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Arterial pulse wave velocity in coronary arteries

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Abstract— **Pulse wave velocity is related to arterial stiffness. Pulse wave velocity changes with age and disease and is a useful indicator of cardiovascular disease. Different methods are used for evaluating pulse wave velocity in systemic vessels, but none is applicable to coronary arteries.**

In this study we first compare values of wave speed (c) calculated from measurements of pressure (P) and velocity (U) using different analytical methods: PU-loop, β stiffness parameter, characteristic impedance, foot-to-foot method, and the sum of squares (Σ^2), a novel way of calculating the wave speed (calculated from the square root of the sum of the ratio of the dP^2 and dU^2 over a complete cardiac cycle). Results from human measurements using Doppler ultrasound on carotid arteries show good correlation between the PU-loop method, β stiffness parameter and Σ^2. Characteristic impedance calculations show the greatest variation of all methods. The Σ^2 method was further assessed in vitro for use in coronary vessels.

Pressure and velocity measurements were obtained from human coronary arteries following Angiographic studies. The measurements were made invasively by co-locating two wires with pressure and velocity transducers. Pressure and velocity data in the left anterior descending, circumflex, left main stem and right coronary arteries were acquired simultaneously along with the ECG signal. Wave speed was calculated using Σ^2. Wave intensity analysis was used to determine forward and backward traveling waves at different times in different locations, for which wave speed, approximate distance and timings between waves need to be known.

I. INTRODUCTION

Arterial stiffness is as an important predictor of cardiovascular events [1]. Various indices have been applied to quantify arterial stiffness, and they all provide approximations due to the nonhomogeneous structure of the arterial wall, its structural variation at different locations, changes in smooth muscle tone and non-linear stress-strain relationship with varying blood pressure. Measures of arterial stiffness include: distensibility, compliance, elastic modulus, volume elastic modulus, Young's modulus, pulse wave velocity (PWV), characteristic impedance, augmentation index, β stiffness parameter, capacitive and oscillatory compliance. PWV is probably the most widely used clinical measure of arterial stiffness, but importantly, none of the previous methods for measuring arterial stiffness can be used in the human coronary arteries.

In this study we explored different techniques for calculating wave speed: the foot-to-foot method, characteristic impedance, the PU-loop method, β stiffness parameter and the sum of the squares (Σ^2). Each of these methods suffers from inaccuracies and difficulties in their calculation and there is no gold standard.

The foot-to-foot method depends upon the transit time of the pressure wave and the distance between two sites of pressure measurement. The time delay can be obtained between two simultaneously recorded pressure waves or by gating each individual pressure measurement with the ECG. The distance between measurement sites generally cannot be measured exactly. This technique relies on the identification of the "foot of the wave" or an easily identifiable feature of the pressure curve and an approximation of the length of the vessels in which the wave speed is to be determined. It provides an average wave speed over the whole of the distance between the measurement sites.

Characteristic impedance employs the average of the impedance moduli over a specified frequency range for which it is assumed that wave reflections are negligible. Many frequency ranges have been suggested by different authors, and no consensus has yet been reached [2]-[6]. An impedance change can be related to changes in elastic properties, cross-sectional area or wall thickness.

The PU-loop method relies upon the identification of a linear portion of the pressure-velocity curve when only forward waves are present [7]; its slope is equal to ρc (where ρ is the density of blood). This technique provides information of the local wave speed at a single measurement site. However, it depends on the correct selection of the linear portion of the slope that corresponds to unidirectional wave travel. The absence of a period of unidirectional waves makes this method unsuitable for wave speed calculation in the coronary arteries.

The β stiffness parameter relates the logarithm of the ratio of systolic and diastolic pressure and the relative changes in diameter which determine the elastic properties of the vessel, $ln(P/P_0) = \beta(D - D_0)/D_0$, for calculating wave speed as $c_\beta = (\beta P/2\rho)^{1/2}$ (ρ being blood density) [8] . It can be measured non-invasively using ultrasound techniques, however, wall tracking of the vessel is essential and no consensus has yet been reached regarding the vessel layer that should be tracked.

Σ^2 requires simultaneous measurements of pressure (P) and velocity (U) at a single point over a cardiac cycle. It is calculated as

$$c = \frac{1}{\rho}\sqrt{\frac{\sum dP^2}{\sum dU^2}} \qquad (1)$$

It does not rely upon there being a period when only

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unidirectional waves are present and therefore can be used in the coronary arteries, unlike the other methods [9]. However, theoretically it can provide erroneous results when measurements are done very close to a large reflection site so that there is significant concurrence between forward and backward waves.

A. Wave Intensity Analysis

Wave intensity analysis refers to the energy flux per unit area (W/m^2) carried by a wave [10]. It uses one-dimensional flow equations of mass and momentum conservation solved through the method of characteristics, thus accounting for non-linear components of flow in elastic arteries and holding the advantage of time domain treatment. Flow is assumed unsteady, incompressible and inviscid in an impermeable, uniform elastic tube. It requires the knowledge of the wave speed for performing wave separation into their forward and backward going components. This technique has recently been used for elucidating the nature of waves in the coronary arteries in health and disease [11]. Wave speed calculation is important for timing wave interaction in different vessels throughout the cardiac cycle, thus providing knowledge of large reflection sites and the energy flux of blood flow to the coronary tree during cardiac muscle contraction.

II. METHODS

A. In-vivo, non-invasive human data measurements

All in vivo studies were approved by the St. Mary's Hospital local ethics committee and performed in accordance with institutional guidelines; all participants provided full informed consent. Non-invasive measurements of pressure and velocity in left and right carotid arteries were obtained from subjects with no stenosis and no haemodynamically significant atheroma (8 males; aged 23 - 31 years). ECG R wave was used as a fiducial marker. Flow velocity was measured using an Aloka 5500SV ultrasound machine (Aloka, Inc.) It also provides an in-built wave intensity analysis system and uses an e-tracking technique from which a pressure waveform is obtained assuming that changes in diameter are linearly related to changes in pressure [12]. Brachial blood pressure was measured using a validated automated device (Omron HEM-705-CP). Applanation tonometry was also used for obtaining a secondary pressure waveform [13].

To minimise inter-observer errors on the e-tracking location point, measurements were made on both carotid arteries (right and left)[14]. Furthermore, measurements were done at the intima (inner boundary) and intima-media complex at about 2 cm proximal to the bifurcation (completing a total of 4 data sets per subject).

The slope of the PU-loop was calculated using an automated program for selecting the most probable linear segment of the curve using a Bayesian statistical algorithm implemented in Matlab (The MathWorks, Inc.) The characteristic impedance calculation to determine wave speed used five different algorithms previously proposed in the literature (see Table I).

TABLE I
CHARACTERISTIC IMPEDANCE ALGORITHMS TESTED

Z_1	Milnor et al. (1978)	7 to 15 harmonics $>$ 1.3 Hz
Z_2	Stergiopulos et al. (1999)	3^{rd} to 10^{th} harmonic
Z_3	Van Huis et al. (1987)	20 harmonics $>$ 7 Hz
Z_4	Cox et al. (1975)	9 to 18 Hz
Z_5	O'Rourke et al. (1967)	15 to 25 Hz

B. In-vitro experimentation

For in vitro validation of Σ^2, P and U measurements were recorded in thin walled elastic latex tubes (0.8 mm diameter, 100 cm long and 0.25 ± 0.08 mm wall thickness). Because thin walled elastic latex tubes are manufactured by dipping, wall thickness decreases along the tube. The tubes were cut in half (50 cm length) and classified into two groups according to their averaged measured wall thickness. A constant steady laminar flow system was built in such a way that it minimised reflection sites and maintained a constant high velocity in a floating elastic latex tube with an open end configuration. The experimental system provided the possibility of imposing a sudden sharp pulse that travelled along the latex tube, generating unidirectional waves that travelled and reflected back from the tube end. Pressure and Doppler guide wires (5-Star WaveWire and FloWire, Volcano Corp.), and WaveMap and FloMap consoles (Volcano Corp.) were used. Data acquisition was performed using a BNC2090 DAQ board (National Instruments) and Labview (National Instruments). Wave speed was calculated using the Moens-Korteweg equation, the foot-to-foot method, the PU-loop method using the same Bayesian statistical best fitting program and Σ^2 technique.

C. In-vivo, invasive human coronary data measurements

Simultaneous ECG and intra-arterial pressure and velocity measurements were made from patients undergoing coronary angiography whose arteries have been judged to be angiographically normal. Measurements were taken in the aorta, left anterior descending, circumflex, left main stem and right coronary arteries. Pressure and Doppler velocity measurements were made using the same equipment as in the in-vitro studies. Measurements were recorded for 1 min in each vessel, and in the aorta the wires were pulled-back and measurements taken every 10 cm starting from the aortic root. Wave speed in the coronaries was calculated using Σ^2 and in the aorta Σ^2 was compared with the foot-to-foot method.

III. RESULTS

A. In-vivo, non-invasive human data measurements

A Wilcoxon signed rank sum test rendered a non-significant difference between both tracking sites. We presume that the sample size was small for obtaining significant results. In practice, the intima-media complex tracking proved easier to perform.

It is not a priori expected to obtain exact same wave speed values on both left and right carotids. Results show that

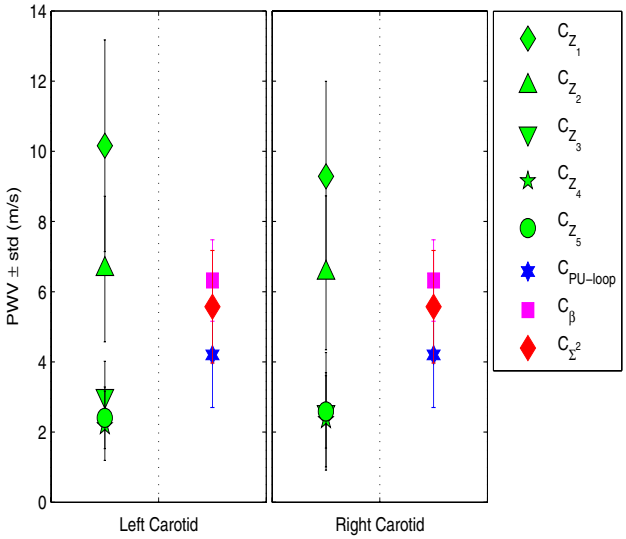

Fig. 1. PWV (avg± std dev) in left and right carotid arteries using intima-media complex tracking. Characteristic impedance (at the left column of each graph) was calculated using algorithms described in Table I. PU-loop, β stiffness parameter and Σ^2 plotted at the right columns.

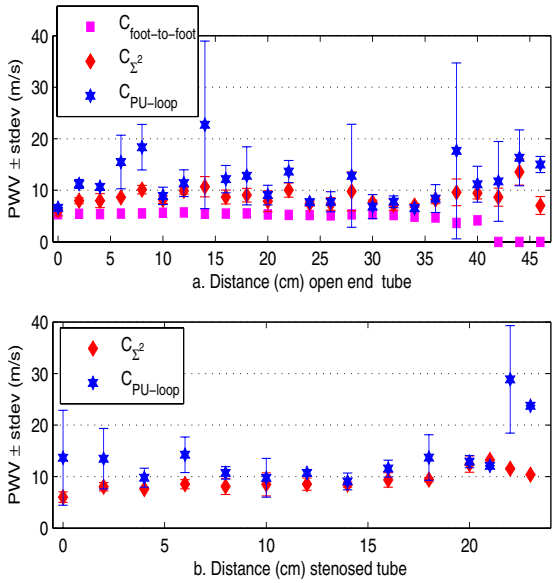

Fig. 2. PWV (avg± std dev) measured every 2 cm in thin walled, elastic latex tubes using the foot-to-foot, PU-loop and Σ^2 methods; (a.) in an open end configuration and (b.) with a 50% stenosis at 23 cm.

wave speed in the right carotid was slightly lower than wave speed in the left carotid (see Fig. 1), but most important are the values in which PWV calculated using characteristic impedance algorithms range (plotted in left column of each graph). The standard deviations are visibly larger for characteristic impedance techniques. Higher harmonic ranges provide lower PWV values and viceversa. In the right columns of each vessel data in Fig. 1, PWV calculated using PU-loop, β stiffness parameter and Σ^2 show high correlation. Standard deviations are generally smaller, and a Wilcoxon signed rank sum test rendered C_{Z_1} as the highest value (rank 8), followed by C_{Z_2} (rank 7), C_β (rank 6), C_{Σ^2} (rank 5), $C_{PU-loop}$ (rank 4), C_{Z_3} (rank 3), C_{Z_5} (rank 2) and C_{Z_4} (rank 1), being the lowest.

B. In-vitro experimentation

PWV was calculated every 2 cm along the thin-walled latex tube (see Fig. 2). Wave speed as calculated using Σ^2 agrees closely with the results of the PU-loop method and ranks in between this method and the foot-to-foot method. Total average numerical values can be observed in Table II.

Σ^2 method standard deviation is lower than that of the PU-loop method. All methods fail when used for data measured very close to a major site of reflection since, as effectively, there is no period when there are unidirectional waves and foot-to-foot measurements are impossible. In principle, use of higher sampling rates should overcome this problem, but this is limited in practise. However, it is important to note that Σ^2 still provides a reasonable approximation of wave speed in this circumstance.

The different wall thicknesses used for the classification of the elastic tubes is reflected in the wave speed calculations as observed in Table II. It also shows the theoretical wave speed as obtained using the Moens-Korteweg equation (C_{MK}), which employs the Young modulus, wall thickness and diameter.

TABLE II

WAVE SPEED IN THIN, ELASTIC LATEX TUBES (M/S) ± STD ERROR

	Avg wall thickness (mm)	C_{PU}	C_{Σ^2}	C_{FtF}	C_{MK}
Open end	0.21	13.5±1.0	9.4±0.3		5.6
	0.14	11.7±0.8	8.7±0.3	5.2±0.1	4.2
Stenosed	0.21	17±1.2	11.1±0.7		
	0.14	13.7±1.4	9.3±0.5		

C. In-vivo, invasive human coronary data measurements

Pressure and velocity measurements were obtained from angiographically normal patients from aorta, left main stem, left anterior descending, circumflex and right coronary (Fig. 3). The local PWV was calculated using Σ^2 (see Table III.)

IV. DISCUSSION

A reliable method for estimating local wave speed in the coronaries is needed for performing wave separation and, with the exception of Σ^2, no existing techniques can do this.

TABLE III

WAVE SPEED (M/S) IN CORONARY ARTERIES

	Root Aorta	Renal Aorta	LMS	LAD	CX	RCA
Wave speed	5.65	7.54	11.13	12.79	10.72	13.12

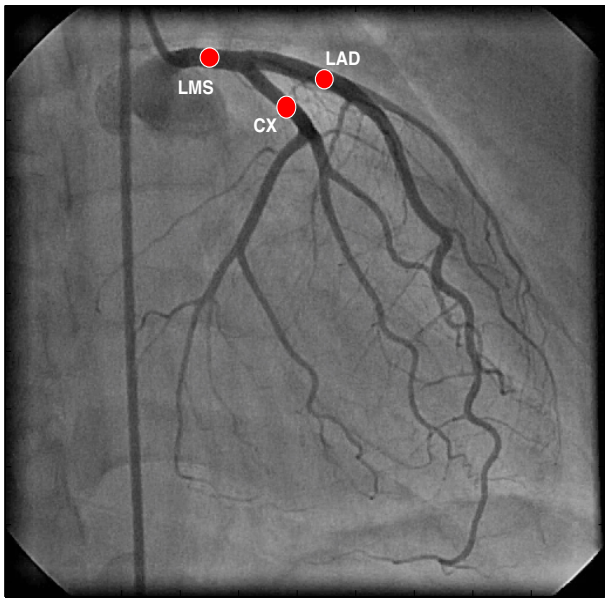

Fig. 3. Left main stem (LMS), left anterior descending (LAD), circumflex (CX) arteries: location of the pressure and velocity measurement sites.

However, wave speed is not simply a parameter in wave equations, since it provides a measure of vessel stiffness, and sets the distance-time frame for assessment of propagating waves and reflection sites. The approach presented in this paper offers a novel approach to this problem, but further analysis and validation is an ongoing research.

V. CONCLUSIONS AND FUTURE WORKS

A. Conclusions

There is no Gold Standard technique for calculating wave speed. The sum of the squares method (Σ^2) provides a good estimate of wave speed with low variation. It is easily applicable to data collected in any artery, including the coronaries, but particular care must be taken in regions close to major reflection sites.

The clinical relevance of wave intensity analysis is receiving increasing attention as a diagnostic tool, as it provides data on the source of waves, wave interaction and wave propagation in the arterial system, including the coronary tree [11]. Wave mapping can also provide a better insight into the mechanisms of coronary blood flow.

B. Future Works

Wave separation in coronary arteries allows us to distinguish the origin of each wave that contributes to the characteristic waveform in any blood vessel. In the coronary arteries multiple waves are evident throughout the cardiac cycle and the patterns of waves also differ by vessel location and the propagation of contraction in the heart muscle. Mapping wave travel in the cardiovascular system with the knowledge of the timings of waves in different vessels, the wave speed and the spatial location of pressure and velocity measurements is an important future goal.

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