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In-vivo Pulse Wave Imaging for arterial stiffness measurement under normal and pathological conditions

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***Abstract*—Numerous studies have identified arterial stiffening as a strong indicator of cardiovascular pathologies such as hypertension and abdominal aortic aneurysm (AAA). Pulse Wave Imaging (PWI) is a novel, noninvasive ultrasound-based method to quantify *regional* arterial stiffness by measuring the velocity of the pulse wave that propagates along arterial walls after each left ventricular contraction. The PWI method employs 1D cross-correlation speckle tracking to compute axial incremental displacements, then tracks the position of the displacement wave in the anterior wall of the vessel to estimate pulse wave velocity (PWV). PWI has been validated on straight tube aortic phantoms and aortas of healthy humans as well as normal and AAA murine models. This paper presents and compares preliminary PWI results from normal, hypertensive, and AAA human subjects. PWV was computed in select cases from each subject category. The measured PWV values in hypertensive (N = 5) and AAA (N = 2) subjects were found to be significantly higher than in normal subjects (N = 8). In all subjects, the spatio-temporal profile and waveform morphologies of the pulse wave were generated from the displacement data for visualization and qualitative evaluation of the pulse wave propagation. While the waveforms were found to maintain roughly the same shape in normal subjects, those in the AAA and most hypertensive cases changed drastically along the imaged aortic segment, suggesting non-uniform wall mechanical properties.**

***Index Terms*—Arterial stiffness, abdominal aortic aneurysm (AAA), pulse wave, speckle tracking, ultrasound.**

I. INTRODUCTION

Increasing arterial stiffness has been found to be associated with many cardiovascular risk conditions[1] including hypertension[2] and abdominal aortic aneurysm (AAA)[3]. Thus, the currently unavailable accurate, reliable, and noninvasive quantification of arterial stiffness may have a widespread impact on detection and diagnosis of cardiovascular disease. In terms of AAAs, there also exists the clinical need for a reliable method of predicting aneurysm rupture, which carries a 75-90% mortality rate[4].

One of the most recognized methods for quantification of vascular stiffening is measurement of the pulse wave velocity (PWV)[5-7], which is the propagation speed of pressure, flow velocity, and vessel wall displacement waves arising from the natural pulsation of arteries[8]. The current clinical gold standard for PWV estimation involves dividing the distance between two remote sites in the arterial tree (commonly the carotid and femoral arteries) by the time it takes for the pressure waveform to traverse that distance[5,7]. However, such a method faces several limitations. First, the result is a global average of the PWV over the length of the arterial tree based on the simplistic assumption that arterial geometry remains uniform between two remote measurement sites. More importantly, many cardiovascular diseases such as aneurysms are characterized by localized changes in vessel properties[3]. In this sense, a global averaging method may be unable to detect developing aneurysms, resulting in silent progression of the condition.

Pulse Wave Imaging (PWI) is a novel ultrasound-based technique developed by our group to non-invasively visualize pulse wave propagation and measure its velocity within the imaged segment. The method uses a fast normalized 1D cross-correlation algorithm[9] to track moving speckle between consecutive radiofrequency (RF) frames and calculate incremental (inter-frame) displacements. The position of the displacement wave in the anterior aortic wall is tracked over one cardiac cycle and plotted against arrival time to estimate PWV. This method has been validated in straight tube aortic phantoms and in vivo in healthy subjects[10] as well as healthy and AAA mouse models[11].

This paper presents preliminary results from PWI in hypertensive and AAA patients and compares them to the results from healthy volunteers.

II. METHODS

A. Data Acquisition

In vivo studies approved by the Institutional Review Board of St. Luke's-Roosevelt Hospital Center were conducted on three categories of human subjects –healthy (normotensive, age range 23-66, and with no previous cardiovascular pathology), hypertensive, and AAA.

Each subject was asked to lie in the supine position while a 3.3 MHz curved linear transducer (Sonix RP, Ultrasonix, Burnaby, Canada) was used to image the infrarenal descending abdominal aorta. The transducer was oriented so that the pulse wave propagated from right to left (proximal to distal end of the aorta) in the ultrasonic window. RF signals were collected in 2.5-second trials to ensure capture of at least one cardiac cycle. Since the distance of the aorta from the transducer varied among subjects, imaging depths ranged from 7-15 cm, which resulted in frame rates of 284-426 Hz.

B. Dating Processing

A fast normalized 1D cross correlation technique[9] was used to compute incremental axial (parallel to the ultrasound beams) displacements in mm over entire frames using a 3.5-mm window size with 80% overlap. In order to normalize by the frame rate, the displacement values were converted to incremental velocities by multiplying by frame rate. The anterior wall of the aorta was then manually segmented. In images where poor echographic image obstructed the view of the entire aorta, only the visible part of the wall was selected.

The axial velocities in the anterior wall were plotted over time to generate a spatio-temporal profile of the pulse wave propagation. From this profile, the foot of the waveform "seen" by each beam was tracked and its arrival time plotted against the position of the beam along the imaged segment. The slope of the linear regression was assumed equal to the PWV. For this study, the foot was defined as 50% of the upstroke of the waveform.

III. Results

Fig. 1 depicts the anterior wall segmentation, spatio-temporal profiles, and waveform plots of one healthy subject, one hypertensive subject, and one AAA subject. In the healthy subject, the waveform amplitude decreases in magnitude as they propagate along the aorta, but their general morphology remains similar. However, the shape of the waveform changes significantly with increasing distance in the hypertensive and AAA cases.

Fig. 2 shows successive B-mode image frames overlaid with incremental axial velocities of the same three subjects.

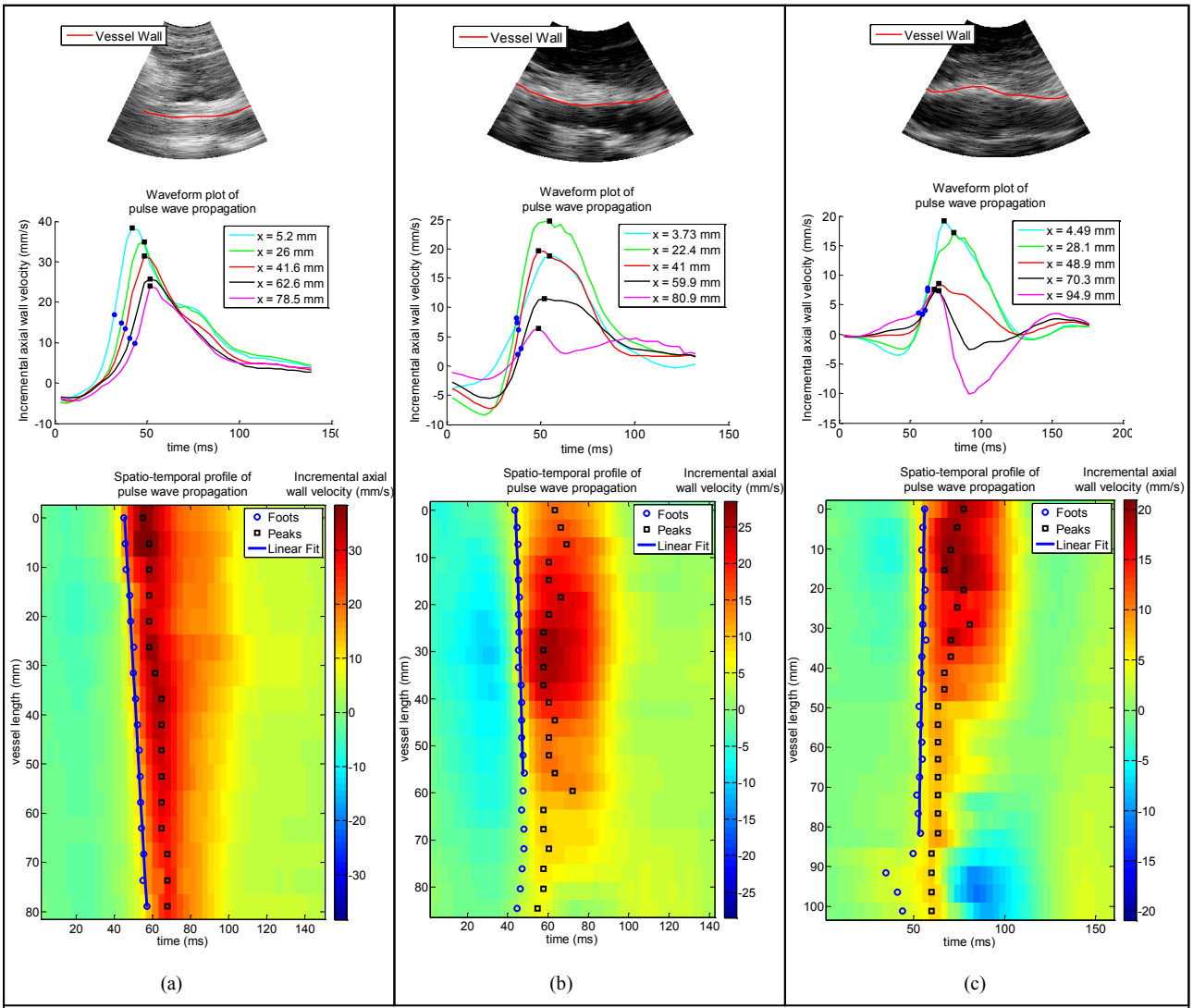

Fig. 1. Aortic anterior wall segmentation, waveform plots, and spatio-temporal profiles of (a) healthy (25 y.o.), (b) hypertensive (83 y.o., blood pressure 153/84), (c) AAA (68 y.o., 3.3 cm diameter aneurysm) subjects. Positive incremental axial wall velocities indicate movement wards the transducer. The blue and black dots indicate the approximate locations of the foots and peaks of the waveforms, respectively. In the hypertensive and AAA cases, waveforms whose morphology deviated drastically from the rest were excluded from linear regression. Thus, not all foot points are part of the linear fit. Steeper linear fits and smaller wall velocities in the hypertensive and AAA cases indicate a stiffer aorta. Direction of blood flow is from right to left in the ultrasonic window in all cases.

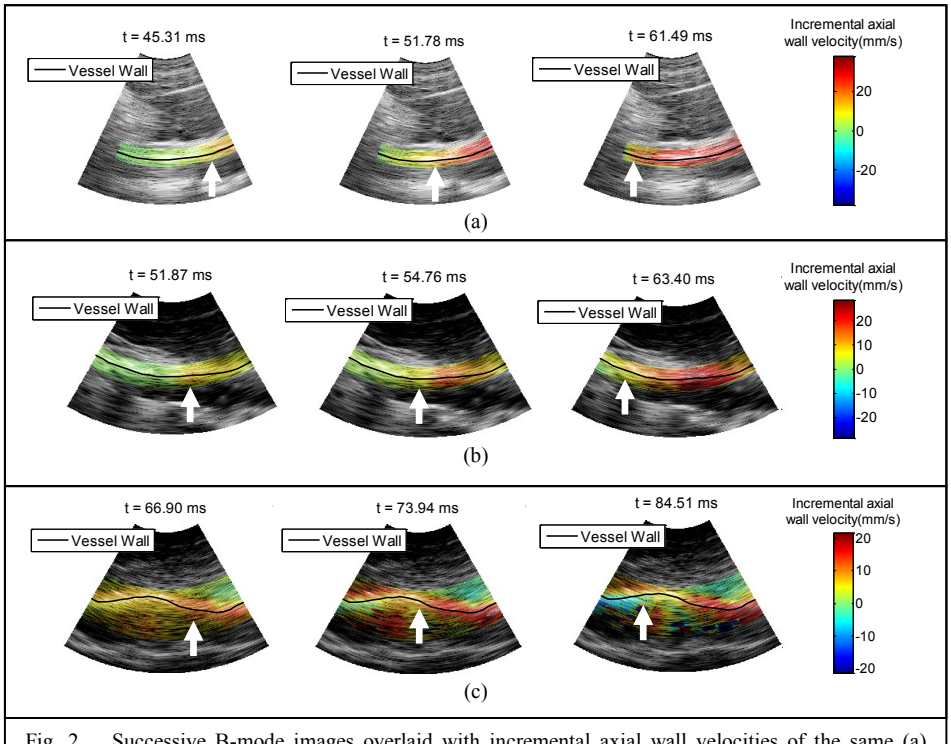

Fig. 2. Successive B-mode images overlaid with incremental axial wall velocities of the same (a) healthy, (b) hypertensive, and (c) AAA subjects shown in Fig. 1. Direction of blood flow is from right to left in the ultrasonic window in all cases. White arrows indicate the approximate locations of the foot of the pulse wave.

From these sequences of images, the pulse wave is shown to induce positive (towards the transducer) axial velocities in the anterior wall and its surrounding tissue.

Fig. 3 shows the spatio-temporal profiles of two additional AAA subjects. The waveform duration and peak axial wall velocity both decrease when the pulse wave reaches the aneurysm sac, similar to the AAA case in Fig. 1.

The PWV values estimated in select subjects using the PWI method are shown in Table 1. Due to highly non-uniform pulse wave morphology, only about 20% of AAA subjects and 25% of hypertensive subjects scanned were included in the PWV measurements.

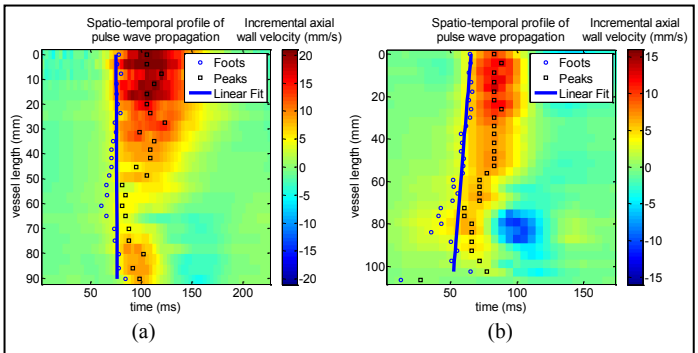

Fig. 3. Spatio-temporal profiles of two additional AAA subjects, ages (a) 68 and (b) 66, with 4.2 and 8.2-cm aneurysms, respectively.

IV. Discussion

PWI has the capability to provide clinicians with a noninvasive method to measure the relative regional stiffness of any artery that can be visualized using ultrasound imaging. However, it is important to note that the estimated value of the PWV is dependent upon the segmentation of the vessel wall. In this study, segmentation was done by qualitatively setting boundary samples along the anterior wall of aorta in the first B-Mode image frame. The displacements at these same points in every frame were used to map the pulse wave and compute its velocity. Thus, if the displacements were to reach a level at which the initial points are not contained within the wall, those displacements would not be reflective of the true wall displacement. However, the maximum incremental displacement in all subjects was $\leq$ 0.13 mm, much less than the thickness of the aorta. Nonetheless, due to the variability of PWV measurement with inter-operator segmentation and cardiac cycle, it was deemed necessary to average PWV over multiple cardiac cycles.

In theory, there is a maximum PWV that can be measured with each given frame rate. The pulse wave must propagate over at least two frames to allow for confident estimation of the PWV. In this study, the average length of the imaged aortic segment was 90 mm. This means that at the frame rates of 284-426 Hz used, the range of maximum measureable PWVs is roughly 12.78-19.17 m/s. However, the measured PWV for one of the AAA subjects in Table 1 exceeded this range, suggesting that the frame rate was insufficient. In general, stiffer arteries result in higher PWV, which in turn require higher frame rates to measure.

In addition to the frame rate limitation, another factor that confounded PWV measurement in hypertensive and AAA subjects was the non-uniformity of the waveforms. Even in normal subjects, the waveforms at successive positions along the aorta varied in shape, rendering it difficult to identify a consistent feature for tracking. For example, in the AAA case shown in Fig. 3b, the linear regression returned a negative PWV due to changing waveform morphology to-

wards the distal end of the imaged aorta. To mitigate this problem, in most of the hypertensive cases presented in Table 1, waveforms that deviated drastically from the rest were excluded from linear regression. Nonetheless, the standard deviations [correlation coefficients] of the PWV measurements in hypertensive and AAA subjects were much greater [smaller] than those in healthy subjects.

The spatio-temporal profiles of the AAA subjects show that in the aneurysmal sac, the magnitudes of the incremental axial wall velocities are smaller and the duration of the pulse wave waveform decreases, indicating increased stiffness in that region.

Table 1. PWV measurements from select normal and hypertensive subjects.

Subject Age	*PWV (averaged over 4+ cardiac cycles) in m/s*	*Correlation Coefficient*
Healthy:		
23	4.82 ± 0.36	0.985 ± 0.007
25	5.51 ± 0.20	0.991 ± 0.005
31	4.32 ± 0.19	0.983 ± 0.002
39	5.77 ± 0.36	0.938 ± 0.004
43	6.04 ± 0.14	0.971 ± 0.006
55	6.82 ± 0.54	0.962 ± 0.021
56	4.65 ± 0.26	0.953 ± 0.019
66	7.65 ± 0.65	0.955 ± 0.017
Hypertensive:		
45 (BP 153/94)	5.48 ± 0.36	0.989 ± 0.006
51 (BP 134/74)	8.27 ± 0.84	0.923 ± 0.029
55 (BP 133/80)	9.37 ± 1.59	0.722 ± 0.018
83 (BP 153/84)	9.79 ± 1.10	0.922 ± 0.037
87 (BP 142/82)	11.23 ± 1.29	0.764 ± 0.027
AAA:		
68	19.93 ± 1.30	0.723 ± 0.075
68	17.33 ± 2.76	0.539 ± 0.091

BP = Blood Pressure

V. Conclusion

PWI is a promising technique with the potential to accurately quantify regional arterial stiffness by measuring pulse wave velocity, which could aid in the early detection of many cardiovascular diseases. By spatio-temporally mapping the pulse wave propagation, PWI provides both a quantitative and qualitative evaluation of the pulse wave in both normal and pathological aortas *in vivo*. However, two key confounding factors in PWI-guided PWV measurement are the frame rate limitation and the non-uniformity of successive waveforms. Along these lines, further research is required to optimize PWI.

In terms of AAA rupture, PWI can potentially detect trends that are unique to AAA cases, providing insight into the underlying biomechanics that govern AAA onset and progression.

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