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Pressure reservoir-wave separation applied to the coronary arterial data

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***Abstract*— Pressure waveforms measured at different locations in the coronary arteries are similar. Previous work has shown the cardiovascular system can be modelled as a Windkessel and wave system. [1] We now suggest that simultaneously measured coronary pressure, P, and velocity, U, can be used to calculate the separated reservoir, $\bar{P}$, and wave, p, pressure such that $P = \bar{P} + p$. This separation enables us to deduce the resistance of the coronary microcirculation as it varies with time; resistance during systole being almost double the resistance during diastole. Wave intensity analysis is used to separate forward and backward waves. This requires knowledge of the local wave speed, c, which is determined from the data using the sum of squares technique. [2] Wave timings differ at different sites in the coronary tree, revealing the complexity of wave propagation. [3] Their mapping give a fairly complete picture of wave travel in the coronary network and insight into the physiology of coronary artery flow in health and disease. [4]**

I. INTRODUCTION

Reverend Stephen Hales, in 1733 in his book Haemostatics, was the first one to describe the concept of peripheral resistance and the cushioning effect of the arterial system to maintain nearly constant blood flow to the tissue. It was afterwards that Otto Frank described the model quantitatively in 1899. He suggested an air chamber or *windkessel* model [5], which highlights the importance of the arterial compliance in transforming the discontinuous cardiac output into a more steady pressure and flow in the arteries and microcirculation. If arteries were rigid, pressure changes would occur at the same time everywhere in the system, and the blood flow into the microcirculation would be instantaneously equal to the blood flow out of the ventricle, leading to zero blood flow during diastole.

The windkessel model is a good model to explain diastole, but it fails to explain systole. Euler in 1775 described the basic one-dimensional partial differential equations for inviscid flow in elastic arteries employing the conservation of mass and momentum [6]. These equations were solved by Lambert in the time domain using Riemann's [7] method of characteristics, while Womersley solved them in the frequency domain using Fourier analysis. [8] Both solutions show that pressure and flow can be separated into forward and backward waves [9], [10]. However, forward and backward waves fail to explain pressure and flow waveforms during diastole. Wang et al. [1] proposed a unifying windkessel-wave theory that fully explain pressure and flow waveforms in the root of the aorta. They separated the measured pressure into a Windkessel and an excess pressure in the time domain employing simultaneously measured flow. [1]

In this study we extend that approach to the coronary arterial network, where the exponential diastolic decay of pressure waveforms in diastole are very similar to those measured at the root of the aorta even when measured velocities are extremely different to the velocities observed in the systemic arteries (as shown in figs 1 and 2). We therefore calculate a time-varying reservoir pressure $\bar{P}(t)$ and a distance- and time-varying wave pressure $p(x,t)$ by fitting an exponential function to the diastolic decay of the measured pressure P; defining that $P(x,t) = \bar{P}(t) + p(x,t)$. We explored the implications of applying the technique to *in-vivo* human data.

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II. METHODS

A. Experimental Methods

Simultaneous ECG and intra-coronary P and U measurements from patients with arteries judged to be angiographically normal were made in Left Anterior Descending (LAD), Circumflex (CX), Left Main Stem (LMS), Right Coronary (RCA) and Aorta (Ao) using a ComboWire and ComboMap (Volcano Corp.) All subjects gave written informed consent in accordance with the protocol approved by the local ethics committee.

B. Theoretical Methods

Assuming that $\bar{P}$ is determined from the conservation of mass:

$$\frac{\mathrm{d}V}{\mathrm{d}t} = Q_{in} - Q_{out}, \tag{1}$$

that the arterial system is compliant and the microcirculation exerts a resistance to flow and that we can approximate Q_{in} as being proportional to the difference between P and $\bar{P}$ [1]. Q_{in} can be written as $Q_{in} = a(P - \bar{P})$, where a is a rate constant (s^{-1}) which will depend upon a number of factors including the local wave speed. Re-stating:

$$\frac{d\bar{P}}{dt} = a(P - \bar{P}) - b(\bar{P} - P_v), \tag{2}$$

where $b = 1/\tau$ is also a rate constant of the system with units (s^{-1}). P_v is the venous pressure.

Inflow to the arterial system is equal to zero ($Q_{in} = 0$) when the aortic valve is closed (for $T_N \leq t \leq T$, where T_N is the time of the pressure notch and T is the time when the heart beat ends). During this period of time equation (2) reduces to

$$\frac{d\bar{P}}{dt} = -b(\bar{P} - P_v), \qquad T_N \leq t \leq T. \tag{3}$$

Solving (3) we obtain:

$$\bar{P} - P_v = (\bar{P}(T_N) - P_v)e^{-b(t-T_N)}, \quad T_N \leq t \leq T. \quad (4)$$

Since the reservoir is the main driver of the exponential pressure fall off in diastole, we can estimate the constant parameters in (4), $\bar{P}(T_N)$, P_v and b by fitting them to experimental data P using an unconstrained non-linear optimization algorithm. We assumed $P_v = 0$ since the venous pressure is unknown.

For systole, (2) can be solved explicitly using the integration factor $e^{(a+b)t}$ as

$$\bar{P} = \frac{b}{a+b}P_v + e^{-(a+b)t}\left[\int_0^t aP(t')e^{(a+b)t'}dt'\right] + e^{-(a+b)t}\left[\bar{P}_{(t=0)} - \frac{b}{a+b}P_v\right], \quad (5)$$

where $\bar{P}_{(t=0)}$ corresponds to the diastolic P, since little wave activity is expected at the end of the previous beat. To determine the unknown parameter a we enforce continuity of $\bar{P}$ at $t = T_N$, which yields

$$\bar{P}(T_N) = \frac{b}{a+b}P_v + e^{-(a+b)T_N}\left[\int_0^{T_N} aP(t')e^{(a+b)t'}dt'\right] + e^{-(a+b)T_N}\left[\bar{P}_{(t=0)} - \frac{b}{a+b}P_v\right]. \quad (6)$$

The parameter a is also fitted from experimental data. Then $\bar{P}$ is determined for the entire period from (4) and (5).

The time-varying resistance was calculated as

$$R(t) = \frac{\bar{P}(t) - P_v}{U(t)}. \quad (7)$$

III. Results

Measurements were performed in normal human subjects during angiography. Figure 1 shows ECG gated ensemble averaged P waveforms measured in the aorta and four different coronary arteries in a single subject. Figure 2 shows simultaneously measured U at the same location. Notice how all coronary and aortic P waveforms are extremely similar; but the coronary U waveforms vary significantly to the systemic waveforms; this due to the coronary flow systolic impediment (CFSI).

Fig. 3 shows the measured P and reservoir component $\bar{P}$ calculated for the left anterior descending artery (LAD). The lower panel shows the wave pressure $p(x,t)$ in comparison to the simultaneously measured velocity U at the same location. We suggest that an extra element can be introduced to the analysis; that is, a time-varying resistance, $R(t)$, (fig. 4) calculated as described in equation 7. Notice how the resistance in systole in some cases can be almost fourfold that in diastole. After estimating the wave speed in the vessel, we can perform wave separation and therefore look at the proximally and distally generated waves for pressure and velocity, as shown in fig. 5. Notice that proximally and distally generated wave interaction due to reflections and

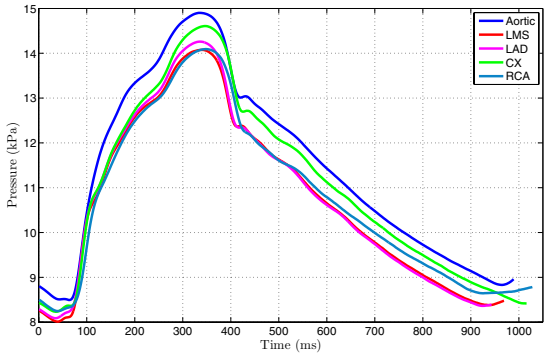

Fig. 1. P measured at the aorta, left main stem (LMS), left anterior descending (LAD, circumflex (CX) and right coronary (RCA) arteries.

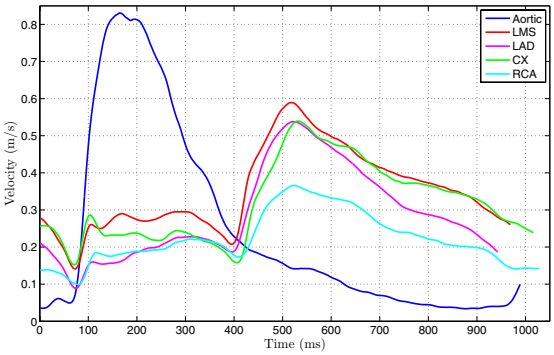

Fig. 2. U measured at the aorta, left main stem (LMS), left anterior descending (LAD, circumflex (CX) and right coronary (RCA) arteries.

muscle contraction account for differences between wave pressure and measured velocity.

Finally, wave intensity analysis was calculated for each of the measurements (fig. 6); from which wave reflection and interaction can be studied to further understand coronary haemodynamics. Before ejection occurs, there is a backward compression wave (pushing wave) generated by the reduction in the diameter of the distal arterioles during isovolumic contraction in systole (thus the increase in resistance). Flow to the myocardium decreases, but as contraction progresses, a forward compression wave is generated from the proximal end, due to the increase in pressure in the aorta at ejection. Blood ejection from the left ventricle to the aorta generates a slight increase in flow towards the myocardium. From the separation of waves (fig. 5) we can clearly observe a slight decline in the backward compression wave (pushing wave generated distally) with the progression of the muscle contraction. These equal but opposite pressure waves during systole are the responsible for the CFSI and could help increase the heart muscle stiffness before ejection. In the middle of systole wave intensity is small. It is right before the closure of the aortic valve that both a forward expansion and a backward expansion waves occur, but the forward expansion wave generally dominates (fig. 6). This means that before aortic valve closure, a suction wave is generated at the proximal or aortic side, while a backward expansion

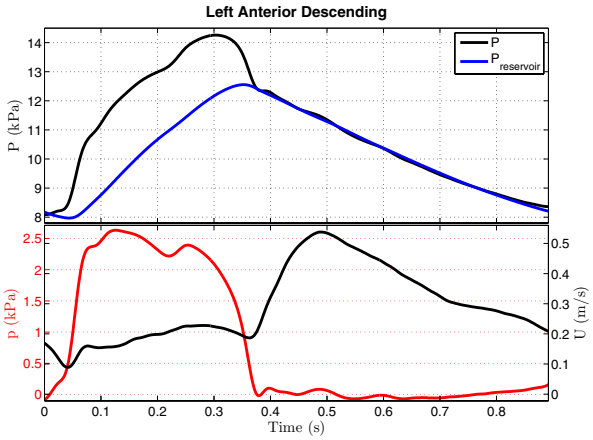

Fig. 3. Measured data and reservoir-wave pressure components from the Left Anterior Descending coronary (LAD).

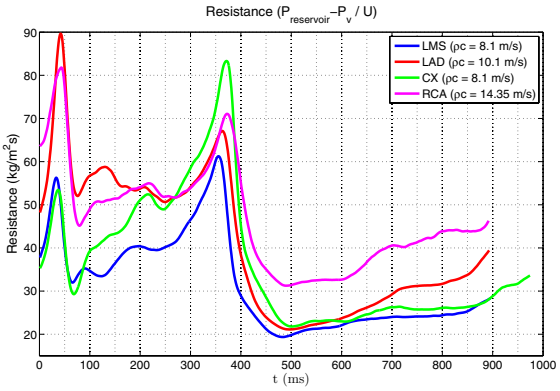

Fig. 4. Time varying resistance, $R(t)$, calculated in 4 different coronary arteries from a human subject.

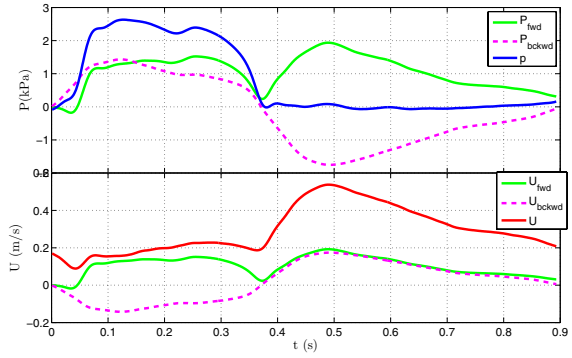

Fig. 5. Separated waves with and without the reservoir component in LAD from a human subject.

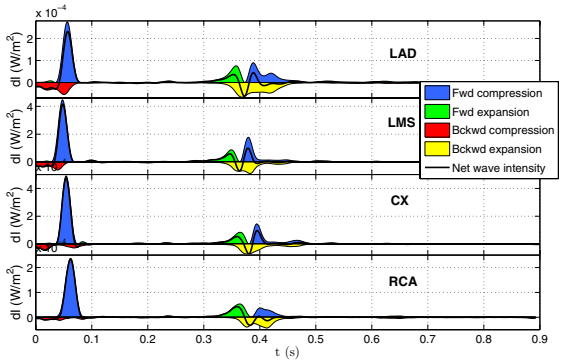

Fig. 6. Wave intensity analysis calculated in 4 different coronary arteries from a human subject.

(suction) wave is generated distally due to the sudden change in resistance, thus allowing the inflow of blood to the muscle. It is at the time of the dicrotic notch that the reservoir effect on the coronary flow begins to dominate. The forward compression (pushing wave travelling from the aorta) and backward expansion waves (suction wave travelling from the distal or myocardial side) as a result from the lower resistance distally, allow blood to perfuse the myocardium during diastole. Notice in fig. 5 that there are simultaneous self cancelling pressure waves travelling from both proximal and distal locations. This is regarded as the reservoir effect, since the same pressure decay exists in the vessels at approximately the same time, so flow to the myocardium is an active mechanism of suction due to the muscle relaxation and the windkessel in the aorta. Wave intensity during diastole is small.

The appearance of waves at different times and in different intensities at the various locations is the result of the spatial location of the coronary measured, the region it perfuses and the inhomogeneous way the muscle contracts.

IV. CONCLUSIONS AND FUTURE WORKS

A. Conclusions

A reservoir plus a wave pressure may be a useful model for coronary artery haemodynamics. Resistance to flow in the coronaries varies throughout the cardiac cycle (up to fourfold during systole). Mapping of the wave intensity of the separated wave pressure gives a fairly complete picture of wave travel in the coronary network and may provide insight into the physiology of coronary artery flow.

B. Future Works

There is still great controversy on the mechanisms of coronary haemodynamics. We are employing and developing new tools to be able to analyse and elucidate the complex interaction of muscle contraction and wave propagation in the coronary arterial tree and that could be of use in the clinical setting. We believe that the reservoir-wave separation in combination with wave intensity analysis will be able to provide some new knowledge on that subject.

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