Full-range imaging of eye accommodation by high-speed long-depth range optical frequency domain imaging

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Abstract: We describe a high-speed long-depth range optical frequency domain imaging (OFDI) system employing a long-coherence length tunable source and demonstrate dynamic full-range imaging of the anterior segment of the eye including from the cornea surface to the posterior capsule of the crystalline lens with a depth range of 12 mm without removing complex conjugate image ambiguity. The tunable source spanned from 1260 to 1360 nm with an average output power of 15.8 mW. The fast A-scan rate of 20,000 per second provided dynamic OFDI and dependence of the whole anterior segment change on time following abrupt relaxation from the accommodated to the relaxed status, which was measured for a healthy eye and that with an intraocular lens.

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1. Introduction

Optical coherence tomography (OCT) is a rapidly developing biomedical imaging modality, which provides high-resolution cross-sectional images of biological tissues in a noninvasive, noncontact way [1,2]. The structural information with this technique is derived from light backscattered at the interfaces between regions with different optical properties within the object.

OCT emerged from low-coherence interferometry [3]. Now, two detection schemes are used in OCT instrumentation. The conventional method is time-domain OCT (TD-OCT), where a profile of the in-depth distribution of scatterers (A-scan) is extracted by varying the length of the reference arm [1]. Significant advances have recently been achieved in Fourier domain OCT (FD-OCT), which is based on spectral analysis of the interferometric signal recorded as a function of the wavelength [3–5]. Significantly better performance can be achieved by FD-OCT in terms of sensitivity and speed than with TD-OCT [6–8]. In FD-OCT, an A-scan profile is calculated by Fourier transformation of the recorded interferometric signal. Two methods are used for FD-OCT to record this. In spectral domain OCT (SD-OCT), it is recorded with a spectrometer with a line-scan camera [9,10]. In optical frequency domain imaging (OFDI) it is recorded with a single detector with a rapidly tunable laser used as a light source (swept source, therefore OFDI is also called SS-OCT) [11,12].

Ophthalmic imaging of the retina and anterior segment by OCT has attracted a great deal of attention since its early development. Anterior segment OCT (AS-OCT) provides the advantage of producing non-contact images of the anterior segment under static and dynamic conditions [13–32]. AS-OCT was first reported by Izatt *et al.* using a TD-OCT system with a superluminescent diode light source at 800 nm [13]. Radhakrishnan *et al.* demonstrated deeper penetration into the anterior tissue around angle using a longer wavelength range near 1300 nm [14]. The usefulness of AS-OCT for both static and dynamic measurements was demonstrated using TD-OCT by a few researchers [15–18].

The first publication of anterior segment imaging with SD-OCT was reported by Kaluzny *et al.* [19]. Two years later they presented the first ultrahigh resolution images of the human cornea in vivo measured by an SD-OCT system with a supercontinuum light source [20]. Clinical imaging of the anterior segment with high-resolution SD-OCT has proven the capabilities of applying this technique to diagnosing corneal diseases as well as monitoring postoperative healing processes [21–25]. Recent work using SD-OCT has demonstrated dynamic imaging of the entire anterior segment of the eye from the cornea to the posterior part of the crystalline lens [26,27]. Anterior segment OCT imaging using the OFDI method has also been demonstrated [28–34].

Accommodation is the process where the eye maintains sharp focus on an object while it changes its distance. Research on understanding accommodation and restoring the accommodative power of the eye with presbyopia and surgery have attracted a great deal of attention in the ophthalmic research community [35–40]. Accommodation occurs through changes in the shape of the crystalline lens and its thickness, and in distances between major refractive surfaces. Observing changes in these dimensions with accommodation in various subjects of different ages, before and after surgery, or other factors is useful for making diagnoses. AS-OCT can effectively be used to image these changes both under static and dynamic conditions even immediately after surgery because of its non-contact nature. Baikoff *et al.* [15,16] and Richade *et al.* [17] explored modifications to the anterior chamber and lens thickness with aging and accommodation using TD-OCT. However, more useful information on accommodation can be obtained by simultaneously imaging the whole anterior segment (cornea, iris, anterior chamber, and crystalline lens), which cannot be accomplished with commercial TD-OCT systems because of limitations in the imaging depth as well as imaging speed.

Two significant developments with the SD-OCT method, i.e., successful dynamic imaging of the whole anterior segment while the eye accommodated were recently demonstrated [26,27]. To overcome the limited imaging depth with SD-OCT, Grulkowski *et al.* used a method of eliminating complex ambiguity [26]. Full-range real-time video imaging that is free of complex ambiguity is expected to contribute to clinical accommodation research and diagnoses. However, if only a single OCT channel is used, the technique requires multiple images to remove the complex ambiguity in SD-OCT, which reduces the speed at which data can be acquired. Another limitation is that sufficient lateral resolution cannot be achieved over the entire image with a single objective lens. To mitigate these, Zhou *et al.* developed a dual-channel dual-focus OCT for imaging accommodation [27]. However, the whole lens was not imaged in their system because the added length of 7.7 mm of the two SD-OCT systems was not enough to cover the whole anterior segment. They arranged the system to image the posterior lens region and the region from the cornea to the anterior lens, losing the image of the region in the central crystalline lens.

Large imaging-depth ranges with OFDI of 4 mm at 43.9 kHz axial scan rate and 8 mm at 200 kHz axial scan rate were demonstrated by Kerbage *et al.* [29] for the former and Gora *et al.* [33] for the latter. They could image the human anterior segment from the cornea to the anterior surface of the lens at the 1300 nm wavelengths, but could not include the posterior surface of the crystalline lens in the same B-scan images. High-speed reflective Fabry-Perot tunable lasers (RFPTL) in the 1050 and 1300 nm regions with a coherence length of more than about 13 mm have recently become commercially available [41]. Potsaid *et al.* [34] performed an imaging-depth range of 10 mm using a RFPTL at wavelengths of 1050 nm. They demonstrated the anterior segment imaging at 100 kHz axial scan rate, but could not show imaging of the entire lens because their wavelength was 1050 nm and did not have as high penetration as the 1300 nm wavelengths. The coherence length is sufficiently long to enable the full anterior segment to be imaged with OFDI from the cornea to the posterior surface of the crystalline lens with a single system and with a single beam, without the need to remove complex ambiguity. RFPTL at wavelengths of 1300 nm is shipped with k-clock (data sampling clock) output for an imaging depth of 5 mm. To attain longer imaging depths, we introduced an external Mach-Zehnder interferometer to generate k-clock for a depth range of 12 mm. We demonstrated the dynamic imaging of change for a full anterior segment from the cornea to the posterior surface of the lens associated with abrupt relaxation from the accommodated status both for a healthy eye and that with an intraocular lens (IOL). To this end, we measured the curvature for the anterior surface of the lens as first step, though we need to measure whole curvature of the lens.

2. Experimental system and performance

Figure 1 is a schematic of our OFDI experimental system. The swept source is a commercial reflective Fabry-Perot tunable laser (RFPTL) [41] (Axsun Technologies, model SSOC-1310). The laser was operated at a tuning rate of 20 kHz. The averaged power at laser output measured with an optical power meter (Yokogawa, model AQ2160-02) was 15.8 mW. The averaged spectrum measured with an optical spectrum analyzer (Yokogawa, model AQ6370) is shown in Fig. 2 (left). The center wavelength was $\lambda_0 = 1310$ nm and the sweep width was 99.7 nm. The effective wavelength span we used was 87 nm. The expected axial resolution obtained by Hanning window apodization was 14 μ m. The dependence of laser output power on time is shown in Fig. 2 (right). We only used data acquired when the laser scans in forward direction, and the data acquisition duty was 55%. Because output power of the backward scan direction have significantly worse properties as shown in Fig. 2 (right).

Fig. 1. Experimental set up for optical frequency domain imaging system. PC: polarization controller, DAQ: data acquisition board, D/A: digital to analog converter, CL: collimator, PB: pellicle beamsplitter, OL: objective lens, LED: light emitting diode, GM: galvano mirror.

The swept source outputs a sampling clock at 15-GHz intervals. If we used the clock, the imaging optical depth would be 5 mm, which is not long enough to measure the full anterior segment. To generate a k-clock signal for a longer imaging depth, 1% of the laser output was tapped and directed to a Mach-Zehnder interferometer (k-MZI) with an air gap of 12 mm, which generated a k-clock with a 6.25-GHz frequency interval. The k-MZI consisted of two 50:50 couplers, two optical delays (General Photonics) and a balanced detector (Thorlabs, model 110C). The output of the balanced detector was connected to the channel-2 input of the data acquisition board (DAQ, National Instruments, model PCI-5124). The k-MZI generated a chirped sinusoidal interference signal and re-scaling processing was done as described below.

To generate the OCT interference signal, 98% of the laser output was directed to OCT-MZI (Fig. 1). The optical power incident on the eye was 13 mW, which met the safety requirements of the ANSI standards for a short exposure time [42]. The Mach-Zehnder configuration of the OCT-MZI was similar to that reported by a previous paper [9]. The

output of the balanced detector of the OCT-MZI in the present system was detected with the balanced detector (Thorlabs, model 110C) and its output was sampled by using Ch. 1 of the DAQ. The DAQ card was inserted in a computer (Epson, model Endeavor Pro 3500). The two channels of the DAQ were simultaneously sampled at a sampling rate of 200 MS/s by using a internal clock with 12-bit resolution, synchronously to A-scan trigger output from the swept source. To capture a B-scan image, a galvano mirror (GM, Cambridge technologies, model 6210H) was scanned by a digital to analog converter (D/A converter, National Instruments' model PCI-6733) synchronously to the A-scan trigger.

Light out of the fiber was collimated in the sample illumination optics with an aspheric lens collimator (CL) with a 20-mm focal length to a 4-mm diameter beam and focused onto the sample with an achromatic-doublet 100-mm focal-length objective lens (OL). The calculated confocal length was 4.2 mm and the lateral resolution at the focal plane was 10 μm in air. The focal plane was adjusted at 6 mm from the reference position of zero optical delay (OPD = 0) between the sample and reference arm. The position of OPD = 0 was set a little deeper than the posterior surface of the lens. With the imaging depth range of 12 mm, this set up for the optics provided excellent quality imaging of the whole anterior segment and the posterior surface of the lens was imaged clearly. However, the lateral resolution at the image depth of 12 mm was expected to be 250 μm . The deterioration in the lateral resolution at positions away from the focal plane was a significant disadvantage of the present single-focus configuration. However, the depth resolution is important to enable distances in the depth direction to be measured.

Fig. 2. Left: Normalized time-averaged output spectrum of laser source. Wavelength range of 87 nm was effectively used in experiment. Right: Output power as a function of time (lower plot) and A-scan trigger signal (upper inset). Vertical scale does not show voltage level of A-scan trigger, which is 1.4 V at high and 0 V at low. Rising edge of A-trigger signal was used to trigger A-scan. Output power was used for measurement at 55% duty.

Both k-MZI and OCT-MZI signals were synchronously sampled at 5,500 data points with an acquisition rate of 200 MS/s triggered by the A-scan trigger signal out of the swept source. We selected 2,600 data points for FFT analysis for the real-time display. The number of data points was pre-determined by post processing following the nearest neighbor check algorithm proposed by Huber *et al.* [43]. The post processing for re-scaling after data were acquired was always done to obtain a final OCT image. The Fourier transform of 5,500 k-MZI data was zero padded to 16,384 points in the post processing to increase accuracy. The zero padded data were inverse Fourier transformed. A 2,600 data set, corresponding to the local minimums and maximums of the processed k-MZI signal, was determined by the nearest neighbor check algorithm. Similar processing was also done for the OCT signal and 2,600 corresponding data were determined. The data set, zero padded to 4,096 points data, was Fourier transformed and 2,048 data points for an A-scan were obtained. LabVIEW software (National Instruments) was used for the numerical processing and also to control the acquisition of data.

Figure 3 (left) shows the point spread function (PSF) measured at various depths. The PSF was measured with a reflectance mirror placed at a sample position with -55 dB optical attenuation in the sample arm including losses in the set up. The sensitivity values were calculated as 20 times the logarithm of the ratio between the peak maximum value and the noise floor measured by cutting the sample beam. A maximum sensitivity value of 112 dB was observed at a depth of 0.1 mm. This value was 14 dB worse than the calculated shot noise limit of about 126 dB for a given source parameter using the formula in Ref [9]. The dotted line plots a value 6 dB less than the maximum sensitivity. The effective coherence length of the system was estimated to be about 10 mm where the PSF peak took this value. Figure 3 (Right) plots the axial resolution determined by FWHM of PSFs as a function of depth. The resolution is about $16\text{ }\mu\text{m}$ over the entire depth range and worse than the calculated value by $2\text{ }\mu\text{m}$.

Fig. 3. Left: Point spread functions at different depths, measured with -55 dB optical attenuation in sample arm including losses. Right: Axial resolution plotted as a function of depth.

3. Results and discussion

The dynamic process of the eye to relaxation from accommodation was imaged. As seen in Fig. 1, a pellicle beamsplitter (PB) with 5% reflectance was placed between the OL and subject's eye. The subject's eye was fixated at the light-emitting diode (LED) target via the PB. Figure 4 shows a sequence of cross-sectional images acquired after subjects' eyes abruptly relaxed from accommodation to the target at a diopter of 10 D. After relaxation, subjects effectively viewed the target at infinity. The frame size was 2048 (axial) $\times$ 390 (lateral) pixels, i.e., 12 mm (axial) $\times$ 16 mm (lateral). We recorded 114 successive frames (B-scans) for 2.3 s durations at equal time intervals. The scale bars in the figures indicate a distance of 1 mm.

Figure 4 (left) has a movie of the normal right eye of A who was a volunteer subject (32-year old, male). Figure 4 (right) has a movie of the left eye of B who was another volunteer (37-year old, male) with IOL. In both movies, increase in the anterior depth, decrease in the lens thickness, and an increase in the pupil diameter as the eyes relax can clearly be observed. A decrease in the anterior and posterior surface of the lens can also be observed. The subject blinked about 1.7 s after relaxation as seen in Fig. 4 (right).

Fig. 4. Movies showing OCT imaging of dynamical change in whole anterior segment of eye after abrupt relaxation from accommodation to target at 10 D to effectively see infinity. Structural elements including cornea, iris and crystalline lens are visible. Image size is 2048 (axial) $\times$ 390 (lateral) pixels, i.e., 12 mm (axial) $\times$ 16 mm (lateral). 114 frames were recorded during 2.3 s. Left: (Media 1) Normal eye (subject A). Right: (Media 2) eye with IOL (subject B). Subject blinked about 1.7 s after abrupt relaxation.

Image warping due to refraction at the tissue boundaries and the difference between the physical and optical length must be corrected to calculate the dimensions of the anterior segment. Only the latter correction is required to determine the dimensions between major reflective surfaces. The light ray that passes through the apex of the cornea was chosen, which intersects the reflective surfaces practically at right angles, and the distances between reflective points are corrected by the refractive index between the points. The dependence of axial dimensions on time determined this way are shown in Fig. 5 for subject A and Fig. 6 for subject B, at selected times of the movies shown in Fig. 4. We used the refractive index values of 1.3771 for the cornea, 1.3374 for the aqueous humor, and 1.42 for the crystalline lens [44]. And we used the refractive index value of 1.44 for IOL as the collamer lens. These are not rigorous values in the 1310-nm wavelength range. Therefore, the calculations of dimensions in this report should be regarded as being preliminary. Only approximate values and relative changes can therefore be discussed.

The calculated dependence of the anterior chamber depth and lens thickness of subject A (left movie in Fig. 4) on time are depicted in Fig. 5(a) for the former and Fig. 5(b) for the latter. The anterior chamber depth was calculated as the distance between the posterior surface of the cornea and the anterior surface of the lens. We measured the thickness data five times on one axial scan near the central reflection. With relaxation from accommodation, the anterior chamber depth increased and the lens thickness decreased. The addition of both lengths, i.e. the length between the posterior surface of the cornea and the posterior surface of the lens took a constant value of about 7.1 mm within the experimental accuracy. Because the calculated corneal thickness was constant, the axial distance between the corneal surface and the posterior surface of the lens was kept constant during relaxation from accommodation.

Fig. 5. Dependence of (a) anterior chamber depth and (b) lens thickness of subject A on time after abrupt relaxation from accommodation at fixation object at 10D to effectively see infinity.

Fig. 6. Dependence of selected dimensions of eye with IOL after abrupt relaxation from accommodation on time. (a) Anterior chamber depth. (b) Lens thickness. (c) Distance from posterior cornea surface to anterior IOL surface. (d) Distance from posterior IOL surface to anterior crystalline lens surface. Subject blinked at about 1.7 s, which is indicated by shaded vertical bar.

The calculated dependence of the anterior chamber depth, lens thickness, the distance between the posterior surface of the cornea and the anterior surface of IOL (C-IOL distance), and the distance between the posterior surface of IOL and the anterior surface of the crystalline lens (IOL-CL) on time for subject B are plotted in turn in Figs. 6(a), 6(b), 6(c), and 6(d). With relaxation from accommodation, the anterior chamber depth increased and the lens thickness decreased. Also, the addition of anterior chamber depth and lens thickness took a constant value of about 6.6 mm for the subject with IOL within the experimental accuracy. Subject B in the measurement session had a shorter relaxation time than subject A. We did not carry out repeated measurements to check dependence from session to session. However, we

can claim there is the possibility of determining accommodation-relaxation speed from the present preliminary measurements.

The IOL moved toward the crystalline lens as the subject's eye relaxed from accommodation as shown in Figs. 6(c) and 6(d). Because the refractive power of the eye depends on the position of IOL, the capability of being able to measure the dynamic IOL position may be useful in IOL design.

Fig. 7. Distortion corrected OCT image of subject A. Image size is 2048 (axial) $\times$ 1500 (lateral) pixels, i.e., 12 mm (axial) $\times$ 16 mm (lateral). Acquisition time was 75 ms.

Fig. 8. Distortion corrected OCT image of subject B. Image size was 2048 (axial) $\times$ 500 (lateral) pixels, i.e., 12 mm (axial) $\times$ 16 mm (lateral). Acquisition time was 25 ms.

Image warping due to refractions at tissue boundaries must be corrected to determine the lateral dimensions. We applied Snell's law at each boundary for correction [45], which is similar to the method proposed by Westphal *et al.* [46]. The distortion in the OCT images is mainly caused by the curved boundary between the cornea and air. However, refraction at the boundary between the cornea and aqueous humor causes warping that is non-negligible to determine the anterior radius of the curvature of the lens and the pupil size. To determine the radius of the curvature of the posterior surface of the lens, not only refraction at the anterior

surface boundary but also curving light rays inside the crystalline lens due to the inhomogeneous refractive index must be corrected. We did not try to correct these.

Figure 7 has an example of a warp-corrected OCT image for subject A and Fig. 8 has one for subject B. The refraction was only corrected at both boundaries of the cornea. The original image size for Fig. 7 was 2048 (axial) $\times$ 1500 (lateral) pixels, i.e., 12 mm (axial) $\times$ 16 mm (lateral). The acquisition time was 75 ms. The original image size for Fig. 8 was 2048 (axial) $\times$ 500 (lateral) pixels, i.e., 12 mm (axial) $\times$ 16 mm (lateral). The acquisition time was 25 ms. The scale bars in the figures indicate a distance of 1 mm.

For rough estimation of lens deformation, we chose images at three time periods of 0.02, 1.12, and 2.22 s, from the movies in Fig. 4 and corrected warp at both surfaces of the cornea. First of all, to determine the radius of the curvature of the anterior lens, we selected four points of *a*, *b*, *c*, and *d* on the anterior lens surface manually as shown in Fig. 7. Next, the intersection of each perpendicular bisector of segment *ab* and segment *cd* is automatically calculated as center of a circle O. Finally, the mean value of segment *Oa*, *Ob*, *Oc*, and *Od* is calculated, and it is assumed to be the radius of the curvature. We did not correct for the distortion due to the IOL interface for subject B when calculating the radius of the curvature of the anterior lens. The calculated pupil diameters and the radius of the curvature of the anterior lens surface are listed in Table 1. Although we only used three time periods, we could calculate the dependence of pupil size and the radius of the curvature of the anterior lens surface on time. With relaxation from accommodation, the pupil diameter and the radius of the curvature of the anterior lens surface increased. These preliminary calculations indicated the usefulness of the present method for investigating the dependence of the lateral dimensions of the eye on time during changes in accommodation.

Table 1. Dependence of selected dimensions of eyes on time

	Time (s)		
	0.02	1.12	2.22
Subject A			
Pupil diameter (mm)	3.65	3.88	3.99
Radius of curvature of anterior lens surface (mm)	7.69	8.69	9.33
Subject B			
Pupil diameter (mm)	3.47	3.91	4.03
Radius of curvature of anterior lens surface (mm)	7.31	9.72	10.29

4. Conclusions

We developed a single-channel single-focus OCT system for real-time imaging of the accommodation of the eye. This experimental system provided simultaneous imaging of the whole anterior segment from the surface of the cornea to the posterior surface of the lens as a function of time while the eye changed accommodation. Thus, changes in distances between major reflective surfaces, the lens thickness, and radii of the curvature of the anterior surface of the lens with accommodation could be studied non-invasively using high resolution OCT. The curvature of the posterior surface of the lens, that is necessary for the correction of refraction against the anterior surface of the lens, remains for future work. The preliminary results presented in this paper also demonstrated the possibility of applying OCT to assess IOL under dynamical accommodation.

The main disadvantage of this work is that lateral resolution depends on the image depth and the best resolution can only be achieved within a short distance near the focal plane.

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