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3 **Comparison between Reflection-mode**
4 **Photoplethysmography (PPG) and Arterial Diameter**
5 **Change Detected by Ultrasound at the Region of Radial**
6 **Artery**

7

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12 Running head: Comparison between PPG and arterial diameter change

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23

Abstract

Continuous monitoring of arterial blood pressure (ABP) can provide vital information on the cardiovascular system in clinical practice and research. To achieve this, methods have been developed to determine ABP continuously and non-invasively, including the wrist volume clamp method, which uses reflection-mode photoplethysmography (PPG) to indicate the volume change of the radial artery. However, this kind of indication is reportedly not accurate enough, and an in vivo test for its accuracy is still lacking. As ultrasound can detect the arterial diameter accurately, we have developed a sensor comprised of a PPG sensor and an ultrasound transducer, which can collect reflection-mode PPG and A-mode ultrasound signals simultaneously. Tests on fifteen volunteers were conducted under the similar conditions of using wrist volume clamp method for a comparison between the PPG signal and the radial arterial diameter. It was observed that there were obvious differences between the shapes of these two signals, mainly between their drifting trend parts, with the pulsatile components of the signals matching very well. The mean RMS value of the differences of the trend parts (0.287 ± 0.072) was found to be much larger than that of the pulsatile parts (0.107 ± 0.028). The results indicated that using PPG signal as a reference for ABP measurement at the wrist region might be not accurate enough, and ultrasound has the potential for replacing it in the wrist volume clamp method for more accurate ABP determination.

Keywords: blood pressure, wrist volume clamp method, reflection-mode photoplethysmography, PPG, arterial diameter, ultrasound.

1. Introduction

Arterial blood pressure (ABP) is one of the most important hemodynamic characteristics of the cardiovascular system. It not only changes with the heart pulsation, but also varies naturally throughout the day as part of the circadian rhythm. In addition, ABP also changes in response to stress, drugs or diseases. Thus, the development of an accurate and reliable method for continuous ABP measurement has attracted much research effort. Although both invasive and non-invasive methods have been developed, the latter are more desirable for replacing the invasive method that is currently used in clinical practice [1, 2].

Some methods have been developed for continuous non-invasive ABP measurement, such as the tonometry method [3] and the finger volume clamp method [4]. Tonometry method is based on the coplanar measurement, in which a tonometer is applied to squeeze a superficial artery against a bone until the amplitude of the oscillations on the collected pressure signal reach to its maximum. In this state, with calibration by a sphygmomanometer at the brachial artery, the measured pressure signal can be scaled up to the continuous ABP waveform. However, it has some problems as difficulty in placing the tomometer precisely and stably over the artery and the fact that its results will be affected by the viscoelastic properties of the surrounding tissues. The most criticized one is that it requires calibration and this is not convenient in clinical use [5]. The finger volume clamp method, commercially available as Finometer and Portapres devices (Finapres Medical Systems BV, Arnhem, Netherlands) and the CNAP™ Monitor 500 (CNSystems Medizintechnik AG, Graz, Austria), is perhaps the

1 most widely used method. In this method, the volume of finger arteries is detected by an
2 infrared transmission-mode photoplethysmography (PPG) sensor, and the pressure of an
3 inflatable air bladder is adjusted by a servo controller with a response quick enough to follow
4 the pulsation. The PPG sensor and air bladder are both built in a band wrapped around the
5 finger. The volume of finger arteries is kept constant at a “set point value” by the bladder in
6 spite of the pulsatile changes in ABP. This set point value corresponds to the unloaded state of
7 the arterial walls, which means that the external pressure from the air bladder always equals
8 the intravascular blood pressure. This allows for continuous ABP measurement in finger
9 arteries [4]. However, this method has not yet been fully accepted by physicians and
10 researchers because there is a large difference between the finger and brachial ABP values,
11 and the latter are more valuable in clinical use [6]. Although an experiential transfer function
12 from the finger ABP to the brachial ABP has been used with the results further calibrated
13 using a traditional sphygmomanometer, the accuracy and reliability of this method are still not
14 satisfactory [7-9]. Furthermore, congestion may occur in the finger tissues after they are
15 clamped under the external pressure for several minutes [10].

16

17 Recently, a modified volume clamp method called the wrist volume clamp method (or wrist
18 volume compensation method) was reported, which changed the measurement position from
19 the finger to the wrist [11]. It is assumed that the radial ABP value measured at the wrist
20 region is much closer to the brachial blood pressure. The wrist contains two arteries, the radial
21 artery and ulnar artery, and both of them can provide arterial blood to the hand. In the wrist

1 volume clamp method, a pad-type bladder is used to apply external pressure only on the radial
2 artery. As the blood supply from the ulnar artery is not influenced, the congestion problem
3 resulting from the finger method would not occur in the hand even after a long time
4 measurement [12]. The volume change of the radial artery is indicated by a reflection-mode
5 PPG sensor, instead of the transmission-mode sensor used in the finger version. The results of
6 this method have been compared with those obtained by the simultaneous measurement of
7 invasive radial artery pressure in healthy subjects [13]. The averaged bias and precision of
8 systolic blood pressure (SBP) and diastolic blood pressure (DBP) were -0.5 ± 2.1 mmHg and
9 0.6 ± 1.8 mmHg, respectively, while the largest differences reached $+5.7/-8.3$ mmHg and
10 $+8.8/-4.5$ mmHg in SBP and DBP, respectively.

11
12 PPG is an optical technique that is widely used to study the characteristics of the
13 cardiovascular system, such as oxygen saturation, pulsatile perfusion, and pulse transit time.
14 Despite its simplicity, attempts to quantify the amplitude of PPG signals have been largely
15 unsuccessful, especially for the reflection-mode PPG [14, 15]. This is because the intensity of
16 the received light is associated not only with the arterial volume change but also with the
17 optic properties of the surrounding tissues, the depth and movements of the large artery, the
18 orientation of the red blood cells which changes with the blood flow velocity, the volume
19 change of the veins and capillaries with sympathetic tone and respiration, and the position,
20 optic active area and light wavelength of the optic sensors [14-19]. Furthermore, the PPG
21 signal is also easily affected by ambient light and motion artifacts. Therefore, the accuracy of

1 the wrist volume clamp method depends on whether the reflection-mode PPG signal
2 measured on the wrist can accurately indicate the volume change of radial artery. However,
3 effort to test the reliability of this kind of indication is lacking in the literature. As the
4 diameter of a larger artery, such as the radial artery, can be measured non-invasively and
5 accurately using ultrasound in vivo [20-22], we investigated the relationship between the
6 reflection-mode PPG signal and the radial arterial diameter detected by ultrasound in this
7 study. The ultrasonic echoes from anterior and posterior arterial walls were tracked with both
8 high temporal and spatial resolutions and were used for the calculation of the arterial diameter.
9 Through this study, we hope to further investigate the accuracy of the arterial volume change
10 as indicated by the reflection-mode PPG signal in the wrist volume clamp method and to
11 explore the feasibility of replacing the PPG signal with the arterial diameter as determined by
12 ultrasound, with the aim of improving the accuracy of this method.

13

14 **2. Methods**

15 *2.1. Experimental Set-up*

16 An integrative sensor was fabricated from a 10 MHz single element ultrasonic transducer with
17 a diameter of 3 mm (Shantou Institute of Ultrasonic Instruments, Shantou, China), an infrared
18 light emitting diode (LED) with a 940 nm peak-output-wavelength, and a light-to-frequency
19 converter (LFC) with a light sensing range of 320 nm to 1050 nm and an optic active area of
20 0.92 mm^2 (TSL235R, TAOS Inc., Plano, TX, USA). These components were embedded in a
21 piece of hot-melt adhesive material. As shown in **Fig. 1(a)**, the flat arrangement of the sensor
22 made it easy to be kept steady on the wrist. The distance between the LED and the LFC was

1 approximately 10 mm with the ultrasonic transducer fixed in between. The output signal of
2 the LFC was a square wave with a frequency directly proportional to the intensity of received
3 light. The frequency was measured by a NIDAQ data collection card (National Instruments
4 Co. Ltd., Austin, TX, USA). A Panametrics-ndt 5900PR ultrasonic pulser/receiver (Olympus
5 NDT Inc., Waltham, MA, USA) was used to drive the ultrasonic transducer. The A-mode
6 ultrasonic radio frequency (RF) signal was digitized by a high speed A/D converter card,
7 Cobra CompuScope digitizer (Gage Applied Technologies Inc., Canada) with a sampling rate
8 of 125 MHz. The PPG signal and ultrasound RF signal were collected and saved
9 synchronously by a custom-designed Labview program (National Instruments Co. Ltd.,
10 Austin, TX, USA). The frame rate of the A-mode RF ultrasound signal and the sampling rate
11 of the PPG signal were both 100 Hz.

12

13 2.2. *Experimental Procedure*

14 Referring to the protocol for comparing the accuracy of the blood pressure measurement
15 device to the invasive measurement suggested by the American Academy of Insurance
16 Medicine (AAIM), fifteen healthy young volunteers (25-35 years old, eleven males and four
17 females) were invited to participate in this study. The subjects were instructed to be seated
18 still in front of the experiment table and to put his/her left wrist on a soft pad. As
19 demonstrated in [Fig. 1\(b\)](#), the sensor was placed at the site where the radial artery crosses the
20 most protuberant spot of the distal end of the radius, as specified in the wrist volume clamp
21 method [12]. The three components in the sensor were aligned along the axis of radial artery.

1 To avoid the interferences to the PPG signal, the measurement was conducted far away from
2 the ambient light source, and the sensor was covered by a piece of black adhesive plaster as a
3 light shield. Ultrasound coupling gel was applied between the transducer and skin, and it also
4 helped to keep the sensor more stable on the skin surface. The transducer was adjusted until
5 both of the echoes from the opposite arterial walls reached their maximal amplitudes and
6 remained stable. Similar to the protocol used in the wrist volume clamp method, an
7 appropriate external pressure was exerted on the sensor to make the amplitude of the PPG
8 pulsation reach its approximate maximum. After the sensor was carefully moved to a
9 satisfactory position and the external pressure on it was adjusted to a proper level, data
10 collection was started. Each data collection period took about 30 – 60 seconds, and five
11 collections were performed on each subject. All data were saved for further analysis.

12

13 Another experiment was performed to verify if the pulsatile components of the
14 reflection-mode PPG signal still existed when the external pressure was increased to make the
15 radial artery fully occluded. During the experiment, the sensor was first placed on the
16 measurement position with almost no external pressure. Then the external pressure exerted on
17 the sensor was gradually increased by the operator until no pulsation appeared on the
18 ultrasonic echoes from the arterial walls, which meant the radial artery was fully occluded
19 with no blood running through. Both the signals were collected and analyzed.

20

21 *2.3. Data Analysis*

1 The saved data were processed with Matlab (Mathworks, Natick, MA, USA). **Fig. 2(a)** shows
 2 the RF signals of the echoes reflected from the anterior and posterior arterial walls. An
 3 M-mode ultrasonic image was formed using the ultrasonic RF signals. As shown in **Fig. 2(b)**,
 4 the motion of arterial walls could be seen along the vertical axis, and the ranges of their
 5 displacements could be easily determined. The echoes from the anterior and posterior arterial
 6 walls were manually selected from the first frame of the RF signal and automatically tracked
 7 using a cross-correlation method [23]. Then, the relative displacements of the two opposite
 8 arterial walls were plotted, and the change of the radial arterial diameter was calculated.
 9 Under the applied external pressure, the reflection-mode PPG signal and arterial diameter
 10 change are opposite in phase. The larger the arterial diameter, the smaller the received light
 11 intensity by the LFC would be, and vice versa. Therefore, only the shapes of the two signals
 12 were comparable, rather than their absolute values. For this purpose, the two signals were
 13 separated into pulsatile parts and low-frequency trend parts. Pairs of maximal and minimal
 14 values in each pulsation were detected, and the mean values from each pair were interpolated
 15 by a trend line using shape-preserving piecewise cubic interpolation. The pulsatile and trend
 16 parts were then separated and normalized using the following equation:

$$17 \quad D_{norm}(i) = \frac{D(i) - \text{mean}(D)}{\max(D) - \min(D)}, \quad D(i) \in D, D_{norm}(i) \in D_{norm}, i = 1, \dots, N; \quad (1)$$

18 where D is the array of raw data, D_{norm} is the array of normalized data, and i and N are the
 19 indexes of the data point and the length of the array, respectively. Finally, the results were
 20 biased to the range from -0.5 to 0.5 for a convenient comparison. The root mean square (RMS)
 21 values of the differences between the normalized trend parts and pulsatile parts of the two

signals were calculated for every single subject. The frequency spectra of the two signals were also calculated.

3. Results

Fig. 3 shows the typical frequency spectra of the reflection-mode PPG signal and the signal representing the change of arterial diameter of a male subject. We can observe from the spectra that there were large components with frequency close to zero, which represented the baselines of signals. **Fig. 4(a) and (b)** show the normalized trend, and the pulsatile parts of the two signals, respectively. It was observed from the figures that the two trend signals were obviously different. Additionally, the differences between the pulsatile parts were much smaller compared with those between the trend parts, indicating that the trend part contributed to the main differences in the shapes of the two signals. Further data analysis also supported this finding. Table 1 shows the RMS values of the differences of the normalized trend part and pulsatile part between the two signals calculated for every subject. The data ranges of the normalized signals were -0.5 to 0.5. The value of RMS difference of the trend part, 0.287 ± 0.072 (mean \pm SD), was significantly ($p < 0.001$, paired t-test) larger than that of the pulsatile part, 0.107 ± 0.028 . This result further demonstrated that the differences between the two signals largely came from the trend part.

In the current wrist volume clamp method, the set point value is determined by the trend part of the reflection-mode PPG signal. If the amplitude of the PPG signal is kept constant at the

1 set point, the radial arterial volume is also treated as not changing in the unloaded state. But
2 our study demonstrated that there are often some differences between the two signals, especially in
3 their trend parts. For example, if the trend part of the PPG signal increases, but the arterial
4 volume doesn't change, to keep the PPG signal at the set point will make the measured blood
5 pressure overestimated. That's why using the PPG signal to indicate the arterial volume will
6 influence the accuracy of the wrist volume clamp method. Since the differences between
7 the two signals largely come from the trend parts, theoretically, in the current wrist
8 volume clamp method, the accuracy of the systolic blood pressure, diastolic blood
9 pressure and mean blood pressure values will be more affected than the relative pulse
10 blood pressure values.

11

12 The two signals collected with the external pressure exerted on the sensor showed an obvious
13 difference. For the ultrasound signal, with the external pressure increasing, the pulsation
14 amplitude of arterial diameter first increased and then decreased. When the artery became
15 fully occluded, and the pulsatile motion of both arterial walls failed to be detected. In the PPG
16 signal, a similar pattern of the pulsatile parts could also be noted. However, after the artery
17 was fully occluded, pulsations still appeared in the PPG signal. This indicated that besides the
18 radial arterial diameter change resulting from the heart beat, other factors could also affect the
19 pulsatile part of the reflection-mode PPG signal, such as the blood volume changes in the
20 arterioles, capillaries and venules in the surrounding tissues. As mentioned earlier, this would
21 influence the accuracy of the wrist volume clamp method.

4. Discussion

In this study, a sensor capable of collecting both reflection-mode PPG and ultrasound signals at the region of the radial artery was developed, and the results from the two signals were compared to observe their relationship. The results were used to judge whether ultrasound could be used in the wrist volume clamp method for more accurate continuous ABP determination. The differences in the shapes of the two signals observed in this study showed that using the PPG signal might be not accurate for the measurement of the radial arterial volume and that the ultrasound method could be potentially used to replace the PPG for monitoring ABP more accurately.

The relationship between reflection-mode PPG signals and arterial volume has been studied in vitro by a previous study, which reported that the amplitude of reflection-mode PPG signals could be affected by two processes [24]. One process is the attenuation of back-reflected light, whereby light is reflected by the deeper tissue and “backlights” the superficial artery. Thus, the larger the arterial diameter is, the less light that can reach the sensor, just like the transmission-mode PPG signal. The other process is the light reflection by the arterial wall. In this case, the arterial extension causes more light to reach the sensor and counteracts the attenuation mentioned above. The shape of PPG pulsations depends on the combined effects of these two processes. When the position of the optic sensor is changed, such as increasing the relative “depth” of the sensor versus the artery to some level, inversion of the pulsatile parts in the PPG signal would be observed because the reflection dominates the processes.

1 But in our experiments, with stable external pressure exerted on the sensor, this “inversion”
2 phenomenon of reflection-mode PPG signal did not occur, just like in the wrist volume clamp
3 method.

4 It was reported in a previous study, which was conducted on the isolated aorta of cats using
5 ultrasound for arterial diameter measurement, that positioning of the ultrasonic transducer is
6 very critical [20]. The echoes would disappear when the transducer axis was deviated by more
7 than 1 degree from the radial direction and by more than 10 degrees from the longitudinal axis
8 of the artery. Obvious and stable echoes from the opposite walls of the artery only occurred
9 when the transducer was targeted at the axis of the artery directly and vertically. In our in vivo
10 study, the A-mode ultrasonic method for arterial diameter measurement was also found to be
11 very sensitive to the relative position between the transducer and artery. We adopted a simple
12 method for positioning the sensor at the point where the echoes from both arterial walls
13 reached their maximal amplitudes and remained stable.

14 Some previous studies have revealed that when the PPG sensor is placed on a larger, distinct
15 artery, such as the radial artery, the amplitude of the PPG signal is not only related to the
16 pulsation in the larger artery, but also to the blood volume changes in the arterioles, capillaries
17 and venules in the surrounding tissues [24, 25]. That might explain the phenomenon observed
18 in our experiment that even after the artery was fully occluded, there were still pulsatile
19 components in the PPG signal. The pressure was mainly performed onto the radial artery until
20 no pulsatile motion of the arterial walls was detected. This only meant the radial artery was
21 fully occluded, but not all the other small vessels in the surrounding tissues. The pulsatile

1 blood volume changes in these vessels still influenced the PPG signal. In addition, an earlier
2 study has reported to extract the respiration signal from PPG, because the oxygen level in the
3 blood would affect the magnitude of PPG [26]. Temperature could also reportedly affect the
4 PPG signal and the ABP values [19, 27]. When the temperature of the hand was decreased to
5 a low level, the blood pressure of the radial artery would increase as well as its diameter. At
6 the same time, vasoconstriction of the capillaries would cause a decreased transmission of
7 arterial blood to the veins. Therefore, the whole blood volume (arterial blood and venous
8 blood) would decrease. As a result, regardless of their pulsatile parts, the average level of the
9 intensity of the received light would also increase during this process, as would the arterial
10 diameter. In this case, a different variation in trend between these two signals would result
11 from their normally negative correlation. Therefore, temperature change might also have
12 contributed to the larger difference observed in the trend parts of the two signals in
13 comparison with that of their pulsatile parts.

14 The results of the experiment showed that the shapes of the two signals were obviously
15 different. Separating the signals into trend and pulsation parts revealed that the differences
16 mainly came from the trend part. As addressed above, the blood volume changes of the veins,
17 arterioles, venules and capillaries due to sympathetic tone and temperature might have caused
18 the differences. As ultrasound measurement of the arterial diameter tends to be accurate and
19 reliable, the differences between the PPG and ultrasound signals called into question the
20 accuracy of the PPG signal used in the wrist volume clamp method for ABP measurement.
21 The results from this study have demonstrated the feasibility of using ultrasound for the

1 measurement. Our next step is to replace the PPG sensor in the wrist volume clamp method
2 with an ultrasonic transducer for the aim to ultimately achieve a better continuous
3 non-invasive ABP measurement method.

4 In summary, an integrative sensor for simultaneously measuring reflection-mode PPG and
5 A-mode ultrasound signals was developed, and a preliminary test was conducted to compare
6 the PPG signal and arterial diameter change detected with ultrasound. The results revealed
7 several differences between the two signals, particularly in the drifting trends. Since the artery
8 diameter is a direct measure for the blood volume inside the artery, we thought that using PPG
9 for the wrist volume clamp method might cause some inaccuracy. Meanwhile, we propose
10 that ultrasound has great potential to replace the PPG signal for a more accurate non-invasive
11 ABP measurement using the wrist volume clamp method. Further research effort to develop
12 an ultrasound-based wrist volume clamp method is required to make a more solid conclusion
13 for the findings in this study.

14

15

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5

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11

12

1 Table 1. The root mean square (RMS) values of the differences of the normalized trend parts
 2 and pulsation parts between the PPG signal and the arterial diameter calculated for every
 3 subject.

Subject	RMS	RMS
(gender)	Trend parts	Pulsation parts
Subject1 (M)	0.381	0.085
Subject2 (M)	0.174	0.105
Subject3 (M)	0.246	0.155
Subject4 (F)	0.297	0.153
Subject5 (M)	0.181	0.109
Subject6 (M)	0.278	0.127
Subject7 (M)	0.275	0.113
Subject8 (M)	0.241	0.115
Subject9 (F)	0.306	0.090
Subject10 (F)	0.197	0.062
Subject11 (M)	0.313	0.081
Subject12 (M)	0.405	0.084
Subject13 (M)	0.308	0.143
Subject14 (M)	0.301	0.080
Subject15 (F)	0.394	0.103
Mean \pm SD	0.287 \pm 0.072	0.107 \pm 0.028

Figure Captions

Fig. 1. (a) The sensor fabricated for this study which contains a single element ultrasonic transducer, an infrared light emitting diode (LED), and a light-to-frequency converter (LFC).

(b) The position and direction of the sensor in the experiment.

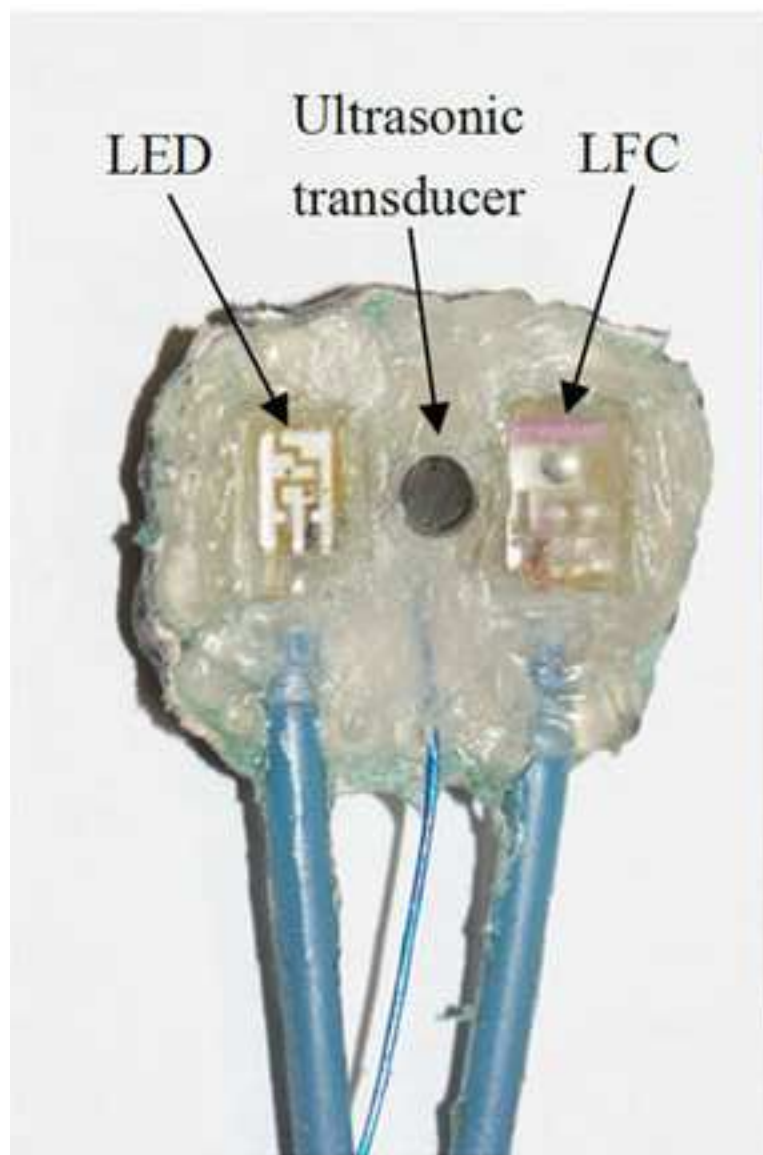
Fig. 2. (a) One typical frame of A-mode ultrasonic radio frequency (RF) signal which shows the echoes from the opposite radial arterial walls. **(b)** One M-mode ultrasonic image which shows the pulsation of the opposite radial arterial walls.

Fig. 3. Frequency spectra of the reflection-mode PPG signal and the signal of arterial diameter change.

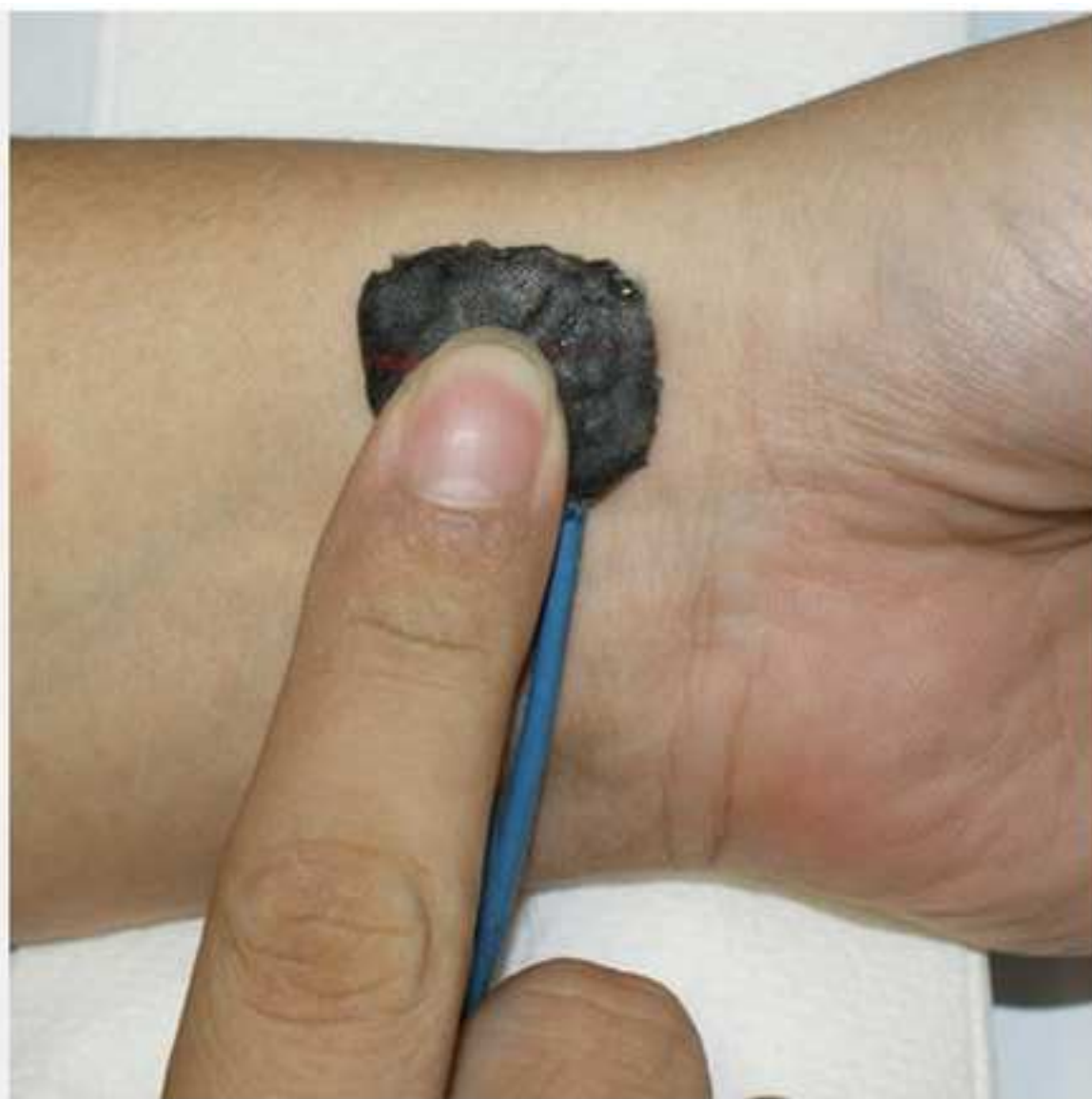
Fig. 4. (a) Comparison of the trend parts of the normalized PPG and arterial diameter signals.

(d) Comparison of the pulsatile parts of the two signals.

Figure 1a-b
[Click here to download high resolution image](#)



(a)



(b)

Figure 2a
[Click here to download high resolution image](#)

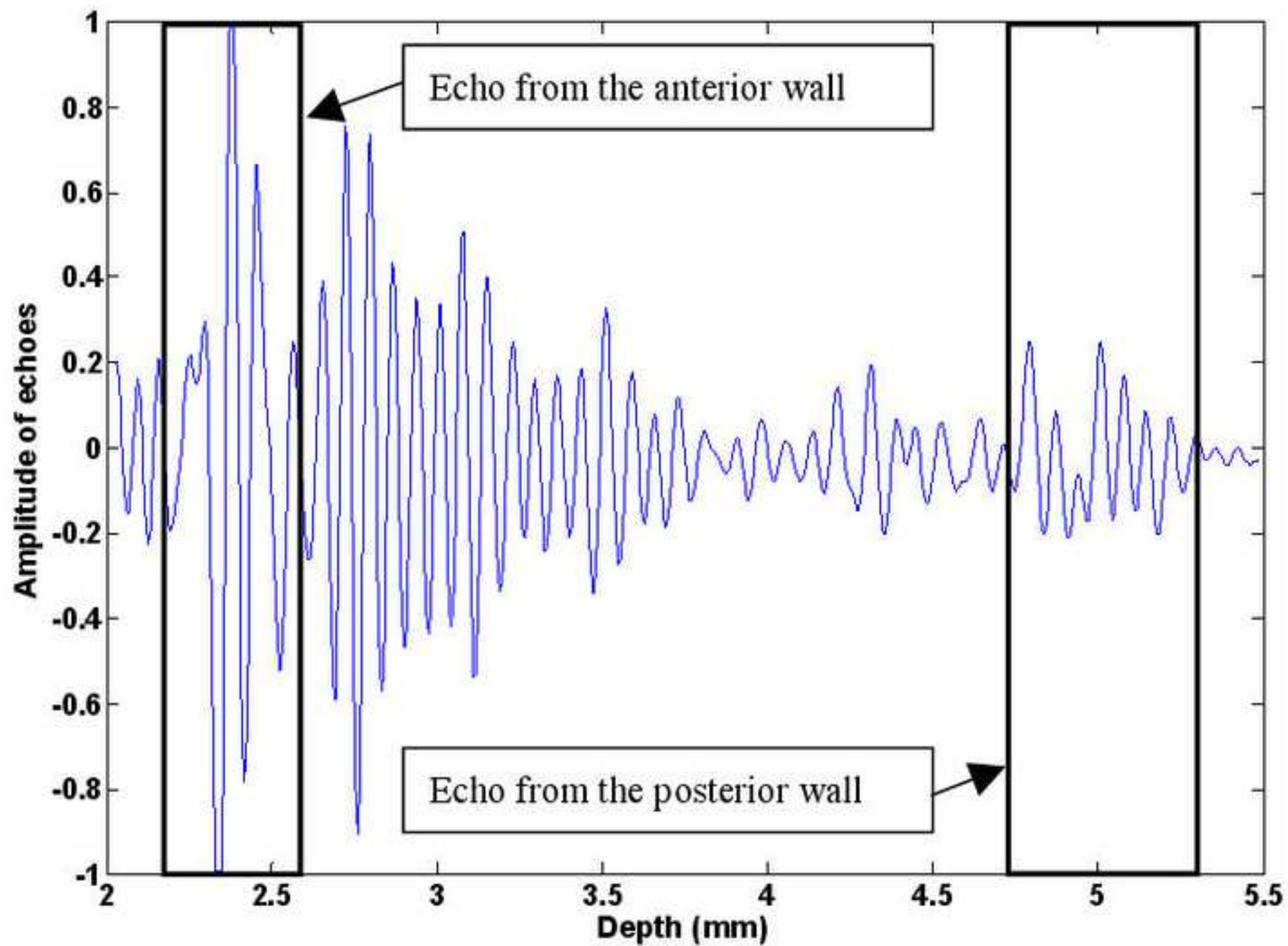


Figure 2b
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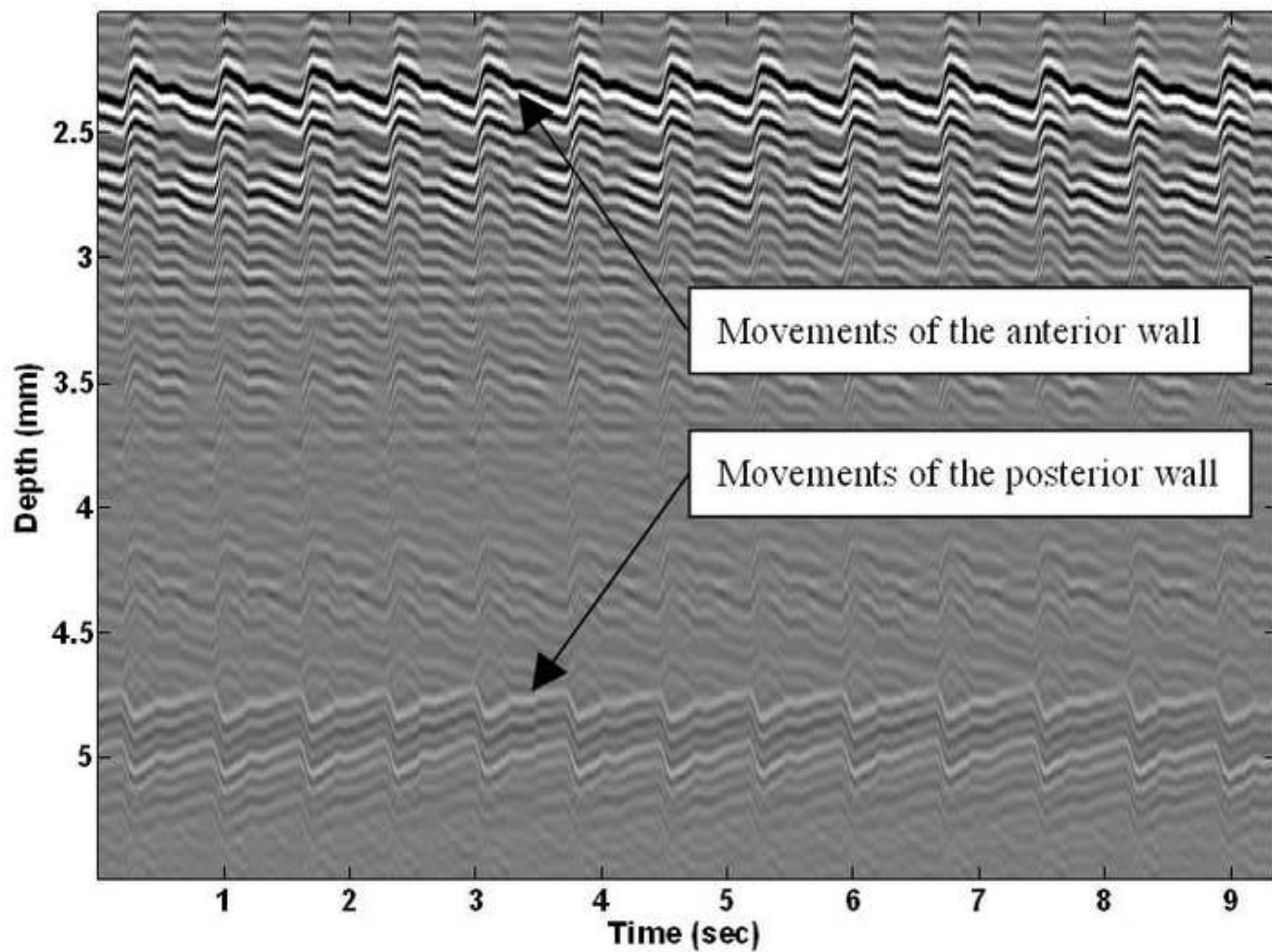


Figure 3
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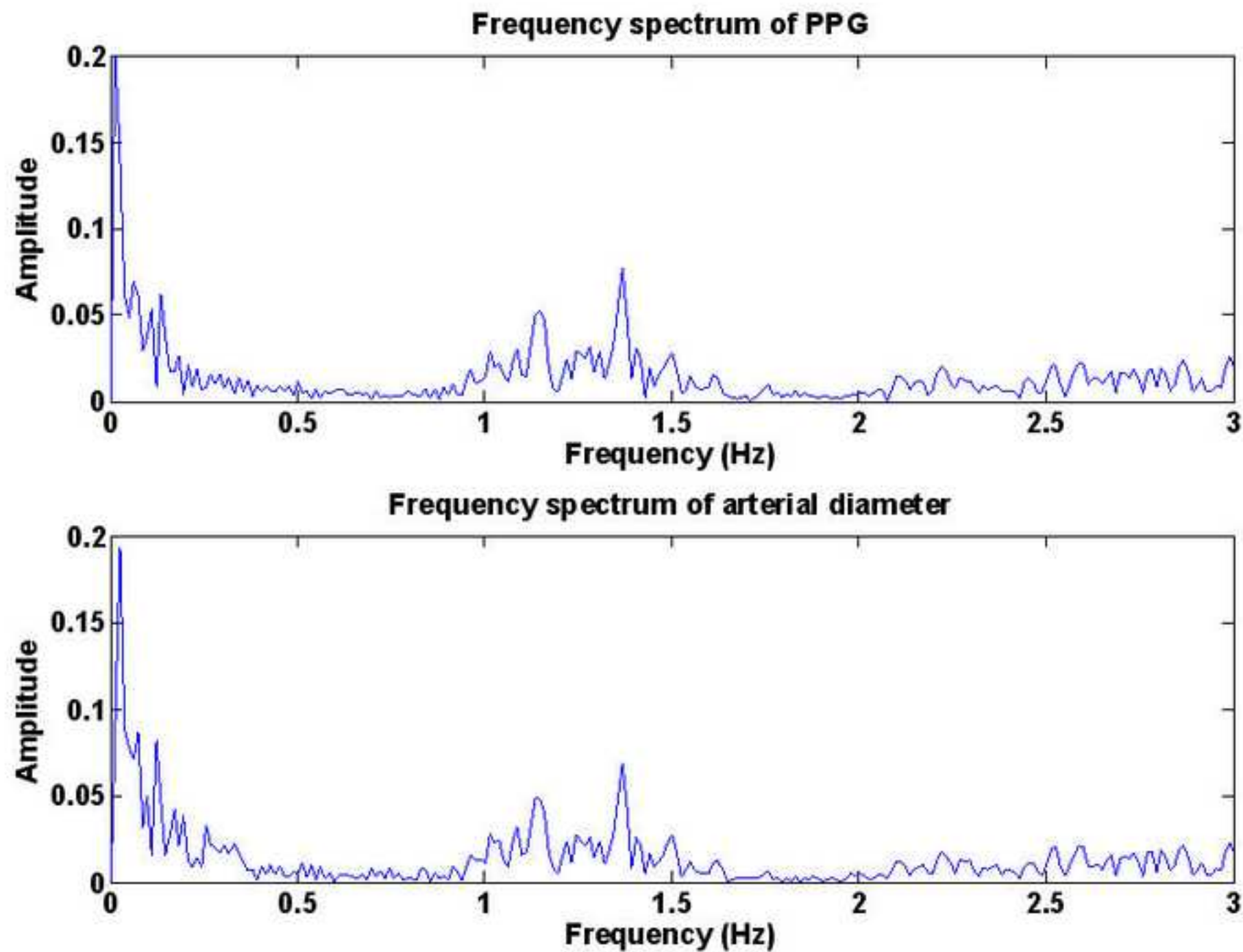


Figure 4a
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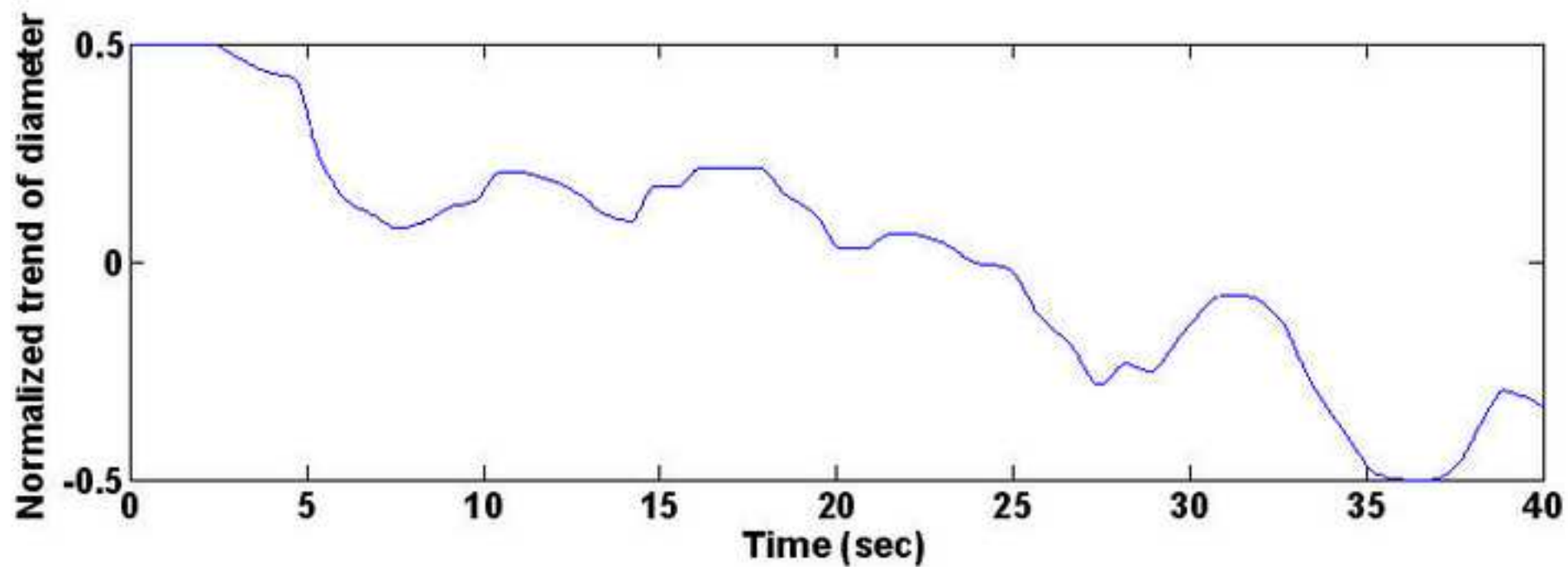
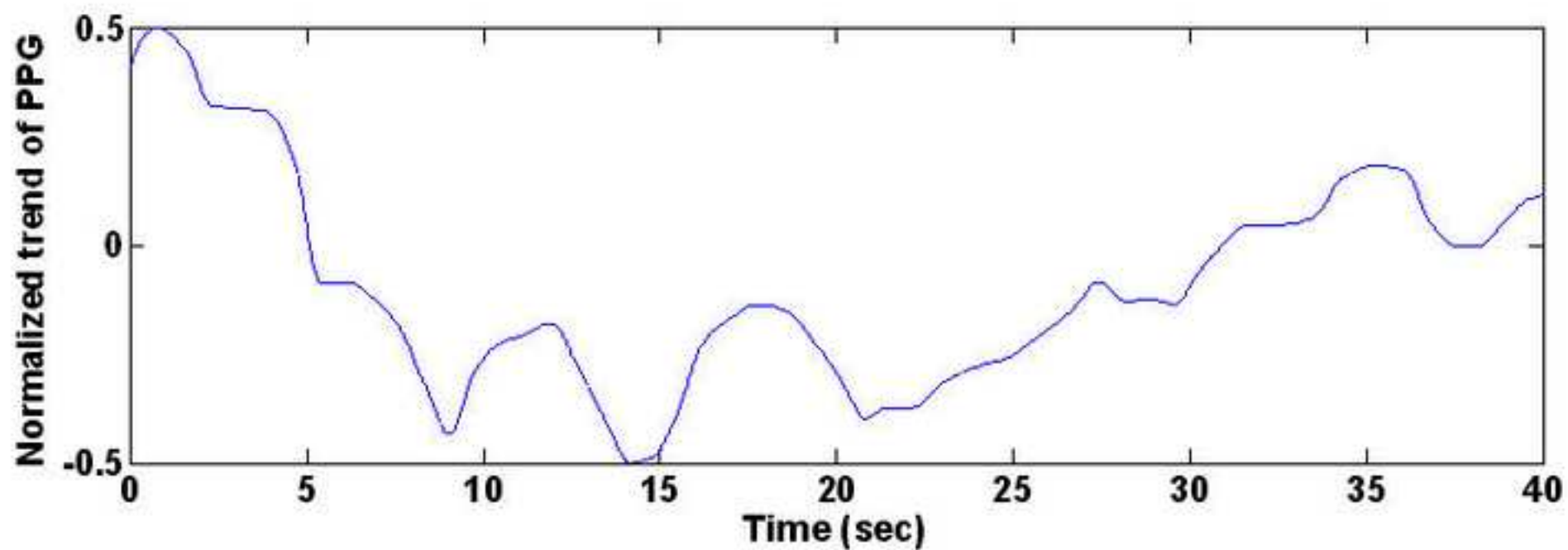


Figure 4b
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