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Performance assessment and optimization of Pulse Wave Imaging (PWI) in *ex vivo* canine aortas and *in vivo* normal human arteries

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***Abstract*—The amplitude, velocity, and morphology of the arterial pulse wave may all provide valuable diagnostic information for cardiovascular pathology. Pulse Wave Imaging (PWI) is an ultrasound-based method developed by our group to noninvasively visualize and map the spatio-temporal variations of the pulse wave-induced vessel wall motion. Because PWI is capable of acquiring multiple wall motion waveforms successively along an imaged arterial segment over a single cardiac cycle *in vivo*, the *regional* morphological changes, amplitudes, and velocity (i.e. pulse wave velocity, or PWV) of the pulse wave can all be evaluated. In this study, an *ex vivo* setup was used to assess the effects of varying PWI image acquisition variables (beam density/frame rate and scanning orientation) and signal processing methods (beam sweep compensation scheme and waveform feature tracking) on the PWV estimation in order to validate the optimal parameters. PWI was also performed on the carotid arteries and abdominal aortas of six healthy volunteers for identification of several salient features of the waveforms over the entire cardiac cycle that may aid in assessing the morphological changes of the pulse wave. The *ex vivo* results suggest that the PWI temporal resolution is more important for PWV estimation than the PWI spatial resolution, and also that the reverse scanning orientation (i.e. beam sweeping direction opposite the direction of fluid flow) is advantageous due to higher precision and less dependence on the frame rate. In the *in vivo* waveforms, the highest precision PWV measurements were obtained by tracking the 50% upstroke of the waveforms. Finally, the dicrotic notch, reflected wave, and several inflection points were qualitatively identified in the carotid and aortic anterior wall motion waveforms and shown in one representative subject.**

I. Introduction

"If we were able to read all the messages in the arterial pulse waves, then all we need for noninvasive diagnosis is to observe these waves in some conveniently located arteries. If the messages are clear and unequivocal, then the art of noninvasive diagnosis would have been moved ahead a big step." – Y.C. Fung [1].

The pulse wave is generally referred to as the pressure and flow velocity wave generated by each contraction of the left ventricle that propagates throughout the arterial tree and induces displacements in the vessel walls, giving rise to the natural pulsation of the arteries [1,2]. Utilizing high-fidelity pressure sensors, the most common and trusted clinical method for recording and quantifying the pulse wave is based on applanation tonometry, which records the oscillatory time-dependent function of pressure at conveniently located extracorporeal sites (i.e. the radial, femoral, and carotid arteries) [3]. Clinical applications of pulse wave studies are generally aimed at detecting and explaining arterial pathologies such as atherosclerosis, stenosis, and aneurysm, locating sites that need surgical treatment, and inferring the condition of the heart [1].

The observation of significant differences between the peripheral and central (i.e. in the aorta and carotid artery) pressure pulse [4] has resulted in an increased interest in noninvasively recording the central pulse wave and measuring its pressure, which may be more patho-physiologically relevant than the brachial or radial pulses due to its proximity to the heart. By means of applanation tonometry, this is done by recording the radial or carotid pressure waveform and calibrating based on generalized transfer functions obtained from catherized patients [2,4]. Use of a generalized transfer function assumes that the arterial properties between the two sites are the same in all subjects and under all conditions, which is not the case since such properties are dependent upon a variety of factors such as age, blood pressure, pathology, and composition of the vessel wall constituents [1,2]. Despite the reported good reproducibility of the tonometry measurements [4], the most accurate central pulse wave recordings would intuitively be made directly at the aorta.

One of the most theoretically sound parameters in characterizing arterial mechanical properties is the pulse wave velocity (PWV), which is directly and quantitatively related to the Young's modulus of the artery by the well-known Moens-Korteweg equation [2,4]. Estimation of the PWV requires recording the pulse waveform at two or more sites. In applanation tonometry, this is typically done by synchronizing the carotid and femoral pressure waveforms using the ECG, then measuring the time delay (Δt) between the waveforms and estimating the distance (Δd) between the two sites extracorporeally using a tape measure [4]. The result is a global PWV measurement that is based on the invalid assumption of uniform arterial elasticity and geometry within the entire arterial tree. Imaging-based methods using tissue Doppler [5] and MRI [6] to measure the regional PWV over short segments typically suffer from lack of temporal and/or spatial resolution.

Pulse Wave Imaging (PWI) is an ultrasound-based method developed by our group [7-9] to noninvasively image and map the estimated pulse wave-induced displacements of the vessel walls (i.e. diameter wave). By tracking a fiduciary point in each displacement waveform, the regional PWV can be estimated over a single cardiac cycle. The advantage of PWI over other imaging-guided methods for pulse wave analysis is that multiple waveforms (i.e. equal to the number of ultrasound beam lines) can be acquired successively along the imaged arterial segment over the same cardiac cycle, allowing for assessment of changes in the waveform contour as it propagates along the arterial segment.

An initial clinical feasibility study using PWI [11] showed that PWV alone may not be sufficient to differentiate between normal and hypertensive aortas. This calls for further analysis of the waveforms to supplement the PWV as a biomarker for vascular pathology. In addition, tradeoffs exist between the spatial resolution (i.e. beam density), temporal resolution (i.e. frame rate), and fundamental upper limit on the PWV estimate obtainable with PWI. Thus, the purpose of this paper is twofold:

1. To assess the effects of PWI image acquisition variables (beam density/frame rate and scanning orientation) and signal processing methods (beam sweep compensation and waveform feature tracking) on the PWV measurements in order to validate the optimal parameters.
2. To identify salient features in the displacement waveforms obtain using PWI that may aid in pulse wave analysis.

Benchtop experiments using an excised *ex vivo* canine aorta were performed to provide a controlled environment in which the image acquisition parameters could be readily varied while maintaining the exact same field of view. PWI was also performed in the carotid arteries and aortas of normal human subjects to obtain physiological waveforms over complete cardiac cycles.

II. Methods

A. Considerations for PWI Performance Assessment and Optimization

Since estimation of the PWV using PWI is based on spatio-temporal mapping of the pulse wave-induced displacements, the accuracy of the PWV measurements is contingent upon the spatial resolution (i.e. the beam density) and the temporal resolution (i.e. the frame rate), which are interdependent, i.e. decreasing the beam density will increase the frame rate, and vice versa. Theoretically, the temporal resolution will be of greater importance because there is an upper limit to the PWV that can be measured with a given frame rate. Since the pulse wave must be captured by least two frames to allow for velocity estimation, the upper limit (i.e. maximum measurable PWV) can be expressed as

$$PWV_{max} = \frac{(Arterial\ segment\ length)*(Frame\ rate)}{2} \quad (1)$$

In conventional ultrasound scanners, the beam sweeping induces delays in the acquisition of each RF line (and hence the motion estimation), which necessitates the compensation for beam sweeping in order to estimate the true PWV. The beam sweep compensation scheme depends on whether the transducer is oriented such that beam sweeping and pulse wave propagation occur in the same (i.e. forward scan) or opposite (i.e. reverse scan) directions. Previous applications of PWI have employed the beam sweeping compensation scheme [11,12] shown in Fig. 1. However, it has not been validated across multiple beam densities (which governs the time delay between consecutive RF lines) and both scanning orientations.

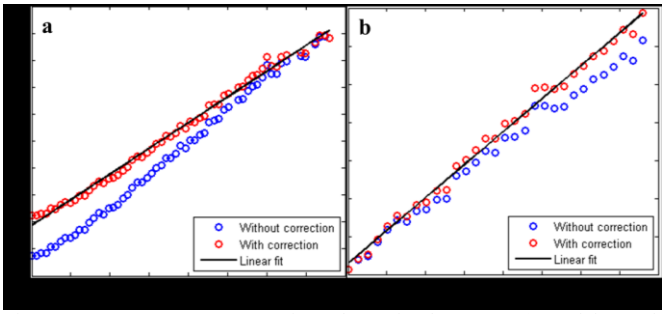

Fig. 1. Beam sweep compensation scheme for the reverse (a) and forward (b) scan orientations. Since beam sweeping typically occurs from left to right in the ultrasonic window, the beginning of the vessel (length = 0) corresponds to the rightmost beam for the reverse scan and the leftmost beam for the forward scan.

B. Ex vivo Setup

The schematic of the setup used for *ex vivo* experiments is shown in Fig. 2. A peristaltic pump (Manostat Varistaltic, Barrington, IL) was used to generate pulsatile flow through an *ex vivo* canine aorta embedded in phosphate-buffered saline (PBS). Ultrasound radiofrequency (RF) signals were acquired using a 10-MHz linear array transducer (SonixTouch, Ultrasonix Medical Corp., Burnaby, Canada) at a constant 25 x 38 mm field of view while varying the beam density from 24 – 128 for both forward (i.e. beam sweeping in the same

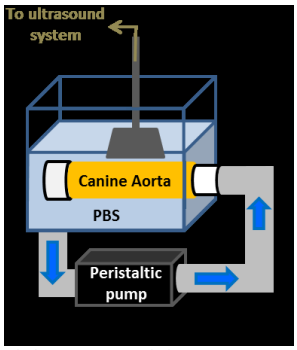

Fig. 2. Schematic of the setup used for *ex vivo* experiments. The pump cycles PBS from the bath through the specimen and back into the bath.

direction as the fluid flow) and reverse scan orientations. The inter-frame axial wall displacements were estimated using a 1D cross correlation-based motion estimation method [10], and the upper limit of the measurable PWV given the frame rate associated with each beam density was calculated using Eq. 1. The PWV was estimated, both with and without a previously described beam sweep compensation scheme [11,12], by tracking the foot of the upper wall displacement waveform for all combinations of beam density and scanning orientation. All PWV measurements were averaged over five pump cycles.

C. In vivo Human Carotid Artery and Aorta

PWI was performed as described in the previous section on the carotid arteries and infrarenal abdominal aortas of six normal human subjects (age range 23 – 56 y.o.) in the supine position using a 3.3 MHz curvilinear array transducer (SonixTouch, Ultrasonix Medical, Burnaby, BC, Canada). To minimize rigid motion, each subject was requested to perform breath-holding for the entire duration of the 2.5-second RF acquisition. The carotid arteries were imaged with 32 beams

at a depth of 2.5 cm to achieve a frame rate of 505 Hz. The aortas were imaged with beam densities of 16-32 and depths of 6-9 cm, resulting in frame rates between 309 and 462 Hz. In order to normalize by the frame rate, the inter-frame displacements were converted to incremental wall velocities by multiplying by the frame rate. The precisions of the PWVs obtained by tracking different features of the aortic anterior wall motion waveform (i.e. foot, peak, and upstrokes) were assessed.

III. Results

A. Ex vivo Experiments

Fig. 3a shows the spatiotemporal map of the upper wall motion over one pump cycle in the canine aorta. Red denotes motion towards the transducer. Fig 3b shows the pulse waveforms at three locations along the imaged segment as indicated by the red, blue and black lines in 3a. In 3b, the purple dots represent the foot of each waveform, and the propagation of the waveform along the segment is clearly shown.

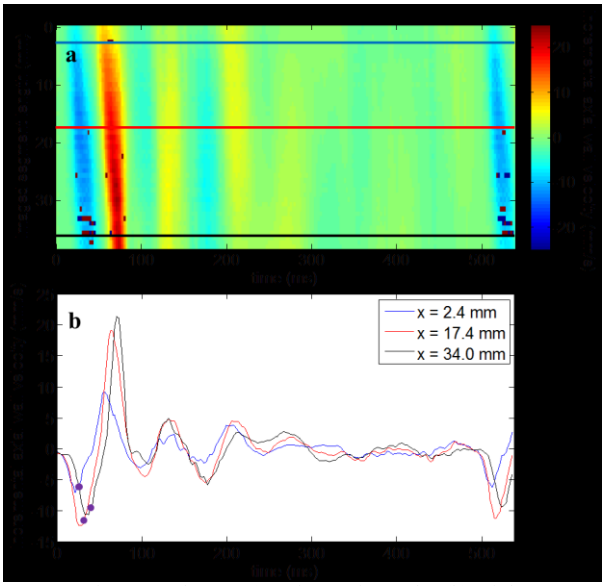

Fig. 3. Spatiotemporal map (a) and waveform plot (b) of the upper wall motion over one pump cycle in the canine aorta. The purple dots in (b) represent the foot of the waveform at 3 locations along the imaged segment (shown by the red, blue, and black lines in (a)).

Fig. 4 shows the effects of beam density, scanning orientation, and beam sweep compensation on the *ex vivo* PWV measurements and the upper limit of the PWV estimation. For all beam densities, the forward scan overestimated the PWV relative to the reverse scan. However, the post-compensated PWV values remained relatively steady across all beam densities, averaging out to 2.61 ± 0.13 m/s for the reverse scan and 2.79 ± 0.24 m/s for the forward scan. Decreasing beam density (i.e. increasing frame rate) resulted in smaller discrepancies between the uncompensated forward and reverse scan PWV estimates. The PWVs obtained using the reverse scan orientation exhibited higher precision and lower deviation from the post-compensated PWVs, which fell between the uncompensated forward and reverse scan estimates.

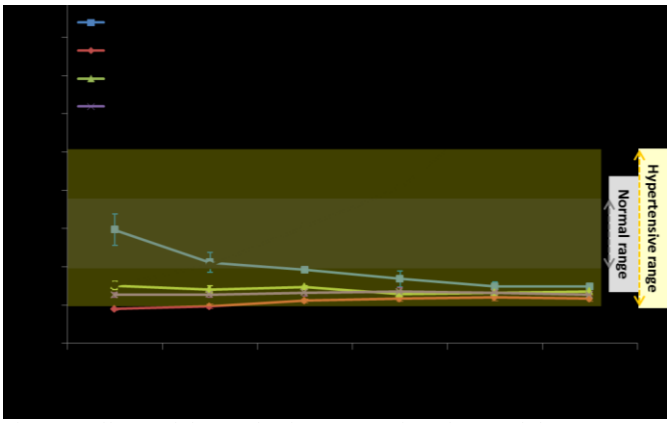

Fig. 4. Effects of beam density, scan orientation, and beam sweep compensation on the *ex vivo* PWV measurements. The black line represents the upper limit of the measurable PWV given the frame rate associated with each beam density. The shaded areas represent the range of compensated PWVs measured using PWI in normal and hypertensive human aortas, obtained from a previous *in vivo* feasibility study [11].

B. Waveform analysis in vivo in normal human carotid arteries and aortas

For the *in vivo* aortic waveforms, the highest precision PWV measurements were obtained by tracking the 50% upstroke. By qualitatively comparing the waveforms in the carotid artery and aorta of the human subjects over a full cardiac cycle, several common characteristics of the pulse wave were identified across subjects. Fig. 5 shows the pulse waveform obtained from the central beam line in the anterior wall of the aorta (a) and carotid artery (b) of the same healthy volunteer. It is important to note that the waveforms are not necessarily synchronized in time. The end-systolic point of the pulse wave was defined as the maximum of the upstroke phase, and the end diastolic point was identified as the point at which the upstroke begins (i.e. foot).

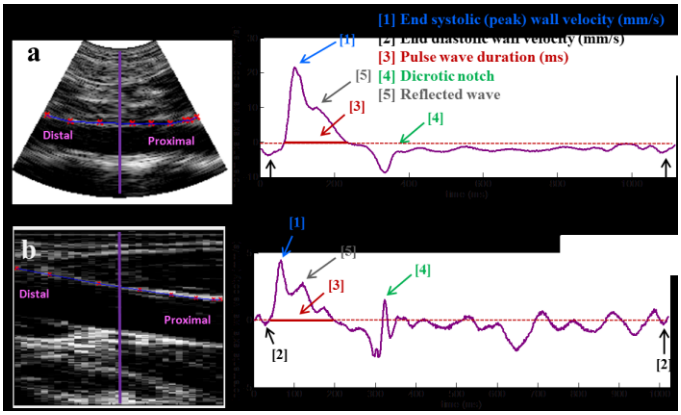

Fig. 5. Pulse waveform obtained over one complete cardiac cycle from a single ultrasound beam line (shown in purple in the B-Mode field of view) in the anterior wall of the aorta (a) and carotid artery (b) of the same healthy volunteer.

Another common feature observed in all waveforms was that the wave amplitude falls below zero just before the major upstroke and also on the tail end of the downstroke. By measuring the time lapse between these two zero-crossing points, we define the "width" of each successive waveform as

the wave duration. In the carotid waveforms, the reflected wave was more pronounced that in the aortic waveforms.

IV. Discussion

PWI is capable of imaging and mapping the arterial pulse wave as a diameter wave at multiple sites along the imaged segment (i.e. high spatial resolution) and at high frame rates (i.e. high temporal resolution) over a single cardiac cycle. Such a method may provide new avenues for pulse wave analysis and PWV estimation because multiple waveforms can be acquired locally along any major artery, allowing for analysis of consecutive waveforms and estimation of the regional PWV over one cardiac cycle.

Increasing the frame rate caused the PWVs obtained using the two different scan orientations to converge towards the post-compensated PWV values, despite the reduction in beam density. Thus, the *ex vivo* results indicated that the PWI temporal resolution is more important for accurate PWV estimation than the PWI spatial resolution.

The *ex vivo* results also suggest that the reverse scan orientation is advantageous due to higher precision and underestimation of the PWV relative to the forward scan (Fig. 4). From a physical standpoint, if the pulse wave were to propagate in the same direction and at the exact same speed as the beam sweeping, the PWV would appear to be infinite when it is actually finite (disregarding beam sweep compensation). Thus, the apparent PWV measured using PWI in the forward scan orientation would be overestimate the true PWV, and vice versa for the reverse scan. This means that reverse scanning "slows down" the apparent pulse wave so that higher PWVs can be measured with the same beam density and its associated frame rate.

Although the beam sweep compensation scheme adjusted the estimated PWV to values in between the uncompensated forward and reverse scan values, complete validation of the beam sweep compensation scheme requires knowledge of the exact value of the true PWV. This can be done through mechanical testing to find the Young's modulus of the specimen and using the Moens-Korteweg equation to derive PWV. However, the Moens-Korteweg equation is based upon several major simplifying assumptions including uniform vessel geometry and zero wave reflections [2] which do not apply in our *ex vivo* experiments nor *in vivo*. Future work will focus on the utilization of pressure sensors and Doppler ultrasound to find the true PWV through flow velocity and pressure wave measurements in *ex vivo* canine aortas.

If the typical ranges of the PWV measured using PWI in normal and hypertensive aortas [11] are considered (shaded areas in Fig. 4), a beam density of 32 (i.e. frame rate of 642 fps) would be required to reliably measure the PWV in both normal and hypertensive aortas, assuming a constant 25 x 38 mm field of view.

Finally, the *in vivo* results suggest that for clinical PWI on human aortas, tracking the 50% upstroke will yield the most consistent PWV estimates. Regarding the features of the *in vivo* waveforms, the waveform at any given site in the arterial tree is a combination of the forward incident wave and any reflected waves originating from further down the vasculature [1,2]. The observation of common features in the PWI carotid and aortic waveforms across all subjects means that in order to improve the clinical utility of PWI for more accurate diagnosis and characterization of cardiovascular disease based on pulse wave analysis, the entire wealth of information obtainable from the images should be utilized to supplement the PWV estimation.

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