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CHAPTER FOUR

HEARTBEAT INDUCED AXIAL MOTION ARTIFACTS IN OPTICAL COHERENCE TOMOGRAPHY MEASUREMENTS OF THE RETINA

Abstract

We investigated the cause of axial eye motion artifacts that occur in optical coherence tomography (OCT) imaging of the retina. Understanding the cause of these motions can lead to improved OCT image quality and therefore better diagnosis. Twenty-seven measurements were done on 5 subjects. We collected spectral-domain OCT images at the macula over periods up to 30 seconds. We calculated the axial shift of every average A-scan with respect to the previous average A-scan by calculating the cross-correlation. The frequency spectrum of the calculated shifts versus time was determined. The heart rate was determined from blood pressure measurements at the finger using an optical blood pressure detector. The fundamental frequency and higher order harmonics of the axial OCT shift were compared with the frequency spectrum of blood pressure data. In addition, simultaneous registration of the movement of the cornea and the retina was done using a dual reference arm OCT set-up and movements of the head were also analyzed. We found a correlation of 0.90 between the fundamental frequency in the axial OCT shift and the heart rate. Cornea and retina move simultaneously in the axial direction. The entire head moves with the same amplitude as the retina. Axial motion artifacts during OCT volume scanning of the retina are caused by movements of the whole head induced by the heartbeat.
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4.1 INTRODUCTION

Motion artifacts in medical imaging have been a topic of great interest for many years. Motion artifacts during image acquisition of a patient can be caused by muscular, peristaltic, cardiovascular and/or respiratory activity. Degradation of image quality resulting from motion can lead to ambiguous clinical interpretation and even erroneous diagnoses. Investigating the causes of these involuntary motions can lead to a better understanding of the underlying physiology and improve clinical interpretation. Moreover, information of the origin of the motions can be used for image correction, during, or after imaging. Although motion artifacts are mostly considered as disturbing, they can also contain valuable functional information on the patients' health state.

In ophthalmology, OCT is mainly used for imaging the central retina, where the retina-vitreous interface, sub- and intra-macular edema and the retinal thickness can be monitored. Around the optic nerve the thickness of the nerve fiber layer (NFL) is especially important for diagnosis and follow-up of glaucoma patients. In addition to morphological imaging, OCT also can provide information about (retinal) blood flow using the Doppler shift of the backscattered light. Moving red blood cells, cause a Doppler frequency shift of the backscattered light from which the speed of the moving particle can be derived.

For OCT imaging of the retina, motion artifacts can be easily removed by using image alignment in image post-processing. For Doppler OCT, bulk motions by the sample need to be corrected to accurately determine the absolute blood flow velocity. With the higher imaging speeds (of more than 100,000 A-lines per second) that are reached in Fourier domain OCT, some of these motion artifacts have been ameliorated. However even in these systems movements by a patient can still cause significant image quality degradation and can be clearly visible in 3D OCT volume scans of the whole retina.

When OCT is used to visualize the retina, movements towards and away from the laser beam (axial movements) are often visible during acquisition of subsequent cross-sectional images, B-scans, in the so-called slow scanning direction in a 3D or volume scan. A typical 3D scan of the macula that is made in our clinic is shown in Figure 4-1. The slow scanning direction is indicated with x. The axial motion of the retina is clearly visible as an oscillation of the retina-vitreous interface.
In this study, we first investigate the relation between axial motions visible in OCT scans of the retina and the heart rate of the subject by simultaneous OCT measurements and non invasive optical blood pressure measurements on the finger from which the heart rate is derived. Secondly, simultaneous registration of the axial movement of the cornea and the retina is done using a dual reference arm OCT set-up. Thirdly, we investigate axial head movements with OCT scanning of the teeth. In addition, the axial position of the retina is recorded when a subject is lying down to decrease the influence of head movements.

4.2 MATERIALS AND METHODS

4.2.1 OCT IMAGING SETUP

We used a spectral domain optical coherence tomography (SD-OCT, OCP840SR Thorlabs GmbH) set-up to image the human retina. The sample arm of the SD-OCT set-up was adjusted to an ophthalmic configuration, i.e., the entrance beam in the sample arm was first collimated. To create a telescopic entrance beam two objective lenses (L1 and L2 in Figure 4-2) were placed at a distance of two focal lengths of each other. With the scan mirror in the focal point of L1, the pivot point of the collimated beam was situated in the pupil plane, resulting in a large field of view of the retina (no mydriatic was needed to dilate the pupil). The SD-OCT set-up contained a super luminescent diode with a center wavelength of 848 nm and an optical bandwidth of 30 nm. The optical bandwidth limited axial resolution in air was 10.5 μm, the measured axial resolution in air was 11.5 μm. The scan rate of the
line scan camera system was 5000 lines per second. The sensitivity, defined as the ratio between the signal amplitude and the standard deviation of the noise, was 104.9 dB at 200 μm from the zero path length difference location measured on a mirror placed in a model eye (15) and using an OD filter. The measured 3 dB sensitivity roll off was at 1.2 mm from the zero delay point. The maximal imaging depth was 3.5 mm. The output power measured at the position of the cornea was less than 700 μW. We positioned the OCT setup on an optical table, with the chin rest mounted at the end of the sample arm onto the same optical table. The scanner is not directly attached to the chin rest and the setup is not able to move.

To investigate the simultaneous axial movement of the retina and the cornea, a dual reference arm was implemented in the OCT setup (16) (see Figure 4-2). The light in the reference arm was split by a 50-50% beam splitter cube into a reference arm set to a distance for corneal imaging and a reference arm set to a distance for retinal imaging. The difference in optical path length between both reference arms was matched to the axial length of the examined eye. Light in the sample arm was partly focused by a cylindrical lens (CL in Figure 4-2-II, f=2.3 mm) in order to create two focal points (astigmatic focusing). One plane of the sample arm light beam was focused by the cylindrical lens onto the cornea. The collimated light in the perpendicular plane was focused by the human eye onto the retina. Light of both focal points was combined with light of both reference arms and projected on the spectrometer resulting in a combined OCT image of the cornea and the retina. The scan mirror (MS1) was kept stationary to image at the same position.

Figure 4-2: Optical coherence tomography setup with three (I,II,III) sample arm configurations that are used for experiments on the retina, dual reference arm measurements and measurements at the teeth, respectively. $\lambda_c =$ central wavelength of light source; 50:50BS = beam splitter; MR = mirror reference arm; MS = scanning mirror sample arm; L = spherical lens; CL = cylindrical lens.
For measurement on the teeth, the cylindrical lens in the sample arm that was used for the simultaneous registration of the cornea and the retina was replaced with a spherical lens (L3 in Figure 4-2-III, f=50 mm). Also the scan mirror (MS1) was kept stationary to measure on the same position at the teeth.

4.2.2 HEARTBEAT MEASUREMENT

To determine the heart rate, the blood pressure was measured simultaneously and continuously during OCT imaging using a Nexfin blood pressure monitor (Bmeye B.V.). This device used a volume clamp method with a pressurized cuff around the finger of the subject to obtain continuous non-invasive blood pressure. The blood pressure waveform (sample frequency 200 Hz) and derived parameters e.g. heart rate were stored to file after the measurement. At the start and at the end of the OCT scanning, an electric trigger signal was send to the Nexfin, and the trigger signal was stored in the blood pressure data set. In post-processing the data of these triggers were used to synchronize the blood pressure measurement with the OCT measurement.

4.2.3 DATA ACQUISITION AND ANALYSIS

Consecutive cross-sectional OCT B-scans of the macula with a lateral scan length of 2.0 mm were collected in time. The time of acquisition of each B-scan was recorded. Each B-scan consisted of 40 axial depth scans (A-scans), which were summed to calculate an averaged A-scan. In this way structural differences between consecutive images were minimized, signal-to-noise ratio and sample rate were increased. The axial OCT shifts were determined by a cross correlation between the \( i \)-th and \( (i+1) \)-th averaged A-scan (17). The position of the \( (i+1) \)-th averaged A-scan was aligned with the difference in position relative to the 1st averaged A-scan. The calculated total shifts, relative to the 1st averaged A-scan, were displayed versus time. A frequency spectrum of the averaged A-scan shift in time, with a minimal frequency resolution of 0.05 Hz, was determined to analyze its frequency content.

4.2.4 MEASUREMENTS

To investigate the influence of the heartbeat on the axial motions a total of 27 measurements were done on 5 healthy subjects. The mean age of the subjects was 31 ± 8 years. All subjects were healthy without any known ocular pathology and with clear ocular media. The subjects were asked to fixate and relax while they placed their head on a chin rest. Furthermore, they were asked not to blink their eyes, and to avoid large head movements. In the frequency spectrum of the axial OCT shift, peaks that were clearly visible above noise level were located manually and were analyzed. Peaks with frequencies lower than 0.5 Hz were excluded from
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analysis. The uncertainty in the central frequency of the peak is determined by the resolution of the frequency spectrum. From the blood pressure measurement the corresponding part was selected using the start and stop triggers as a reference. A frequency spectrum was made of the blood pressure signal, and the fundamental frequency, i.e. the heart rate, was selected and used in further analysis.

Secondly, the movement of the retina and the cornea were measured simultaneously where the signal from the cornea was displayed in the upper part and the signal from the retina was displayed in the lower part of the B-scan image. Seventeen measurements were done on 2 subjects. During these measurements the scan mirror was not rotating. The average A-scan was segmented in a retinal image and a corneal image. The position analysis was performed on both images to determine the shift of the retina and the cornea.

Thirdly, to register axial head motions 10 measurements were performed on the teeth of 1 subject. The same cross correlation method was used to calculate the axial OCT shift and to determine the frequency of the motion.

Finally, the effect of the heart rate on head motions was further investigated on six subjects, who were asked to lie down, resting with the backside of the head on the floor during OCT imaging of the retina. In this way, head movements toward and away from the illuminating beam were restricted since gravity kept the head position constant. Five measurements per subject were done in this position and the same method was used in the analysis of the OCT images.

All research adhered to the tenets of the Declaration of Helsinki. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

4.3 RESULTS

Figure 4-3(a) shows a typical measurement of the axial shift of the retina versus time in one subject. A spiking axial motion with a period of ~ 1 s and average peak to peak amplitude of 81 µm ± 3.5 µm is observed. This spiking motion is observed in all subjects albeit with some variability in amplitude and period. The slowly varying shift with a period of ~5 s in Figure 4-3(a) is attributed to breathing of the subject. The simultaneously measured blood pressure is displayed in Figure 4-3(b). This graph shows a typical blood pressure waveform. The rise from diastolic pressure to the systolic blood pressure level (upstroke) is relatively sharp. During the decline to diastolic pressure often a local maximum can be seen which is due to a reflection of the systolic pulse in the arterial tree (mainly in the abdomen of the subject). It can be easily observed that the peaks in the shift of the retina occur simultaneously with the peaks in the blood pressure.
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Figure 4-3: (A): The axial OCT shift of the retina, relative to t=0, measured with optical coherence tomography has an average peak-to-peak amplitude of $81\mu m \pm 3.5\mu m$.

(B): Measured blood pressure at the index finger. The peak of the systole corresponds to the peak shift of the retina (indicated by dashed vertical lines).

The frequency content of the OCT shift and blood pressure signals is shown in Figure 4-4(a) and 5-4(b). In Figure 4-4(a) the fundamental frequency of the OCT shift at 1 Hz and the higher harmonics of this fundamental frequency are clearly visible. The fundamental frequency of the motion artifact is $0.95 \pm 0.02$ Hz. The peak at 0.2 Hz in Figure 4-4(a) is the slowly varying shift that is caused by breathing. The fundamental frequency of the blood pressure is $0.95\pm0.05$ Hz, which is the heart rate. The fundamental and higher harmonic frequencies of the OCT shift and the fundamental frequency of the heart rate are used in subsequent analysis of the frequency spectra.

Figure 4-4: (A)
Frequency spectrum of the axial shift of OCT images of the retina.

(B): Frequency spectrum of the blood pressure pulse. Note that the higher order harmonics are visible in both the axial position of the retina and in the blood pressure.

In Figure 4-5 all identified frequency components of the axial shift in the OCT image for 26 measurements (displayed in the figure with □) are plotted against the heart rate.
The line trough the data is used as guide to the eye, with each line having a slope that is a multiple of the slope of the heart rate. The 2\textsuperscript{nd} order harmonic is visible in 21 measurements (displayed in the figure with ●), the 3\textsuperscript{rd} order harmonic is visible in 20 measurements (displayed in the figure with ○) and the 4\textsuperscript{th} order harmonic of the axial shift of the retina (displayed in the figure with Δ) is visible in 10 measurements. We find a clear correlation between the heart rate and the fundamental frequency of the axial motion (R=0.90) and also high correlations between the harmonics of the OCT shift and the heart rate (R=0.92, R=0.95, R=0.89 for the 2\textsuperscript{nd} order, 3\textsuperscript{rd} order and 4\textsuperscript{th} order harmonic, respectively).

Next, we investigate in a series of experiments what movement is causing the axial retinal motion.

Firstly, we measure the axial shift of the cornea and retina simultaneously; see Figure 4-6(a). This measurement indicates that the cornea moves simultaneously with the retina because the phase of the signals is similar. However, the amplitude of the motion of the retina is larger than the amplitude of the motion of the cornea, especially in large amplitude excursions.

Secondly, the axial OCT shift measured on the teeth of one subject is displayed versus time in Figure 4-6(b). The fundamental frequency in the OCT motion is at 0.8
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Hz corresponding to the fundamental frequency of the heart rate of the subject. The amplitude has a similar magnitude as the amplitude measured on the retina: 89.0±7.1 µm.

Figure 4-6(A): Shift in axial direction of the retina (black line) and cornea (grey line) measured with a double reference arm OCT.

(B): Typical measurement of the shift in the axial direction measured on the teeth of one volunteer. The heartbeat-induced motion artifact is clearly visible; its amplitude is similar to that in the retina.

(C): Typical measurement of the axial Shift of the retina of one volunteer while the subject is lying down. Head movements are minimized and the heart rate is not visible.

Thirdly, subjects were lying down while OCT imaging is performed on the retina. The result of one measurement is displayed in Figure 4-6(c). The motions have a mean peak-peak value of 21.3±8.0 µm. It is clear that the amplitude of the motion in the lying down position is much smaller than the amplitude shown in Figure 4-6(b). This was obtained for all subjects.

4.4 Discussion

In this study we have shown that the fundamental frequency in the axial motion of the retina and the heart rate are highly correlated. Figure 4-3 and the frequency analysis in Figure 4-4 show a typical measurement of the OCT shift and the blood pressure. The similar fundamental frequencies in the OCT shift and the blood
pressure indicate that the heart rate causes the periodic axial shifts in the OCT images of the retina. The axial shift of the retina is clearly visible when the subject is situated quietly with their head positioned on the chin rest. Indicating that our home built OCT system is stable and sensitive enough to measure axial motions induced by the heartbeat, validation measurements were performed on a static phantom eye model, with no axial motions visible.

In Figure 4-3 a low frequency movement is also visible which we observed to be due to whole body movement during breathing of the subject during acquisition of the OCT scan. Breathing causes a slow and small amplitude movement of the subject’s head, which is resting on the chin rest. The frequency spectrum of Figure 4-4(a) shows that this movement has a frequency of 0.2 Hz, which is similar to typical breathing rates for humans in rest (around 12 times per minute). We therefore neglected the signals in the frequency analysis.

In Figure 4-5 the frequency components in the OCT shift signal are plotted versus the heart rate (the frequency component due to breathing is not shown in Figure 4-5). It is clear that all frequency components of 27 measurements are either the fundamental frequency or higher order harmonic frequencies of the heartbeat. The number of detected higher order harmonics decreases with increasing order, because they were either too weak or the noise was too high. Note that for a very spiky periodic axial motion in time, such as for the measured axial motion of the retina, the frequency spectrum consists of a large number of harmonics. The result of the frequency analysis is in agreement with this sharply peaked axial motion artifact. We conclude that the axial motions in OCT imaging of the retina are caused by the heartbeat.

Axial motion artifacts during OCT measurements are often regarded as eye movements caused by micro-saccades or unstable fixation(18). We investigated the effect of lateral eye motions by rotating the eye several times from left to right over 8 degrees during continuous OCT acquisition. No effect on the axial motion was observed which is in agreement with gaze stability measurement reported in a previous study(19) and it was also calculated(3) that the error of depth position for a rotation of ~1° for a healthy volunteer is smaller than 1.5 μm, which is lower than our resolution.

Figure 4-6(a) shows that the corneal surface moves in phase with the retinal surface implying an entire head movement. However, the amplitude of the retinal movement is somewhat larger (especially at large movements). Note that for a whole head movement the shifts of both the retina and the cornea should be similar as only the path length in air changes for both interfaces. However, the sensitivity measured on the retina is 22.1 dB lower with this configuration due to the use of the cylindrical lens in the sample arm (measured using a phantom eye model(15)
with a mirror as retina). The observed difference between both amplitudes might therefore be due to the accuracy of the cross correlation. The cross correlation can be less accurate since the A-scan of the retina has multiple peaks with similar amplitude and lower signal to noise ratio. The A-scan of the cornea shows a strong single reflection at the air-cornea interface and therefore its autocorrelation is more accurate.

Previous studies (20, 21) show that the axial length changes due to the heartbeat cycle. However, axial length changes during a heartbeat cycle that were measured with low coherence interferometry are in the order of 3.5 µm and are not in agreement with our results. Also, our axial resolution is limited by the optical bandwidth of the light source and we are not able to measure axial length difference smaller than the coherence length. Heartbeat related motions were furthermore confirmed in an animal study (22). They showed that motions in the retina during OCT scanning can be caused by the heart rate. However, the measurements in this study were done on rodents and the blood pressure was not synchronized with OCT scanning. Partially in agreement with our measurements, they found an identical movement of the cornea and retina both in phase but also in amplitude presumably caused by heartbeat, but the motions were not measured simultaneously. Also, they measure choroidal thickness changes during a heartbeat cycle. This can be a very interesting topic for a successive study with a double reference arm OCT setup, because this can be an indicator for the progression of eye diseases that involve changes in perfusion of the retina. However, to do this we have to measure with larger wavelength for a larger penetration depth with OCT.

The effect of whole head movement was further investigated by OCT imaging on the teeth (Figure 4-6(b)). The heartbeat-induced axial motion is clearly visible and the amplitude is similar to what we measure on the retina.

Finally, we reduced the effect of the heart rate on head motions by performing OCT measurements on the retina when the subject was lying down. In this case the head does not easily move towards the illuminating beam during the measurement and heartbeat-induced motions of the head are therefore very much reduced during the measurement (Figure 4-6(c)). This indicates that axial motions are mainly caused by movements of the head and probably not causing a compression of the eye. The measured amplitude of the retina or entire eye motion has a lot smaller amplitude than the amplitude of the whole head movement measured on the teeth. In our view, these small motions in Figure 4-6(c) containing mainly 2.3 to 3.0 Hz motions are unlikely to be caused by the heartbeat and the motions are in disagreement with the amplitude and frequency of the shift in our earlier measurements (Figure 4-6(b)). Our OCT setup provides the opportunity to investigate the origin of the remaining axial motions that are visible in Figure 4-6(c) (e.g. muscular contraction).
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4.5 CONCLUSION

Based on all our measurements we conclude that the retinal axial motions are largely caused by an entire head movement that is caused by the heart rate. Axial motions are not movements of the whole eye within the eye socket, nor movements of the retina relative to the cornea (involving a compression / expansion of the eye). Although we measured different amplitudes between cornea and retina, we hypothesize that the heartbeat causes an arterial blood pressure pulse in the arteria carotis that induces a head movement that is translated to the eye and visible during OCT scanning of the retina. In summary, we have elucidated a major cause of imaging artifacts in OCT of the retina. Our results can help in a better quantification of (Doppler) OCT data and improve medical diagnosis with OCT.

4.6 REFERENCES