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Comparison between multi-channel LDV and PWI for measurement of pulse wave velocity in distensible tubes: Towards a new diagnostic technique for detection of arteriosclerosis

Adriaan Campo[a,b,1,2], Grzegorz Dudzik[c,3], Jason Apostolakis[a,1], Adam Waz[c,3], Pierre Nauleau[a,1], Krzysztof Abramski[c,3], Joris Dirckx[b,2], Elisa Konofagou[a,1,*]

[a] Ultrasound Elasticy Imaging Laboratory (UEIL), Department of Biomedical Engineering, Columbia University, 51 Engineering Terrace 1210 Amsterdam Avenue, New York 10031, USA
[b] Biophysics and Biomedical Physics Laboratory (Bimef), Department of Physics, Antwerp University, 171 Groenenborgerlaan; Antwerp, Antwerp 2020, Belgium
[c] Laser and Fiber Electronics Group (LFEG), Wroclaw University of Technology, Wybrzeze Wyspianskiego 27, Lower Silesia, Wroclaw 50-372, Poland

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ABSTRACT

The aim of this work, was to compare pulse wave velocity (PWV) measurements using Laser Doppler vibrometry (LDV) and the more established ultrasound-based pulse wave imaging (PWI) in smooth vessels. Additionally, it was tested whether changes in phantom structure can be detected using LDV in vessels containing a local hardening of the vessel wall.

Results from both methods showed good agreement illustrated by the non-parametric Spearman correlation analysis (Spearman-$\rho = 1$ and $p < 0.05$) and the Bland–Altman analysis (mean bias of −0.63 m/s and limits of agreement between −0.35 and −0.90 m/s).

The PWV in soft phantoms as measured with LDV was 1.30±0.40 m/s and the PWV in stiff phantoms was 3.6±1.4 m/s. The PWV values in phantoms with inclusions were in between those of soft and stiff phantoms.

However, using LDV, given the low number of measurement beams, the exact locations of inclusions could not be determined, and the PWV in the inclusions could not be measured. In conclusion, this study indicates that the PWV as measured with PWI is in good agreement with the PWV measured with LDV although the latter technique has lower spatial resolution, fewer markers and larger distances between beams. In further studies, more LDV beams will be used to allow detection of local changes in arterial wall dynamics due to e.g. small inclusions or local hardenings of the vessel wall.

1. Introduction

Cardiovascular disease (CVD) is the most important cause of death worldwide and its prevalence is steadily rising [1]. An important factor in the etiology of CVD is arterial stiffness. Increased arterial stiffness increases the load on the heart and can cause damage to peripheral organs due to reduced compliance and reflection phenomena. An increase in large artery stiffness is an indicator for stroke, heart failure and overall mortality amongst other risks [2–4].

Arterial stiffness can be estimated in vivo through several approaches such as the pressure-area (PA) relationship [5], the water-hammer equation [6], and the pulse wave velocity (PWV) [7]. Our work will focus on the latter method, and is commonly used in the form of the so-called "carotid-femoral" PWV. Carotid-femoral PWV has been extensively validated, and it is currently considered to be the gold standard for in vivo arterial stiffness detection. This method renders a stiffness estimate for a long stretch of the aorta between the common carotid artery (CCA) and the femoral artery (FA).

However, the carotid-femoral PWV is a coarse measurement and has been proven to be prone to error [8–12]. The PWV is dependent on the artery characteristics. As the pulse wave passes through the CCA, the descending aorta, the abdominal aorta, the iliac artery and eventually the FA, it is modified due to different mechanisms, including

Abbreviations: ARFI, Acoustic radiation force impulse; BMI, Body mass index; CCA, Common carotid artery; CVD, Cardiovascular disease; FA, Femoral artery; LDV, Laser Doppler vibrometry; PA, Pressure-area; PTT, Pulse transit time; PWI, Pulse wave imaging; PWV, Pulse Wave Velocity; SWE, Shear wave elastography; TSI, Thermal strain imaging.

* Corresponding author.
E-mail address: ek2191@columbia.edu (E. Konofagou).

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changing blood velocity, pulse amplification and reflection amongst others. The result of this is twofold: the carotid-femoral PWV will render an averaged PWV, and the change in shape of the pulse wave makes calculation of exact arrival time of the pulse in each location difficult [13]. Also, the trajectory is composed of a combination of central and more peripheral, elastic and muscular arteries. It has been reported that stiffness of these arteries is differently affected by such factors as age and disease [14], and this also applies to the CCA and the FA [15]. Furthermore, the actual distance between CCA and FA as traveled by the pulse wave is difficult to accurately measure, and is biased in patients with high BMI or high age [8,16]. Therefore, research is ongoing to develop alternative methods for cardiovascular screening.

Several findings suggest that CCA PWV is a promising alternative to carotid-femoral PWV. CCA stiffness is shown to be linked to arteriosclerosis [17,18], and additionally, CCA stiffness is an indicator of plaque formation in the CCA [19].

Plaque formation is a natural phenomenon of arterial aging. However, not all plaques are considered dangerous when the level of stenosis is within certain limits. Plaques that are considered vulnerable plaques are more prone to rupturing and causing stroke when present in the CCA [20]. It is believed that these plaques show different features than non-vulnerable plaques such as a lower degree of calcification or a liquid core [21]. Quantifying plaque vulnerability non-invasively remains a great challenge in medical science today, and recent findings suggests that local PWV assessment in the CCA can provide a valuable tool for plaque characterization [22], amongst other techniques such as acoustic radiation force impulse (ARFI) imaging [23], shear wave elastography (SWE) [24] and thermal strain imaging (TSI) [25].

The PWV of a short stretch of the CCA can be detected non-invasively in patients with several methods by tracking certain features of the pulse wave. MRI uses the time difference in flow velocity profiles inside the artery to determine the PWV [26,27], while ultrasound uses the wall displacement of the artery [28–32]. Optical methods use skin displacement of the skin overlaying the CCA [33–35].

In this and previous studies [33], laser Doppler vibrometry (LDV) is presented as an alternative over other local PWV detection techniques. A related method of local PWV measurement is Pulse wave Imaging (PWI) [13], which is an ultrasound-based method capable of measuring pulse wave propagation in arteries and phantoms non-invasively and with high spatial and temporal resolution. PWI is being used for PWV detection in vivo in the CCA [36] and even the aorta [37], and its potential as a tool in clinical diagnosis and fundamental research is well documented [28,29].

The aim of this study will be to compare LDV with PWI measurements in vitro and validate them against PWV values derived using PA testing. It is also hypothesized that local changes in phantom structure can be detected using LDV. For this purpose, PWV will be measured in smooth vessels, and vessels containing a local hardening of the vessel wall. Additionally, PWV values will compared against ground-truth stiffness values of the vessel wall.

2. Methods

2.1. Phantom setup

Soft silicone gel was prepared with a 10:1 weigth ratio of Silicone Soft Gel Part A (A-341, Factor II, Lakeside, AZ, US) and Silicone Soft Gel Part B (A-341-C, Factor II, Lakeside, AZ, US) (Table 1). Stiff silicone gel was prepared with a 3:2 weight ratio of Silicone Elastomer Part A (A-RTV-05, Factor II, Lakeside, AZ, US) and Silicone Elastomer Part B (A-RTV-05, Factor II, Lakeside, AZ, US) (Table 1). Starch was added to the composition as a scatterer to enhance visibility using ultrasound. Using a mold, 4 different silicone vessels (phantoms) were created: phantom 1: uniformly soft silicone; phantom 2: uniformly stiff silicone; phantom 3: soft silicone with a 1 cm long, ring-shaped stiff silicone inclusion in the center; phantom 4: soft silicone with a 4 cm long, stiff silicone inclusion in the center (Table 1). All phantoms were 16 cm long, with outer diameter of 12 mm and inner diameter of 7 mm according to mold dimensions.

Table 1
Phantom overview with geometry of 4 different phantoms.

		Phantom composition		
Phantom	1		16 cm soft silicone	
	2		16 cm stiff silicone	
	3	7,5 cm soft silicone	1 cm stiff silicone	7,5 cm soft silicone
	4	6 cm soft silicone	4 cm stiff silicone	6 cm soft silicone

The phantoms were installed in a plastic box with a slab of absorbing rubber on the bottom, and embedded in gelatin in order to mimic human surrounding tissue. Phantoms were covered by 10 mm of gelatin. The gelatin was regular powdered gelatin (Knox Unflavoured Gelatin, Treehouse Foods, Oak Brook, Illinois, USA), with 30 g of gelatin per liter of water used.

Additional silicone tubes connected at the inlet and outlet allow pulse generation and filling and emptying of the phantom vessels (Fig. 1).

Pressure pulses were generated by manually pinching-and-releasing the connected tube upstream from the measurement setup by use of a large paper clamp. Pressure pulse propagation in the phantoms was measured in five different configurations: (1) the measurement device centered in the middle of the phantom 1, (2) the measurement device centered in the middle of phantom 2, (3) the second beam of the LDV device centered in the middle of the 1 cm long inclusion in phantom 3, (4) the measurement device centered on the transition of soft to stiff silicone in phantom 4 with the pressure pulse propagating from soft to stiff silicone; and (5) the measurement device centered on the transition of stiff to soft silicone in phantom 4 with the pressure pulse propagating from stiff to soft silicone. In all cases the center of the LDV device and the ultrasound probe for PWI was in the same location.

2.2. LDV measurements

For PWV measurements a custom-built 4-channel 1550 nm LDV system was used as developed by Waz et al. (Laser & Fiber Electronics Group, WrUT, Wroclaw, Poland) [38–40]. Laser heads were positioned parallel to each other and perpendicular to the gelatin surface, detecting out-of-plane displacement of the gelatin surface caused by pressure variation inside the phantom. Beams were positioned such that they were incident on the surface with a mutual distance of 15 mm, i.e. the distance between outer beams was 45 mm (Fig. 1). In each configuration, 10 to 15 measurements were performed, with a duration of 2 s at sampling rate of 500 kHz. In order to reduce noise, LDV data was downsampled until a smooth waveform was obtained, still retaining the necessary detail for pulse wave analysis. The data was downsampled to a sampling rate of 5 kHz, and smoothed with a moving average filter (window-size of 150 points).

2.3. Ultrasound measurements

A linear ultrasound array (Philips L7-4, Philips, Amsterdam, NL) connected to a customized system (Vantage 256, Verasonics, Kirkland, Washington, USA) was positioned directly above the phantom with the direction of the beams perpendicular to the phantom surface. The central frequency was 5.2 MHz, the sampling frequency was 42 MHz, the imaging depth was 40 mm and the width of the field of view was 38 mm with 128 beams. In every configuration, 10 to 13 measurements were performed, with a duration of 1.3 s at a framerate of 8.3 kHz. The data was downsampled to a sampling rate of 5 kHz, and smoothed with a moving average filter (window-size of 150 points).

The phantoms were imaged using plane waves, and beamforming was performed according to Montaldo et al. [41]. Using ultrasound, PWI measurements were performed. PWI uses the different elements