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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

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0. 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.

Keywords: Laser Doppler Vibrometry; Common Carotid Artery; Arteriosclerosis; LDV; CCA; PWV.

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.

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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 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 weight 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.

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 (Figure 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.

Phantom	Phantom composition			
	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

Table 1: Phantom overview with geometry of 4 different phantoms.

Figure 1: Picture (a) and schematic rendition (b) of the LDV setup. In (a) 4 LDV heads (1) are aimed through mirrors (2) at the surface of gelatin-embedding the phantoms (3). The negative pressure pulses are generated by releasing the paper clamp (4). In (b) 4 LDV heads (LDV 1-4) are aimed on the stiff phantom (dark gray). The three other phantoms are also embedded in the same container. Light gray indicates soft silicone material, dark gray indicates stiff silicone material.

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 (Figure 1). In each configuration, 10 to 15 measurements were performed, with a duration of 2 seconds 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 seconds 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 in the linear array, to measure the distension of the vessel along the array over time. Since distension and pressure are closely related, the progression of the pressure wave can be detected along the array over time. This way, the PWV can be measured [42]. The PWI post-processing methodology utilized in the current study is described in [22].

2.4. Pressure-Area measurements

In an identical setup as in the previous section, a pressure catheter (PCU-2000, Millar, Houston, Texas, USA; MPR-500, Millar, Houston, Texas, USA) was inserted in the phantom within the field of view of the ultrasound probe. Pressure and wall displacement measurements were simultaneously recorded. The recorded pressure waveform was sampled at 50 kHz. From the displacement waveforms of both top and bottom wall, the crosssectional area of the vessel lumen was derived assuming circular profile of the vessel. The pressure data was downsampled to a sampling rate of 5 kHz, and smoothed with a moving average filter (window-size of 150 points) in order to make comparison with the displacement waveforms. Then, from the PA curve from a whole measurement, an estimate of the PWV was made using the Bramwell-Hill equation:

$$PWV = \sqrt{\frac{dP * A}{\rho * dA}} , \quad (1)$$

where dP denotes the change in pressure, dA the change in area of vessel lumen, A the vessel lumen and ρ the water density. The Bramwell-Hill equation theoretically links PWV, distensibility and pulse pressure. It was derived from the Moens-Korteweg equation which, under modeling assumptions (e.g. vessel wall thickness is small compared to the diameter and the circulating fluid within the vessel is incompressible and nonviscous), relates arterial stiffness and PWV [43].

2.5. Data analysis

The propagation of the pressure wave, or pulse transit time (PTT), was analyzed in both datasets using the 50% upstroke of the out-of-plane displacement of the gelatin displacement (LDV) or the change in lumen diameter (PWI) as the respective tracking feature. This point in the displacement waveform is the time-point, at which the displacement of the gelatin surface/change in lumen diameter reaches 50% of the maximum displacement/change in lumen diameter due to pressure changes in the vessel as compared to the resting state. The pressure pulse used in this setup was generated by releasing a paper clamp, thus generating a negative pressure wave. Therefore, the area of the vessel lumen decreases and the gelatin surface indents at the negative peak of the pressure pulse. From the PTT and the measurement positions (D) along the phantom, the PWV was calculated by evaluating the slope of the linear relation between PTT and D (Figure 2). Additionally, an R^2 value was calculated from this linear relationship and was used to assess the quality of the PWV measurements [37]. In the graphs to be shown, the mostly upstream measurement positions would be the closest to the origin. The measured waveforms from the 4 LDV beams were interpolated linearly in the spatial domain to have 10 waveforms in order to facilitate PWV analysis and qualitative comparison with PWI data (see Figure 2).

In order to analyze whether PWI and LDV can accurately characterize and differentiate between the soft and stiff phantoms used using PWV, a non-parametric Wilcoxon ranked sum test [44] was performed on the PWV data of phantom 1 and 2. This test is a non-parametric test to detect difference between matched samples.

To analyze whether LDV and PWI give similar results, a non-parametric Spearman correlation test [45]. This non-parametric test assesses how well the relation between two samples can be described with a monotonic function on the data of configurations 1-5 (see Figure 6).

Additionally, a Bland-Altman analysis [46,47] was performed on the data of configurations 1-5. This method analyses the degree of agreement between two measurement methods (see Figure 6).

Since the LDV measurements are sensitive to nanoscale displacements, vibration from the research setup (i.e. the optical table containing the setup as depicted in Figure 1) and the larger surroundings (i.e. the lab area and its surroundings) disturbed the signals significantly in some measurements. Also, phase aberration was present in the signals due to scattering effects from the phantom wall. It can be assumed, that these artifacts the measured relation between PTT and measurement position D , as evaluated by the R^2 value. Therefore, to ensure highest quality, a threshold was placed on the LDV measurements, discarding any measurement with an R^2 value less than 0.5.

3. Results

3.1. LDV measurements

The maximum amplitude of gelatin displacement is $85 \pm 16 \mu\text{m}$ in the uniformly soft phantom and $78 \pm 28 \mu\text{m}$ in the uniformly stiff phantom (see Table 2). In the uniformly soft phantom, the PWV is $1.30 \pm 0.40 \text{ m/s}$ and in the uniformly stiff phantom the PWV is $3.6 \pm 1.4 \text{ m/s}$. In configuration 3, the PWV is $1.6 \pm 0.89 \text{ m/s}$; in configuration 4, the PWV is $3.5 \pm 2.7 \text{ m/s}$ and in configuration 5, the PWV is $1.5 \pm 1.6 \text{ m/s}$ (see Table 2, Table 3, Figure 2, Figure 2, Figure 3, Figure 4). Values are being reported in mean $\pm$ standard deviation (SD).

Figure 2: Spatiotemporal maps of interpolated (4 to 10) LDV measurements in soft (a) and stiff (b) phantoms and PWI measurements in soft (c) and stiff (d) phantoms. The x-axis represents the time-domain, the y-axis represents the measurement position, and the colour indicates change in lumen diameter of the vessel (c and d) or out-of-plane displacement of the gelatine surface (a and b). The dashed line indicates the 50% threshold of maximum displacement/change in lumen diameter as used for calculating PWV. The red rectangle in (d), delineates the zone zoomed in upon in Figure 2e. The linear relation between measurement position and 50% upstroke point is clearly visible (e).

Figure 3: In (a), relation of average pulse transit time (PTT) and measurement position is indicated as measured with LDV. In (b), average maximum amplitude of surface displacements is displayed along the measurement position as measured with LDV. The different line styles represent the five different investigated configurations as described in the Methods section.

3.2. PWI measurements

The maximum incremental increase in lumen diameter between frames is $295 \pm 50 \mu\text{m}$ in the uniformly soft phantom and $97 \pm 12 \mu\text{m}$ in the uniformly stiff phantom (see Table 2). In the uniformly soft phantom, the PWV is $2.39 \pm 0.83 \text{ m/s}$ and in the uniformly stiff phantom the PWV is $4.7 \pm 1.4 \text{ m/s}$. In configuration 3, the PWV is $3.3 \pm 1.4 \text{ m/s}$; in configuration 4, the PWV is $4.5 \pm 2.6 \text{ m/s}$ and in configuration 5, the PWV is $2.787 \pm 0.050 \text{ m/s}$ (see Table 2, Table 3, Figure 2, Figure 2, Figure 4).

configuration	Method (N)	Max change in lumen diameter (PWI, μm) or max displacement of gelatin surface (LDV, μm)		
		Soft	Stiff	Soft
1	PWI (10)	295 ± 50	N/A	N/A
	LDV (10)	85 ± 16		
2	PWI (10)	N/A	97 ± 12	
	LDV (10)		78 ± 28	
3	PWI (10)	250 ± 28	91 ± 28	357 ± 30
	LDV (10)	54 ± 15	53 ± 15	63 ± 18
4	PWI (10)	277 ± 32	89 ± 31	N/A
	LDV (9)	73 ± 16	44 ± 11	
5	PWI (10)	N/A	107 ± 11	378 ± 33
	LDV (10)		46.1 ± 9.1	81 ± 16

Table 2: Increase in diameter (PWI) and displacement amplitude (LDV) in five different configurations.

Method	Configuration	Average PWV $\pm$ SD (m/s)	Average R $\pm$ SD	N
LDV	soft	1.30 ± 0.40	0.9878 ± 0.0090	10
	stiff	3.6 ± 1.4	0.915 ± 0.085	10
	1 cm	1.6 ± 0.89	0.932 ± 0.066	10
	soft-stiff	3.5 ± 2.7	0.91 ± 0.12	9
	stiff-soft	1.5 ± 1.6	0.9870 ± 0.0088	10
PWI	soft	2.39 ± 0.83	0.981 ± 0.010	10
	stiff	4.7 ± 1.4	0.9936 ± 0.0031	10
	1cm	3.3 ± 1.4	0.920 ± 0.031	10
	soft-stiff	4.5 ± 2.6	0.950 ± 0.079	10
	stiff-soft	2.82 ± 0.98	0.941 ± 0.016	10
PA	soft	1.341 ± 0.015	/	3
	stiff	2.787 ± 0.050	/	3

Table 3: The PWV of different phantoms in five different configurations as measured with PWI and LDV. N indicates sample number.

3.3. Pressure-Area Measurements

Static pressures inside the phantoms at the beginning of the experiment are between 600 and 650 Pa, pressures during the propagating pulse are between 0 and 850 Pa. The lumen area inside the phantoms is between 55 and 70 mm² for the soft phantom and 80 and 86 mm² for the stiff phantom. The PWV of the soft part is 1.341 ± 0.015 m/s, the PWV of the stiff part is 2.787 ± 0.050 m/s (see Figure 5).

3.4. Precision and accuracy estimation

PWV is determined by evaluating the slope of the linear relation between detected timepoints of 50% upstroke (T) and associated measurement location (D). Thus, PWV is a function of input quantities D and T: $PWV = f(D,T)$ and is estimated from n pairs (D_i, T_i) with ($i = 1, 2, \dots, N$) as follows:

$$PWV = f(D,T) = \frac{\sum_{i=1}^N (T_i - \hat{T}) * (D_i - \hat{D})}{\sum_{i=1}^N (T_i - \hat{T})^2} \quad (2)$$

With $\hat{D}$ and $\hat{T}$ being the means of the respective input quantities D and T. D and T are being determined by manual measurement (LDV) or manufacturers probe characteristics (PWI). Thus, the precision of D_i is estimated 1.0 mm in the case of LDV and 0.30 in the case of PWI. The precision of T_i is estimated as the sample frequency, which is 0.20 ms.

We will not consider precision nor accuracy in the phantoms containing inclusions, since these are non-ideal situation. I.e. the linear relationship between T and D is strongly biased. The combined standard precision for the smooth phantoms (i.e. the ones without inclusions) is determined using the standard deviations on the PWV, i.e. experimentally

determined precision. This standard precision is 1.4 m/s both for PWI and LDV, in this particular setup.

The accuracy is expressed as the difference between the expected PWV value and the measured PWV value:

$$\text{accuracy} = \text{expected PWV value} - \text{measured PWV value} \quad (3)$$

with measured PWV values being the PWV determined by PWI and LDV, and the expected PWV value being determined by the PA experiments. The accuracy is -0.81 ± 1.4 m/s for the LDV and -1.9 ± 1.4 m/s for PWI.

Figure 4: Comparison of the PWV as measured by three different methods. *: $p < 0.001$; **: $p < 0.0005$; ***: $p < 0.0001$ with p being the probability that results are from the same population.

Figure 5: Example of a simultaneously measured lumen area (blue graph) pressure (red graph) in soft (a) and stiff (b) phantoms.

3.5. Comparison of methods

The non-parametric Spearman correlation analysis of all five measured configurations comparing 2 measurement techniques, shows a Spearman- ρ 1 at a significance level of $p < 0.05$. The Bland-Altman analysis of all five measured configurations comparing 2 measurement techniques shows a mean bias of -0.63 m/s and limits of agreement between -0.35 and -0.90 m/s (see Figure 6).

Figure 6: Correlation plot (left) and Bland-Altman plot (right) of the PWV as measured with PWI and LDV. The Spearman correlation analysis returns a Spearman- ρ 1 with $p < 0.05$; the Bland-Altman analysis shows a mean bias of -0.63 m/s and limits of agreement between -0.35 and -0.90 m/s.

Figure 8: B-mode Image of a uniformly soft phantom as acquired with the ultrasound (PWI) method.

4. Discussion

4.1. Introduction

Arterial stiffness is an important parameter in the aetiology of CVD and research is ongoing to assess arterial stiffness to acquire a better understanding of this parameter and to use it for cardiovascular screening. Several approaches are currently being explored for reliable measurement of local CCA stiffness. CCA stiffness has clinical significance as a putative indicator of large artery stiffness, and it is suspected to be an indicator of vulnerable plaque formation. Recently, LDV is being developed for local stiffness detection. The aim of this study was to compare LDV with the more established PWI technique *in vitro* and validate both techniques against ground-truth PWV values derived using PA testing. Additionally, it was tested whether local changes in phantom structure can be detected using LDV. For this purpose, PWV was measured in vessels containing a local hardening of the vessel wall.

4.2. Comparison of PWV measurements in smooth vessels

The spatial resolution of LDV was 30 times lower than PWI's. Moreover, PTT was evaluated based on the waveform (using the 50% upstroke method). The origin of the waveform, is very different in both techniques, with the waveform evaluated in PWI being the change in diameter of the vessel lumen, and the waveform evaluated in LDV being a displacement of

the gelatine surface covering the vessel. Thus, although the reference point is the same from a signal processing perspective, the physical meaning will be different. Nevertheless, both methods yielded similar findings (see Table 3 and Figure 4) as reflected in the correlation (see Figure 6a) and the Bland-Altman analyses (see Figure 6b). Additionally, both PWI and LDV were capable of distinguishing soft from stiff phantoms (see Table 3 and Figure 4), and PWV values measured in these phantoms were in line with theoretical “ground-truth” PWV values as derived from the PA relationship.

4.3. Comparison of PWV measurements in vessels containing an inclusion

Soft phantoms containing a stiff inclusion, had a higher overall PWV value compared to their uniformly soft counterpart (see Figure 4). It can be assumed that the velocity of the pulse wave was affected locally by the local changes in artery stiffness [22]. However, since only 4 measurement points were used, these local changes in PWV could not be readily observed using LDV. It should be noted that the measurement errors are in general larger, when measuring on a reflection site, as is the case in situations 3-5 (coefficient of variation is on average $34\pm 4\%$ for the smooth vessels, and $62\pm 26\%$ for the vessels containing an inclusion). At the site of the inclusion, where the pressure wave propagates from the soft-to-stiff, or from the stiff-to-soft part of the phantom, reflections and other significant perturbations of the system emanate locally, causing variability in the measurement outcome. Moreover, the traditional way of estimating PWV (in contrast to e.g. piece-wise pulse wave analysis [22]), assumes that distensibility does not change along the vessel. However, when evaluating the PWV over an inclusion with altered distensibility, this assumption is violated, resulting in biased PWV results.

In the displacement results (see Figure 3), it could be observed that the wall displacement and diameter change is larger in the softer parts and smaller in the stiffer parts (70-80 μm compared to 50-60 μm and 250-280 compared to 80-110 μm respectively), representing the phantom structure accurately. It should be stressed that the discordance between displacement and diameter values (table 2), is because they have a different physical meaning: the values originating from PWI measurements represent change in lumen diameter, i.e. the change due to combined downward movement of the upper wall and upward movement of the lower wall of the vessel; while the values originating from LDV measurements represent downward displacement of the surface of the gelatine covering the vessel. However, for a LDV-driven quantitative assessment with exact pinpointing of the location of the structural differences within the phantom, a higher number of beams is likely to be required, potentially even to match spatial resolution of PWI (128 beams per 38 mm).

4.4. Translation to the clinic: where are we now?

In the uniform vessels, the standard precision was determined as 1.4 m/s both for PWI and LDV and the accuracy was determined as -0.81 ± 1.40 m/s for the LDV and -1.9 ± 1.4 m/s for PWI measurements. However, the authors stress that the uncertainties from a measurement setup will not transfer readily to a real-life biomedical situation. The artefacts in this environment very different, and are likely to pose additional challenges. Carotid-femoral PWV, is extensively described in the literature. Reference “healthy” and “at-risk” values have been determined for each age group, and the relation between carotid-femoral PWV and several pathologies has been described. E.g., in a healthy, young (<30

years old) population, the carotid-femoral PWV can be expected to fall between 4.7 and 7.6 m/s [48], while in hypertensive patients, a carotid-femoral PWV above 13 m/s is a strong predictor of cardiovascular mortality [49]. However, similar extensive research has not yet been accomplished for CCA PWV. Although the literature suggests that CCA PWV values generally fall in the range of 4.3 to 8.3 m/s (e.g. [31,36]) in young healthy volunteers, research is scarce, and very little is known about CCA PWV in age and disease, and CCA PWV for use in plaque determination is in early stages of exploration [50]. Future research will reveal what requirements are needed on the level of precision and accuracy with current approaches, either for stiffness detection or for plaque determination.

4.5. The benefits and weaknesses of LDV as apparent from this experiment

At present, the spatial resolution of LDV is low compared to PWI. Moreover, LDV measures displacements at the nanoscale level [51,52], making a measurement susceptible to all kinds of artefacts, such as ringing and other vibrations in the measurement environment, or involuntary body motions [33]. Also, it should be noted, that the LDV only measures displacement information of the outer wall of the CCA, possibly masking stiffness information of the inner wall. This in contrast to PWI, which is capable of measuring displacement information of both inner and outer CCA wall (see Figure 8) while additionally providing valuable information such as blood velocity, degree stenosis and plaque anatomy. Also, accurate and reproducible positioning of the LDV device is challenging, especially in elder or obese patients, while lacking the window on the CCA anatomy as is the case with PWI. Finally, CCA anatomy differs between subjects, with the CCA sometimes lying deeply hidden in the flesh, or close or under other moving structures such as the jugular vein. Not only does this make it difficult to detect the trajectory of the CCA, but it can also contaminate the displacement signal [53].

On the other hand, the readout of the displacement measurement is direct with no extensive post-processing of large datasets, such that results can be acquired in real time. The technique is non-contact, avoiding any interference with artery mechanics during measurements [33].

General limitations of local PWV detection include susceptibility to reflections, the effect of various artefacts on modulus estimations and accurate positioning of the measurement probe [37].

4.6. Conclusions

In conclusion, PWV values as measured with LDV and PWI are in concordance, despite fundamental differences in measurement approach. Additionally, PWV values as measured with LDV correspond to ground-truth PWV values. The low spatial resolution of LDV prohibits exact pinpointing of the local inhomogeneities of the vessel wall, either with PWV of local displacement data. It is likely that an increase in beam density will enhance performance for inclusion detection. The translation of the LDV system to the medical practice is at current not feasible due to the bulky setup, the susceptibility to artifacts due to the high sensitivity, and the low beam density.

4.7. Future directions

Despite the limitations of LDV for PWV detection, the method is promising for development of a medical device. Recently, there is an emergence of experimental and industrial systems for multi-point vibrometry (up to 48 channels in some recent models). Also, on-chip integrated LDV arrays are under development, potentially decreasing cost and size of a measurement device [54].

Using fibre technology, or on-chip integration, a high number of beams could be incorporated in a compact head or even a wearable. The high temporal resolution of LDV can be used to have closely spaced channels. In combination with the high measurement sensitivity [51,52], this can potentially aid in finding deeper arteries, it could help detection of local inhomogeneities in the vessel wall as previously demonstrated with PWI and piecewise PWV analysis [22] or PWI and pulse wave inverse problem analysis [55], or even distinguish between vulnerable and non-vulnerable plaques based on the properties both on the level of local PWV behaviour and wall displacement.

In future work, a LDV device with higher spatial resolution will be developed and tested in an *in vivo* validation study. The biggest challenges will be accurate and reproducible positioning of the measurement system and the test subject. For optimal performance, a higher number of closely spaced channels will be required in a small portable head. Additional channels may aid in the detection of topical vessel pathologies caused by atherosclerosis, detection of stiffness, and possibly even discrimination of different types of plaques.

5. References

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