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Application of a New 4-Channel Vibrometer for Determination of Atherosclerosis

Further Advances Towards a Handheld Device

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***Abstract*—Cardiovascular diseases (CD) are the leading cause of death worldwide and their prevalence is expected to rise. Important in the etiology of CD is the stiffening of the large arteries (arteriosclerosis) and plaque formation (atherosclerosis) in the common carotid artery (CCA). Increasing evidence shows that both arteriosclerosis and atherosclerosis can be detected by assessing pulse wave velocity (PWV) in the CCA, and several techniques focus on the detection of PWV in this structure. In previous studies, laser doppler vibrometry (LDV) was proposed as an approach to detect the arterial system. In the present work, a compact 4-channel LDV system is introduced for PWV detection. Four phantom arteries were assessed mimicking real life cardiovascular pathologies. Due to the high sensitivity and the increased spatial and temporal resolution of the LDV system, PWV could be assessed, and even local changes in phantom architecture could be detected. The system could potentially be use to detect arteriosclerosis and plaque during cardiovascular screening.**

Keywords—arterial stiffness; cardiovascular diseases; laser doppler vibrometry; plaque

I. INTRODUCTION

A. General Background

According to the World Health Organization (WHO), cardiovascular diseases (CD) are the leading cause of death worldwide, and the annual number of casualties is expected to rise. Therefore, an early detection of cardiovascular risk to prevent or delay cardiovascular events is needed [1].

The most important conditions in the etiology of CD are arteriosclerosis and atherosclerosis, as is backed by an impressive corpus of evidence. As a consequence, research for screening methods focusses on the detection and evaluation of these conditions [2].

Arteriosclerosis or increased large artery stiffness is known to cause damage to the heart and the arteries over time. There exists a well-documented relationship between arteriosclerosis and cardiovascular risk, with increased large artery stiffness being involved in hypertrophy of the heart, alteration of myocardial perfusion and increased systolic dysfunction. Atherosclerosis or plaque formation in the arteries, on the other hand, is the main cause of stroke and ischemia. Although a different condition than arteriosclerosis, it is related since local stiffening of the artery is known to precede plaque formation [3].

B. Pulse Wave Velocity

During a cardiovascular cycle, a pressure wave emerges from the heart and propagates through the arterial system. Arteriosclerosis can be monitored by assessing velocity of this pulse wave or PWV as PWV is a function of arterial stiffness. PWV is usually measured by detecting the pulse transit time (PTT) between 2 or more pressure waves at known locations, usually between the common carotid artery (CCA) in the neck and the femoral artery (FA) groin, or the so called carotid-femoral PWV or cfPWV. When the distance D between measurement sites is known, PWV can be readily calculated as PWV = D/PTT (1). cfPWV is assumed to reflect stiffness of the large arteries, and it has been shown to be a very robust predictor for cardiovascular morbidity and mortality [1].

C. Local Pulse Wave Velocity in the Common Carotid Artery

However, cfPWV provides a measure of the average arterial stiffness over a long trajectory, and it returns an averaged PWV value with contributions of arterial segments that may respond differently to aging and disease. Also because of the long trajectory, pulse shape and PWV changes significantly between measurement sites, rendering a relevant PTT determination problematic. Finally, the distance D in (1) is difficult to measure accurately in elderly and obese patients [4].

Therefore, methods to assess arterial stiffness locally are of interest. Methods for local stiffness detection mainly focus on the CCA, for it is an interesting target: the CCA is easily accessible and it's a large elastic artery possibly being representative for overall large artery stiffness [3]. Moreover, as the CCA is frequently affected by plaque formation, increased stiffening of the CCA is a predictor of atherosclerosis and even stroke [5].

D. Local Pulse Wave Velocity Detection

Pulse wave imaging (PWI) is an ultrasound based technique that allows local detection of the PWV in the CCA. Recently, the possibility was investigated to use PWI for plaque detection by Shahmirzadi *et al.* [6]. In this study, a similar approach is tested using a 4-channel laser Doppler vibrometer (LDV) system as developed by Waz *et al.* [7]–[9]. LDV provides a non-contact, non-invasive method to assess out-of-plane displacement of the skin overlaying the CCA. The motion of the CCA wall and its surrounding tissues (skin) is in direct relation to the pressure inside the vessel. Therefore, it is possible to detect the pulse wave at multiple known locations along the trajectory of the vessel and to calculate the PWV. Previous experiments indicate that LDV can be used to measure cfPWV and local carotid PWV [10], [11]. In this study, we assess the feasibility of the 4-channel vibrometer system to assess PWV velocity of phantoms with varying architectural traits, mimicking gross arterial pathologies. The setup is built to mimic real life conditions in the CCA, with some phantoms showing entire or local increases of stiffness, or local hardening of the vessel wall.

Our hypothesis states that the high temporal resolution, and number of channels, allows not only determination of phantom stiffness, but also allows detecting local changes in arterial restructuring, thereby making LDV also a possible tool for atherosclerosis detection.

II. METHODS

A. Experimental Setup

Latex tubes with an inner diameter of 6 mm, a wall thickness of 200 µm and length of 10 cm were used as phantoms. The dimensions and the stiffness were chosen to resemble a human CCA. In order to mimic conditions of arterial disease, 4 different modifications to the latex tubes were created: specimen 1 consisted of a single layer of latex, mimicking a normal condition; specimen 2 consisted of a double layer of latex, mimicking increased arterial stiffness, specimen 3 consisted of a single layer, with the last 5 cm downstream of the tube being fortified with a longitudinal stretch of non-elastic tape (5x50 mm), mimicking local calcifications; specimen 4 consisted of a single layer, with the last 5 cm downstream of the tube consisting of a double layer of latex, mimicking locally increased stiffness. All specimens were embedded in gelatin, approximately 1 cm below the surface to mimic the tissue surrounding the CCA (Fig. 1.). The specimens were connected to a system that was able to subject them to heart-like pressure pulses: a container with water level at 1 m from the top of the test tube was connected to a valve. For a pressure pulse, the valve opened for 0.5 s, projecting a pressure pulse trough the specimens. Downstream from the valve but upstream from the test tubes a small Windkessel was mounted to round the profile of the pressure pulse. The system ended in a reservoir with water level 15 cm above the top of the test tube in order to keep tubes open at all times. The height difference between the reservoirs was 85 cm or 64 mmHg, which is in the same order as human pulse pressure amplitude. More details about the setup can be found in [11].

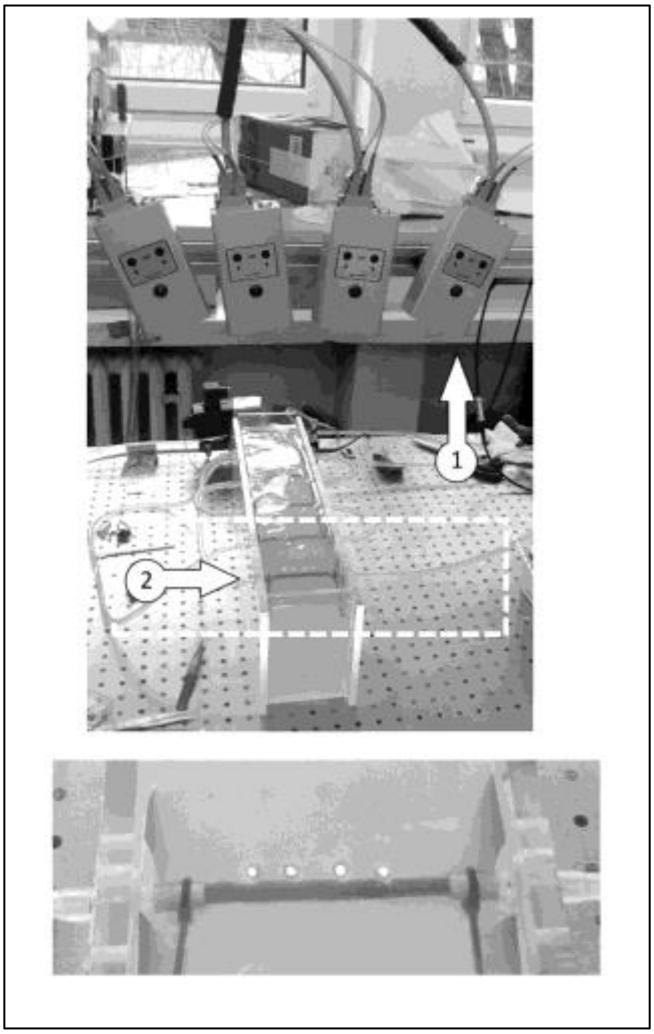

Fig. 1. Depiction of the measurement setup. In the upper pane, the 4 measurement heads of the LDV system are shown (arrow 1), as aimed on specimen 1 embedded in gelatin (arrow 2). In the lower pane, a close up shows the embedded specimen with the 4 measurement beams aimed on the gelatin surface.

B. *LDV Setup*

Out-of-plane displacements of the gelatin surface straight above the tube were recorded with a 4-channel LDV system as described by Waz *et al.* at the Wroclaw University of Technology (Poland) [7]–[9]. LDV measures the displacement of a moving object using heterodyne detection of scattered light, in a non-contact and non-invasive way. A low power laser beam (<10mW at 1550 nm eye-safe radiation) is aimed at the object. When the object moves, the frequency of the reflected light is shifted due to the Doppler effect. The LDV detects a heterodyne signal which gives the displacement of the moving object after IQ demodulation and signal processing [12]. Displacements of tube wall and the surrounding structures, is function of the pressure inside the tube. By measuring gelatin displacement right above a surfacing tube, pressure waves can be tracked such that PWV can be determined (Fig. 1). The 4 measurement beams were aimed on the surface a distance of 1-2 cm apart. In specimen 3 and 4, the 2 first beams were aimed at the first halve of the tube, and the 2 last beams were aimed at the modified part of the tube (i.e. the part with non-elastic tape and the part with double layer of latex respectively). Each measurement, displacements were monitored for 1 s with a sampling rate of 1 MHz (Fig. 2.). The valve from the experimental setup was triggered 10 ms after the start of a measurement. All 4 specimens were measured 10-11 times.

C. *Signal Analysis*

Prior to any processing, out-of-plane displacement signals were filtered with a 5th order low-pass Bessel filter with cutoff frequency of 100 kHz. Waveforms were further smoothed with a 2nd order Savitsky-Golay filter (window size 11). The distance between measurement points on the specimen surface was measured with a ruler. Prior to analysis, the dataset was interpolated between measurement locations, in order to have 10 time series that appear to be equally spaced between the first and the last measurement point. This allows better visual inspection, and it eases signal processing as shown in Fig. 3. The propagation of the pulse wave in the 10 different time series was determined by finding the point where the displacement exceeds 50% of its first maximum of displacement. PWV was then derived by evaluating the relation of these points in time, with the distance between measurement points. This was done using a least squares approximation. Subsequently, the R-squared value was calculated for this relationship. Due to the high sensitivity of the measurement apparatus, distorting ripples from the building and the measurement setup were assumed to be present. Despite precautions, and based on visual inspection, 3 of 40 measurements were determined unsuitable due to contamination with ripples from external origin. All calculations were performed using Matlab (Matlab R2015a, MathWorks, Nattick, USA).

III. RESULTS

A. *Specimens 1-2*

Using the 4-channel vibrometer, displacement of the vessel wall could be tracked in specimens 1 and 2. Out-of-plane displacements of the first maximum of upstroke are 10-100 μm which is comparative to skin displacements above the CCA in a human subject [13]. By tracking the 50% of maximum upstroke, the PWV can be determined. PWV values are between 4 and 6 m/s as shown in Table I. These values are in the same order as PWV measured in human subjects [14]. The properties in specimens 1 and 2 are those of a tube with uniform wall which results in propagation of the pulse wave with uniform velocity as can be appreciated in Fig. 2 and Fig. 3. Also, due to the uniform nature of the tube wall, there is a sound linear relationship between propagation of the wave-front in time and the traveled distance of the wave-front, as reflected in the R-squared values which are between 0.95 and 0.99 (see Table I).

B. *Specimens 3-4*

Properties of specimens 3 and 4 are those of a tube with changing wall properties at some point, hereby affecting propagating velocity.

Displacements of the first maximum of upstroke are 10-150 μm which is comparative to skin displacements above the CCA in a human subject. By tracking the 50% of maximum upstroke, it can be observed that determination of the PWV is not straightforward anymore.

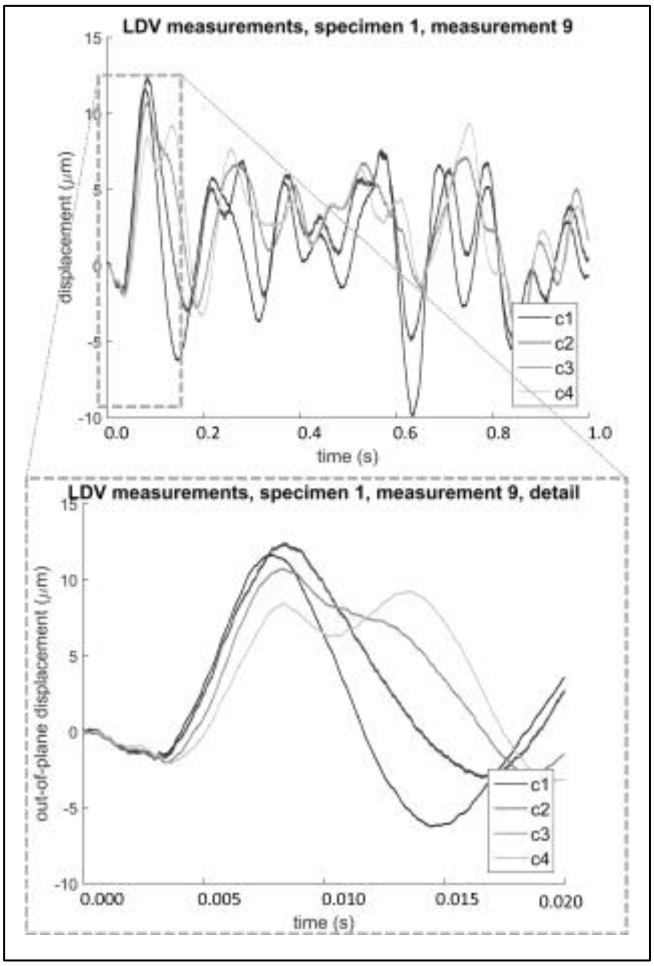

Fig. 2. Assessment of the pressure waveform in a uniform tube (specimen 1). Measurement beams were spaced 1-2 cm apart along the tube. C1-4 denotes the order of position with c1 being more upstream. Detail of the waveform shows the shift of the incoming wave-front in time (lower pane). By tracking this wave-front, PWV can be determined.

The linear relationship between propagation of the wave-front in time and the traveled distance of the wave-front is lost, as reflected in the R-squared values which are between 0.70 and 0.90 (Table I). By assessing the propagation of the pulse wave in time, changes in wall structure and location of these changes can be determined as can be seen in Fig. 4. Despite the complex nature of the signal, waveforms are reproducible in all 4 specimens, showing the same features between measurements.

I. Discussion and Conclusion

In this study, a 4-channel fiber-based LDV system was used for stiffness determination in a phantom setup for the first time using 4 different specimens. The different types of phantoms studied mimic different disease states of the artery, some with local hardening or stiffening of the wall.

Specimens 1 and 2 had uniform wall properties. Since PWV is expected to remain constant when properties remain identical, the uniform wall structure is visible in the linear relationship between propagation of the wave-front in time and the traveled distance of the wave-front. This is reflected in the high R-squared value: the closer this value gets to 1, the more ideal is the linear relationship (see Fig. 1.).

Specimens 3 and 4, however, had dramatic change in wall properties for the last 5 cm of the tube causing the PWV to change locally. The 4 channels allowed visualization of the change in vessel structure by displaying the change in pulse propagation. The distorted linear relationship is reflected in the lower R-squared value.

Despite local increase in stiffness, PWV values are very similar between samples. This is probably due to the heterogeneous nature of the vessel walls, with local increase of stiffness being masked by the average PWV. Therefore, R-squared value has more potential as a measure for uniformity of the vessel wall as demonstrated in [15] (Table I).

The system in this study is promising for development of a medical device since the amount of channels can be extended, and since the technology is fiber based. The latter means that the channels can be incorporated in a compact head that can be easily moved around and positioned on the patient CCA. The high temporal resolution makes that wave fronts can be followed with very narrow spacing of the measurement locations. We hypothesize, that with a larger amount of closely spaced LDV channels much smaller inhomogeneities in the vessel wall can be tracked as was already demonstrated with PWI [15], or maybe even more detailed information about plaque structure can be visualized as suggested in [16].

TABLE I. PWV AND R-SQUARED VALUES[a]

Specimen	***PWV (m/s)±SD***	***R-squared±SD***	***N***
1	4.9±0.6	0.98±0.02	8
2	5.3±0.2	0.96±0.01	11
3	3.6±0.1	0.87±0.01	10
4	4.6±0.9	0.79±0.04	9

[a] PWV and R-squared values are averages with standard deviation (SD). N is the number of samples. In specimen 1 and 4, 2 and respectively 1 measurements were omitted due to unwanted artifacts.

The latter is much of clinical importance: While plaque formation is a natural phenomenon of arterial aging, not all plaques are considered dangerous when stenosis is within certain limits. Vulnerable plaques on the contrary, are more prone to rupture and causing stroke when present in the CCA [17]. It is believed that these plaques show different features than non-vulnerable plaques [18], and a technique to identify the latter type of plaques is therefore much sought after. Currently, ultrasound-based techniques are being developed to quantitatively characterize vulnerable plaque [19], [20]. However, none of the quantitative techniques are ready for commercial use.

Local carotid PWV can also be measured using magnetic resonance imaging (MRI) (e.g. [21], [22]) and pulse wave imaging (PWI) (e.g. [14], [23]). However, vibrometry potentially offers some added value over other local PWV detection techniques: the LDV device can be made compact and handheld, and no bulky ultrasound or MRI equipment is needed. Also, the readout of the measurement is direct with no laborious post-processing of huge datasets, such that results can enter the statistics easily. This makes introduction in the clinical practice feasible, and also allows for large scale studies. Finally, the technique is non-contact, avoiding that any interference with artery mechanics during measurements.

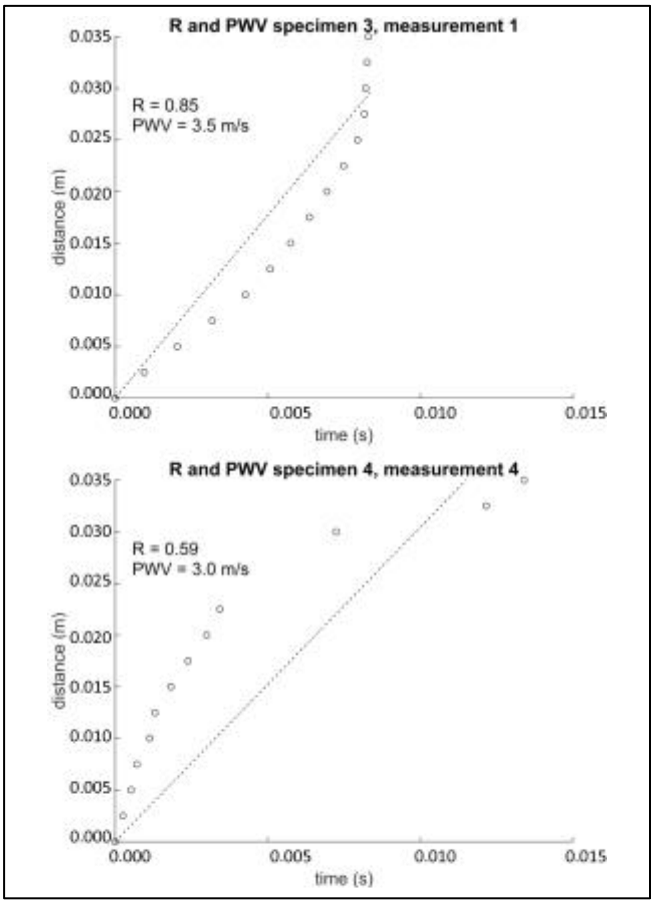

Fig. 3. When evaluating propagation of the wave-front in specimens 3 and 4, it can be noticed that PWV changes along the trajectory as caused by local changes in structure. This deviation from the normal linear relationship is reflected in the R-squared value of the different specimens.

In conclusion, the 4-channel vibrometer is a promising tool for PWV detection in a phantom setup. Current study focusses on measurement in phantoms. However, displacement amplitudes, size of the specimens and carotid PWV are in the same order of magnitude as in vivo conditions [13]. Therefore, we assumed that the transition to in vivo measurements is feasible, and in vivo measurements are currently ongoing. The biggest challenges are limited to positioning of the measurement system and the test subject. For introduction in a clinical setting, a higher amount of closely spaced channels will be required in a small portable head. The higher amount of channels, possibly allows for detection of topical vessel pathologies caused by atherosclerosis, detection of stiffness, and maybe even discrimination of different types of plaques.

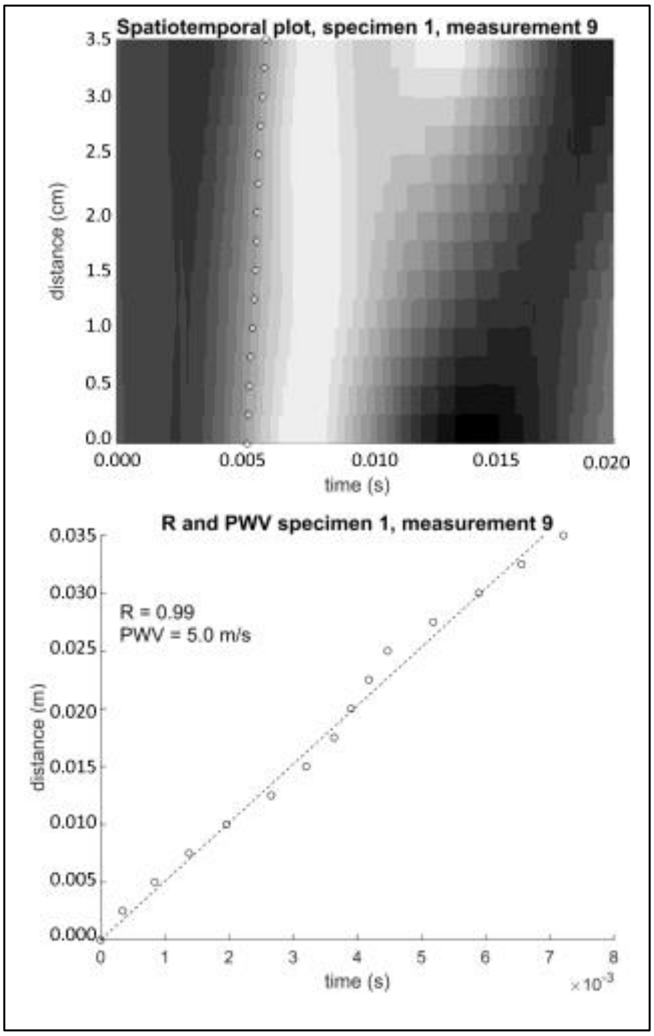

Fig. 4. In order to allow better visual inspection of the measurement, 4 time-series were interpolated to have 10 time-series. A spatiotemporal plot of time versus measurement position allows then visualization of the propagating wave-front in the tube, as assessed with the vibrometer system (upper pane). The grey color code of the upper pane represents arbitrary units of displacement amplitude. Evaluation of the 50% of maximum upstroke against measurement location, allows determination of PWV and R-squared value.

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