A method to implement the reservoir-wave hypothesis using phase-contrast magnetic resonance imaging

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GRAPHICAL ABSTRACT
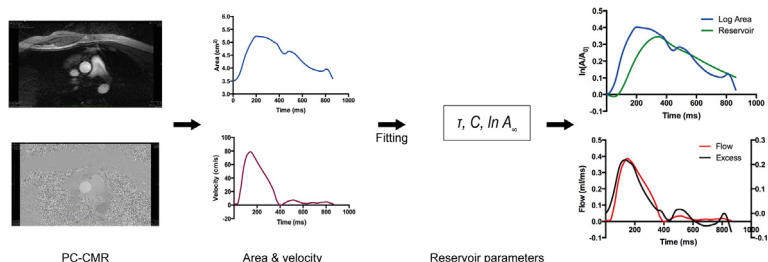
ABSTRACT

The reservoir-wave hypothesis states that the blood pressure waveform can be usefully divided into a "reservoir pressure" related to the global compliance and resistance of the arterial system, and an "excess pressure" that depends on local conditions. The formulation of the reservoir-wave hypothesis applied to the area waveform is shown, and the analysis is applied to area and velocity data from high-resolution phase-contrast cardiovascular magnetic resonance (CMR) imaging. A validation study shows the success of the principle, with the method producing largely robust and physically reasonable parameters, and the linear relationship between flow and wave pressure seen in the traditional pressure formulation is retained. The method was successfully tested on a cohort of 20 subjects (age range: 20–74 years; 17 males).

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This paper:
- Demonstrates the feasibility of deriving reservoir data non-invasively from CMR.
- Includes a validation cohort (CMR data).
- Suggests clinical applications of the method.

Methods

Rationale

The reservoir (Windkessel) model of arterial mechanics [1] represents the arteries as a single compliant compartment and with a single outflow resistance. This model predicts exponentially falling pressure in diastole, but not the sharp rise in pressure seen in systole. The more modern wave theory separates the pressure waveform into a combination of forward and backward travelling waves [2]. This analysis provides a good description during systole, where the separation produces an initial forward compression wave followed by backward reflected waves. However, in diastole this approach predicts large cancelling forward and backward waves to explain a falling pressure and a zero velocity [3]. The reservoir-wave hypothesis is an attempt to combine these two methods and benefits from the good predictions of the wave theory in systole and the reservoir theory in diastole.

In the reservoir-wave hypothesis [4], the pressure waveform in diastole is fitted with a single exponential model from which the reservoir parameters are extracted. We can then calculate the reservoir pressure and the excess pressure, which refers to the remaining part of the pressure waveform when the reservoir is subtracted. The latter is found to have the interesting property of being proportional to the flow into the arterial system. This indicates that the nearly identical excess pressure (P_{ex}) and inflow (Q_{in}) waveforms result only from forward-traveling compression and decompression waves generated by the left ventricle [5].

The reservoir-wave parameters describing the reservoir and excess pressure have been shown to have physiological and pharmacological significance. Their importance has been discussed in various areas including as a measure of left ventricular relaxation [6], as being related to hypertension [7], as a possible therapeutic target [8] and as a significant predictor of cardiovascular events carrying information for selection of pharmacological therapies [9].

Considering the clinical value of the reservoir-wave model, an implementation of the method for medical imaging, and cardiovascular magnetic resonance (CMR) imaging in particular, is desirable.

Implementation

The analysis is incorporated in a Python script. CMR data provides area (A) and velocity (U) as functions of time, sampled with a set temporal resolution (approximately 10 ms), and hence the flow $Q_{in} = UA$.

In complete analogy to the derivation of the reservoir pressure, we derive the reservoir area as follows. We have an equation for the reservoir pressure [3]:

$$\frac{dP_{res}}{dt} = \frac{(P_{res} - P_{\infty})}{RC} = \frac{Q_{in}(t)}{C} \tag{1}$$

where R and C are the resistance and compliance of the arterial system respectively, Q_{in} is the flow of blood into the arterial system and P_{∞} is the pressure at which flow through the circulation ceases. We

formulate a relationship between pressure and area using distensibility [10]

$$D = \frac{1}{A}\frac{dA}{dP} = \frac{d\ln A}{dP} \tag{2}$$

and we can then rewrite an expression for the reservoir pressure in terms of lnA

$$\frac{d\ln A_{res}}{dt} + \frac{(\ln A_{res} - \ln A_\infty)}{RC} = \frac{D}{C}Q_{in}(t) \tag{3}$$

and solve to

$$\ln A_{res} = \ln A_\infty + (\ln A_0 + \ln A_\infty)e^{-\frac{t}{\tau}} + \frac{D}{C}e^{-\frac{t}{\tau}}\int_0^t Q_{in}(t')e^{\frac{t'}{\tau}}dt' \tag{4}$$

where $\tau = RC$. t=0 is defined to be the start of systole and $\ln A_0$ is the value of lnAat that time.

During diastole which starts at time $t = T$, we assume that the inflow $Q_{in} = 0$, and Eq. (4) becomes

$$\ln A_{res} = \ln A_\infty + (\ln A_0 - \ln A_\infty + \ln A_T)e^{-\frac{t}{\tau}} \tag{5}$$

where

$$\ln A_T = \frac{D}{C}\int_0^T Q_{in}(t')e^{\frac{t'}{\tau}}dt' \tag{6}$$

Area is thus a function of the three reservoir parameters

$$\ln A_{res}(\ln A_\infty, \tau, C) = \ln A_\infty + (\ln A_0 - \ln A_\infty + \ln A_T(\tau, C))e^{-\frac{t}{\tau}} \tag{7}$$

The cut-off time T is set as the time when the inflow Q_{in} first goes to 0. The three parameters are then found by fitting Eq. (5) to the data after this point with the Levenberg-Marquardt nonlinear fitting algorithm using the Lmfit package in Python [11].

This allows derivation of reservoir-wave information non-invasively based on CMR data. The derived parameters τ and C are the same as those produced from invasive pressure measurements. The third parameter $\ln A_\infty$ is not, but would be expected to carry important information analogously to P_∞ from the pressure formulation of the analysis.

An important difference from the pressure formulation is that the analysis requires knowledge of $Q_{in}(t)$ in order to calculate $\ln A_T$. This means the analysis is limited to the ascending aorta where we can obtain a measurement of the volume flow rate into the whole arterial system.

Validation

In order to assess the feasibility of the analysis, area and velocity data was acquired by CMR from the ascending aorta position in a small cohort of subjects (n = 20; age range: 20–74 years; 17 males). Ethical approval for analysis of CMR data for research purposes was in place. Data were acquired with a 1.5 T scanner (Avanto, Siemens, Erlangen, Germany) using two spine coils and one body-matrix coil. The imaging plane was planned just above the sinotubular junction, using orthogonal long axis cine images of the ascending aorta. The sequence was a prospectively triggered, spiral, velocity encoded spoiled gradient echo acquisition accelerated with SENSE [12]. The time resolution was 9.56 ms and the spatial resolution was 2.1×2.1 mm. The breathhold was approximately 11 s and VENC was set at 180 cm/s in all cases. A and U signals were extracted by automatic segmentation propagation of the aorta using nonrigid registration, as described in detail elsewhere [13]. $\ln A_\infty$ and Q_{in} time series were calculated from these data, and then the reservoir analysis was run in Python as described. The resulting parameters are displayed in Fig. 1. In 19 of the 20 cases, the fitting algorithm worked robustly and converged onto parameters than are physically realistic and with a reasonably tight distribution. The range of values was 121.05–2069.01 ms, while the values of $\ln A_\infty$ ranged from 0.08 to 1.90. A representative case is shown in Fig. 2, exemplifying the reservoir signal fitted to the raw log-area data,
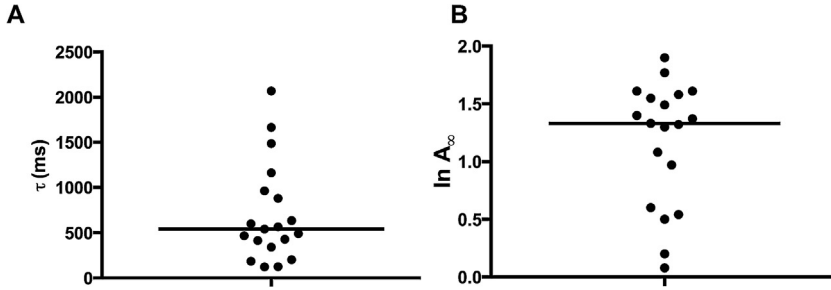
Fig. 1. The reservoir area analysis gives physically reasonable and well-distributed τ and $\ln A_\infty$ parameters. Note that the fitting was not completed successfully in one patient, likely due to the noisiness of the area signal in that specific patient. Horizontal bars represent the median.
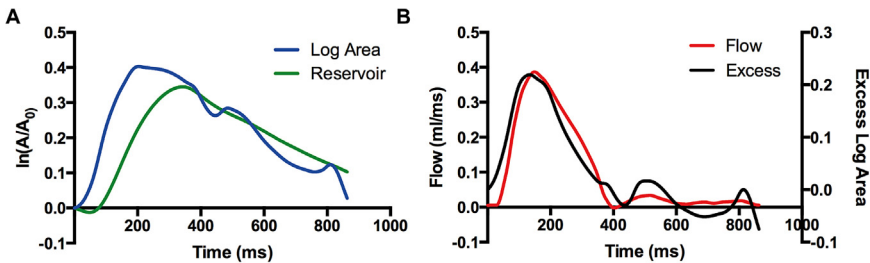

Fig. 2. Representative example data and reservoir-wave results. (A) Normalised log aortic area waveform (blue) and reservoir log area (green), which is found by fitting to the data in diastole. (B) Aortic flow (red) and excess log area (black) which is found by subtracting the reservoir from the raw data. The approximately linear relationship between flow and excess, which demonstrates the validity of this approach, is seen.

and the flow and excess log-area, in analogy to prior observations based on the pressure-formulation [3].

In the majority of cases, the fitting was completed without issue and was robust. In most cases the Nelder-Mead simplex algorithm was also able to perform robust fitting. However, in some cases, a bounding of the fitting to physically reasonable parameters, such as setting $\tau < 10,000$ was required. In one case, even bounding could not achieve a successful fit. We discuss this in the next section.

A second important consideration is diastolic flow. This is assumed to be negligible, but in many cases is not. This will affect the analysis and the fitted parameters and so should be taken into consideration, particularly if the analysis were to be performed in descending aortic data. A potential extension to this work would be a fitting of a general form of equation 4 to the data, not assuming negligible diastolic flow.

Clinically relevant applications in the future may include studying hypertensive patients, but also refining analysis of ventriculo-arterial coupling in patients with congenital heart disease, offering additional insight into arterial mechanics in scenarios where arterial wall properties (and hence the reservoir effect) can be compromised.

Limitations

We found that our method converged to seemingly reasonable parameters in 19 of 20 cases. Despite this, we have found the method has certain limitations. In particular, noisiness in the data can fairly easily confound the fitting algorithm. If noise or some other defect causes the diastolic log-area waveform to deviate too strongly from a simple decaying exponential then the parameter space

becomes extremely flat and the fitting fails. Signal-to-noise ratio and clean data are thus of paramount importance for this method, and smoothing of the data could also be used to enable the fitting algorithm to converge.

Whilst the effect of non-perpendicular positioning of the plane with respect to aortic flow was not systematically tested, it is well known that care should be taken in planning the slice for flow quantification perpendicular to the direction of flow to avoid errors in velocity quantification [14] which in turn could have an effect on flow quantification (Q_{in}). In our case, the aortic plane was always carefully planned perpendicular to the direction of flow; this, together with the knowledge that velocity quantification is relative insensitive to small deviations to true perpendicular within an error of $20°$ [14], would suggest that Q_{in} was not affected. Also, the effect of inaccuracies in U estimation due to setting VENC too high or too low were not systematically tested and can be explored further.

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