Quantification of the ciliary muscle and crystalline lens interaction during accommodation with synchronous OCT imaging

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Abstract: Two SD-OCT systems and a dual channel accommodation target were combined and precisely synchronized to simultaneously image the anterior segment and the ciliary muscle during dynamic accommodation. The imaging system simultaneously generates two synchronized OCT image sequences of the anterior segment and ciliary muscle with an imaging speed of 13 frames per second. The system was used to acquire OCT image sequences of a non-presbyopic and a pre-presbyopic subject accommodating in response to step changes in vergence. The image sequences were processed to extract dynamic morphological data from the crystalline lens and the ciliary muscle. The synchronization between the OCT systems allowed the precise correlation of anatomical changes occurring in the crystalline lens and ciliary muscle at identical time points during accommodation. To describe the dynamic interaction between the crystalline lens and ciliary muscle, we introduce accommodation state diagrams that display the relation between anatomical changes occurring in the accommodating crystalline lens and ciliary muscle.

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1. Introduction

A better understanding of the biomechanics of the ageing accommodative apparatus is necessary to guide the development of new approaches aimed at restoring the ability to accommodate in presbyopes [1,2]. The development of strategies aimed at restoring accommodation such as accommodating intraocular implants, crystalline lens refilling techniques and femtosecond laser softening, have also created the need for in vivo imaging instrumentation that can objectively demonstrate their clinical efficacy [3]. One particular challenge is the difficulty in imaging the ciliary muscle and its interaction with the crystalline lens during accommodation.

The crystalline lens and/or the ciliary muscle have been imaged at static accommodation states using MRI [4–8], ultrasound [9–11], Scheimpflug imaging [12–18] and transscleral imaging with commercial time-domain (TD) OCT systems operating at wavelengths around 1300 nm [19–24]. These longer wavelengths enhance light penetration through the sclera and improve the visibility of the ciliary muscle in the OCT images.

The age-related changes in ciliary ring diameter and lens shape during accommodation have been quantified using magnetic resonance imaging (MRI) [25]. MRI provides distortion-free images of the entire eye, but its slow acquisition speed limits its application to the study of static accommodation. Recently, Shao et al [26,27] demonstrated joint but asynchronous acquisition of anterior segment and ciliary muscle images during accommodation using two separate SD-OCT units operating at central wavelengths of 840 nm and 1310 nm. The lack of precise synchronization combined with the moderate acquisition speed (~7-8 frames per second) of their systems limits the ability to accurately and precisely characterize the mutual temporal relationship between the dynamic changes occurring in the ciliary muscle and the resulting changes in the crystalline lens.

We previously described an extended depth SD-OCT system operating at a central wavelength of 840nm that enabled 2D imaging and full-length ocular biometry during dynamic accommodation [28]. We also recently demonstrated high-resolution live and 3D imaging and biometry of the ciliary muscle during dynamic accommodation using a transscleral SD-OCT system operating at a central wavelength of 1325 nm [29]. In this paper, we describe the combination and synchronization of these two SD-OCT systems and a dual-channel accommodation target to image the accommodative apparatus during dynamic accommodation. The dual SD-OCT system enables simultaneous and precisely synchronized acquisition of OCT sequences of the crystalline lens and ciliary muscle at an imaging speed (~13 frames per second) that is sufficient to characterize the dynamics of the response. We also present the first results showing the interaction between the crystalline lens and ciliary muscle during accommodation.

2. Methods

2.1. OCT imaging system

The imaging unit consists of two separate SD-OCT systems operating at central wavelengths of 1325 nm (CM-OCT, Fig. 1(A)) and 840 nm (AS-OCT, Fig. 1(C)) for imaging the ciliary muscle and the anterior segment, respectively. Details about the individual OCT systems were previously reported [28, 29]. Briefly, imaging at 840 nm of the eye ranging from the cornea to the lens along the horizontal plane is achieved by stitching two OCT frames consecutively acquired at different depths using a high-speed optical switch implemented in the reference arm. The system features an axial resolution of about 8 μm (in air) and is operated at an axial scan rate of up to 40,000 A-lines/s. The optical probe of the CM-OCT unit (Fig. 1(B)) was configured for transscleral illumination of the ciliary muscle (Fig. 1(D)). This unit is based on a commercially available OCT platform (TELESTO, Thorlabs Inc., NJ) that produces images with an axial resolution of 7.5 μm (in air) over an axial range of 2.5mm (in air). The system can be only operated at three fixed imaging speeds (6,000, 28,000 or 91,000 A-lines/s).
sample arm of the AS-OCT system consists of a set of X-Y transversal galvanometer scanners followed by an achromatic lens (AC254-100-B, f = 100 mm, Thorlabs, USA) that provides telecentric scanning along the horizontal plane. The sample arm of the system operating at 1325 nm integrates a color camera with a set of X-Y transversal galvanometer scanners followed by an objective lens (LSM03, EFL = 36 mm, Thorlabs, USA) configured to produce quasi-telecentric fields in both directions. The calculated diameter of the anterior segment OCT beam is 52 μm at the waist, which was positioned at the anterior surface of the crystalline lens. The calculated diameter of the transscleral OCT beam is 15 μm at the beam waist, which was positioned near the interface between the ciliary muscle and the sclera (Fig. 1(D)). The power delivered to the eye was 750 μW at 840 nm and about 3 mW at 1325 nm.

![Fig. 1. Schematic of the accommodation OCT system. (A) The SD-OCT system at 1325 nm (CM-OCT). (B) The delivery probes of the OCT systems and the accommodation unit. (C) The SD-OCT system at 840nm (AS-OCT). (D) Schematic of the anterior segment and OCT images of the ciliary muscle (CM) (red) and cornea, anterior chamber and lens (blue) generated by the system. Scale bar = 1mm (in air).](image)

2.2 Delivery unit

The delivery probes of the two SD-OCT systems and the custom-built accommodation unit were mounted on a motorized ophthalmic table equipped with a slit-lamp microscope mount, a patient contour head frame, an adjustable height chin rest, and a joystick (Fig. 1(B)). A dichroic mirror was used to optically couple the NIR light of the AS-OCT delivery system with the visible light produced by the accommodation unit [28]. The accommodation module consists of two optical channels, each based on a variation of the Badal optometer, that were combined to produce a monocular accommodation step stimulus while minimizing ocular convergence during the imaging procedure [28]. The OCT probe of the AS-OCT system is
mechanically coupled to the accommodation module so that it can be rotated and translated to allow precise alignment of the anterior segment OCT image plane with the optical axis of the eye while the subject fixates on the visible target. The delivery probe of the CM-OCT system is attached to a 4-axis positioning stage that is mounted on the rotation arm of the table.

2.3 SD-OCT systems synchronization

Ideally, the two OCT systems should acquire images at the exact same time points to precisely correlate the dynamic changes occurring in the anterior segment and ciliary muscle during accommodation. To ensure exact frame-to-frame synchronization, image acquisition must be triggered at the same time point for the two OCT units and the frame rate of the two OCT units must be equal.

Two computer workstations (Dell T5500, dual 3.6 GHz processor, 3 GB memory and Dell T5500, dual 3.6 GHz processor, 3 GB memory) with two different commercial software packages (Bioptigen, Inc. Research Triangle Park, NC and ThorImage OCT 4.0, Thorlabs Inc., NJ) were individually used for the real-time acquisition and display of the OCT data acquired at 840 nm and 1325 nm. Both software packages provide two imaging modes: alignment and acquisition. The graphical user interface (GUI) of both software packages includes a button to start the system in alignment mode and another one to elicit an acquisition of an OCT image sequence. Scanning parameters including acquisition speed and OCT image density are modified using the GUIs.

Since the commercial software packages for OCT image processing and display could not be modified to synchronize the two OCT imaging systems, we developed a microcontroller-based timing unit to trigger a simultaneous acquisition (Fig. 2). The timing unit synchronizes the OCT systems by processing the sawtooth voltage waveform that drives the X galvanometer scanner of the AS-OCT system (X-GS840 – Fig. 2(A)).

The timing unit synchronizes the beginning of an acquisition of the two SD-OCT systems and triggers the step stimulus produced by the accommodation unit at a specific time during the recordings through the following steps (Fig. 2(A)):

Step 1 – The systems are in alignment mode. The operator clicks on the acquisition button on the GUI of the AS-OCT (Fig. 2(A–1)) to start a synchronized acquisition.

Step 2 – The time control unit detects the first rising edge of the sawtooth waveform during acquisition of the AS-OCT (Fig. 2(A–2)) and triggers an interrupt of Microcontroller 1.

Step 3 – The interrupt routine of Microcontroller 1 is programmed to position the mouse pointer of the CM-OCT system over the acquisition button of the GUI and click and release to trigger an image sequence acquisition (Fig. 2(A–3)).

Step 4 – At each rising edge of the X-GS840 signal an interrupt event of Microcontroller 2 is triggered. The interrupt routine of Microcontroller 2 alternately switches the position of the optical switch in the reference arm of the AS-OCT system to acquire two frames at two different depths and triggers the accommodative step stimulus at a specific time during the acquisition that corresponds to a specific frame number, N. The stimulus onset time is manually set by the operator by defining the frame number N at the beginning of which the step stimulus is triggered. (Fig. 2(A–4)).

To match the frame rates of the two imaging systems, we adjust the scanning parameters as follows: we operated the CM-OCT unit at 28,000 A-lines/s with 897 A-lines per frame and a X-galvanometer fly-back time of 183 lines, corresponding to a frame rate of 25.926 fps. The AS-OCT system was operated at 12,500 A-lines/s with 400 A-lines per frame, and X-galvanometer fly-back of 82 lines corresponding to a frame rate of 25.934 fps.
Figure 2(B) shows the timing diagram of the two systems when a simultaneous acquisition is triggered. At the beginning of an imaging session both OCT systems run in alignment mode. When the acquisition button is pressed, the AS-OCT system transitions from alignment mode to acquisition mode (Step 1, Fig. 2(B–1)). During the transient between alignment and acquisition mode, the X galvanometer voltage signal of the AS-OCT system (X-GS<sub>840</sub> – Fig. 2(B)) is set to a constant voltage by the software (Fig. 2(B)). Once the first falling edge of the X galvanometer signal of the AS-OCT system is detected (Step 2, Fig. 2(B–2)), the chain of events shown in Fig. 2(A) triggers an acquisition of the CM-OCT system, which starts recording frames beginning with the one that is currently being acquired (Fig. 2(B–3)). This synchronization procedure introduces a random time delay ΔT (Fig. 2(B–3)) between the two temporal OCT sequences that produces an uncertainty of ± 1 frame, or ± 38.6 ms. In other words, the two SD-OCT systems are synchronized within ± 38.6 ms.

Fig. 2. (A) Schematic of the timing unit and synchronization operations between the SD-OCT systems operating at 840 nm and 1325 nm. (B) Time diagram of the synchronous acquisition between the two OCT systems.
2.4 Subjects and imaging protocol

The study was approved by the Institutional Review Board at the University of Miami Miller School of Medicine and followed the tenets of the Declaration of Helsinki. Written informed consent was obtained for all participants. The experiments were performed on the left eye of a 22 year-old non-presbyopic and of a 45 year-old pre-presbyopic subject with spherical equivalent refraction of \(-3\) D and \(-9\) D, respectively. The right eye was covered with an eye patch. Subjects were seated at the ophthalmic table with their head stabilized by the chinrest and the contour head frame. The distance channel of the accommodation module was adjusted until the patient was able to see the target in focus. The dynamic accommodative response of the 22 year old-subject to step stimuli of 2 D and 4 D amplitude was imaged with the system. For the 45 year-old subject, the dynamic response to a step stimulus of 2 D was recorded. The response to the 4 D stimulus was not recorded because the accommodation amplitude of this subject was insufficient.

A full dynamic recording consisted of two synchronized OCT image sequences which were acquired over a period of 6.170 s. The accommodation step stimulus onset was triggered after the first 40 frames were recorded \((t_S = 1.542\) s). After processing of the two OCT sequences was performed (see Section 2.5 below), the effective frame rate of the dynamic sequences was 13 fps.

2.5 Image post-processing and data analysis

**Anterior segment OCT image processing:** Each dynamic sequence acquired with the SD-OCT system at 840 nm consists of 160 OCT images that were alternately acquired at two different depths (Fig. 3(A)).

![Fig. 3. Schematic of the image processing applied on the OCT temporal sequence acquired over the anterior segment. (A) 160 images alternately acquired at two different depths over the anterior segment. (B) 80 images of the anterior segment ranging from the cornea to the posterior lens. (C) Intraocular distances including central corneal thickness (CCT), anterior chamber depth (ACD) and lens thickness (LT) extracted from automatic segmentation.](image-url)
Consecutive image pairs were combined [28] to obtain a new sequence of 80 OCT images ranging in depth from the cornea to the posterior lens (Fig. 3(B)). A custom automated segmentation algorithm was applied to each of the 80 OCT images of the anterior segment to detect the boundaries of the cornea and lens (Fig. 3(C)). The optical distances between the surface boundaries were then measured along the A-line passing through the center of pupil. The crystalline lens thickness (LT) and the shift of the anterior (ALS) and posterior (PLS) surfaces of the lens toward the cornea were obtained by dividing the optical distances by the group refractive index of the corresponding ocular media at 840nm ($n_{LENS} = 1.415$, $n_{AQUEOUS} = 1.341$) [28]. The geometrical shift of the crystalline lens center (LS) toward the cornea was calculated as the difference between ALS and PLS.

**Ciliary muscle OCT image processing:** Spatial registration of the ciliary muscle OCT sequence was performed to reduce the effect of motion artifacts [30]. Averaging of consecutive OCT image pairs was then applied to the entire sequence to reduce background noise and enhance the visualization of deeper structures such as the inner surface of the ciliary muscle and the inner apex (Fig. 1(D)). As a result, a sequence consisting of 80 averaged OCT images was obtained (Fig. 4(B)).

![Image](image-url)

Fig. 4. Schematic of the image processing applied on the OCT temporal sequence acquired over the ciliary muscle (CM). (A) 160 consecutive images of the ciliary muscle. (B) 80 averaged ($\times 2$) images of the ciliary muscle obtained from (B). (C) Manual segmentation of the ocular surface boundaries applied to the images in (B). Segmentation sample of the conjunctival surface (blue), CM outer surface (red), CM inner surface (green), anterior chamber boundary (yellow). (D) Distortion correction of the segmented boundaries in (C). (E) Ciliary muscle maximal thickness.

Manual segmentation of the OCT images of the ciliary muscle was performed independently by three examiners familiar with ocular anatomy to outline the contour of the conjunctiva (Fig. 4(C) – Blue line), the outer surface of the ciliary muscle (i.e. interface between sclera and ciliary muscle) (Fig. 4(C) – Red line), the inner surface of the ciliary muscle (i.e. interface between ciliary muscle and pigmented epithelium) (Fig. 4(C) – Green line), and the anterior chamber boundary (Fig. 4(C) – Yellow line). The segmented contours of the conjunctiva and ciliary muscle were corrected for distortion due to refraction of the beam at consecutive image boundaries (Fig. 4(D)) using a custom algorithm that was previously described [29]. The group refractive indices used for distortion correction and for calculation of thicknesses were 1.415 for the conjunctiva and sclera and 1.380 for the ciliary muscle at 1325nm [29]. Flat-field correction to minimize fan distortion introduced by the optical scanner was automatically corrected by the processing software of the CM-OCT.
system. After correction was performed, the maximum thickness of the ciliary muscle (CMT) was measured as the distance between the ciliary muscle outer surface and the inner apex along the direction perpendicular to the ciliary muscle outer surface (Fig. 4(E)). The inner apex was extracted from the segmented boundaries as the innermost point of the pigmented epithelium.

3. Results

3.1 Dynamic imaging of accommodation

Figure 5 shows the accommodative response to a step stimulus from 0 D to 2 D (Fig. 5(A) Visualization 1) and from 0 D to 4 D (Fig. 5(B) Visualization 2) in the 22 year-old subject and from 0 D to 2 D in the 45 year-old subject (Fig. 5(C) Visualization 3). The movies display composite OCT images including the ciliary muscle (Fig. 5(A)-5(C) left) and anterior segment surfaces (Fig. 5(A)-5(C) right) acquired according to the protocol previously described. The orientation of the ciliary muscle image is adjusted so that the iris in the two images is aligned. The OCT image of the ciliary muscle is magnified with respect to the one of the anterior segment to emphasize the anatomical changes. During accommodation, changes in shape of the crystalline lens and ciliary muscle contraction are observed in both subjects.

![Fig. 5. Real-time display of lens and ciliary muscle response during accommodation in a 22 year-old subject for (A) a 2D (see Visualization 1) and (B) a 4D (see Visualization 2) step stimulus and in a 45 year-old subject (see Visualization 3) for a 2D step stimulus. The OCT images were acquired at 13 fps during the accommodative responses from the relaxed state to the accommodative state. The movies are displayed at twice the acquisition speed (26 fps).](image)

3.2 Dynamic biometry of accommodation

For each subject and accommodation stimulus we extracted the time course of the shift of the lens surfaces and center (ALS, PLS, LS – Fig. 6(A)-6(C)), the lens thickness (LT – Fig. 6(D)-6(F)) and the maximum thickness of the ciliary muscle (CMT – Fig. 6(G)-6(I)) in response to a step change in accommodation. The shift and thickness of the crystalline lens and the thickness of the ciliary muscle are steady (relaxed state) until the accommodation stimulus is
applied (Fig. 6(A)-6(I)). The changes during accommodation follow an exponential type behavior, with a rising phase leading to the steady accommodated state.

Fig. 6. Dynamics of the crystalline lens position (A-C) and thickness (D-F), and ciliary muscle thickness maximal thickness (G-I) in a 22 year-old and a 45 year-old in response to step accommodation stimuli. The ciliary muscle thickness data points and error bars represent the average and standard deviation of measurements obtained by three independent operators on the same OCT images using a custom-made manual segmentation program. (A-C) Time response of the anterior (ALS), posterior (PLS) and central (LS) lens position. (D-F) Time response of the lens thickness (LT). Red squares indicate changes occurring during the LT rising phase (between 5% and 95% of the final lens thickness). Black squares indicate steady states or LT changes occurring outside the rising phase. (G-I) Time course of ciliary muscle maximal thickness (CMT). Red squares indicate CMT changes occurring during the rising phase of LT. Black squares indicate steady states or CMT changes occurring outside the LT rising phase. Exponential fit of LT and CMT traces according to Eq. (1) are reported in blue. (J-L) Accommodation state diagrams reporting LT changes (D-F) as a function of CMT changes (G-I). Data points (LT, CMT) corresponding to the rising phase of LT are indicated with red empty squares. The relaxed and accommodated states of the lens are indicated with red, solid squares. The transition path from the relaxed to the accommodated state is indicated with a red line. Steady states or LT changes occurring outside the rising phase are indicated with black, empty squares. Linear regression of the rising phase plot is reported in blue.
To quantify the change in dimensions, mean and standard deviation of the biometric parameters were calculated over the first 20 images acquired before the stimulus onset (relaxed state) and the last 20 images acquired in the sequence (accommodated state) (Table 1). During accommodation, the lens increases in thickness and moves toward the cornea. The shift of the lens center is mainly produced by a forward movement of the anterior surface, while the posterior surface position remains essentially steady. The ciliary muscle apex moves inward during accommodation.

### Table 1. Mean and standard deviation of the change in crystalline lens thickness (LT), anterior (ALS), posterior (PLS) and central (LS) axial shift of the crystalline lens and maximum thickness of the ciliary muscle (CMT) during accommodation in 22 year-old and 45 year-old subjects.

| Age | Step stimulus | LT [mm]       | ALS [mm] | PLS [mm] | LS [mm] | CMT [mm] |
|-----|---------------|---------------|----------|----------|---------|----------|
| 22  | 0D            | 3.438±0.002°  | 0±0.008° | 0±0.008° | 0±0.008°| 0.478±0.006° |
|     | ↓             | 3.563±0.007°  | 0.134±0.011° | 0.099±0.002° | 0.072±0.010° | 0.525±0.009° |
|     | 2D            | 3.453±0.004°  | 0±0.011° | 0±0.010° | 0±0.010°| 0.471±0.011° |
|     | ↓             | 3.667±0.008°  | 0.205±0.012° | -0.009±0.012° | 0.098±0.012° | 0.543±0.019° |
| 45  | 0D            | 4.291±0.001°  | 0±0.021° | 0±0.021° | 0±0.021°| 0.608±0.016° |
|     | ↓             | 4.381±0.003°  | 0.092±0.021° | +0.001±0.022° | 0.046±0.021° | 0.697±0.015° |

The 0D data corresponds to the average (red lines in Fig. 6(D-I)) and standard deviation of measurements obtained from 20 images acquired before the onset of the stimulus (t =1.542 s). The 2D and 4D data correspond to the average (red lines in Fig. 6(D-I)) and standard deviation of measurements acquired on the last 20 images of the session.

The dynamic responses of the crystalline lens and ciliary muscle to a step change in vergence are similar to those previously recorded using A-scan ultrasonography and OCT [26–28, 31, 32]. We fit the lens and ciliary muscle thickness time traces with the following first order exponential growth (Fig. 6(D)-6(I)) [31]:

$$x(t) = x_0 + \Delta x \times \left(1 - e^{\left(\frac{-t}{2\tau}\right)}\right).$$

where \(t\) is time elapsed from the beginning of an acquisition, \(x(t)\) is the time dependent thickness, \(x_0\) is the value in the relaxed state, \(\Delta x\) is the total thickness change, \(\Delta t\) is the latency, which is the time elapsed between the application of the step stimulus (\(t_s = 1.542\) s) and the start of the accommodation response and \(\tau\) is the time constant of the response. Table 2 reports the estimated latency time, time constant and peak velocity for the time traces reported in Fig. 6(D)-6(I). The thickness changes, time constants and latencies are similar to previously published values found using ultrasonography and Purkinje imaging [31, 33].

3.3 Quantification of the crystalline lens and ciliary muscle interaction

The ability to acquire precisely synchronized (within ± 38.6 ms) images of the lens and ciliary muscle at a frame rate of 13 Hz allows us to produce accommodation state diagrams (Fig. 6(J)-6(L)) that describe the interaction between the crystalline lens and the ciliary muscle during dynamic accommodation. The diagrams (Fig. 6(J)-6(L)) were produced by plotting the synchronized values of the crystalline lens and ciliary muscle thickness (LT vs. CMT) from Fig. 6(D)-6(F) and Fig. 6(G)-6(I), for each subject and accommodative stimulus amplitude.
Table 2. Parameters of the exponential fits of the changes in the lens and ciliary muscle thickness during accommodation for the 22 year-old and 45 year-old subjects

| Age | Step stimulus | Parameter | \( x_0 \) [mm] | \( x \) [mm] | \( \Delta t \) [s] | \( \tau \) [s] | \( v_{\text{Peak}} \) [mm/s] | \( \Delta X_{\text{DELAY}} \) [µm] |
|-----|---------------|-----------|----------------|-------------|----------------|-------------|-----------------|-----------------|
| 22  | 2D            | LT        | 3.438          | 0.124       | 0.515          | 0.279       | 0.444           | 16.9            |
|     |               | CMT       | 0.476          | 0.045       | 0.448          | 0.255       | 0.176           | 6.7             |
|     | 4D            | LT        | 3.456          | 0.215       | 0.469          | 0.406       | 0.530           | 20.1            |
|     |               | CMT       | 0.471          | 0.070       | 0.226          | 0.821       | 0.085           | 3.2             |
| 45  | 2D            | LT        | 4.291          | 0.090       | 0.564          | 0.428       | 0.210           | 7.9             |
|     |               | CMT       | 0.608          | 0.086       | 0.105          | 1.002       | 0.086           | 3.3             |

*Thickness during the relaxed state \((x_0)\), overall thickness change \((\Delta x)\), latency \((\Delta t)\), time constant \((\tau)\), and peak velocity \((v_{\text{Peak}})\) are reported for the lens and ciliary muscle, for each subject and stimulus amplitude. The maximum predicted thickness change in lens or ciliary muscle thickness \((\Delta X_{\text{DELAY}})\) produced over a period of about 38 ms and calculated at the peak velocity of accommodation \((v_{\text{Peak}})\) is reported. The thickness \((x_0)\) and overall thickness change \((\Delta x)\) were extracted from the exponential fit of Eq. (1) and for this reason might slightly differ from the mean values calculated over 20 samples reported in Table 1.

The data points \((LT, CMT)\) corresponding to the rising phase of the lens thickness (Fig. 6(J)-6(L) – red, empty squares) were connected with lines (Fig. 6(J)-6(L) – red line) to show the sequence between the relaxed and accommodated states. In the younger subject, the absolute change in mean ciliary muscle thickness between the relaxed state and the first data point of the rising phase of the lens thickness is very small (<0.005 mm), which indicates that minimal contraction of the ciliary muscle is needed to produce a change in lens thickness. As the ciliary muscle continues to contract, the lens thickens until the accommodated state is reached. In the older subject, the change in ciliary muscle thickness between relaxed state and the first data point of the rising phase of the lens thickness is significantly larger (0.030 mm for 2 D step stimulus), which suggests that the ciliary muscle of the older subject needs a greater contraction to elicit an accommodative change of the lens. In order to quantify the relationship between lens thickness change and ciliary muscle thickness change, we calculated the slope of the linear regression of the diagrams during the rising phase (Fig. 6(J)-6(L) – blue line). The slope of the linear regression was 2.190 mm/mm and 2.133 mm/mm for a 2 D and 4 D stimulus in the 22 year-old subject, respectively, and 1.223 mm/mm in the 45 year-old subject for a 2 D stimulus. The steeper slopes for the younger subject indicate a stronger response in lens thickness per unit change in ciliary muscle thickness.

4. Discussion

We precisely synchronized two SD-OCT systems operating at 840 nm and 1325 nm and an accommodation target to image the anterior segment during dynamic accommodation. The accommodation target is a two-channel Badal optometer that provides step stimuli during OCT image acquisition. Our system enables the synchronous recording of temporal OCT image sequences of the anterior segment and the ciliary muscle at 13 frames per second during accommodation.

The microcontroller-based timing unit that we developed to synchronize the acquisition of the two temporal image sequences and control the stimulus onset time together with the selected imaging parameters provides synchronization with a delay within ± 38.6 ms. The effect of this small delay on the quantitative analysis of the correlation between lens and ciliary muscle dynamics is minimal. In our experiments, the maximum predicted thickness change in lens or ciliary muscle thickness \((\Delta X_{\text{DELAY}})\) produced over a period of about 38 ms and calculated at the peak velocity of accommodation (Table 2) varied between only 3.2 µm and 6.7 µm for the ciliary muscle and between 7.9 µm and 20.1 µm for the lens (Table 2). These values are comparable to the axial and lateral resolutions of the two SD-OCT systems (Section 2.1) and to the variability of thickness measurements (0.001 to 0.021 mm – Table 1). Thus, the lens and ciliary muscle OCT sequences can be considered synchronized within the precision of our measurements.
The ability to acquire synchronized images of the lens and ciliary muscle at a frame rate that is significantly faster than the time constants of accommodation enables us to characterize, for the first time, the relation between ciliary muscle contraction and changes in lens shape dynamically during accommodation. The only previous report on the biometry of the crystalline lens and ciliary muscle during dynamic accommodation used a combination of two SD-OCT systems which acquired images asynchronously with different frame rates for the lens and ciliary muscle (8.33 and 7.0 fps, respectively) [26, 27]. The asynchronous image acquisition, lower frame rate, and uncertainty in time delay between image acquisition and onset of the accommodation stimulus resulted in large variability and uncertainty in the measured dynamic parameters significantly impacting the ability to gain insight into the dynamics of accommodation [26].

One of the challenges in imaging the inner structures of the ciliary muscle is the attenuation of light by the sclera and ciliary body, which in turn decreases the image contrast, making structures such as the ciliary body inner apex more difficult to visualize [19]. OCT imaging at long wavelengths (~1300 nm) enables deeper visualization of the posterior ciliary muscle boundary and the inner apex [19, 34], which is the key to obtaining accurate ciliary muscle thickness measurements. To increase the visibility of the ciliary muscle, we registered and averaged consecutive pairs of OCT images during dynamic acquisition. The trade-off of averaging is that the temporal resolution is reduced by a factor of two. We also tested if image contrast could be further improved by positioning the inner apex near the zero delay position [27]. However, we did not notice an improvement in image contrast compared to positioning the conjunctival surface near the zero delay position.

Compared to previous studies using OCT for ciliary muscle imaging [19–24, 26, 27, 35], we obtain increased contrast of the posterior ciliary muscle and inner apex [19]. Despite this improvement in contrast, we still found significant inter-operator variability in the manual measurements of ciliary muscle maximum thickness (Fig. 6(G)–6(I)). For example, the measurements obtained by three different examiners led to time constants equal to 0.401 s, 0.924 s and 1.426 s, latencies equal to 0.384 s, 0.318 s and 0.002 s and thickness changes equal to 0.089 mm, 0.058 mm and 0.071 mm respectively in the 22 year-old subject responding to a step stimulus of 4 D. The segmentation and measurement variability introduces a relatively large uncertainty in the dynamic fit parameters extracted from ciliary muscle images. The purpose of this study is to assess the ability to record the synchronous dynamic response of the crystalline lens and the ciliary muscle with OCT. More studies are needed to improve the model for the dynamic response of the ciliary muscle and crystalline lens and fully evaluate the variability and subjectivity of the analysis. However, our preliminary findings suggest that caution must be exercised when evaluating time constants and latencies of the ciliary muscle thickness during accommodation if manual segmentation is used, especially if the image contrast over the ciliary muscle apex is low [26, 27]. Semiautomatic segmentation algorithms and analytical methods for morphological data extraction from OCT images of the ciliary muscle have been recently proposed [19, 35], which may help reduce the variability and subjectivity of the analysis.

We previously described the impact of motion artifacts while imaging and performing full-length biometry of the eye during accommodation using SD-OCT with a dual-channel monocular accommodation target. The accommodation module is designed to reduce ocular movements during accommodation [28]. The real-time displays of the accommodative process shown in Fig. 5 suggest that ocular convergence and movements are minimal during the imaging process. In this study, we can use the variability of the lens thickness and position during steady accommodative states to estimate the effect of eye movements on the measurement accuracy. In our measurements (Table 1), the maximum variability of lens thickness (0.008mm) and position (0.021mm) during steady states is relatively small, which indicates that the dynamic measurements are not significantly affected by ocular movements occurring during the relatively long recording time (6.170s). The lens position of the older...
subject shows higher variability (0.021mm) compared to the one of the younger subject (0.010) during sustained accommodation in response to 2D (Fig. 6(A), 6(C)). We believe that the variability of the lens position during steady accommodative states is mainly produced by actual fluctuations in lens position rather than ocular movements since for both subjects and accommodative stimuli this variability is much less than the variability in lens thickness (Table 1). If the variability in lens position would be caused by eye movements, we would expect similar variability in the lens thickness measurements.

Precise synchronization of the crystalline lens image sequence, the ciliary muscle image sequence and accommodation stimulus enabled us to introduce accommodation state diagrams describing the interaction between the crystalline lens and the ciliary muscle during dynamic accommodation. The preliminary results obtained from these diagrams suggest that: a) in the younger subject, a contraction of the ciliary muscle from the relaxed state produces an immediate response in the crystalline lens while in the older subject the contraction of the ciliary muscle needs to reach a certain threshold before eliciting a response in the crystalline lens; b) the younger subject produces a larger change in lens thickness per unit change in ciliary muscle thickness than the older subject. The accommodation state diagrams can be used as a tool to investigate and quantify the interaction between the crystalline lens and ciliary muscle during accommodation as a function of age and different accommodative stimulus amplitudes. Currently, there is no widely accepted method for measuring the morphological changes in the ciliary muscle during accommodation [34]. In this study, we used the maximal ciliary muscle thickness to quantify the change in ciliary muscle dimensions in the accommodation diagram. However, a different metric, such as thickness at multiple positions, length, or cross-sectional area [19, 23, 24, 34, 35], may be used to generate accommodative diagrams.

5. Summary

We combined and precisely synchronized two SD-OCT systems and an accommodation target to produce two synchronous OCT image sequences of the anterior segment and the ciliary muscle with high imaging speed (~13 fps) during accommodation. The fast imaging speed of the system and the precise synchronization enabled the quantification of the dynamic transients of the crystalline lens and ciliary muscle thicknesses, and the characterization of the relationship between ciliary muscle contraction and resulting changes in lens thickness during accommodation.

Author disclosure

The University of Miami and authors MR, FM, and JMP stand to benefit from intellectual property in the OCT technology used in this study.

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