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Repeated measurements of the anterior segment during accommodation using long scan depth optical coherence tomography

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Abstract

Objectives—To determine the repeatability of ultra-long scan depth spectral domain optical coherence tomography (SD-OCT) measurements of the ocular anterior segment during accommodation.

Methods—The center wavelength of the SD-OCT light source was 840 nm with a bandwidth of 50 nm. The ocular axial resolution of the system was ~6.0 μm , and the scan depth was 7.2 mm in air. Twenty eyes of twenty healthy subjects were imaged with a custom-built, ultra-long scan depth SD-OCT during two visits. The anterior segment images were acquired during non-accommodative and maximal accommodative states. After image processing and correction, the true values of the morphometric dimensions of the anterior eye were obtained. The variables of the two states from two visits were compared.

Results—For the corrected anterior segment images, the variables did not significantly differ from one visit to the next. The values of anterior chamber depth, pupil diameter, and the radius of the lens anterior surface curvature during accommodation were significantly smaller than those during the non-accommodative state. The lens thickness significantly increased with accommodation. There was no significant difference in the posterior surface curvature of the lens between the two states.

Conclusions—Ultra-long scan depth SD-OCT holds promise for quantifying dimensional changes in the eye during accommodation. The instrument demonstrated good repeatability of ocular anterior segment dimensional measurements during accommodation.

Keywords

accommodation; optical coherence tomography; anterior segment; lens; pupil

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INTRODUCTION

The accommodation system of the human eye is highly dynamic and sensitive. It responds differently to targets of various distance, color, luminance and contrast. The response of the system is related to refractive error, pupil size, and convergence.^{1, 2} Accommodative responses, including accommodative lead and lag, have been identified and studied for decades. Abnormalities in this system may cause several clinical symptoms. Presbyopia, which is defined as a decrease in the amplitude of the accommodative response, occurs with aging.^{3–6} The optical power changes of the eye during accommodation have been characterized previously. The accommodative response, including accommodative lead, lag and microfluctuation, has been quantified.^{7, 8} These studies provided insight into the accommodation system. However, studies on dioptric changes were not sufficient to fully understand the accommodation system. During accommodation, the crystalline lens changes its shape and plays a significant role in the power change of the ocular optical system. Meanwhile, other optic media of the eye, such as the anterior chamber, change accordingly. Thus, it is essential to study the changes in ocular optic media dimensions during accommodation.

To quantify dimensional changes during accommodation in vivo, advanced imaging technology is required. Optical coherence tomography (OCT) is a rapid and non-contact method and is thus an ideal tool to study the eye.^{9–12} Recently, an ultra-long scan depth spectral domain OCT (SD-OCT) was built at the Bascom Palmer Eye Institute.¹³ With this instrument, the anterior segment of the eye from the front surface of the cornea to the posterior surface of the crystalline lens can be imaged simultaneously. The purpose of this study was to determine the repeatability of ultra-long scan depth SD-OCT measurements of the ocular anterior segment during accommodation.

MATERIALS AND METHODS

Subjects

This study enrolled 20 healthy subjects (9 female and 11 male; mean $\pm$ standard deviation age: 33.1 ± 5.8 years) after receiving approval from the Institutional Review Board of the University of Miami. The mean spherical equivalent of the subjects was -2.76 ± 2.61 D (range: 0 $\sim$ -6.88 D). The astigmatism of the subjects ranged from 0 to -1.75 D. All subjects had a visual acuity of 20/20 or better in each eye with their habitual Rx. The subjects had no ocular diseases, trauma, or any history of ophthalmic surgery. Each subject was treated in accordance with the tenets of the Declaration of Helsinki, and informed consent was obtained.

OCT Instrument

Acustom-built ultra-long scan depth SD-OCT with high resolution was used to image the ocular anterior segment. This instrument has been previously described in detail.¹³ Briefly, the center wavelength of the superluminescent diode-based light source (Superlum, Broadlighter, D840-HP, Superlumdiodes Ltd., Moscow, Russia) was 840 nm with a bandwidth of 50 nm. The ocular axial resolution of the system was ~ 6.0 μ m. A custom spectrometer was developed to achieve an extended depth range of 7.2 mm in air. The total exposure power was 1.30 mW, which is within the safe range for the human eye according to ANSI Z136.1.¹⁴ The beam passed through an optical isolator and was split by a 50:50 fiber coupler into reference and sample arms. A charge-coupled device camera (Aviiva-SM2010, 2,048 pixels; Atmel, e2v Inc., Elmsford, NY, USA) was equipped with a volume holographic diffraction grating (1,800 lines/mm; Wasatch Photonics, Logan, UT, USA). Two-dimensional cross-sectional scans (B-scans), consisting of 2,048 line scans (A-scans)

with 2,048 points per A-scan, were used to image the anterior segment of the eye. The OCT was connected to an optical delivery system with a video camera. An x-y galvanometer pair served as a scanner. The x-y galvanometer pair allowed alignment of the scanning position at both the horizontal and vertical meridians. To precisely align the OCT scanning position, “X-Y cross aiming mode” was built in the OCT driving software.¹⁵ When the operator began aligning the image, this mode was launched as a guide, and the OCT probe began to scan the eye at both horizontal and vertical meridians. Thus, the operator was able to monitor the images of both meridians on the software interface (Fig. 1). The image should be acquired when the specular reflection of the corneal apex could be seen at both meridians. Thus, the “X-Y cross aiming mode” ensured that the corneal apex was precisely centered during image acquirement.

A fixation target system was also built. A liquid-crystal display monitor was attached to the probe. It was 20 cm in front of the test eye. A white “E” fixation target with a black background was displayed on the monitor. The “E” was a 20/100 letter according to the Snellen visual acuity chart. The position of the monitor was adjustable to enable guiding of the subject’s fixation. Meanwhile, a lens holder was mounted 8 cm in front of the test the eye. Trial lenses were placed in the holder to compensate for the subject’s Rx and to induce non-accommodative and maximal accommodative states of each subject (Fig. 2).

As previously demonstrated, mirror artifacts arise from the Fourier transformation used in SD-OCT systems.^{16, 17} Thus, two OCT images are produced that are symmetrical around the zero-delay line. This phenomenon has been analyzed and was used to image the full range image of the human anterior chamber.^{18, 19} In addition, Fourier-domain instruments lose sensitivity with increased distance from the zero-delay line. This loss occurs because finer interference signals are produced at increased distances from the zero-delay line, and the resolution of the spectrometer is finite.^{16, 17} In the present study with extended scan depth SD-OCT, the zero-delay line was set at the anterior portion of the lens during OCT imaging to allow the full range of the anterior segment to be imaged (Fig. 3A). The mirror images overlapped each other and contained the anterior chamber and the lens (Fig. 3A). In this way, the corneal plane was far away from the zero-delay line. Although the intensity of the cornea decreased, the boundaries of the cornea could be defined using our imaging processing method. After processing the raw OCT image using custom software, we were able to obtain the anterior segment dimensions from the cornea to the posterior surface of lens simultaneously without using a complicated phase shift technique.^{16, 18}

Study Procedure

The habitual Rx and maximal amplitude of accommodation of each subject were tested. All subjects had a visual acuity of 20/20 or better in each eye with their habitual Rx, and the maximal amplitude of accommodation of the test eyes was recorded. Therefore, the distances between the fixation target, trial lens and test eye (Fig. 2) as well as the habitual Rx and maximal amplitude of accommodation were already known. The proper power of the trial lenses during non-accommodative and maximal accommodative states for each subject was calculated using custom software. The OCT images were collected in a consulting room that was kept dark. One randomly selected eye of each subject was tested. Two visits were scheduled for each subject at the same time on two consecutive days. During each visit, the subject was asked to look forward at an internal “E” fixation target using the test eye while the other eye was covered. To relax accommodation, trial lenses with proper power were placed in front of the test eye. Meanwhile, the OCT image was aligned at both the horizontal and vertical meridians under the “X-Y aiming mode”. Being able to visualize the specular reflection of the corneal apex at both meridians indicated that the corneal apex was precisely centered (Fig. 1). After the subject reported that the target could be seen clearly, a 14.5-mm cross-sectional OCT scan at the horizontal meridian was collected. The raw images of the

anterior segment with both mirror artifacts were acquired during the non-accommodative state (Fig. 3A). The trial lenses were then replaced to induce the maximal amplitude of accommodation of the subject, and another OCT scan was collected (Fig. 3D).

Image Processing

Image processing was divided into two steps. First, the raw anterior segment images with both mirror artifacts (Fig. 3A, 3D) were processed and reconstructed using custom software to obtain full-range anterior segment images (Fig. 3B, 3E). We then applied the semi-automatic segmentation process to detect the boundaries of the cornea, iris and crystalline lens. It should be mentioned that the intensity of the cornea seemed low, so we placed 4 points on the interface to define the boundaries through our segmentation method.

Secondly, an algorithm was developed to optically correct the images because the OCT light is distorted as it passes through the eye.²⁰ After the positions of all interfaces in the OCT image were semi-segmented, the surface extraction algorithm was used to produce a set of positions for well-defined interfaces. The refraction correction algorithm was then applied based on Snell's principle,²⁰ and for each ray, we calculated the new corrected position of the second interface. After image correction, the true surface positions of the lens were obtained. We used the least squares method to fit the lens surfaces with circle equation. The obtained curvature of the fitted circle was defined as the curvatures of the lens surfaces. It should be indicated that the anterior chamber depth was defined as the distance from the back surface of the central cornea to the anterior vertex of the lens. The lens thickness was defined as the distance from the anterior vertex to the posterior vertex. We validated this algorithm on an ocular imaging eye model (OEMI-7, Ocular[®] Instruments Inc., Bellevue, WA, USA) with a polymethyl methacrylate (PMMA) cornea and intraocular lens. The eye model was imaged by both OCT and a Zygo Interferometric Optical Surface Profiler (Zygo[™] Corporation, Middlefield, CT, USA). The anterior and posterior curvature measurements of the PMMA cornea and intraocular lens by the OCT and the Zygo profiler were consistent. In addition, with the 840-nm wavelength of the present SD-OCT instrument, the refractive indices of the cornea and lens used in the calculations were 1.38 and 1.40, respectively.^{10, 21} The OCT images were optically corrected (Fig. 3C, 3F), and the true values of the ocular morphometric dimensions were obtained.

Data Analysis

The data from the uncorrected and corrected images are presented as the mean $\pm$ standard deviation. Data analyses were conducted using the Statistical Package for the Social Sciences (version 15.0, SPSS Inc., Chicago, IL, USA). The mean values of the morphometric dimensions and the average differences between the repeated measurements on two consecutive days were calculated. The differences between repeated measurements were determined with repeated measures analysis of variance (Re-ANOVA) and Bland-Altman plots.²² Paired t-tests were used to test the differences between the dimensions of the non-accommodative and accommodative states.

RESULTS

The anterior segment dimensions during non-accommodative and maximal accommodative states in 20 eyes of 20 subjects were obtained before (Table 1) and after image correction (Table 2). For the corrected anterior segment images, there were no significant differences in any of the variables between the two measurements acquired on separate days (Re-ANOVA, $P > 0.05$, Table 2). The Bland-Altman plots revealed that the mean differences in the values between the two repeated measurements were close to zero. The limits of agreement were defined as the mean difference $\pm$ 1.96 times the standard deviation of the difference (Fig. 4).

The anterior chamber depth, pupil diameter, and radius of the lens anterior surface curvature during accommodation were significantly smaller than in the non-accommodative state (paired t-test, $P < 0.05$, Table 2). Meanwhile, the lens thickness significantly increased with accommodation ($P < 0.05$). There was no significant difference in the posterior surface curvature of the lens between the two states ($P > 0.05$).

DISCUSSION

Several studies on dimensional changes of the anterior eye using various imaging technologies have contributed to our understanding of the accommodation system.^{23–25} For instance, magnetic resonance imaging (MRI) and Scheimpflug photography can capture the full range of the anterior segment.^{23, 24} However, these methods have relatively low resolution. MRI was reported to have an in-plane resolution of 0.156 mm,²³ whereas the changes in lens thickness and lens surface curvatures have been reported to be 0.045 mm and 0.61 mm, respectively, per diopter.²⁴ In the present study, the mean changes in lens thickness and lens surface curvatures during accommodation were much less than the resolution of MRI. Thus, imaging technology with micrometer-scale resolution was required to study the crystalline lens. The present Scheimpflug instrument, which uses visible blue light²⁴, cannot compete in resolution with SD-OCT, which uses a near-infrared light source.¹² Moreover, the scan speed of MRI is slow, and it is difficult to control eye movement and accommodative amplitude during imaging.²³ The natural accommodative process may be altered by the use of mydriatics and the stimulation of visible scan light during Scheimpflug photography.²⁴ Furthermore, the scan light is not set against the axis of the cornea, and the position of the camera is inclined. The inclined scan light is refracted by the cornea, tumor and crystalline lens. This may induce optical distortion, especially the prismatic effect.^{24, 26–28} Ultrasound biomicroscopy is a contact method and requires a water bath between the probe and eye,²⁵ making it difficult to maintain natural accommodation.

Because the accommodation system is highly dynamic, precise and sensitive, advanced imaging technology is necessary to overcome technical limitations of the current imaging method. SD-OCT is a rapid, non-invasive method with a high scan speed and high resolution.¹² The use of invisible near-infrared light makes it possible to maintain the natural accommodative process of the human eye during imaging. SD-OCT has been used to study the characteristics of tear film and was demonstrated to be an ideal tool without stimulating the eye.²⁹ However, commercially available SD-OCT instruments have shallow scan depths no deeper than 3–4 mm that cannot image the anterior chamber and lens simultaneously,^{26, 30, 31} thus limiting their application in accommodation research. In the present study, the custom-built ultra-long scan depth SD-OCT was able to image the full range of the anterior segment. Moreover, a software package was developed for image processing. Most importantly, we took advantage of the symmetrical mirror artifacts of SD-OCT that effectively doubled the scan depth to approximately 14 mm. The image could be optically corrected using a custom algorithm to yield true anterior segment dimensions. This enabled a rapid way to dynamically image the entire anterior segment.

Because some portions of the lens image overlapped in the mirror images of the anterior segment, the details inside the lens could not be examined. However, after image reconstruction, the boundaries of the cornea, iris and lens were clearly visualized. In this pilot study of accommodation, we focused primarily on changes in lens shape. The absence of detailed changes inside the lens did not alter our findings.

In the present study, we observed good repeatability of measurements collected during two separate visits. The values of the anterior segment dimensions, including anterior chamber depth, pupil diameter, lens thickness, and the radius of the lens of both surfaces curvatures

were consistent with previous studies.^{23, 24, 26, 31} The changes in the anterior segment dimensions during accommodation could be quantified. The cornea was regarded as a reference plane because the position of the cornea does not change during accommodation.³² The anterior surface of the lens became steeper and moved forward during accommodation so that the anterior chamber became shallower while the pupil contracted.

Interestingly, the lens posterior surface curvature and the distance from the back surface of the cornea to the posterior lens surface, i.e., the sum of the anterior chamber depth and lens thickness, did not change significantly during accommodation. This indicated that the posterior lens surface remained static. Thus, the lens became thicker with the change in anterior surface. Some studies have given contradictory results.^{30, 33, 34} For instance, the lens was reported to be pushed towards the cornea during accommodation because of the hydraulic pressure of the vitreous.³³ However, other studies suggested that the posterior lens surface moved backward during accommodation.^{30, 34} This may be due to differences in age, refractive error, and accommodative amplitude as well as possible measurement error using low-resolution image modalities. Because there are few reports related to posterior lens surface in accommodation, further studies using this rapid, non-invasive SD-OCT with a wide range of the ages and refractive errors are needed to resolve these issues.

There were some limitations in the present study. First, the details inside the lens may be lost after image processing. The hardware and software of the SD-OCT instrument need to be improved to present the internal structure of the lens. Second, the OCT system had only one focal plane, which was not sufficient to match the long scan depth. A dual-focus OCT system may improve the signal-to-noise ratio. Third, the dimensional changes other than the horizontal meridian during accommodation remained untested. In the future, complementary a metal-oxide semiconductor (CMOS) camera may be used to boost the scan speed.³⁵ Thus, three-dimensional changes of the anterior segment during accommodation can be obtained.

In summary, the custom-built SD-OCT with ultra-long scan depth holds promise for imaging the ocular anterior segment accurately. This instrument demonstrated good repeatability of the dimensional measurements of the anterior segment in both accommodative and non-accommodative conditions.

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FIGURE 1. The illustration of the “X-Y Cross aiming mode”

The “X-Y cross aiming mode” was built in the OCT driving software. When the operator began aligning the image, this mode was launched as a guide, and the OCT probe began to scan the eye at both horizontal and vertical meridians. The operator was able to monitor the images of both meridians on the software interface. The image should be acquired when the specular reflection of the corneal apex could be seen at both meridians. Thus, the “X-Y cross aiming mode” ensured that the corneal apex was precisely centered during image acquirement.

FIGURE 2. Diagram of the fixation target system

A liquid-crystal display monitor was attached to the probe, which was 20 cm in front of the test eye. A white "E" fixation target with a black background was displayed on the monitor. The position of the monitor was adjustable to enable guiding of the subject's fixation. Meanwhile, a lens holder was mounted 8 cm in front of the test the eye. Trial lenses were placed in the holder to compensate for the subject's Rx and to induce non-accommodative and maximal accommodative states of each subject.

FIGURE 3. SD-OCT images of the ocular anterior segment in non-accommodative and accommodative states

In these images of a subject's left eye, both mirror artifacts were present in the raw OCT images of the anterior segment during non-accommodative (A) and accommodative states (D). The raw images were processed using custom software (B, non-accommodative state; E, accommodative state). Finally, they were optically corrected to yield the true morphometric dimensions of the anterior segment (C, non-accommodative state; F, accommodative state). Bars = 1 mm.

FIGURE 4. Bland-Altman plots of the difference between two repeated measurements Mean differences of variables between two repeated measurements during non-accommodative (A-E) and accommodative (F-J) states. The mean differences of values between two measurements were near zero. The dashed lines indicate the limits of agreement. ACD, anterior chamber depth; PD, pupil diameter; ASC, radius of lens anterior surface curvature; PSC, radius of lens posterior surface curvature; LT, lens thickness.

TABLE 1

Anterior Segment Dimensions before Image Correction during Non-accommodative and Accommodative States

Variables	Non-accommodative State	Accommodative State
ACD 1 [†]	4016 ± 451	3913 ± 418
ACD 2 [‡]	3986 ± 447	3921 ± 449
Diff	30 ± 97	-8 ± 69
PD 1 [†]	5960 ± 617	5018 ± 738
PD 2 [‡]	5824 ± 994	5006 ± 792
Diff	136 ± 977	11 ± 369
LT 1 [†]	5024 ± 293	5110 ± 263
LT 2 [‡]	5060 ± 245	5146 ± 279
Diff	-36 ± 170	-36 ± 77
ASC 1 [†]	19433 ± 4837	14570 ± 3302
ASC 2 [‡]	18684 ± 4203	15302 ± 3507
Diff	399 ± 4336	-731 ± 1688
PSC 1 [†]	5569 ± 310	5347 ± 587
PSC 2 [‡]	5515 ± 436	5504 ± 485
Diff	54 ± 420	-157 ± 833

Measurements in micrometers; n = 20 eyes of 20 subjects; ACD, anterior chamber depth; PD, pupil diameter; LT, lens thickness; ASC, radius of lens anterior surface curvature; PSC, radius of lens posterior surface curvature; Diff, difference between two repeated measurements.

[†]Mean ± standard deviation for the first measurement of each eye.

[‡]Mean ± standard deviation for the second measurement of each eye.

TABLE 2

Anterior Segment Dimensions after Image Correction during Non-accommodative and Accommodative States

Variables	Non-accommodative State	Accommodative State	P value ^{//}
ACD 1 [†]	3011 ± 348	2951 ± 317*	0.000
ACD 2 [‡]	3003 ± 315	2968 ± 322*	0.037
Diff	8 ± 87	-17 ± 47	
P value [§]	0.677	0.124	
PD 1 [†]	4903 ± 807	4221 ± 775*	0.002
PD 2 [‡]	5025 ± 779	4412 ± 846*	0.001
Diff	-121 ± 670	-191 ± 520	
P value [§]	0.427	0.126	
LT 1 [†]	3687 ± 247	3798 ± 265*	0.004
LT 2 [‡]	3719 ± 253	3790 ± 234*	0.012
Diff	-32 ± 108	9 ± 55	
P value [§]	0.200	0.484	
ASC 1 [†]	11791 ± 1919	10028 ± 2114*	0.000
ASC 2 [‡]	11653 ± 2258	10263 ± 2120*	0.012
Diff	318 ± 2071	-235 ± 2310	
P value [§]	0.500	0.654	
PSC 1 [†]	5761 ± 887	5511 ± 612	0.255
PSC 2 [‡]	5716 ± 766	5444 ± 845	0.178
Diff	45 ± 1129	67 ± 853	
P value [§]	0.861	0.728	

Measurements in micrometers; n = 20 eyes of 20 subjects; ACD, anterior chamber depth; PD, pupil diameter; LT, lens thickness; ASC, radius of lens anterior surface curvature; PSC, radius of lens posterior surface curvature; Diff, difference between two repeated measurements.

[†]Mean ± standard deviation for the first measurement of each eye;

[‡]Mean ± standard deviation for the second measurement of each eye;

[§]The P values were for comparison between two repeated measurements.

^{//}The P values were for comparison between non-accommodative and accommodative states.