

**Forward and Inward Movement of the Ciliary Muscle Apex
with Accommodation in Adults**

THESIS

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Abstract

Purpose: to study the inward and forward movement of the ciliary muscle during accommodation and to investigate the effects of one hour of reading on the ciliary muscle behavior in young adults.

Methods: Subjects included 23 young adults with a mean age of 23.7 ± 1.9 years. Images of the temporal ciliary muscle of the right eye were obtained using the Visante™ Anterior Segment Ocular Coherence Tomography while accommodative response was monitored simultaneously by the Power-Refractor. Four images were taken at each accommodative response level (0, 4.0 and 6.0 D) before and after one hour of reading. Ciliary muscle thickness was measured at every 0.25 mm posterior to the scleral spur. SSMAX, which is the distance between scleral spur and the thickest point of the muscle (CMTMAX), was also measured. The change in the ciliary muscle thickness and SSMAX with accommodation from 0 to 4.0 D and 0 to 6.0 D was calculated. Paired t-tests were used to determine if the ciliary muscle thickness and SSMAX for the 4.0 and 6.0 diopters of accommodative response were different after one hour of reading.

Results: Before one hour of reading, for the change from 0 to 4.0 D, CMTMAX increased by $78.09 \pm 64.80 \mu\text{m}$ ($p < 0.0001$), CMT1 increased by $69.25 \pm 61.37 \mu\text{m}$ ($p < 0.0001$) and SSMAX decreased by $-156.57 \pm 265.03 \mu\text{m}$ ($p = 0.0097$). For the change from 0 to 6.0 D, CMTMAX increased by $95.64 \pm 60.86 \mu\text{m}$ ($p < 0.0001$), CMT1 increased by $76.75 \pm 56.80 \mu\text{m}$ ($p < 0.0001$) and SSMAX decreased by $-209.34 \pm 216.53 \mu\text{m}$

($p = 0.0001$). A period of one hour of reading had no effect on CMTMAX, CMT1 and SSMAX for either the 4.0 D condition ($p = 0.4, 0.2, 0.2$ respectively) or the 6.0 D condition ($p = 0.3, 0.3, 0.8$ respectively).

Conclusions: Using the Visante images, we were able to show that during accommodation, the ciliary muscle becomes thicker anteriorly and thinner posteriorly while the muscle apex moves forward, demonstrated by the decrease in SSMAX. The results also suggest that, on average, the amount of thickening or thinning and the forward movement of the ciliary muscle are not altered after an extended period of reading in young adults. Future investigations will consider whether or not the overall dimensions of the ciliary muscle impact the accommodation of the ciliary muscle after extended reading and/or how advancing age affects the forward and inward movement of the ciliary muscle.

Dedication

This document is dedicated to my dearest sister Thu Thuy, for her love and inspiration.

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CHAPTER 1: INTRODUCTION

Accommodation has been a subject of great interest among the scientific community for more than a hundred years. Even though a number of theories have been proposed, details of the accommodative mechanism still remain elusive. One of the main challenges in studying accommodation is that it is difficult to directly observe the ciliary muscle, an important component of the accommodative apparatus, because it is hidden from view behind the iris.¹ As a result, very little is known about the human ciliary muscle, including its contraction during accommodation, its development during overall eye growth, and how it changes throughout adult life.² Recently, imaging techniques, including magnetic resonance imaging, ultrasound biomicroscopy and ocular coherence tomography, have been able to visualize the ciliary body *in vivo*. Using the Visante™ Anterior Segment Ocular Coherence Tomography, the present study investigates the forward and inward movement of the ciliary muscle in young adults. The effect of fatigue created by an extended period of near work on the forward and inward movement of the ciliary muscle is also explored. Data collected from this study provide insights on the change in ciliary muscle morphology during the act of accommodation, thus allowing us to further understand the accommodative mechanism as well as related phenomena such as presbyopia and myopia development.

1. The accommodative apparatus

1.1 Ciliary body

The ciliary body is part of the uveal tract of the eye that extends from the iris root anteriorly to the ora serrata posteriorly.³ It consists of two parts: the posterior, smooth-surfaced pars plana and the anterior pars plicata that is characterized by radiating processes projecting freely into the posterior chamber.⁴ The ciliary body contains six layers, which, from the external aspect to the internal aspect are: the supraciliaris, the muscle layer, the stroma, the basal lamina, the epithelium and the internal limiting membrane.⁵ The supraciliaris is a very thin layer of loose connective tissue consisting of scarce collagen fiber, fibroblasts and melanocytes.⁴ It connects the ciliary body to the sclera and creates a space for the ciliary muscle to contract during accommodation without stretching the sclera.^{3,4} The second layer of the ciliary body is the ciliary muscle, which will be discussed in detail later. Internal to the ciliary muscle is the stroma which is continuous with the iris stroma anteriorly and with the choroidal stroma posteriorly.³ It is a highly vascularized structure with fenestrated capillaries to allow the flow of water and metabolites from the vasculature to the epithelium for aqueous production.⁵ Next to the stroma is the basal lamina. Also known as the external basal membrane, the basal lamina is secreted by the outer pigmented ciliary epithelium and continuous with Bruch's membrane of the choroid.⁶ Internal to the basal lamina is the epithelial layer. It consists of two single layers of epithelium: the pigmented and the non-pigmented ciliary epithelium, facing each other at their apices.³ Gap junctions between the apical surfaces allow the two layers to communicate and probably play an important role in aqueous production.⁷⁻¹⁰ The last layer of the ciliary body is the internal limiting membrane, which

is the basal membrane secreted by the inner non-pigmented ciliary epithelium. It is a direct continuation of the internal limiting membrane of the retina and attachment site for the zonular fibers as well as the fibers of the vitreous base.^{3,5}

The ciliary muscle

The ciliary muscle is largely considered a smooth muscle as it appears unstriated under the microscope and has a less ordered arrangement of its internal contractile fibers than skeletal muscle.⁶ Furthermore, it functions under the command of the autonomic nervous system.³ It is classified as a multi-unit smooth muscle, as opposed to the unitary or visceral smooth muscles in the gastrointestinal tract.¹¹ Multi-unit smooth muscles consist of discrete fibers, each operating independently of the others and are often innervated by a single nerve fiber ending, i.e., similar to skeletal muscle.⁶ Multi-unit smooth muscles such as the ciliary muscle, therefore, respond as rapidly as skeletal muscles⁶.

Even though the ciliary muscle is mostly considered a smooth muscle, it exhibits some significant deviations. In contrast to the smooth muscle cells of the vascular media but similar to skeletal muscle cells, ciliary muscle cells have mitochondria concentrated around the center of the cell while having contractile myofibrils located more in the periphery where they run almost parallel to the cell membrane.¹² In addition, the action potential of the ciliary muscle has been reported as having properties similar to that of skeletal muscle.¹¹ Furthermore, many nerve fibers to the ciliary muscle are myelinated which is unusual in postsynaptic fibers of autonomic nerves.¹³ Myelination increases

conduction velocity of a nerve impulse and is most often found in the motor nerves to skeletal muscles.⁶

The ciliary muscle is attached anteriorly to the scleral spur and the trabecular meshwork and extends as far as to the muscle stars in the suprachoroidal layer.³ The ciliary muscle consists of fibers of three different orientations: the external longitudinal fibers, the intermediate radial fibers and the inner circular fibers.⁴ These three portions of the ciliary muscle, however, are not truly separate entities. During contraction of the ciliary muscle, there is a gradual rearrangement of the muscle fibers in which the circular portion increases at the expense of the longitudinal portion.⁴ In addition, the longitudinal fiber portion shortens and the posterior pole moves anteriorly.¹⁴ The result is the anterior-inward movement of the ciliary muscle, allowing the zonular fibers to relax and the lens to take on a more spherical shape during accommodation.⁴ The anterior movement of the ciliary muscle is supported by a firm anterior attachment made by broad, inelastic, collagenous tendons inserting into the scleral spur and the peripheral cornea.¹⁴ The posterior attachment, on the other hand, contains elastic tendons that allow the ciliary muscle to stretch forward during accommodation and shrink backwards during relaxation.¹⁴

The ciliary muscle is innervated by the autonomic nervous system, including parasympathetic stimulation for contraction and sympathetic innervation for relaxation.¹⁵⁻¹⁷ The ciliary muscle is very densely innervated by the parasympathetic division which releases acetylcholine at the neuromuscular junction.^{4,6} Similar to skeletal muscle and in marked contrast to other smooth muscles outside the eye, the ciliary muscle atrophies

following denervation caused by ciliary ganglionectomy, which suggests that the ciliary muscle is controlled mainly by nerve signals to individual muscle cells rather than by circulating hormones or electrical coupling through gap junctions.^{6,18,19} The fact that gap junctions have not been observed between ciliary muscle cells supports this idea.⁴ In addition to its abundant parasympathetic innervations, the ciliary muscle is under control, though to a much smaller extent, by an inhibitory branch of the sympathetic nervous system, which is mediated primarily by the neurotransmitter noradrenaline on beta-2 receptors.²⁰ The inhibitory sympathetic system is slow, of low magnitude and mediated by concurrent parasympathetic input.²¹ Access to the inhibitory sympathetic system also varies among individuals. A study done by Edward Mallen showed that sympathetic facility in human ciliary muscle was observed only in 27% of emmetropes, 21% of early onset myopes and 29% of late-onset myopes.²⁰

Refractive error and ciliary muscle

A paper by Oliveira et al. in 2005 was the first one to demonstrate that the ciliary body thickness, measured at 2 mm and 3 mm from the scleral spur was negatively correlated with refractive error and positively correlated with axial length in adult patients.²² This result was confirmed by Bailey et al. in a study in children aged 8-15 in 2008.²³ Myopic eyes, therefore, seem to have thicker ciliary muscles in addition to having longer axial length and deeper anterior chambers. Using ultrasound biomicroscopy, Muftuoglu et al. found that ciliary body is thicker in eyes with unilateral high axial myopia than in their relatively normal fellow eyes, further supporting the findings of Oliveira et al. and Bailey et al.²⁴ In a larger sample of 269 children, Pucker et al. found

that the posterior ciliary muscle fibers are thicker in myopia but paradoxically, the apical ciliary muscle fibers are thicker in hyperopia.²⁵ This was likely the first evidence suggesting that increased accommodative workload in hyperopia is associated with a thicker anterior region of the muscle, which is largely composed of circular and some radial fibers.²⁵ This result was confirmed by Kuchem et al. in a study of 29 subjects with at least one diopter of anisometropia.²⁶ The study, however, found no difference between the two eyes for any ciliary muscle thickness measurement, indicating that in anisometropia, an eye can grow longer and more myopic than its fellow eye without resulting in an increase in ciliary muscle thickness.²⁶ This contradicts the findings of Muftuoglu et al. who reported significantly thicker ciliary muscles in myopic eyes than in relatively normal fellow eyes.²⁴ Further investigations are needed to determine the relation between the ciliary muscle configuration and refractive error, as well as the role of the ciliary muscle in myopigenesis.

1.2. The Crystalline Lens

The crystalline lens is a transparent and avascular structure that aids in refracting and focusing light on the retina.²⁷ It is composed of 65% water and 34% protein with variable distribution throughout the lens.²⁸ The high protein content is necessary to produce and maintain its high refractive power.²⁹ The lens can be divided into two parts: the outer cortex and the inner nucleus.³⁰ The inner nucleus can be further divided into embryonic, fetal, adolescent and adult nuclei.⁶ Surrounding the entire lens is an acellular, elastic capsule secreted by the lens epithelium.^{3,31} The capsule is thicker anteriorly than posteriorly, and continues to thicken anteriorly throughout most of life to keep pace with

the increase in size of the lens.^{31,32} Fincham suggested that the elastic properties of the capsule are responsible for increasing the lens curvature when the ciliary muscle contracts.³³ According to Fisher, the elasticity of the lens capsule decreases with age and that might be an underlying cause of presbyopia.³¹ The lens is attached to the ciliary body by the lens zonules (or the suspensory ligament of the lens).³ Although highly elastic, the zonules have no true elastic fibers.^{34,35} Most zonular fibers attach to the lens capsule at the pre-equatorial and post-equatorial regions; few attach at the equator.³⁶ Helmholtz's theory of accommodation suggests that the change in the lens curvature is induced as the zonules apply or release a load on the lens capsules.³⁷ The zonules, therefore, serve as a critical component of the accommodative apparatus.²⁸

2. Accommodation

2.1 Theories of accommodation

Accommodation is the ability of the eye to change its refractive power to bring objects at different distances into focus the retina.⁶ It is generally agreed upon that accommodation in humans is achieved by altering the shape, hence the refractive power of the crystalline lens.³⁸ Our present understanding of the mechanism of accommodation is largely based on Helmholtz's theory.³⁷ In the unaccommodative state, the ciliary muscle is relaxed; the zonules, therefore, are taut, imparting a load on the lens and causing it to flatten. Flatter curvature means a reduction in the refractive power, allowing the eye to focus on distant objects. When the eye accommodates, the ciliary muscle contracts, moving inward and hence, reducing the tension on the zonules. As a result, the stretching force exerted on the lens by the zonules is diminished, allowing the lens to

assume a more curved form. This increases the optical power of the lens, allowing the eye to focus on near objects. Helmholtz also included the iris in his theory, indicating that the iris's pressure is responsible for some of the increase in the curvature of the lens' front surface. A recent study by Crawford et al. showed that maximum accommodation induced by carbachol was 40% less in iridectomized monkey eyes, hence supporting Helmholtz's theory.³⁹

The theory of Helmholtz has been modified by Fincham and Coleman. Fincham proposed that the changes in the lens shape observed during accommodation were caused by the elastic contractile properties of the lens capsule alone.^{33,40} He proposed that the capsule compresses the lens at the equator where the capsule is thicker, allowing it to bulge in the central anterior region where the capsule is thinner. This proposal was not supported by Koretz and Handelman, whose mathematical analysis showed that the capsular forces act evenly over the lens.^{41,42} The vitreous may also play a role in accommodation by acting as a hydraulic diaphragm to support lens thickening, as proposed by Coleman.⁴³ He demonstrated a differential pressure increase in the vitreous space relative to the aqueous space, initiated by the ciliary muscle contraction and the forward translational movement of the lens during accommodation.

An alternative theory of accommodation has been recently proposed by Schachar.⁴⁴ According to his theory, during accommodation, the anterior radial segment of the ciliary muscle contracts towards the sclera, hence increasing the tension on the equatorial zonules. The anterior and posterior zonules, on the other hand, become more relaxed. The increased equatorial zonular tension and decreased anterior and posterior

zonular tension cause central surface steepening, peripheral surface flattening as well as an increase in central lenticular thickness and power.

2.2 Ciliary muscle and accommodation

Despite the ongoing debate about different theories of accommodation, the central role of the ciliary muscle in the process of accommodation is relatively indisputable.

Using newly developed imaging techniques, recent studies have been able to capture and analyze the morphological changes of the ciliary muscle *in vivo* during accommodation.

Using ultrasound biomicroscopy and goniovideography, a study by Glasser and Kaufman in monkeys showed that the ciliary body and the lens equator move away from the sclera and towards the anterior-posterior axis of the eye during accommodation.⁴⁵ The study's result supports Helmholtz's theory and contradicts the recent proposal by Schachar. One shortfall of this study, however, was that the subjects' accommodation was pharmacologically rather than physiologically induced. Ostrin and Glasser found that pharmacologically stimulated accommodation results in a greater increase in the lens thickness, an overall forward movement of the lens and a greater change in dioptric power than Edinger-Westphal-stimulated accommodation.⁴⁶

Another study using three-dimensional ultrasound by Stachs et al. also detected an inward and forward movement of the ciliary muscle's center of gravity with a small decrease with age.¹ Interestingly, the displacement of the plane containing both the ciliary muscle and ciliary processes was larger than that of the plane containing only the ciliary muscle. This supports Hess and Fincham's statement that the ciliary processes move in the direction of the lens during accommodation.^{1,33,47} Stachs's study also reinforces

Helmholtz's theory and counters Schachar's postulation of a centrifugal movement of the ciliary body away from the lens. Using a different imaging method – anterior segment optical coherence tomography (AS-OCT), Lewis et al. and Lossing et al. found a thickening in the anterior portion of the ciliary muscle as well as a thinning in the posterior portion during accommodation.^{48,49} These findings, once again, support the anterior and centripetal contractile shift of the ciliary muscle during accommodation.

3. The near triad

Accommodation is one component of the near-vision triad that consists of convergence, miosis, and accommodation.⁵⁰⁻⁵² Neural pathways that control each of these components are different but interrelated.⁵³ While accommodation increases the optical power of the eye to focus on near objects, convergence directs the eyes towards the object and the pupil constriction increases the depth of focus.^{54,55} Wilson showed that pupil constriction latency is longer than accommodative latency which is in turn longer than convergence latency.⁵⁶ He attributed the longer latency of accommodative and pupillary response to the mechanical constraints of intraocular tissues such as the lens, ciliary muscle and iris musculature.

It has been demonstrated that the magnitude of the pupillary response increased linearly with that of both accommodation and disaccommodation; however, constriction responses in accommodation are faster than similar amplitude dilation responses in disaccommodation.⁵⁷ Interestingly, the amount of pupil change per diopter of refractive change was constant with different amplitudes of accommodation; therefore, the near pupil response may serve as an index of the accommodative effort, similar to the

accommodative convergence to accommodation (AC/A) ratio.⁵⁷ Another study with a cohort of subjects aged 14-45 years indicated an increase in the amount of pupil constriction per diopter of accommodative response with age, but not per diopter of accommodative stimulus, suggesting the near effort per se does not increase with age.⁵⁸

Regarding the AC/A ratio, a number of studies have showed the linkage between elevated AC/A ratio and the development of myopia. Gwiazda et al. found that AC/A ratios are elevated in myopic children, who show reduced accommodation and enhanced accommodative convergence.⁵⁹ Mutti et al. obtained similar results in a study of 828 children aged 6 to 14 years: the response AC/A ratios were highest in myopes, intermediate in emmetropes, and lowest in hyperopes.⁶⁰ In a longitudinal study of myopia development in children, Gwiazda et al. showed that higher AC/A ratios and reduced accommodative response precede myopia onset by at least 2 years.⁶¹ Accommodative convergence, on the other hand, was significantly greater in myopes only at onset.⁶¹ Elevated AC/A ratio and accommodative deficit, therefore, may contribute to myopigenesis, possibly by producing hyperopic retinal defocus during near work.^{59,61}

4. Components of accommodation

Accommodation, as proposed by Heath, consists of four components: reflex, vergence, proximal and tonic accommodation.⁶² Reflex accommodation is the automatic adjustment to obtain and maintain a sharply focused retinal image in response to a blur input. This applies for relatively small amounts of blur, perhaps up to 2 D; beyond that, voluntary accommodative effort is required.⁶³⁻⁶⁵ Reflex accommodation, nonetheless, still serves as the largest and most important component of accommodation under both

monocular and binocular viewing conditions.⁶⁶ Vergence accommodation is the accommodation induced by the innate neurological linking and action of disparity vergence.⁶⁷ It gives rise to the convergence accommodation/convergence (CA/C) ratio.⁶⁸ Proximal accommodation is the accommodation due to the influence or knowledge of perceived nearness of an object, stimulated by targets located within 3 m of the individual.⁶⁹ Finally, tonic accommodation represents the baseline neural innervation from the midbrain to the accommodative apparatus. It is found in the absence of blur, disparity and proximal inputs.

5. Presbyopia and age-related change in the ciliary muscle

One of the most common dysfunctions of accommodation is presbyopia, which is the age-related loss of accommodative amplitude – a universal, consistent, and predictable consequence of human aging.⁷⁰ Even though the topic of presbyopia has been investigated extensively for almost a hundred years, the exact mechanism of presbyopia still remains uncertain. In theory, changes in any of the major accommodative components – the lens, the ciliary muscle, the lens zonules – can alter the balance of forces in the accommodative system and potentially lead to the condition of presbyopia.⁷¹ Current theories of the development of presbyopia can be classified into two main categories: the lenticular theories and the extra-lenticular theories.⁶ The lenticular theories attribute the loss of accommodation with age to the hardening of the lens: the lens cannot assume a more spherical shape for accommodation even if the ciliary muscle retains its power and the capsule most of its elasticity.⁷² There are two prominent variants of the lenticular theories, usually named the Hess-Gullstrand and Duane-Fincham

theories. In the former theory, it is assumed that the amount of ciliary muscle contraction required for each diopter of accommodative change remains constant throughout life.^{6,72} Therefore, it is predicted that as age progresses, an increasing proportion of ciliary muscle contraction will be “latent” in that it has no influence on accommodative status.⁶ In contrast, the Duane-Fincham theory assumes that the amount of ciliary muscle contraction required for a given change in accommodation increases throughout life as the lens becomes more resistant with age.^{73,74} This theory is based on Duane’s finding that atropine generally reduced the amplitude of accommodation faster in older patients than in younger patients. The theory predicts that the muscle will maximally contract once the near point is reached regardless of the amplitude of accommodation. The increase in the response AC/A ratio and the decrease in the response CA/C ratio with age seem to support the Duane-Fincham and refute the Hess-Gullstrand theory.^{50,67,74-79} Fisher’s classical study also supports the Duane-Fincham theory as he found that the relationship between ciliary force and accommodative response is not linear.⁸⁰ However, using magnetic resonance imaging and optical coherence tomography, Richdale et al. found that the changes per diopter of accommodative response in either the ciliary muscle ring diameter or the cross-sectional thickness did not vary with age, thus, supporting the Hess-Gullstrand theory.⁸¹

The extra-lenticular theories of presbyopia attribute the age-related loss of accommodation to the changes in the ciliary muscle and the elastic components of the zonules or ciliary body.⁶ Even though many studies have reported changes observed in the ciliary muscle with age, their contribution to presbyopia is still a subject of debate and

speculation. Several reports have stated that the ciliary muscle contractile ability remains virtually the same throughout the lifespan.^{71,80,82,83} Fisher reported that the contractile force of the ciliary muscle reaches its maximum at the very time when presbyopia becomes clinically manifest.⁸⁰ Therefore, it seems unlikely that a weakening ciliary muscle is the underlying cause of presbyopia. However, important morphological and positional changes in the muscle with age have been observed and might play some role along the development of presbyopia. Using a quantitative morphometric method in a sample of 95 postmortem human eyes (33-87 years), a study by Tamm et al. found that the total area, the length of the ciliary muscle and the distance from its inner apex to the scleral spur show a continuous and significant decrease with age.⁷⁰ In addition, the area of the circular portion increases at the expense of the longitudinal and reticular portion with age.⁷⁰ Thus aging ciliary muscles at rest appear to behave similarly to young ciliary muscles in accommodation. This finding has been confirmed by other studies.^{71,82,83} However, interpretations of this morphological and positional change in the aging ciliary muscle differ substantially among these studies. Tamm et al. suggested that the forward-inward position of the muscle serve to slow down the course of presbyopia, similar to the steepening of the lens curvature observed in aging eye.⁷⁰ Strenk et al., on the other hand, proposed that the anterior-inward movement of the ciliary muscle as well as the increase in lens thickness with age indicate that presbyopia may be caused by the loss in ability to disaccommodate.⁷¹

In conclusion, presbyopia seems to be a multifactorial phenomenon involving both the aging of the lens and the ciliary muscle. Future studies are required to determine whether the change in the ciliary muscle with age is the cause or effect of presbyopia.

6. Imaging techniques

As mentioned above, one of the main challenges in studying accommodation is that it is difficult to directly observe the ciliary muscle, an important component of the accommodative apparatus, because it is hidden from view behind the iris. Our current knowledge about the ciliary muscle, hence, is rather limited. Recent developments in ophthalmic imaging technology have allowed the ciliary muscle to be more easily and accurately imaged *in vivo*. The current techniques for imaging the ciliary muscle *in vivo* include magnetic resonance imaging (MRI), ultrasound biomicroscopy (UBM) and optical coherence tomography (OCT). This section will give an overview of the advantages as well as limitations to each of these methods.

MRI has been proven very useful in investigating the relationship between the ciliary muscle contraction and lens response as it can capture undistorted, three-dimensional images of the entire anterior portion of the eye.⁷¹ It also provides unsurpassed soft tissue contrast and allows the image to be acquired in any desired plane. Besides its apparent advantages, MRI present a number of limitations, including resolution limitations, signal-to-noise ratio limitations, image acquisition time constraints, the difficulty of presenting accommodative stimuli within the confines of the investigator, as well as the requirement that the subject limit head and eye movements

during the scans.⁷¹ MRI is also expensive, making it less desirable to apply to a large-scale study.

UBM has been proven to be an important tool for studying anterior segment structures with high resolution.¹ It has been recently used by a number of investigations to acquire information about the ciliary muscle. Three-dimensional UBM is particularly useful as images can be produced from any scan planes in a manner similar to the MRI method. It also allows an assessment of the ciliary muscle activity in consideration of the ciliary processes.¹ Sections with and without the ciliary processes can be obtained and compared as needed. Additionally, posterior zonules can be identified and used as a marker for posterior margin of the ciliary muscle. Finally, compared to MRI, UBM is more cost effective. Nonetheless, the contact of the UBM probe to the ocular surface and the need for the subject to remain in a supine, unnatural position can be uncomfortable for the subjects and yield less than ideal result.

Our present study utilizes the Vistante™ Anterior Segment OCT (AS-OCT) to visualize the ciliary muscle and uses the semiautomatic extraction algorithm developed by Kao et al. to analyze the images.⁸⁴ The Vistante™ AS-OCT allows fast, non-contact and high resolution imaging of the ciliary muscle while the subject can be positioned in a natural upright orientation. Among the three techniques, it appears to be the best method for studies in children. However, like MRI and UBM, AS-OCT presents a number of limitations. First, it is currently able to capture only two-dimensional images. The plane of acquisition can vary each time the image is taken. Second, it can only image the ciliary muscle, without the ciliary processes. Third, unlike UBM, AS-OCT cannot identify a

reliable marker for the posterior end of the ciliary muscle, making it impossible for the length of the muscle to be accurately measured. This problem raises a question about the validity of Sheppard and Davies' recent method in measuring the thickness of the ciliary muscle at a distance 25, 50 or 75 percent of its overall length from the scleral spur.⁸³ Our study includes the measurement of the maximal thickness of the muscle, which does not rely on the location of the scleral spur or the posterior end of the muscle, nor will it be affected by the application of straight-line calipers across a curved scleral contour.² As noted by Kao and coauthors, the scleral curvature differences can lead to an increased variability in the ciliary muscle thickness measurements especially at an increasing distance from the scleral spur.⁸⁴ To tackle this problem, Kao and coauthors developed the semiautomatic extraction algorithm that is capable of following the scleral curvature. The algorithm has also proven to be repeatable and require only three images of the ciliary body for analysis.

CHAPTER 2: METHODS

1. Subjects

Subjects were recruited within the Ohio State University College of Optometry. Adults between the age of 18 and 30 years with all types of refractive error were eligible to participate in the study as long as they wore their correction (glasses or contact lenses) during all waking hours for at least two weeks prior to their study visit. Exclusion criteria consisted of any ocular diseases, history of strabismus, amblyopia or eye surgery, current pregnancy or breast-feeding and current use of medications known to affect the ciliary body function. The total of 23 subjects was recruited. After a presentation and discussion of the procedures and the purpose of the study, all subjects provided a written informed consent and signed the HIPAA form. Subjects underwent testing at two visits separated by two weeks. Each visit lasted for less than two hours. The study was approved by the Institutional Review Board of The Ohio State University.

2. Visual acuity and accommodative response measurement

High contrast distance visual acuity was measured monocularly at ten feet through habitual correction in normal examination room illumination using the Bailey-Lovie chart. Credit for a line was given if three out of five letters were correctly read. Guessing was encouraged. Visual acuity testing was stopped after three or more errors

were made on a line. Subjects who can read 20/40 or better with each eye were eligible to proceed through the rest of the exam.

Accommodative response of the right eye was measured using the Grand Seiko WR-5100K autorefractor (Grand Seiko Co., Hiroshima, Japan) through the subject's habitual correction. We occluded the left eye so that the subject could view the target through the Badal lens with his/her right eye. Accommodative response was measured at three stimulus levels: 0, 4.0 D and 6.0 D. The mean of five readings at each stimulus level was used for analysis.

3. Ciliary muscle imaging

Images of the temporal ciliary muscle of the right eye were obtained using the Visante™ AS-OCT (Carl Zeiss Meditec). The images were captured in high resolution corneal mode while the subject fixated on a lateral target located on his/her left. Simultaneously, the patient's accommodative response was monitored by the Power-Refractor. The target was moved back and forth until the desired accommodative response was achieved. Four images were taken at each accommodative response level (0, 4.0 and 6.0 D). A diagram of the set-up for the ciliary muscle imaging with concurrent accommodative monitoring is shown in Figure 1.

During the imaging, all subjects wore a special trial frame regardless of their refractive error. If the subjects wore spectacle corrections, trial lenses at their current prescription were placed over their left eye. If the subjects had no refractive correction or wore contact lenses, no trial lenses were needed. The right eye, on the other hand, was covered with a gel filter (Wratten 89B; Kodak, Rochester, New York) that only

transmitted light with wavelengths longer than 680 nm. This filter effectively occluded vision of the right eye, but allowed the infra-red beam from the Vistante™ to go through. If the subjects wore contact lenses, they were asked to remove the one on the right to allow accurate imaging of the ciliary muscle in the right eye.

Most of the time, the Power-Refractor was able to measure the accommodative state of the left eye only, due to a physical blockage over the right eye by the Vistante™. However, due to the highly symmetric accommodation between the two eyes, we assumed that the amount of accommodative response was the same between the left and the right eye.⁸⁵

After the initial set of images was acquired, the subjects were asked to read for one hour in the waiting room. The subjects were allowed to bring in any reading materials of their choices. A variety of magazines were also provided. After one hour of reading, a second set of the ciliary muscle images was taken at 4.0 and 6.0 diopters of accommodative response.

4. Ciliary muscle image analyses

The scleral spur position was selected in each image by one examiner who was masked to both the subject identification number as well as the accommodative state for the image. Using a semi-automatic algorithm, we measured the ciliary muscle thickness at every 0.25 mm from the scleral spur to 3.0 mm posterior to the scleral spur as well as at its thickest point (CMTMAX). We also obtained the distance between the scleral spur and the CMTMAX position (SSMAX) to detect any forward movement of the ciliary

muscle during accommodation. Figure 2 illustrates the muscle outline, scleral spur position, SSMAX, and all thickness measurements.

Below is the list of abbreviations used for the ciliary muscle imaging and measurements:

CMT: ciliary muscle thickness

CMT1: ciliary muscle thickness at 1 mm posterior to the scleral spur

CMT2: ciliary muscle thickness at 2 mm posterior to the scleral spur

CMT3: ciliary muscle thickness at 3 mm posterior to the scleral spur

CMTMAX: ciliary muscle thickness at its thickest point

SSMAX: distance between the CMTMAX position and the scleral spur along the inner surface of the sclera

5. Data analyses

Images of the ciliary muscle from both visits were used to calculate the mean CMT and SSMAX, before and after reading. We plotted the mean CMT at every 0.25 mm posterior to the scleral spur for each accommodative state – 0, 4.0 and 6.0 D (see Figure 3). We used paired t-test to calculate the change in CMTMAX, CMT1 and SSMAX from 0 to 4.0 D and from 0 to 6.0 D before reading. Paired t-test was also used to calculate the change in CMTMAX, CMT1 and SSMAX from before to after reading at 4.0 D and 6.0 D of accommodation. To calculate the change in CMTMAX per diopter of accommodation, we used the following equation:

$$\frac{(\text{Change in CMTMAX from 0 to 4.0 D})/4 + (\text{Change in CMTMAX from 0 to 6.0D})/6}{2}$$

A similar equation was used to calculate the change in CMT1 per diopter of accommodation:

$$\frac{(\text{Change in CMT1 from 0 to 4.0 D})/4 + (\text{Change in CMT1 from 0 to 6.0D})/6}{2}$$

CHAPTER 3: RESULTS

1. Before subjects read for an hour

The study includes 23 subjects with a mean age of 23.7 ± 1.9 years (range 20 to 27 years). Cycloplegic refraction was not measured; however, based on subjects' reported or measured habitual corrections as well as the autorefraction readings of those with no optical corrections, six subjects were emmetropes (spherical equivalent of -0.50 DS to $+0.50$ DS), two were hyperopes (spherical equivalent of more than $+0.50$ DS) and 15 were myopes (spherical equivalent of less than -0.50 DS). Three subjects were Asian, 19 were Caucasian and one was of other race. Nine subjects were male and 14 were female.

Table 1 shows the mean CMTMAX, CMT1 and SSMAX at 0, 4.0 and 6.0 D of accommodation before the subjects read for one hour. Figure 3 depicts the mean CMT at every 0.25 mm from the scleral spur. Three different curves represent CMT at 0, 4.0 and 6.0 diopters of accommodation. The graph shows that qualitatively, the ciliary muscle became thicker anteriorly and thinner posteriorly with increasing amount of accommodation. In addition, SSMAX became smaller as accommodation increased. These changes in the ciliary muscle morphology with accommodation were also apparent in Figure 4, which illustrates the outlines of a sample ciliary muscle at three different accommodative states (0, 4.0 and 6.0 D).

The quantitative changes of CMT and SSMAX from 0.0 to 4.0 D and from 0.0 to 6.0 D of accommodation are summarized by Table 2. The results showed statistical significance for the thickening of CMT1 and CMTMAX at both 4.0 and 6.0 D of accommodation compared to baseline (0.0 D). The amount of thickening of CMT1 and CMTMAX were larger at 6.0 D than at 4.0 D. Additionally, a statistically significant decrease in SSMAX was found at both 4.0 and 6.0 D compared to 0.0 D of accommodation. The change in CMTMAX and CMT1 per diopter of accommodation was 17.7 μm and 15.0 μm respectively.

2. After subjects read for one hour

Table 3 shows the mean CMTMAX, CMT1 and SSMAX at 4.0 and 6.0 D of accommodation measured after the subjects read for one hour. The observed change for the mean CMTMAX, CMT1 and SSMAX from before reading to after reading are summarized in Table 4. Results of pair t-tests showed that a period of one hour of reading had no statistically significant effect on CMTMAX, CMT1 or SSMAX for either the 4.0 D or 6.0 D conditions. The mean change $\pm$ standard deviation in CMTMAX, CMT1 and SSMAX from before to after reading were $-8.96 \pm 48.46 \mu\text{m}$ ($p = 0.4$), -10.91 ± 40.60 ($p=0.2$), $-41.18 \pm 155.36 \mu\text{m}$ ($p = 0.2$) respectively for the 4.0 D condition and $-10.20 \pm 46.17 \mu\text{m}$ ($p = 0.3$), -7.10 ± 34.37 ($p = 0.3$), $-9.70 \pm 150.86 \mu\text{m}$ ($p = 0.8$) respectively for the 6.0 D condition.

CHAPTER 4: DISCUSSION

The present study along with previous reports from our laboratory on the ciliary muscle morphology have shown that the Visante™ is able to image the ciliary muscle *in vivo*. Table 5 compares the change in CMTMAX and CMT1 per diopter of accommodation found in the present study and in three previous reports using similar methods to image the ciliary muscle. Overall, similar increases in CMTMAX and CMT1 were found in the present study and in two other reports from our laboratory by Lewis et al. and Lossing et al. The general agreement among these studies demonstrates that the Visante™ along with the semiautomatic algorithm developed by Chiu Yen Kao is capable of not only imaging but also of quantitatively measuring the change in CMT *in vivo*.⁸⁴ Also using the Visante™, Richdale and co-authors found a relatively greater increase in CMTMAX per diopter of accommodation (26 $\mu\text{m}/\text{D}$) in a cohort of subjects aged 30 to 50 years (no mean age and standard deviation available from the publication).⁸¹ It is important to note that subjects in the study by Richdale et al. were significantly older than in the three studies from our laboratory. Table 6 shows the change in CMTMAX per diopter of accommodation in the four studies in order of youngest to oldest cohorts. The table suggests a general trend in which older cohorts tend to have greater change in CMTMAX per diopter of accommodative response. It is possible that the sample size of 26 subjects with the age range of 30 to 50 years in the

study by Richdale et al. was not big enough to detect any age effect on the ciliary muscle contraction.⁸¹ Future investigations might include larger cohorts with a wider age range to determine if aging and presbyopia have any effect on the ciliary muscle contraction with accommodation.

When looking through our set of the ciliary muscle images, we noticed a wide variation in the ciliary muscle morphology. Qualitatively, thicker ciliary muscles tended to have a more prominent apex. Figure 5 depicts a thick ciliary muscle at rest (top) and at 6.0 diopters of accommodation (bottom). It is not difficult to point out in either image the apex or CMTMAX position. On the contrary, thinner ciliary muscles at rest such as the one depicted in Figure 6 (top image), tended to have a much less obvious apex. Only when the subject accommodated could we easily tell the apical position of the muscle (Figure 6, bottom image). The wide variation in the ciliary muscle morphology and the difficulty in determining the CMTMAX positions in thinner ciliary muscles contribute to the large standard deviations in some measurements. In future studies, we would like to investigate if the thickness of the ciliary muscle is associated with children's ability to sustain accommodation and how that might affect their academic performance. The difference between thick and thin ciliary muscles might also have applications in choosing candidates for accommodative intraocular lens implants.

Compared to previous papers published by our laboratory, the present study offered some important improvements. First, the image of the ciliary muscle was only taken when the desired amount of accommodative response was achieved. We found that the location of the accommodative stimulus required to produce a 4.0 or 6.0 diopter

accommodative response varied greatly among subjects. Accommodative targets had to be moved back and forth in front of each subject until the right amount of accommodative response (4.0 or 6.0 D) was created. This process took considerably more effort than using static accommodative stimuli; however, it ensured that each subject generated the same accommodative response, making the data analysis much simpler and the comparisons between different accommodative states more accurate.

In a published letter, we have attempted to encourage those who measure the ciliary muscle in accommodative studies to include CMTMAX as one measurement as it is independent of the scleral spur location and it does not rely on the accurate identification of the posterior endpoint of the ciliary muscle. In the present study, not only did we include CMTMAX but we also measured the distance between CMTMAX and scleral spur to study another dimension of the ciliary muscle behavior – the anterior–posterior movement of the muscle. The decrease in SSMAX at both 4.0 and 6.0 D showed that the apex of the muscle shifts forward with increasing amounts of accommodation. This result is in agreement with a study published in 2002 by Stachs and coauthors.¹ Using three-dimensional ultrasound to image the ciliary muscle, their study also noted an anterior and inward shift of the ciliary muscle apex with accommodation. These findings support Helmholtz’s classic theory of accommodation which states that the inward and forward movement of the ciliary muscle allows the crystalline lens to adopt a more curved configuration and increase its dioptric power.³⁷ The inward movement of the ciliary muscle found in the present study and others’ also refuted

Schachar's theory which proposed that the anterior segment of the ciliary body contracts towards the sclera during accommodation.⁴⁴

Another improvement in our study design was that we measured CMT at every 0.25 mm along the muscle's length instead of only measuring at 1, 2 and 3 mm posterior to the scleral spur as was previously done by Lewis et al. and Lossing et al.^{48,49}

Measurements at more frequent intervals of the ciliary muscle provided us with a more complete and continuous picture of the muscle's morphology during accommodation *in vivo*. More data points allowed us to build Figure 3, which compares the overall muscle shape at three different conditions – 0, 4.0 and 6.0 diopters of accommodation, represented by three different curves. The graph clearly shows that the muscle apex, represented by the peak of each curve, moves forward and inward with increasing amount of accommodation. Figure 4 demonstrates the same principle by outlining an actual ciliary muscle at three different accommodative states (0, 4.0 and 6.0 D).

In order to explore the effect of fatigue by a prolonged period of near work on the ciliary muscle activity, we measured ciliary muscle thickness and SSMAX after one hour of reading. Our results showed that one hour of reading had no statistically significant effect on CMTMAX, CMT1 or SSMAX for either the 4.0 D or 6.0 D conditions. That amount of fatigue in adult subjects did not alter the overall inward or forward movement of the ciliary muscle. Figure 7 compares the ciliary muscle shape at 4.0 diopters of accommodation before and after reading. The figure shows that the before–reading and the after–reading curves almost overlap each other. Similar result is seen in figure 8, which compares the ciliary muscle shape at 6.0 diopters of accommodation before and

after reading. These results suggest that the same amount of inward and forward movement of the ciliary muscle is needed to generate a certain amount of accommodation whether the ciliary muscle is fatigued or not. We, however, did not record the accommodative stimuli that generated the desired accommodative responses (4.0 or 6.0 D) for each subject. It is possible that after an hour of reading, the accommodative target had to move closer to create the same amount of accommodative response. In future studies, including the location of the target when the right accommodative response is achieved before and after reading might give us a different insight on whether or not fatigue creates strain on the ciliary muscle contraction. Furthermore, it is uncertain if one hour of reading was enough to generate stress on the accommodative system. Differences in reading material, font size and working distance might have also created a significant variability in accommodative demand among different subjects. Increasing the amount of near work to two or three hours and using the same reading material as well as requiring the same working distance among subjects in future studies might be considered to generate an adequate and uniform amount of stress on the accommodative system.

In the present study, all of our subjects were young adults, aged 20-27 years with no known accommodative problems. It would be interesting to repeat the study in subjects with accommodative disorders such as accommodative insufficiency or accommodative excess and to compare the results to those of normal subjects. Also, in our current sample, we were unable to determine if the action of the ciliary muscle differed in thinner ciliary muscles versus thicker ciliary muscles, and this would also be

an interesting topic to consider. Finally, future investigations may also consider how advancing age impacts the inward and forward movement of the ciliary muscle.

Accommodation Level	Measurement Location	Mean (μm)	Standard deviation	Minimum (μm)	Maximum (μm)
0 D	CMTMAX	867.81	92.57	641.69	1025.85
	CMT1	833.92	87.76	623.04	977.36
	SSMAX	900.47	264.01	379.94	1600.45
4.0 D	CMTMAX	945.89	101.28	746.58	1173.61
	CMT1	903.18	100.32	723.46	1131.66
	SSMAX	743.90	216.62	451.50	1278.73
6.0 D	CMTMAX	963.45	90.20	800.53	1142.76
	CMT1	910.68	89.14	753.05	1113.32
	SSMAX	691.12	180.40	366.01	1240.05

Table 1. Measurements of ciliary muscle thickness and position at various accommodative levels before one hour of extended reading. Thickness measurements are for the point of maximum thickness (CMTMAX) and at 1.0 cm posterior to the scleral spur (CMT1). The distance between the scleral spur and CMTMAX (SSMAX) is also shown

Measurement Location	Change: 0 to 4.0 D			Change: 0 to 6.0 D		
	Mean (μm)	Standard deviation	p-Value	Mean (μm)	Standard deviation	p-Value
CMTMAX	78.09	64.80	<0.0001	95.64	60.86	<0.0001
CMT1	69.25	61.37	<0.0001	76.75	56.80	<0.0001
SSMAX	-156.57	265.03	0.0097	-209.34	216.53	0.0001

Table 2. Change in CMTMAX, CMT1 and SSMAX from 0 to 4 diopters of accommodation and from 0 to 6 diopters of accommodation before the reading period. Thickness measurements are for the point of maximum thickness (CMTMAX) and at 1.0 cm posterior to the scleral spur (CMT1). The distance between the scleral spur and CMTMAX (SSMAX) is also shown.

Accommodation Level	Measurement Location	Mean (μm)	Standard deviation	Minimum (μm)	Maximum (μm)
4.0 D	CMTMAX	936.93	77.35	791.02	1074.89
	CMT1	892.27	81.78	748.13	1045.84
	SSMAX	702.72	190.43	444.89	1321.14
6.0D	CMTMAX	953.25	91.36	786.45	1153.04
	CMT1	903.57	88.45	751.83	1103.27
	SSMAX	681.42	140.48	477.03	1082.17

Table 3. Measurements of ciliary muscle thickness and position at various accommodative levels after one hour of extended reading. Thickness measurements are for the point of maximum thickness (CMTMAX) and at 1.0 cm posterior to the scleral spur (CMT1). The distance between the scleral spur and CMTMAX (SSMAX) is also shown.

Measurement Location	4.0D After – 4.0 D Before Reading			6.0D After – 6.0 D Before Reading		
	Mean (µm)	Standard deviation	p-Value	Mean (µm)	Standard deviation	p-Value
CMTMAX	-8.96	48.46	0.4	-10.20	46.17	0.3
CMT1	-10.91	40.60	0.2	-7.10	34.37	0.3
SSMAX	-41.18	155.36	0.2	-9.70	150.86	0.8

Table 4. The difference in ciliary muscle thickness while accommodating 4.0 and 6.0 D from before to after one hour of reading. All measurements are after – before. Thickness measurements are for the point of maximum thickness (CMTMAX) and at 1.0 cm posterior to the scleral spur (CMT1). The distance between the scleral spur and CMTMAX (SSMAX) is also shown.

Study	Change with accommodation ($\mu\text{m/D}$)	
	CMTMAX	CMT1
Present study	17.7	15.0
Lewis's study ⁴⁸	14.2	10.4
Lossing's study ⁴⁹	18.1	12.3
Richdale's study ⁸¹	26	13

Table 5. Comparison of ciliary muscle thickness changes with accommodation from previous studies using similar methods. Thickness measurements are for the point of maximum thickness (CMTMAX) and at 1.0 cm posterior to the scleral spur (CMT1).

Study	CMTMAX change with accommodation ($\mu\text{m/D}$)	Age range
Lewis's study ⁴⁸	14.2	6-12
Present study	17.7	20-27
Lossing's study ⁴⁹	18.1	23-28
Richdale's study ⁸¹	26	30-50

Table 6. Comparison of the change in CMTMAX with accommodation from previous studies using similar methods, in order of youngest to oldest cohorts.

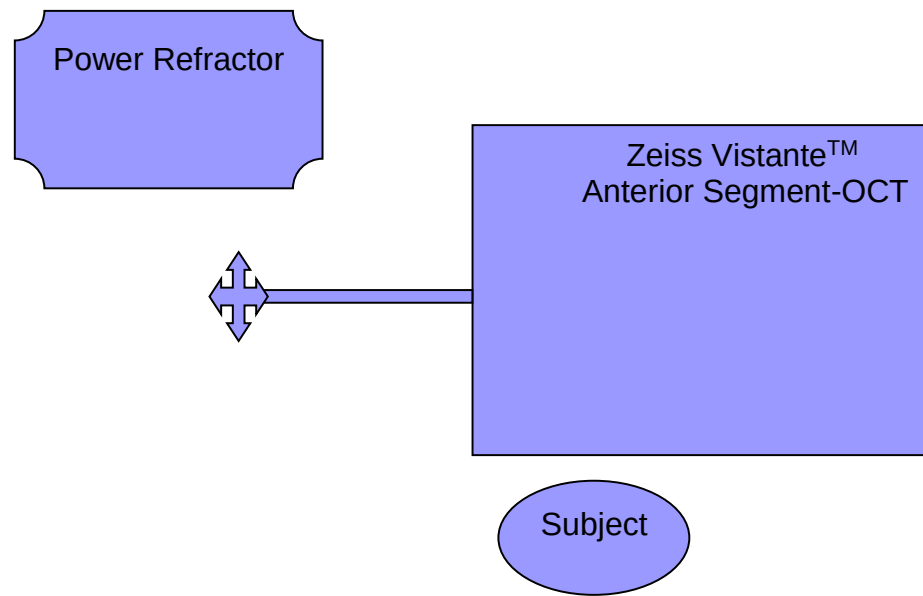


Figure 1. Equipment set-up. The cross symbol represents the target the subject was looking at.

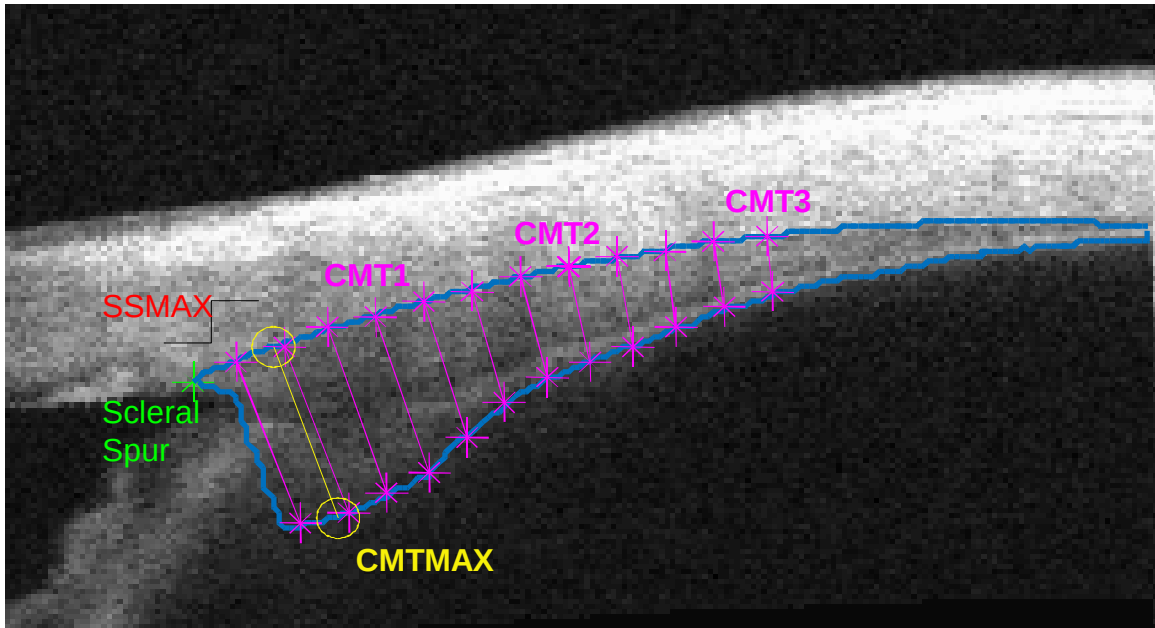


Figure 2. Sample ciliary muscle outline, scleral spur position, ciliary muscle thickness and SSMAX measurements

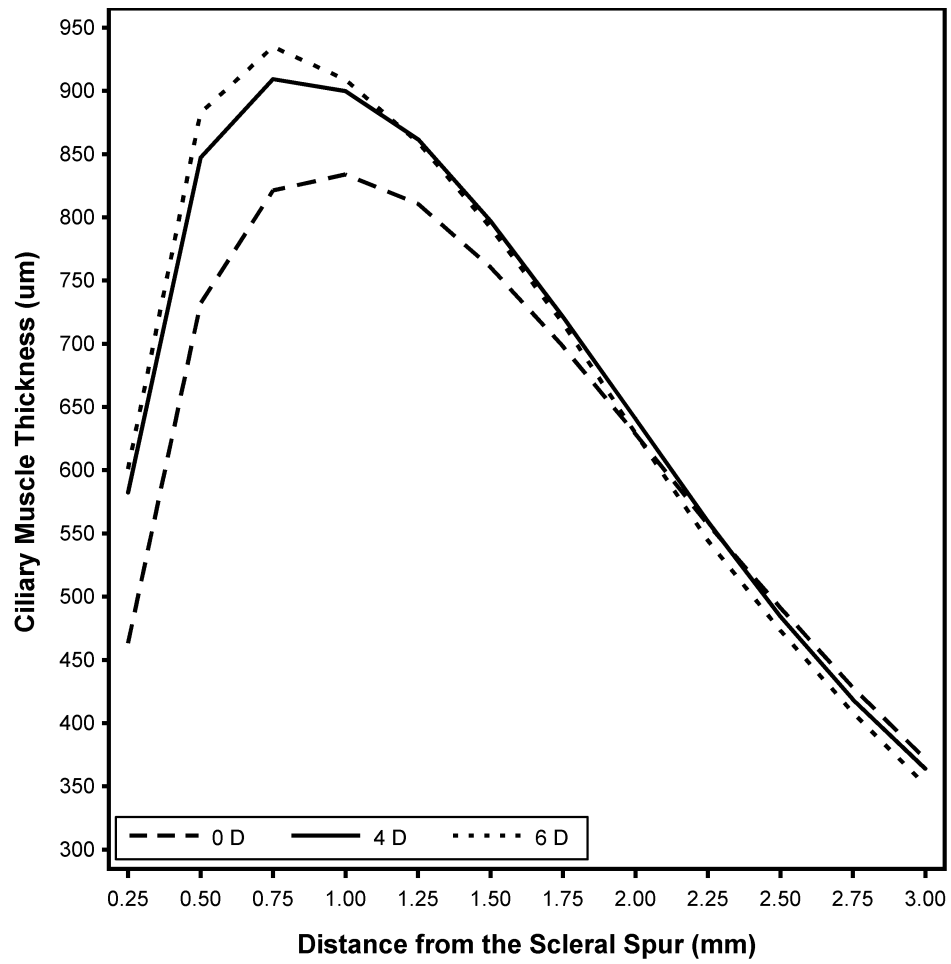


Figure 3. Mean ciliary muscle thickness at every 0.25 mm from the scleral spur in three different accommodative levels (0, 4.0 and 6.0 D)

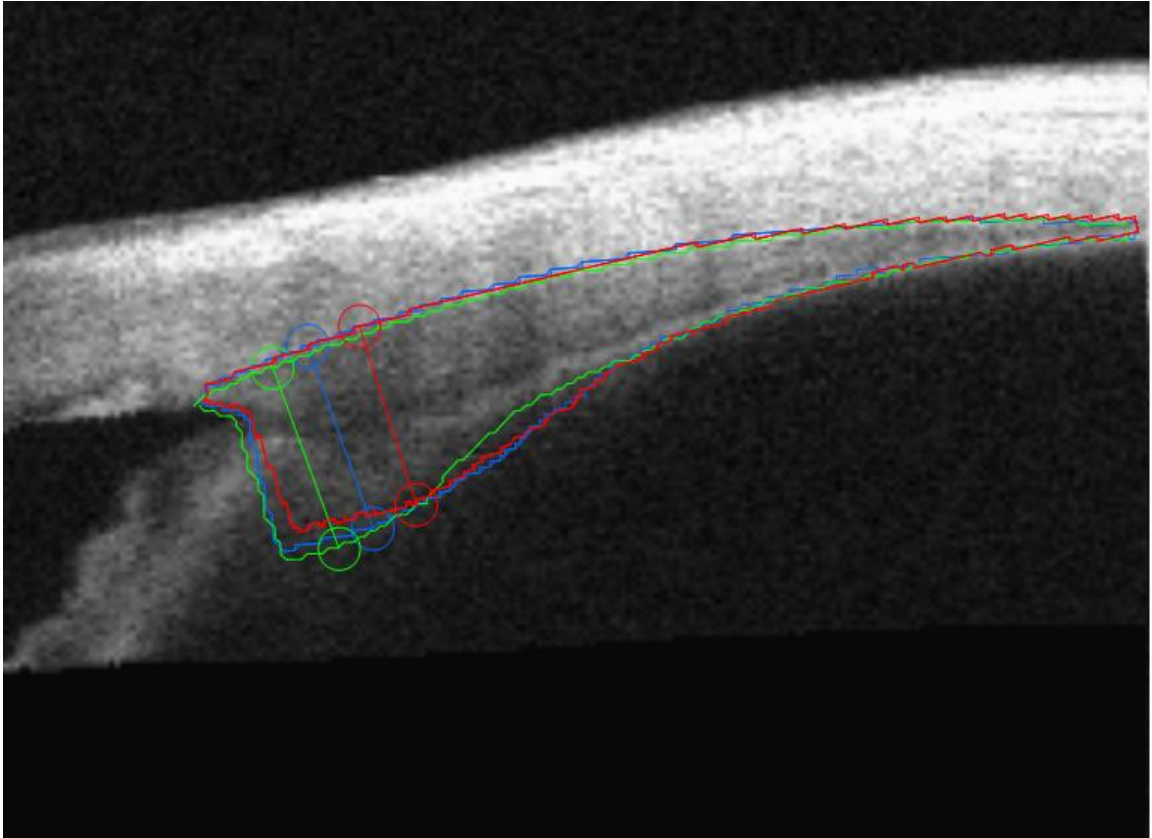


Figure 4. Sample ciliary muscle outline at three different accommodative levels: 0 D (red outline), 4.0 D (blue outline) and 6.0 D (green outline)

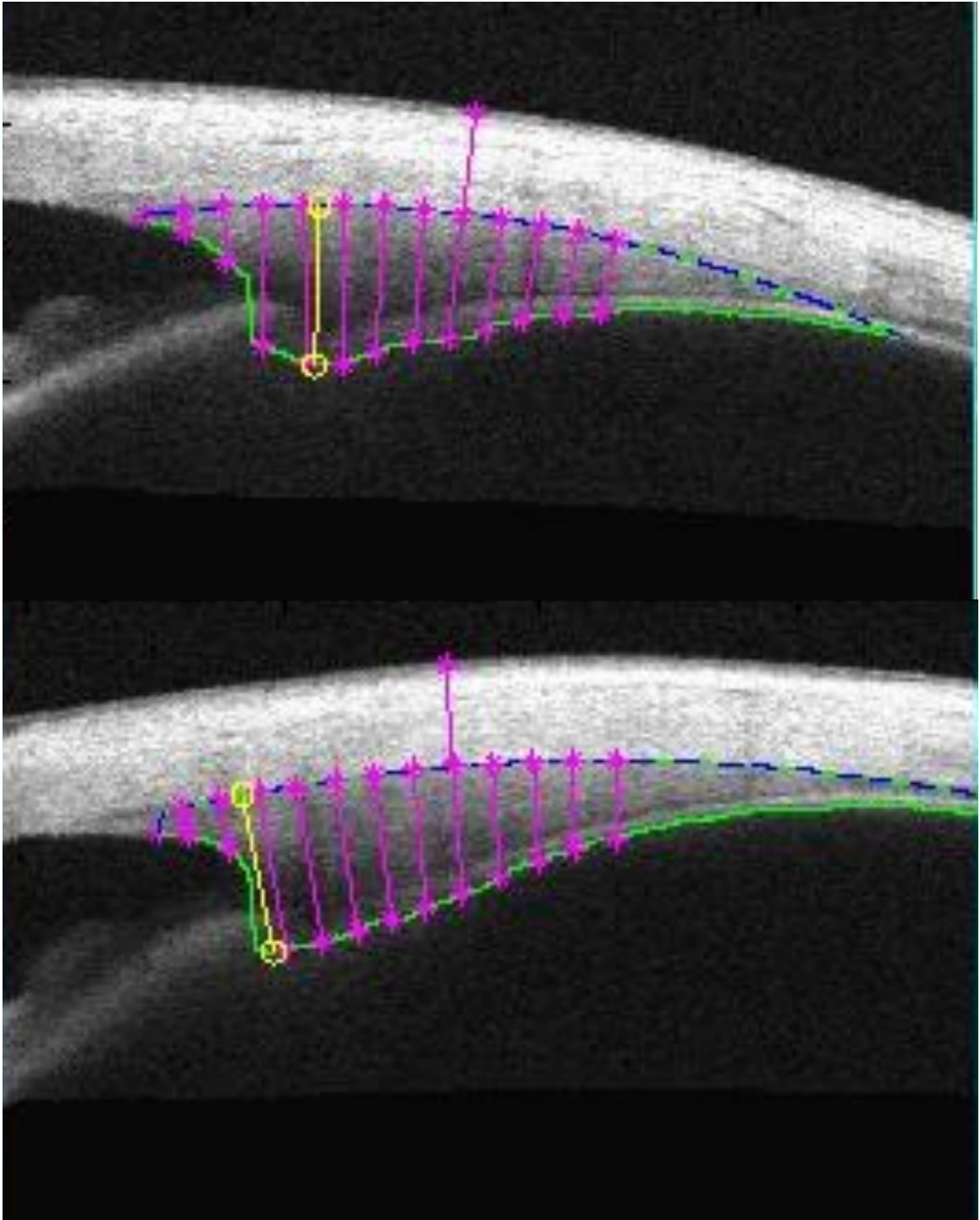


Figure 5. A thick ciliary muscle at rest (top) and with 6.0 diopters of accommodation (bottom)

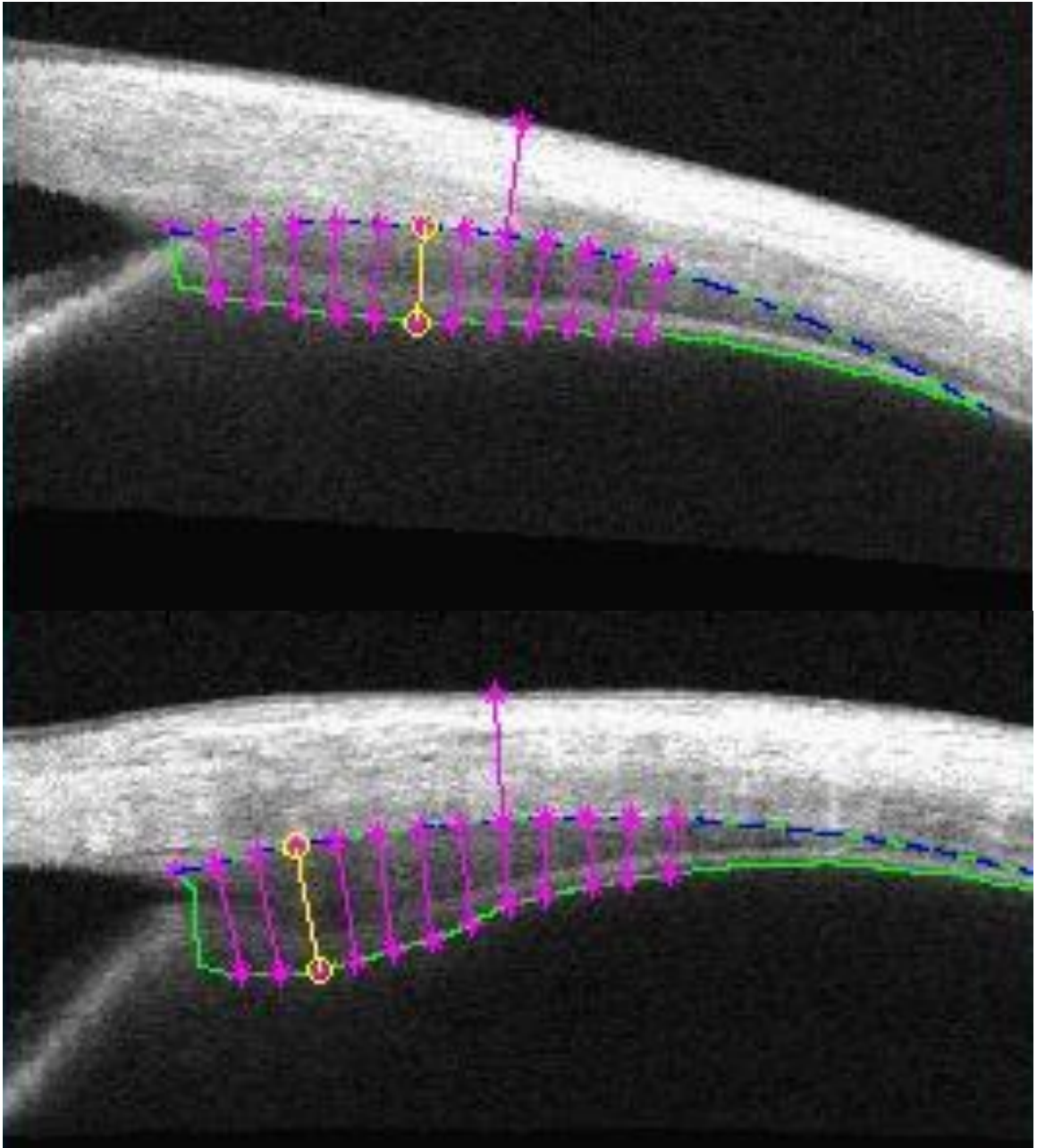


Figure 6. A thin ciliary at rest (top) and with 6.0 diopters of accommodation (bottom)

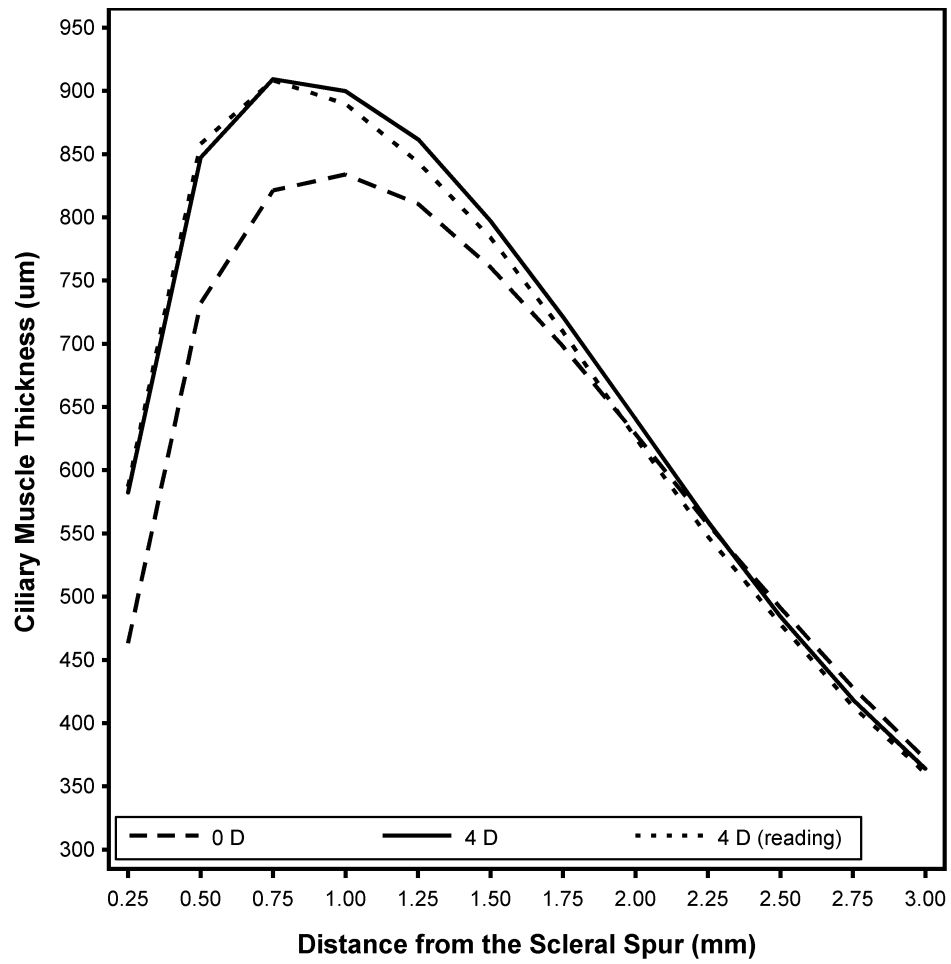


Figure 7. Mean ciliary muscle thickness before and after reading at 4.0 diopters of accommodation

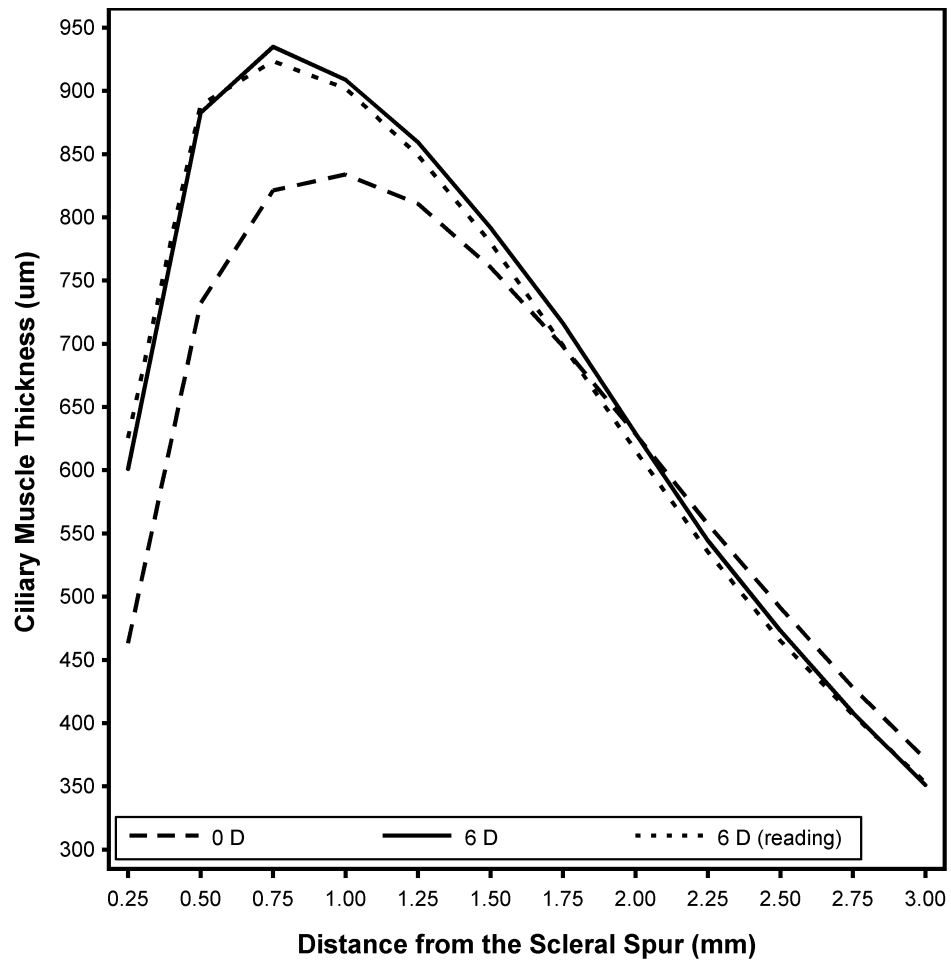


Figure 8. Mean ciliary muscle thickness before and after reading at 6.0 diopters of accommodation

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