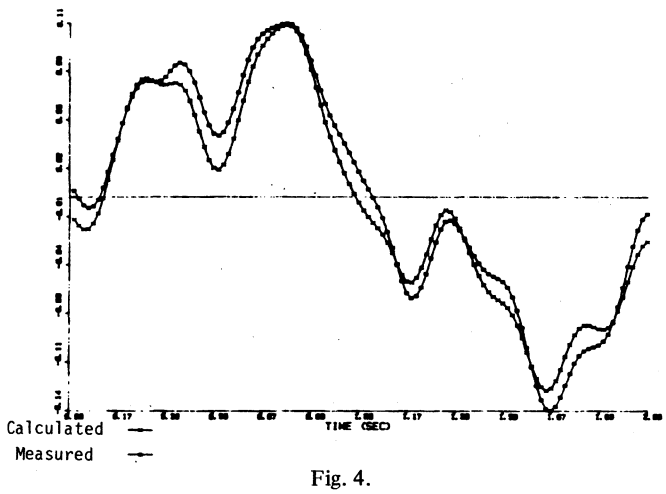

Fig. 4.

as the first model, yet draws from Contini's work to obtain the body segment parameters. The results of this model are seen in Fig. 3. Here again we see a large error in the measured and calculated center of pressure. For the most part, the two results thus far are identical. The explanation probably lies in the fact that the upper body, which is the most massive portion of the body, is modeled identically in both calculations.

Fig. 4 shows results obtained using the general geometric solid model of Hanovan for human body segment parameters. As can be seen, this model provides very good agreement with direct measurement of the center of pressure. The authors believe that these results justify a statistical evaluation of the usefulness of Hanovan's method in quantitative posturography. Such a study is now underway.

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Correlation Between Arterial Blood Pressure Levels and $(dZ/dt)_{min}$ in Impedance Plethysmography

L. DJORDJEVICH, M. S. SADOVE, J. MAYORAL, AND A. D. IVANKOVICH

Abstract—$(dZ/dt)_{min}$, which is the magnitude of the negative peak of the first time derivative of transthoracic electrical impedance Z, plays a key role in impedance plethysmography because it reflects the pumping action of the heart. Its current applications for measuring stroke volume and quantification of myocardial contractility, however, ignore the possibility that $(dZ/dt)_{min}$ may be strongly modified by factors that are independent on the heart. Measurements of $(dZ/dt)_{min}$ on 146 volunteers are statistically correlated with the systolic, diastolic, and mean arterial blood pressure and heart rate. Statistically significant correlations are obtained between the $(dZ/dt)_{min}$ and blood pressures, but not with heart rate. The correlations indicate that $(dZ/dt)_{min}$ is expected to decrease as the arterial blood pressure level increases. This relationship is elucidated with the help of a theoretical model which combines the parallel conductor theory with a mechanical model of an elastic artery. The analysis of the model is in agreement with statistical predictions based on measured data, indicating that $(dZ/dt)_{min}$ explicitly depends on blood pressure level in an inverse manner. It is concluded that the functional dependence of dZ/dt signals on Z and blood pressure levels should be taken into account if valid conclusions from applications of dZ/dt signals are to be drawn. Suggestions are made to use the measured correlations as a means to eliminate Z and blood pressure levels as factors in applications of dZ/dt signals.

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I. INTRODUCTION

Impedance plethysmography [1]-[3] continues to attract the attention of many investigators because of its ability to provide in a noninvasive manner valuable information about intravascular and extravascular fluid volume, heart function, and vascular response to the heart function. Since first suggested by Nyboer *et al.* [4] this method has been used with various degrees of success to measure stroke volume and cardiac output [5]-[8] and total peripheral resistance [9] and to quantify myocardial contractility [10]. The recent evaluation by Schimazu *et al.* [11] of the parallel conductor theory, the physical basis of impedance plethysmography, indicates that the error in measuring the blood component of resistivity caused by this modeling is less than ±2 percent, which shows that the impedance plethysmography signals can be measured with high accuracy.

Ito, Yamakoshi, and Togawa [15]-[17] and Djordjevich *et al.* [12], however, have raised the question of correct application of impedance plethysmography in impedance cardiography and quantification of myocardial contractility; these are based on measurements of $(dZ/dt)_{min}$, which is the magnitude of the negative peak of the first time derivative of the transthoracic impedance Z. They experimentally demonstrated [12] that this peak is proportional to the time-average value of Z, and suggested that this dependence should be taken into account in all applications where the magnitude of the peak is a major factor, such as in stroke volume measured by impedance cardiography, or in myocardial contractility. In addition, the shape and the amplitude of the dZ/dt signal may be expected to be strongly influenced by the dynamic response of the vascular system to the ejection of blood from the left ventricle, which in turn is the consequence of nonlinear, viscoelastic nature of arterial walls. Thus, dZ/dt should also depend on the rate of ejection, the mean arterial blood pressure, and the modulus of elasticity of arterial walls.

This communication presents the directly measured relationship between the $(dZ/dt)_{min}$ peaks and arterial blood pressure in normal subjects, and offers an explanation for this relationship.

II. METHODS

Measurements were done on 146 volunteers of both sexes, who had no known cardiovascular disorder other than hypertension. Normal healthy volunteers were used to avoid possible failure of accurate identification of dZ/dt peaks in various pathological cardiovascular states. The transthoracic electrical impedance Z was measured with volunteers in supine position, after 10 min rest in that position, so that a steady-state circula-

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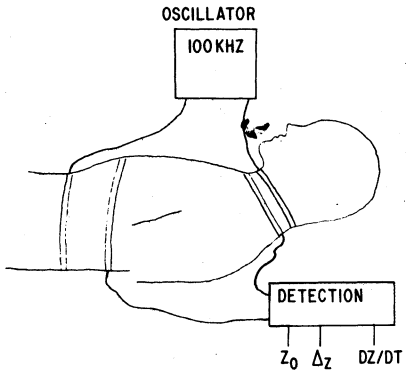

Fig. 1. Electrode attachments for the impedance plethysmograph.

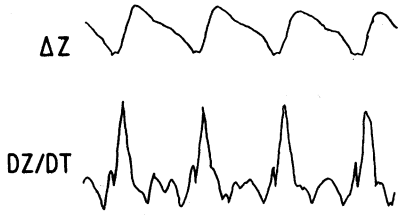

Fig. 2. Recordings of typical signals of Z and dZ/dt.

tion is achieved. Z and dZ/dt were measured with the Impedance Cardiograph, model 200, manufactured by Instrumentation for Medicine. Fig. 1 illustrates electrode attachments. A constant current oscillator produces 4 mA rms current with 100 kHz frequency in the chest region between the two outer electrodes. This combination of current and frequency is considered very safe, with the current level 20 times lower than the threshold of perception. The two inner electrodes serve as measuring electrodes, connected to the detection portion of the impedance meter which measures Z and dZ/dt continuously as functions of time. Typical recordings of the output are shown in Fig. 2.

Z and dZ/dt signals, in the form of voltage, are connected to two input channels of an analog-to-digital converter which is part of a PDP-11/03 minicomputer manufactured by Digital Equipment Corporation. The negative peaks $(dZ/dt)_{\min}$ of the dZ/dt signals are detected in every cardiac cycle by a pattern recognition routine of the computer program, and their magnitudes are stored in an array. Another routine simultaneously samples the values of Z. After 1 min of sampling, the average values of Z and $(dZ/dt)_{\min}$ are calculated and printed.

Simultaneously with impedance measurements, peripheral arterial blood pressures are measured automatically by a Dinamap model 845 (Applied Medical Research Corporation) unit which measures systolic, diastolic, mean arterial blood pressure, and heart rate using a cuff placed on the upper arm. Blood pressure measured in this manner is slightly amplified, but directly proportional to the central arterial pressure.

After each measurement on a volunteer, average values of Z, $(dZ/dt)_{\min}$, systolic, diastolic, mean arterial pressure, and heart rate are stored in a data diskette. When all 146 volunteers were measured, data stored on the diskette were correlated and statistically analyzed by the computer.

III. Results

$(dZ/dt)_{\min}$ represents the average of the absolute values of magnitudes of the negative peaks of the dZ/dt signals, obtained during a 1 min period of measurement on a volunteer (Fig. 2). For each cardiac cycle, there is one such peak corresponding to the maximum rate of change of Z.

The sample size, on the basis of which all correlations below are calculated, is 146. Correlations are obtained by linear regression. The standard deviation around the correlation σ is reported together with the correlation. The statistical significance of the correlation is determined by calculating the value of p, which represents the probability that the regression coefficients are zero. The significance of correlations is determined by the F test of the null hypothesis that regression coefficients are zero, and that there is no relationship between variables. For values of p which are less than 0.01, the correlation is assumed to be statistically significant because there is a 99 percent probability that there exists a true dependence of $(dZ/dt)_{\min}$ on the independent variable.

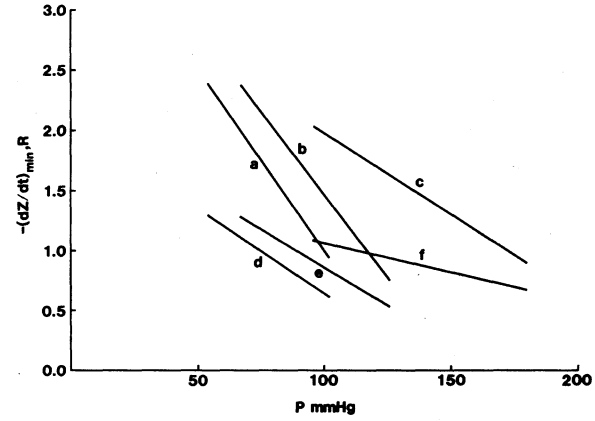

Fig. 3. Correlation of dZ/dt peaks with diastolic pressure a, mean arterial pressure b, and systolic pressure c. Correlation of the ratio R with diastolic pressure d, mean arterial pressure e, and systolic pressure f.

In all correlations below, Z is measured in ohms, dZ/dt in ohms/s, blood pressure in millimeters of mercury, and heart rate in beats/min. The mean value of measured $(dZ/dt)_{\min}$ is 1.6325 Ω/s.

$(dZ/dt)_{\min}$ is first correlated to the mean arterial pressure P_m

$$(dZ/dt)_{\min} = 4.220 - 0.02756P_m \tag{1}$$

with $\sigma = 0.5236$, $p < 10^{-5}$. This correlation is valid for the pressure range between 67 and 126 mmHg.

The correlation with systolic pressure P_s in the range from 96 to 180 mmHg is

$$(dZ/dt)_{\min} = 3.3276 - 0.01352P_s \tag{2}$$

with $\sigma = 0.567$ and $p < 10^{-3}$.

The correlation with diastolic pressure P_d in the range from 54 to 102 mmHg is

$$(dZ/dt)_{\min} = 4.0131 - 0.03016P_d \tag{3}$$

with $\sigma = 0.537$, and $p < 10^{-4}$.

The results are graphically represented in Fig. 3, which shows that all three functions are decreasing.

The correlation with heart rate (HR) has $p > 0.5$ indicating the absence of relationship between $(dZ/dt)_{\min}$ and HR in the range from 51 to 117 beats/min.

An earlier study [12] indicated strong correlation between $(dZ/dt)_{\min}$ and Z_0, which is the time-average value of Z

$$(dZ/dt)_{\min} = 0.0993Z_0 - 0.9038 \tag{4}$$

with $\sigma = 0.2739$ and $p < 10^{-4}$.

Equation (4) is used to eliminate the influence of Z_0 on value of $(dZ/dt)_{\min}$ by forming the ratio

$$R = (dZ/dt)_{\min}/(dZ/dt)_c \tag{5}$$

and the difference

$$D = (dZ/dt)_{\min} - (dZ/dt)_c \tag{6}$$

where $(dZ/dt)_c$ is the predicted value of $(dZ/dt)_{\min}$ calculated from (4), for measured value of Z_0. R and D are then corre-

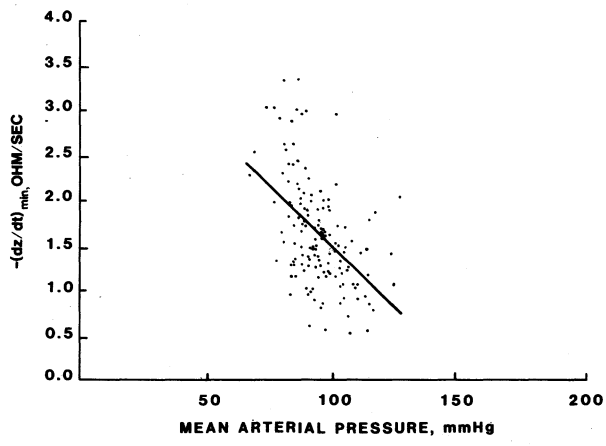

Fig. 4. The distribution of the magnitudes of the dZ/dt peaks (raw data points) as a function of the mean arterial blood pressure (·), and the corresponding linear regression line (—).

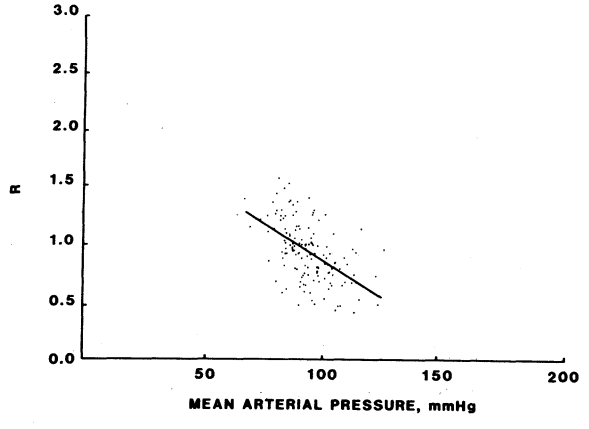

Fig. 5. The distribution of raw data points of the ratio R as a function of the mean arterial blood pressure (·), and the corresponding linear regression line (—).

lated with P_m, P_s, P_d, HR, and Z_0

$$R = 2.1312 - 0.01274P_m \tag{7}$$

with $\sigma = 0.2242$ and $p < 10^{-5}$,

$$R = 1.546 - 0.00487P_s \tag{8}$$

with $\sigma = 0.2522$ and $p < 10^{-2}$, and

$$R = 2.0504 - 0.01413P_d \tag{9}$$

with $\sigma = 0.2299$ and $p < 10^{-5}$. All three equations (7)-(9) represent decreasing functions in the respective domains, as seen in Fig. 3. The slopes of all six correlations depend on the physiologic range of respective blood pressures. Hence, the two correlations with P_d (lines a and d in Fig. 3) are the steepest because the range of P_d is the smallest, while lines c and f are considerably less steep because of the large range of P_s. The typical scattergrams, showing all 146 raw data points, are given in Fig. 4 for $(dZ/dt)_{\min}$, and Fig. 5 for the ratio R. Both show the distribution over the range of the mean arterial blood pressure P_m. The scattergrams over the range of P_s and P_d (not shown to avoid crowding of points) are very similar to Figs. 4 and 5 because the ordinates for each point are identical, while only abscissas differ. This is reflected in small differences between the respective standard deviations.

The correlation of R with HR results in $p > 0.05$ while the correlation with Z_0 results in $p > 0.25$. It is therefore concluded that R does not depend on HR and Z_0. Similarly,

$$D = 2.145 - 0.02408P_m \tag{10}$$

with $\sigma = 0.4048$ and $p < 10^{-5}$,

$$D = 1.2402 - 0.01082P_s \tag{11}$$

with $\sigma = 0.4525$ and $p < 10^{-3}$, and

$$D = 1.931 - 0.02593P_d \tag{12}$$

with $\sigma = 0.4198$ and $p < 10^{-5}$. Again, all three functions (10)-(12) are decreasing in respective domains. Correlation of D with HR gives $p = 0.043$, which is on the borderline of being statistically significant. However, the correlation of R with Z_0 results in $p = 0.88$. Hence, both R and D are independent of Z_0.

The correlations of Z_0 with P_m, P_s, P_d, and HR all resulted in $p > 0.1$, indicating the absence of a functional relationship.

IV. Discussion

The basic finding of this study, as evidenced by (1)-(3), is that the magnitude of the $(dZ/dt)_{\min}$ peaks is a function of arterial blood pressure, in addition to the dependence on Z_0, which was reported earlier [12]. Elimination of the influence of Z_0, using (5) and (6), still leaves the correlation between dZ/dt peaks and blood pressure unchanged, as seen in (7)-(12), indicating that the dependence on blood pressure is direct and not through Z_0. Thus, dZ/dt peaks depend at least on blood pressure levels, Z_0 [12], [15], [16], and rate of ejection of blood from heart (or aortic flow wave) as pointed out by Ito, Yamakoshi, and Togawa [15], [17]. These relationships can be elucidated by analyzing a simple dynamic model of elastic arterial expansion caused by the variation of blood pressure during the cycle.

Starting with the parallel conductor model of impedance plethysmography [11], we can write

$$1/Z = 1/Z_b + 1/Z_c \tag{13}$$

where Z is the total impedance, Z_b is the impedance contributed by volume of blood, which, according to the basic assumption of impedance plethysmography, contains the only variable component of impedance. Z_c is the constant portion, attributed to the rest of the tissues. The first time derivative of Z is therefore

$$dZ/dt = Z^2/Z_b^2 \times dZ_b/dt. \tag{14}$$

On the other hand, the simple relationship between the cross-sectional area (a) of an elastic artery and blood pressure (P) as derived by Bergel [13], can be written as

$$a = a_0[2P/E(K^2 - 1) + 1]^2 \tag{15}$$

where a_0 is unstretched cross-sectional area, which corresponds to $P = 0$, E is the modulus of elasticity of arterial wall, which is a function of P, and K is the ratio of the outer to the inner diameter of the artery in the unstretched state.

Assuming cylindrical geometry of blood vessels in the region of length L between the measuring electrodes, and that the only variable component of impedance signal comes from blood in the vessels, the relationship between a and Z_b is given by

$$a = \rho L/Z_b \tag{16}$$

so that

$$a_0 = \rho L/Z_{b0} \tag{17}$$

where ρ represents the electrical resistivity of blood.

Differentiating (15) we obtain

$$da/dt = [4a_0/(K^2 - 1)^2][2P + E(K^2 - 1)] \cdot [E - P(dE/dP)]/E^3(dP/dt). \tag{18}$$

Differentiating (16) we obtain

$$da/dt = -(\rho L/Z_b^2)(dZ_b/dt). \tag{19}$$

Combining (14) and (17)-(19)

$$dZ/dt = -(Z^2/Z_{b0})[4/(K^2-1)^2][2P + E(K^2-1)] \cdot [E - P(dE/dP)]/E^3(dP/dt). \quad (20)$$

The peak of the dZ/dt signal, $(dZ/dt)_{\min}$, occurs when the absolute value of the right side of the equation (20) is at maximum, which timewise closely corresponds to the moment when the rate of ejection of blood from the left ventricle during the cardiac cycle is at maximum, and which in turn causes dP/dt to be at maximum.

In terms of Z_0, Z can be written as

$$Z = Z_0 + \Delta Z(t) \quad (21)$$

where Z_0 is the time-average value of Z and ΔZ the variable portion of the signal. Typical values of Z_0 are 20-30 Ω, while the maxima of ΔZ are of the order of only 0.1-0.2 Ω. Hence, the predominant portion of signal Z is Z_0.

It is possible now to offer an explanation for the correlations listed in Section III.

According to (20), $(dZ/dt)_{\min}$ is directly proportional to the Z^2/Z_{b0} factor. Hence, in view of (21), the direct proportionality expressed by (4), which statistically confirms the increase of dZ/dt peaks when Z_0 is increased.

The correlations with blood pressure can be explained using (20), by keeping in mind that the modulus of elasticity E is a monotonically increasing nonlinear function of blood pressure [14]. E can be expressed in terms of P either as a polynomial such as

$$E(P) = A_0 + A_1P + A_2P^2 + \cdots \quad (22)$$

of at least second degree, or as an exponential function of P, such as

$$E(P) = B_0 + B_1e^{bP} + B_2e^{cP} + \cdots. \quad (23)$$

In either case, when (22) or (23) are substituted in (20), the resulting function of P is of the negative net exponent because of the predominance of the E^3 term in the denominator in (20). This, in terms of the mechanics, means that as the average blood pressure increases, then the arteries become more distended and more rigid causing the change of their volume during the cardiac cycle to be less pronounced. Therefore, the dZ/dt peaks tend to decrease when blood pressure increases, as statistically confirmed by correlations in Section III. In this model the presence of mechanical factors, such as vasoconstriction, vasodilatation, and total peripheral resistance, is reflected in the magnitude of P, and the numerical values of coefficients A_i or B_i in the expressions (22) or (23) for $E(P)$.

The absence of a conclusive correlation between the dZ/dt peaks and heart rate indicates that the normal physiologic range of heart rates is too narrow, or that the underlying frequencies are too low to significantly induce viscoelastic effects, which otherwise may be expected due to the viscoelastic nature of arterial walls.

V. Conclusions

It was demonstrated by direct measurement that the magnitudes of the dZ/dt peaks depend on blood pressure levels in an inverse manner. It was further shown that this dependence is retained even when the influence of the base impedance Z_0 is eliminated as a factor through dividing the experimentally measured peaks by calculated peaks obtained from the correlation of $(dZ/dt)_{\min}$ with Z_0. Similar results were obtained for the differences between the measured and the calculated peaks. It was also demonstrated that Z_0 and blood pressure are mutually independent. It was therefore concluded that the magnitude of dZ/dt peaks, primarily determined by the rate of ejection of blood from the heart (which is reflected in the magnitude of dP/dt), is also significantly modified by the magnitudes of blood pressure level.

This conclusion is consistent with the analysis of a model of elastic arteries having modulus of elasticity which is a nonlinear function of blood pressure.

dZ/dt peaks play a crucial role in current applications of impedance plethysmography, impedance cardiography, and in quantification of myocardial contractility, but in a manner which tends to ignore the discussed factors. This may lead to inaccurate results and erroneous interpretations. Although the measurements of impedance plethysmography signals and the underlying parallel conductor theory are accurate [11], their applications may not be. The correlations suggest that the ratio R or the difference D, as defined in Section III, are better suited than $(dZ/dt)_{\min}$ for applications in impedance cardiography and the analysis of myocardial contractility because they eliminate the influence of Z_0, which is an artifact in these applications. However, the dependence on blood pressure still remains. It could, perhaps, be eliminated by means of the above reported correlations with blood pressure. In any case, this dependence should be taken into account whenever the dZ/dt signal is a significant factor.

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Use of Time Integrals of the ECG to Solve the Inverse Problem

DAVID B. GESELOWITZ

***Abstract*—With the use of a bisyncytial model of the heart, it is shown that time integrals of *QRS* and *QSR-T* are related to the amplitude (A), area (μ), and activation time (τ) of the cellular action potential (AP) on the closed surface surrounding the ventricles. For the normal heart, solution of the inverse problem would give μ and τ on the heart surface and, by interpolation, in the myocardium, allowing reconstruction of the AP. In the case of ischemia and infarction, μ and $A\tau$ would be available which, while not defining the AP, might provide valuable information. Necrosis introduces an unknown perturbation.**

INTRODUCTION

Miller and Geselowitz have presented a model of the electrocardiogram (ECG) based on a bisyncytial (bidomain) model of the heart [1]. The heart is considered to consist of two interpenetrating syncytia: an intracellular domain and an extracellular domain. Current passes from one domain to the other through the cell membrane. The model predicts that the bioelectric sources in the heart are proportional to the spatial gradient of the transmembrane action potential (AP) [2], [3]. It has been quite successful in accounting for the human electrocardiogram and magnetocardiogram for the normal and ischemic heart [1], [4], as well as for potentials in a tissue bath preparation [3].

The ventricular gradient is defined as the area under the *QRS-T* waveform [5]. Other time integrals, such as the area under *QRS*, can also be considered. With use of the heart model, these time integrals can be shown to be related to three parameters of the action potential: amplitude, activation time, and area. This communication derives these results and explores some of their consequences with regard to the inverse problem.

MODEL

Heart muscle is considered to consist of an intracellular space and an extracellular or interstitial space. These two compartments, or domains, are each taken to occupy the entire tissue space. They are everywhere separated from each other by the cell membrane.

Currents will exist in both domains as a result of active processes in the cell membranes. Each domain will be considered to be a passive conductor. Hence, the current density J in each domain will be proportional to the gradient of the electric potential ϕ. The constant of proportionality is the effective conductivity σ. In the present analysis, we will ignore the anisotropy of the conductivity. The current density and potential are macroscopic quantities which may be considered to be averages over small volumes of tissue including several cells. Subscripts i and e will be used to designate intracellular and interstitial space, respectively.

We invoke one additional condition, namely, that the problem is quasi-static. Under this circumstance, the divergence of J must vanish when one considers the entire tissue space. Note that the divergence of the current density in the individual domains need not vanish. Indeed, the continuity equation demands that the net membrane current per unit volume I_m generated by membrane processes be equal to the divergence of J_e and opposite to the divergence of J_i.

These statements can be cast in mathematical form as follows:

$$J_i = -\sigma_i \nabla \phi_i \tag{1a}$$

$$J_e = -\sigma_e \nabla \phi_e \tag{1b}$$

$$\nabla \cdot J_e = -\nabla \cdot J_i = I_m. \tag{2}$$

The transmembrane potential ϕ_m is

$$\phi_m = \phi_i - \phi_e. \tag{3}$$

Hence,

$$J = J_i + J_e = -\sigma_i \nabla \phi_m - (\sigma_i + \sigma_e)\nabla \phi_e$$
$$= -\sigma_i \nabla \phi_m - \sigma \nabla \phi_e \tag{4}$$

and

$$\nabla \cdot \sigma_i \nabla \phi_m = -\nabla \cdot \sigma \nabla \phi_e \tag{5}$$

where σ, the sum of σ_i and σ_e, is the bulk conductivity of the myocardium.

Equation (5) is Poisson's equation where the term on the left may be interpreted as the source of the extracellular potential ϕ_e. Through the use of vector analysis, one can show that this scalar source term can be expressed alternatively as a vector current dipole per unit volume $\sigma_i \nabla \phi_m$ [6].

This result can also be obtained by the following argument. The potential ϕ_e can be considered to arise from cardiac electromotive forces which can be represented by impressed currents [6]. If J^i is the impressed current density at a point, then the total current J is given by

$$J = J^i - \sigma \nabla \phi_e. \tag{6}$$

A comparison of (5) and (6) leads to the result

$$J^i = -\sigma_i \nabla \phi_m. \tag{7}$$

The source term is unaffected if a constant is added to ϕ_m. It is convenient to select this constant so that the transmembrane potential is measured with respect to the resting potential of a normal cell.

Let us restrict our attention to the ventricles. The ventricular myocardial volume may be considered to be enclosed by a surface which encompasses the endocardial and epicardial surfaces of the ventricles. The endocardial surface is normally in contact with the intraventricular blood mass, while the epicardial surface is in contact with the lungs and other tissues of the thoracic volume conductor.

As long as σ_i and σ_e do not depend on J, the volume conductor is linear and superposition holds. The potential ϕ in the volume conductor and its value V on the surface can be expressed as a weighted sum or integral of the sources throughout the myocardium.

$$V = \int J^i \cdot Z dv = -\int \sigma_i Z \cdot \nabla \phi_m dv \tag{8}$$

where Z is the transfer impedence relating the potential at the observation point to the source at the element of volume dv in the heart. This result is valid even if the volume conductor is inhomogeneous.

From considerations of reciprocity, Z is equal to the lead field, that is, the electric field in the heart arising from unit current injected into the lead V [7]. Since this field arises from sources outside the heart (and the body), the current associated with it, σZ, has zero divergence everywhere. If the heart is homogeneous and isotropic, it then follows that everywhere in

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