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Novel Approach to Admittance to Volume Conversion for Ventricular Volume Measurement

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***Abstract*—The conductance catheter is a widely used tool to determine ventricular volumes in animal models. A tetra-polar catheter is inserted into the ventricle to measure instantaneous conductance, which is a combination of ventricular blood and surrounding myocardium. Various techniques have been used to separate the blood conductance signal from the combined measured signal [1], [2]. The blood conductance is then converted to volume using a linear relationship proposed by Baan [1] or an improved non linear relationship proposed by Wei [3]. We propose a novel approach that uses the combined blood-muscle signal to calculate volume, thereby eliminating the need to subtract out the muscle. *In vivo* experiments were performed in mice to validate this new approach and the results were compared with volumes obtained using ultrasound imaging.**

I. Introduction

LEFT ventricular (LV) pressure volume (PV) loops are considered to be the gold standard for cardiac function assessment. An LV volume signal can be estimated using a tetra polar conductance catheter system [1], [4]. Conductance based techniques have been used to assess ventricular function in animal models with varying degrees of success [5] - [9]. This technique involves the insertion of a four electrode catheter into the LV and injecting a constant AC current through the outer electrode pair to generate an electric field within the LV. The inner electrode pair continuously measures the instantaneous conductance as the LV fills and ejects blood. However, the traditional conductance method fails to accurately correct for the parallel conductance contributed by the myocardium, resulting in overestimation of blood volumes. The hypertonic saline technique [4] developed to determine parallel myocardial conductance is not ideal for small animals since the administration of even small amounts of saline has profound effects on hemodynamics and blood resistivity of the animal. An improved admittance based technique has been proposed by Porterfield *et. al* [2] which exploits the unique capacitive property of myocardium [10] to detect and remove it from the combined blood-muscle signal. The corrected blood conductance is then converted to volume using a linear relationship proposed by Baan [1] or an improved non linear relationship proposed by Wei [3]. The linear Baan equation is acceptable in mice since the electrical field generated by the conductance catheter can be assumed uniformly distributed in the LV. However, in larger hearts, the electrical field strength is inhomogeneous throughout the LV and the non linear Wei's equation is more appropriate.

We propose a new approach to determine ventricular volumes using the combined blood-muscle signal from an admittance catheter without the need for separating out the parallel muscle contribution. We model the catheter to be immersed in blood contained within a cylinder of muscle with infinite wall thickness. Hence, the measured admittance (Y) is the sum of blood (Y_b) and muscle (Y_m) admittances.

$$Y = Y_b + Y_m \tag{1}$$

This approach establishes two limits to the dipole field to admittance relationship. The first of these limits represent an extreme where there is only tissue surrounding the catheter. The second extreme represents an infinite volume of blood where the dipole field does not extend to the boundary of the blood pool and there is hence no muscle contribution to the observed admittance. Using these boundary conditions along with the measured electrical resistivity of blood and myocardium, we can generate a relationship between admittance and cylinder radius for the catheter in the LV.

II. Methods

A. Electrical Field Theory

Consider a tetrapolar catheter of radius 'a_0' with two source electrodes and two sensing electrodes placed in a cylindrical column of conducting fluid, as shown in Fig 1. The source electrodes are separated by distance 'd' and the sense electrodes are separated by distance 'L'. The electrical admittance (Y) measured by this catheter has been derived by Wei *et. al* [3].

$$Y = \frac{\pi \cdot d \cdot \left(d^2 - L^2\right) \cdot \left(\sigma + i \cdot \omega \cdot \varepsilon\right)}{4 \cdot L} \left(\frac{1}{\sqrt{{a_0}^2 + d^2/4}} - \frac{1}{\sqrt{R^2 + d^2/4}} \right) \tag{2}$$

where σ and ε are the electrical conductivity and permittivity respectively, of the fluid.

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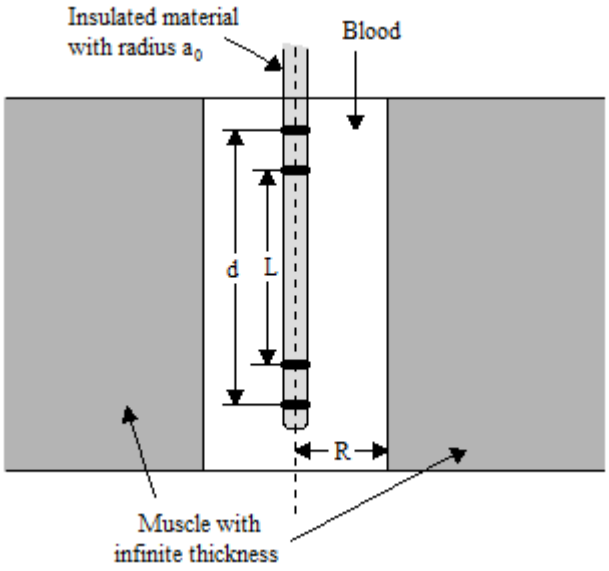

Fig. 1. Catheter placed in a cylindrical column of conducting fluid.

Now consider the situation where the catheter is immersed in a cylindrical column of blood surrounded by muscle of infinite thickness. This matches the physiological condition in the animal where the ventricular blood is surrounded by myocardium. The admittance of a tube of blood of inner radius a_0 and outer radius R is as follows.

$$Y_b = \frac{\pi \cdot d \cdot \left(d^2 - L^2\right) \cdot \left(\sigma_b + i \cdot \omega \cdot \varepsilon_b\right)}{4 \cdot L} \left(\frac{1}{\sqrt{a_0^{\,2} + d^2/4}} - \frac{1}{\sqrt{R^2 + d^2/4}} \right) \quad (3)$$

Similarly, the admittance of a tube of muscle with inner radius R and infinite outer radius is

$$Y_m = \frac{\pi \cdot d \cdot \left(d^2 - L^2\right) \cdot \left(\sigma_m + i \cdot \omega \cdot \varepsilon_m\right)}{4 \cdot L} \left(\frac{1}{\sqrt{R^2 + d^2/4}} \right) \quad (4)$$

The measured admittance (Y) is the sum of blood (Y_b) and muscle (Y_m) admittances with boundary conditions at $R = a_0$ and $R = \infty$. At $R = a_0$,

$$Y_0 = \frac{\pi \cdot d \cdot \left(d^2 - L^2\right) \cdot \left(\sigma_m + i \cdot \omega \cdot \varepsilon_m\right)}{2 \cdot L \cdot \sqrt{4 \cdot a_0^{\,2} + d^2}} \quad (5)$$

At $R = \infty$,

$$Y_{\inf} = \frac{\pi \cdot d \cdot \left(d^2 - L^2\right) \cdot \left(\sigma_b + i \cdot \omega \cdot \varepsilon_b\right)}{2 \cdot L \cdot \sqrt{4 \cdot a_0^{\,2} + d^2}} \quad (6)$$

Substituting (6) in (3) yields

$$Y_b = Y_{\inf} + \frac{\pi \cdot d \cdot \left(d^2 - L^2\right) \cdot \left(\sigma_b + i \cdot \omega \cdot \varepsilon_b\right)}{4 \cdot L} \left(\frac{-1}{\sqrt{R^2 + d^2/4}} \right) \quad (7)$$

The equation for the total measured admittance (1) can now be expressed as

$$Y = Y_{\inf} + \frac{\pi \cdot d \cdot \left(d^2 - L^2\right) \cdot \left(\sigma_m + i \cdot \omega \cdot \varepsilon_m - \sigma_b - i \cdot \omega \cdot \varepsilon_b\right)}{2 \cdot L \cdot \sqrt{4 \cdot R^2 + d^2}} \quad (8)$$

Rearranging the terms and substituting for R^2 in the equation for the volume of a cylinder,

$$Vol = -\pi \cdot L \cdot \left[\frac{d^2}{4} - \frac{\beta \pi^2 d^2 \left(d^2 - L^2\right)^2 \cdot \left(\sigma_m + i\omega\varepsilon_m - \sigma_b - i\omega\varepsilon_b\right)^2}{16 \cdot L^2 \cdot \left(Y - Y_{\inf}\right)^2} \right] \quad (9)$$

Note that the above relation contains a normalization parameter β, to account for the non-cylindrical geometry of the ventricle. The value of β is calculated by forcing the empirically derived stroke volume (SV) to be equal to an independently measured value of SV. Mathematically,

$$\beta = \frac{16 \cdot L \cdot SV \cdot \left(Y_{ED} - Y_{\inf}\right)^2 \cdot \left(Y_{ES} - Y_{\inf}\right)^2}{\pi^3 d^2 \left(d^2 - L^2\right) \cdot \left(\sigma_m + i\omega\varepsilon_m - \sigma_b - i\omega\varepsilon_b\right)^2 \cdot a \cdot b} \quad (10)$$

Hence,

$$Vol = \frac{SV \cdot \left(Y_{ED} - Y_{\inf}\right)^2 \cdot \left(Y_{ES} - Y_{\inf}\right)^2}{\left(Y - Y_{\inf}\right)^2 \cdot a \cdot b} - \frac{\pi \cdot L \cdot d^2}{4} \quad (11)$$

where $a = \left(Y_{ED} - Y_{ES}\right)$ and $b = \left(2 \cdot Y_{\inf} - Y_{ED} - Y_{ES}\right)$

Thus, the calculation of β from a known SV enables the appropriate scaling of volume to transition from an ideal cylindrical model to a less ideal (but still R dominant) model such as the ventricle.

The smallest volume that can be measured based on known values of catheter radius (a_0) and distance between sensing electrodes (L) is

$$Vol_{\min} = \pi \cdot a_0^{\,2} \cdot L \quad (12)$$

Substituting (12) in (11) and rearranging terms results in the final expression for volume.

$$Vol = \pi \cdot L \cdot a_0^{\,2} - \frac{SV\left(Y - Y_{a0}\right)\left(Y_{ED} - Y_{\inf}\right)^2\left(Y_{ES} - Y_{\inf}\right)^2\left(Y + Y_{a0} - 2Y_{\inf}\right)}{\left(Y - Y_{\inf}\right)^2\left(Y_{a0} - Y_{\inf}\right)^2 a \cdot b} \quad (13)$$

We now refer to this relation as the *Dubois equation* in the remainder of this paper. The right hand side of this relation contains both real and imaginary terms and as a practical consideration, the imaginary terms can be neglected since volume is real. Also, $Y_{\inf}$ can be determined for any catheter by immersing it in a large volume of fluid of known conductivity. Y_{a0} is then calculated as the ratio of muscle to blood resistivity multiplied by $Y_{\inf}$.

B. Instrumentation

The admittance magnitude as well as LV pressure was measured using a 1.2Fr tetra polar catheter manufactured by Scisense Inc., Ontario (model FTE-1212B-4518). The catheter contains four platinum electrodes and a high fidelity pressure sensor, as shown in Fig 2.

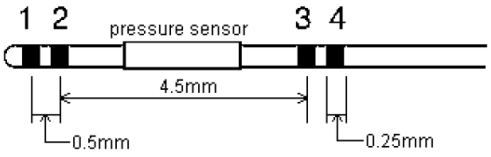

Fig. 2. Tetra polar catheter used for admittance and pressure measurements

The catheter is connected to a control unit (ADVantage™, Scisense Inc, Ontario) that calculates admittance magnitude and pressure. The outputs from the control unit were sampled and analyzed using Labscribe acquisition software (iWorx Systems Inc., Dover, New Hampshire).

The mice were imaged using a Vevo 2100 Ultrasound system (Visualsonics, Ontario) to determine ventricular volumes during systole and diastole. We measured the long axis and two mid-papillary short axis lengths within a long axis view and computed volume using the prolate ellipse method. SV was determined as the difference between EDV and ESV and was used in the Dubois equation to calculate volume.

C. *Murine Studies*

The Institutional Animal Care and Use Committee at Loyola University Medical Center approved all experiments. A total of 8 mice (FVB) were studied by ultrasound imaging and PV catheter measurements. Mice were anaesthetized by administration of 1-2% isoflurane and mechanically ventilated with a MiniVent mouse ventilator (Hugo Sachs, Germany) set at 150 breaths/min (100% O_2). Mice were placed on a heated, temperature-controlled operating table for small animals (Visualsonics, Toronto) and experiments were performed at a murine body temperature of 37° C. The miniaturized conductance catheter was inserted into the LV through the right carotid artery and placed such that electrode #4 was positioned immediately below the aortic valve and electrode #1 was at the apex. The magnitude of admittance as well as LV pressures were measured in the intact beating mouse heart. After the measurements were completed, the heart was imaged using the ultrasound system This verified proper catheter placement in the LV and also provided a second independent measure of ventricular volumes.

III. RESULTS

A. *In vivo Pressure-Volume Loops*

The hemodynamic parameters of six mice used in the study are listed in Table 1. The systolic and diastolic time points were calculated as the points of maximum and minimum rate of pressure change respectively (i.e. dP/dt_{max} and dP/dt_{min}). Two additional mice were excluded from the analysis since their heart rates were below 400 beats per minute.

Mouse	Heart Rate	ESV (µL)		EDV (µL)	
		Dubois	Echo	Dubois	Echo
1	446	20.8	16.5	44.1	37.7
2	474	27.3	19.9	43.6	39.7
3	460	20.0	23.0	42.0	42.9
4	463	22.9	15.2	38.0	36.4
5	535	11.9	13.4	34.4	35.4
6	427	28.7	20.8	41.9	44.7

Table 1. Hemodynamic parameters of n=6 mice used in the study

The real-time PV loops from six mice are shown in Fig 3, where the volumes were calculated using the Dubois equation. The solid lines in the figure indicate the systolic and diastolic volumes determined using ultrasound.

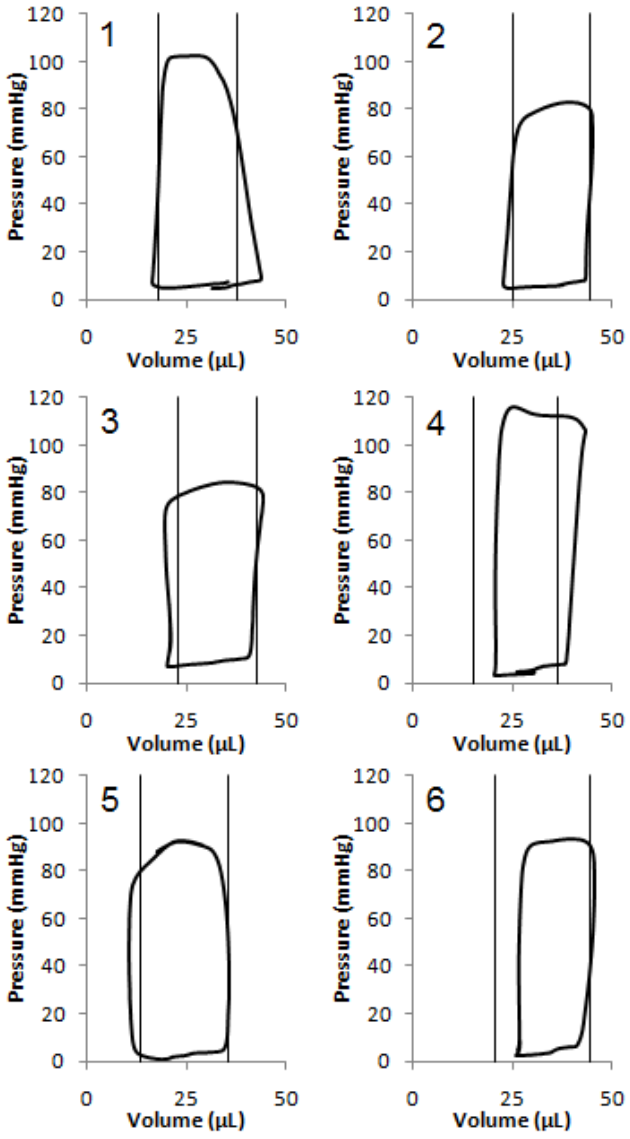

Fig. 3. Pressure-Volume loops from n=6 mice using the Dubois equation. The solid vertical lines indicate the end-systolic and end-diastolic volumes calculated from echo.

B. Statistical Analysis

The real-time volume results obtained using the Dubois equation were compared with volumes from the ultrasound system. Specifically, ESV and EDV values derived using both techniques were compared and the results are presented as a Bland-Altman plot in Fig 4. The mean of the volume difference between the two techniques was 2.50μL with a standard deviation of 4.26μL. The random distribution of the points about the mean indicate that there is no proportional error in the measurement techniques.

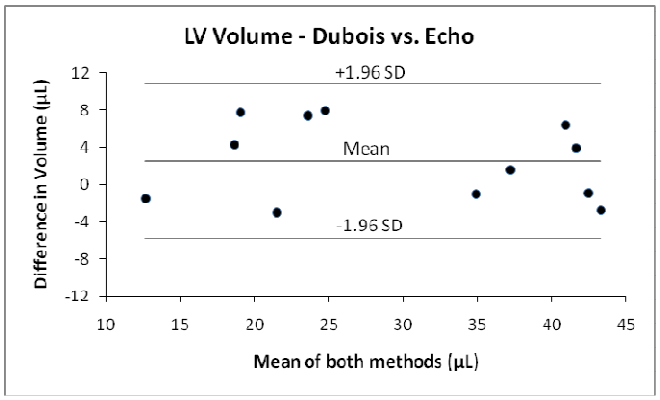

Fig. 4. Bland-Altman plot showing the difference in LV volumes determined by echo and Dubois method (y axis) plotted against the average of both methods (x axis).

IV. Discussion

This study compares volumes determined using the novel Dubois equation with volumes calculated from ultrasound images of the LV during systole and diastole. We have demonstrated that the two techniques provide comparable volumes in mice. It must be noted that the accuracy of volume estimation using ultrasound images is subject to proper LV contour selection, which is user dependent.

The Dubois equation provides several advantages over existing catheter based techniques to determine ventricular volumes. The conventional conductance technique inaccurately assumes a constant value for parallel muscle conductance during a cardiac cycle [11] and uses a non-ideal linear relationship to convert measured blood conductance to volume. Both of these drawbacks are addressed by the Dubois equation. This equation is also computationally simpler than the more recent admittance technique [2], which has been proven to provide accurate LV volumes [2], [12], since it does not require measurement of phase angles or muscle permittivity. A closer look at the Dubois equation also reveals that any scaling or offset parameters in the admittance measurements cancel out due to the subtraction of admittance values in every term of the equation. This makes the system self-calibrating for any electrode or system effects in the measurement of admittance in the LV. However, deviations in catheter placement from the centerline in the LV could introduce inaccuracies in the calculated volume and the extent of this inaccuracy needs to be investigated further.

The Dubois equation can be extended to work in any sized heart by using an appropriately sized catheter. Future work would involve validation of the equation in larger sized ventricles.

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