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Intracardiac Electrical Bioimpedance as a Basis for Controlling of Pacing Rate Limits

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Abstract— **Intracardiac impedance can provide real-time hemodynamic information to automatically control the lower and upper rate limits of a rate-adaptive pacemaker. It is necessary to overcome a number of technical challenges to accomplish this within the constraints of an implantable device.**

I. Introduction

THERE are multiple approaches to controlling the pacing rate of a rate-adaptive pacemaker to provide a heart rate adequate to meet metabolic demand [1]. Several different sensors have been used to assess metabolic demands, including, body acceleration for activity and transthoracic bioimpedance to estimate minute volume MV (Fig. 1). Minute ventilation, the product of breathing rate and tidal volume, correlates well with workload, W_{body}. An ideal rate-adaptive pacing system would automatically control upper and lower rate limits to prevent over pacing [2] and under pacing [3].

Over pacing can take two forms. In the first, the paced heart rate is so high as to impact ventricular filling, putting the heart on the descending limb of the Starling curve and resulting in a decrease in cardiac output. In the second cardiac output is maintained but the heart rate, and therefore cardiac oxygen consumption, is greater than necessary to supply overall metabolic demand. This can promote cardiac ischemia and, potentially, arrhythmias.

The under pacing phenomenon occurs when the sensed demand is low and the paced heart rate is either insufficient to meet metabolic demand or the cardiac output is maintained primarily by increases in preload (i.e., increases in end-diastolic volume and stroke volume) [3]. This situation was common in the early days of fixed-rate pacing and the accompanying increases in wall-stress can promote hypertrophy, fibrosis and heart failure.

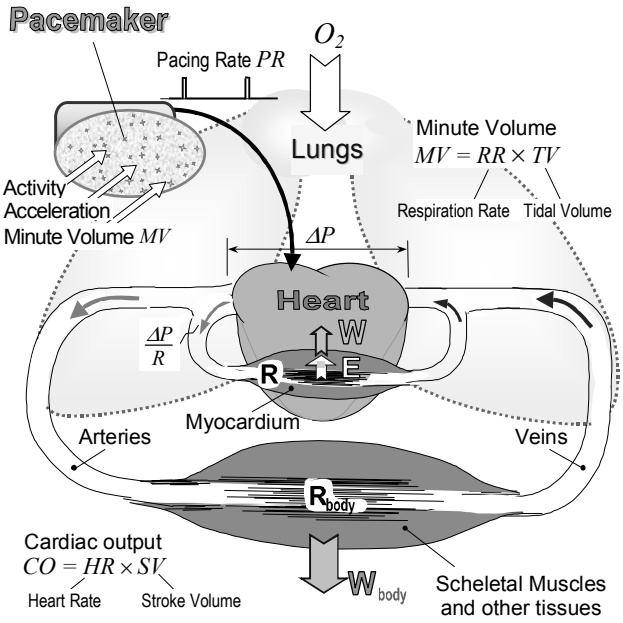

Fig. 1. Implanted cardiac pacemaker with adaptive pacing rate control, and simplified presentation of the cardiovascular system

II. Why is heart rate critical?

It is possible for metabolic demand to exceed the capabilities of a damaged heart. In attempting to meet metabolic demand, an artificial pacing system may drive the heart into failure. Traditionally, the upper and lower pacing rate limits are determined by the implanting physician and are programmed into the pacemaker at the time of implant to avoid over and under pacing of the heart. The actual values may be determined from exercise studies, from algorithms which take into account patient characteristics, or from clinical experience and are set for every patient individually [1].

Incorrect rate limits or rate response can have serious impact on a patient's quality of life. For example, postural hypotension, a sudden drop in blood pressure caused by shifts in blood volume to the lower extremities due to a decrease in hydraulic resistance, R_{body} (Fig. 1), when rising from a seated or supine posture, can lead to syncope and a fall or worse. Neurogenic syncope is a similar problem but even more insidious because the sudden drop in blood

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pressure may occur minutes after the precipitating event. If the normal compensatory vasoconstriction is missing or insufficient, the condition may be ameliorated by an increase in heart rate. Obviously, the timing and extent of this heart rate increase are critical.

A What factors impact patient's upper rate limit?

The ability of heart to work at higher rates is correlated with a better coronary reserve (CR), characterized with a capability to dilate coronary arteries and, therefore, reduce the hydraulic resistance R of myocardium (Fig. 1). Myocardium damaged during an ischemic event or by other disease (e.g., diabetes) will have limited cardiac reserve.

The ability to operate at low heart rates is determined by the ability of the heart to supply adequate cardiac output at rest, CO_{rest} (Fig. 1). Here limitations occur during ventricular filling. Compliant hearts with good diastolic function are able to increase end-diastolic volume with minimal increase in filling pressure and can double stroke volume, and therefore cardiac output, without a rate increase. This is accompanied by an increase in myocardial "stretch" and wall stress [3].

It is critical to maintain a balance between energy demand W and supply E in the heart. Since insufficient myocardial perfusion will lead to hypoxia, ischemia, and infarct, under most circumstances the primary concern must be to maintain adequate cardiac perfusion and to guarantee that $W \le E$.

B Characterization of a myocardial energy imbalance

How does one detect a myocardial energy imbalance?

Useful energy consumption or the external work W of the myocardium during a cardiac cycle can be characterized by the stroke work, the area S_{dem} of the pressure-volume loop (PV-loop), which characterizes the relationship between ventricular volume V and ventricular pressure P, as shown in Fig. 2a. On the other hand, the energy supply E is proportional to the pressure difference between the aortic or arterial and ventricular pressure over the duration of diastole t_{diast} (Fig. 2b). Therefore, the energy supply E is proportional to the area S_{sup} in Fig. 2b.

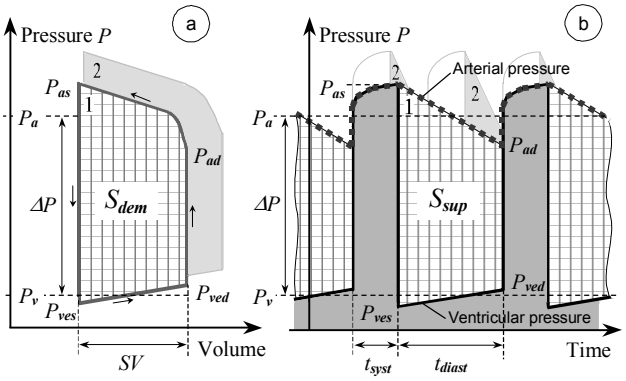

Fig. 2. Ventricular pressure-volume loop (a) and variation of arterial pressure (b).
1. $HR = HR_{initial}$ (e.g. 60 bpm) 2. $HR = 2 \cdot HR_{initial}$ (e.g. 120 bpm)

More precisely, S_{dem} is the external work done by the ventricle during a cardiac cycle pumping blood into the aorta [4, 5]. The roughly triangular area S_{pot} between the average diastolic filling pressure line P_v and the line defining the end-systolic pressure-volume relationship (ESPVR) in Fig. 3 is proportional to the potential energy requirement of myocardium W_{pot} - internal static work [6]. The total energy consumption of myocardium can be expressed as the area $S_{cons} = S_{demt} + S_{pot}$, where $S_{pot} = (V_{es} - V_0) \cdot (P_{as} - P_{ves})/2$ is calculated from the triangle in Fig. 3.

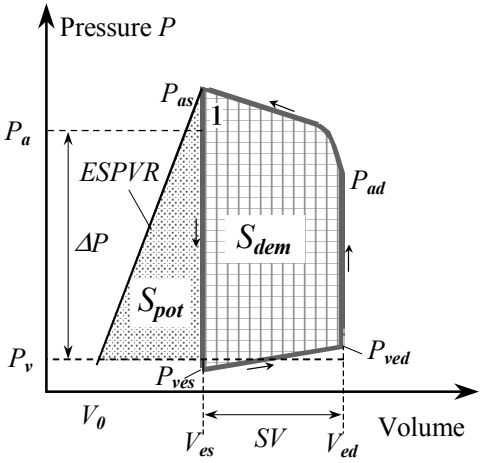

Fig. 3. P-V diagram with the triangular potential energy consumption area S_{pot}, where ESPVR is the end-systolic P-V relationship line.

The total energy consumption S_{cons} of myocardium can be expressed as $S_{dem} \cdot k_{pot}$, where k_{pot} determines the relative role of S_{pot}. The myocardial energy balance can be expressed as $S_{sup} = S_{dem} \cdot k_{pot}$, where k_{pot} depends on relative stroke volume SV/V_{es} (see Fig.4). This equality forms the basis for all subsequent discussions.

From the relationships illustrated in Fig. 4, it appears that the balance conditions depend only weakly on the systolic and diastolic arterial pressure values, P_{as} and P_{ad}. We can, therefore, substitute for them the average arterial pressure P_a.

C How to measure the pressure and stroke volume ?

The area of the P-V diagram in Fig. 2a can be expressed approximately as $S_{dem} = \Delta P \cdot SV$, and the area S_{sup} in Fig. 2b can be approximated as $\Delta P \cdot t_{diast}$, where ΔP is the mean difference between aortic and ventricular pressure. Finally, the area S_{pot} can also be expressed in terms of ΔP.

Since $S_{dem} + S_{pot} = S_{sup}$ at energy balance, ΔP drops out and it becomes unnecessary to make the pressure measurement. Thus to follow changes in energy balance it is necessary to measure only the stroke volume SV, end-systolic volume V_{es}, and the duration of diastole t_{diast}. The time interval t_{diast} can be estimated from the ECG signal as the time from the T-wave to the R-wave, or may be derived from volume or pressure waveforms. Estimation of the stroke volume SV and V_{es} requires more complicated measurements.

The energy demand W_{body} of the patient's body is currently estimated in implantable devices by the minute volume (MV) (Fig. 1), determined through measurement of the electrical

bioimpedance of the torso. Since impedance circuitry is currently available in these devices, it seems reasonable to try to assess stroke volume by the same technique.

D Impedance as a source of physiological information

Intracardiac impedance varies significantly with every stroke of the heart, and thus provides a cardiac signal component that can considered to be an impedance cardiogram (ICG). The respiratory component of the impedance signal corresponds to changes in lung impedance during breathing and is typically used in pacing rate control because it reflects the minute volume *MV* (see Fig. 1). It may be possible to use the cardiac component of the ICG to estimate the stroke volume and to use this information to maintain energy balance by controlling pacing rate.

III. Application of Impedance Measurements

We have shown [2, 3] that not only the absolute value of the *SV* but also the value of SV/SV_{rest} or $V_{es}/V_{es,rest}$ can be useful in discerning an energy imbalance. This approach is technically simpler in that absolute accuracy of the volume measurement is not necessary. Although several problems remain, the results of laboratory experiments are promising [7].

A Experimentation and modeling

Numerical models have also demonstrated the feasibility of determining ventricular volume, and particularly *SV* from intracardiac impedance [8] using a multi-electrode left ventricular catheter. However, this catheter system would be impractical for an implantable device due to the potential for thrombotic events.

In Fig. 5 are shown a comparison between the actual stroke volume measured in an intact canine model by aortic flow and the peak to peak resistance change ΔR during a cardiac cycle measured with a four electrode right ventricular catheter [7]. The relationship is quite linear even with no additional processing.

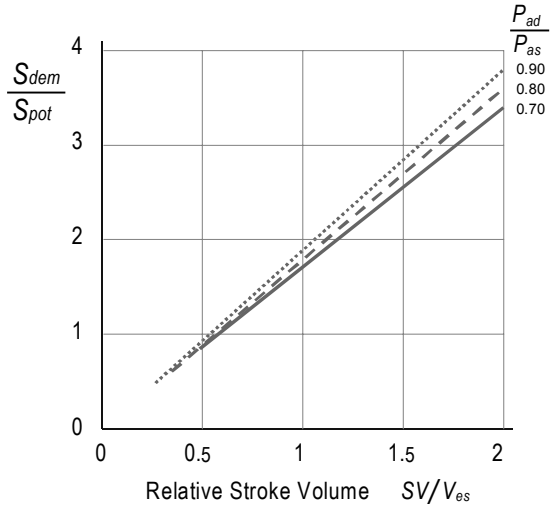

Fig. 4. Relationship of the relative energy demand S_{dem}/S_{pot} versus the relative stroke volume SV/V_{es} for some values of P_{ad}/P_{as}, derived from the simplified geometry in Fig. 3.

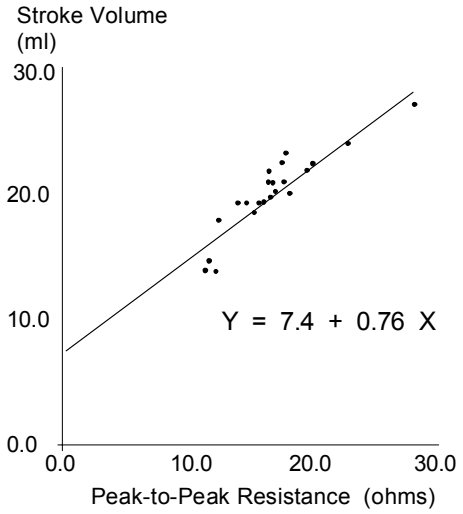

Fig. 5. A comparison between right ventricular stroke volume measured by aortic flow and right ventricular peak-to-peak resistance, ΔR, in a dog during an infusion of dobutamine [7].

The graph in Fig. 6 shows the relationship between actual (horizontal axis) volumes and volumes (vertical axis), that were calculated from the resistances generated by a finite-difference 3D model of heart conductance [8]. In this model, resistance measurements were made across the left ventricle between a coronary venous electrode positioned on the lateral wall and a right ventricular apical electrode. The heart was modeled at several ventricular volumes, corresponding to a cardiac contraction, while maintaining a constant tissue volume. The relationship is quite linear indicating the feasibility of following relative stroke volume changes using a standard implantable electrode system.

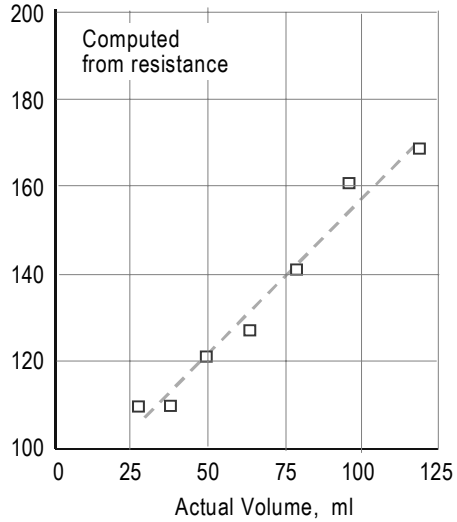

Fig. 6. A comparison between the volumes computed (vertical axis) from resistances measured across the left ventricle (from right ventricular apex to left ventricular free wall) and the actual left ventricular volumes (horizontal axis).

B Stabilizing of the stroke volume

In practice, it is difficult to predict the slope and intercept of the relationship between actual and computed volumes, but for this application it is only necessary to estimate relative changes in volume. Even just knowing the directions of changes (increasing or decreasing) is of interest when trying to stabilize the value of stroke volume [7, 9], using a simple single-input and single-output (SISO) closed loop control system. The control system would be designed to maintain the actual stroke volume SV at the predetermined constant (reference) value SV_{ref}, which does not depend on the pacing rate.

Normally, there is a highly nonlinear relationship between the pacing rate PR and the corresponding stroke volume (see Fig. 7) during exercise. In the closed loop system, the pacing rate will be adjusted automatically to a value, which satisfies the predetermined $SV = SV_{ref}$. The constant stroke volume means that the energy consumption of the myocardium will remain relatively constant for each heartbeat. At the same time, the energy supply diminishes together with a shortening of the diastolic time t_{diast} (Fig. 7) or corresponding increasing of the pacing rate $PR = 60/(t_{syst} + t_{diast})$ in beats per minute (bpm).

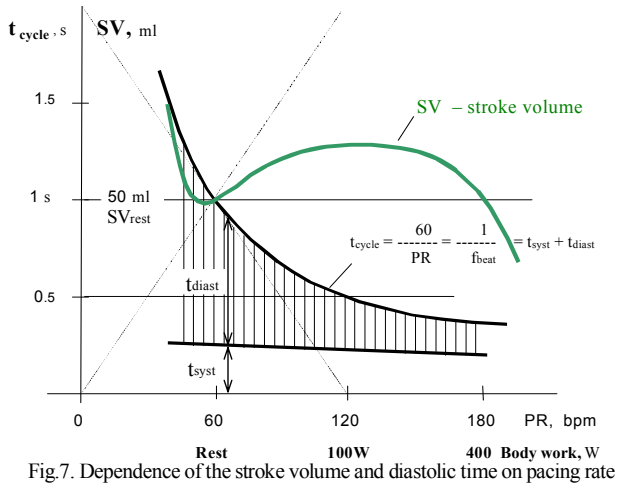

Fig.7. Dependence of the stroke volume and diastolic time on pacing rate

Now, the conditions for energy balance can be expressed directly through the pacing rate PR, knowing that in the case of balance between the energy consumption and supply a following equality takes place $k_{pot} \cdot (SV_{ref}) \cdot \Delta P = (t_{diast}) \cdot \Delta P$.

Substituting $t_{diast} = (60/PR) - t_{syst}$, it appears that the pacing rate must remain below $PR < 60\,SV_{ref}/(1 + k_{pot} \cdot SV_{ref} \cdot t_{syst})$ to avoid over pacing. This inequality is applicable in practice, because the systolic time t_{syst} remains almost constant at different pacing rates (see Fig. 7).

IV. Discussion

Several control methods and different sensors are currently used in rate adaptive pacemakers to improve the quality of life of pacemaker patients. These devices are all used in an open-loop manner and require sophisticated programming to meet patient needs under varying physiological conditions. It is possible to use hemodynamic information from bioimpedance measurements in a feed forward approach to control pacing rate while simultaneously monitoring myocardial energy balance to preclude potentially damaging heart rates. With this approach, the pacing rate is only an available control tool for satisfying the patient's metabolic demands, on the one hand, and the myocardium's energy supply needs on the other. In addition, stabilizing stroke volume would maintain a relatively constant preload and myocyte "stretch" minimizing hypertrophic signaling and subsequent cardiac remodeling.

V. Conclusions

The use of pacing in a population of patients with sick hearts demands increased concern over cardiac efficiency and maintenance of energy balance within the heart. These concerns may be addressed by a novel algorithm that requires only relative stroke volume information, derivable from bioimpedance measurements, applied to a feedback control system. New impedance measurement methods are expected to permit more reliable results to make such feedback systems feasible for rate control [10, 11]. Model based design appears to be a fruitful tool for the synthesis of complicated and nonlinear closed loop systems for pacing rate control.

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