BIOIMPEDANCE BASED CONTROL OF RATE LIMITS IN ARTIFICIAL CARDIAC PACING

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ABSTRACT
The limits of pacing rate can be made dynamically changeable in implantable cardiac pacemakers through the keeping of myocardium’s energy consumption and supply in balance automatically. The energy balance of the myocardium can be estimated indirectly by the aid of measurement of the intracardiac bioimpedance. All the information needed for adaptive control of the pacing rate limits (both, higher and lower limits), can be obtained from analysis of dynamic variations of the measured bioimpedance.

KEY WORDS
Cardiac pacemakers, rate adaptive pacing control, pacing rate limits, intracardiac bioimpedance, myocardium’s energy balance.

1. Introduction

Artificial cardiac pacing by means of implantable pacemakers has become the main method of treating cardiac rhythm abnormalities. As a rule, the abnormalities are the results of some disease or cardiac malfunctioning (like myocardium’s ischemia, infarct, etc.). Evidently, the pacing rate control of a diseased heart can not be carried out in the same way as it is assumed to be suitable for healthy persons.

In general, the pacing rate must be adaptive to the patient’s workload to ensure the required cardiac output \( CO \), which is the product of stroke volume \( SV \) and heart rate \( HR \). Several kind of body sensors (Fig.1) are used to make sure the level of physical work \( W_{\text{body}} \) of the body, e.g. activity and acceleration sensors, and a sensor of minute volume \( MV \) of respiration [1]. The most adequate means for estimating the workload is measurement of variations of the electrical bioimpedance [2] of lungs. In simple cases the pacing rate \( PR \) follows almost linearly the minute volume \( MV \) of respiration, which can be obtained directly from the measured lung impedance. However, in more complicated cases the pacing rate \( PR \) has a badly defined nonlinear dependence on respiration rate \( RR \) and tidal volume \( TV \).

The unhealthy heart can not operate at both, significantly high and low rates because of reducing of the myocardium’s energy supply \( E \) (in comparison with energy consumption for work \( W \)), which is proportional to the blood inflow equal to \( \Delta P/R \), where \( \Delta P \) is the blood pressure difference, and \( R \) is the hydraulic resistance of the vascular system of the heart itself (Fig.1). The limits between which the heart is able to operate without any danger to the myocardium can vary depending on the actual status of an unstably operating diseased organism.

There are certain medical routines established for determining the maximum and minimum cardiac pacing rate values, allowable for the patient with a diagnosed disease [1]. These settings are to be determined as the constants before implantation of the pacemaker, which are periodically re-programmable also after implantation.
Evidently, this kind of rigid or crisp pacing rate limiting between the constant values is far of the best way for pacing control. The real maximum and minimum values for the heart rate can vary depending on the actual status of the heart and patient’s health in general, and the pacing rate limits should be changeable accordingly to ensure well-being of patients.

The pacing rate control is accomplished so that it follows the energy needs of patient’s body $W_{body}$ as good as possible. The $PR$ can be expressed through some set of fuzzy rules via the respiration rate $RR$ and tidal volume $TV$ [3], see Fig. 2.

In practice, the fact that the paced heart is not completely healthy, is taken into account by establishing certain limits to the pacing rate (Fig.2). The limits do not allow to reach the values, at which the oxygen inflow or myocardium’s energy supply $E$ could become insufficient in comparison with the energy consumption (work) $W$ of the myocardium (Fig.1).

It is reasonable to make the upper and lower pacing rate limits automatically controllable depending on the current status of patient’s health. This can be introduced additionally without making any other significant changes in the existing pacing control system or algorithm [3].

The results of measurement and analysis of dynamic variations of intracardiac electrical bioimpedance can be used for getting all the information needed for performing the automatic control of pacing rate limits [1].

2. The Basic Concepts

State-of-the-art solutions use the predetermined, but reprogrammable limiting to avoid the both, too high and too low pacing rates, which can appear in rate adaptive pacemakers due to strict following the control algorithm coping the physical demand of the patient’s organism. The both extreme cases cause the lack of oxygen supply into the myocardium, and consequently a danger of hypoxia and ischemia, and even of the myocardium’s infarct. So, in certain conditions the heart can not fulfill the physiological needs of patient’s organism, and can be get injured itself, if the rate of artificial pacing is not affordable.

The crisp values are dangerous, e.g., in the cases like quick rising up from a bed, serious wounding, taking warm bath or shower, when the blood flow to the body increases very rapidly, and the blood flow to the brain is reduced correspondingly. The body needs more blood, but the cardiac output can not be increased due to rigidly limited pacing rate. The floating limits help to cope the body needs, but one must take into account the limiting factor that sudden decrease of the body resistance $R_{body}$ (see Fig.1) has a similar shunting effect also against the blood supply of the myocardium, thus leading to the lack in energy supply $E$.

The automatic rate limiting can be accomplished easily using different hardware and/or software (mathematical) means. The values for limits determine the range between upper and lower limits within of which the pacing rate can
2.1 The principle of energy balance of the myocardium

If we will be an essential step ahead in pacemaker technology, when we can change the upper and lower limits of pacing rate accordingly to current ability of the patient’s heart keeping the myocardium’s energy consumption $W$ and supply $E$ in balance. The patient can feel more healthy in various everyday life conditions from peaceful sleep to moderate work, including sudden changes in hydraulic resistance of vascular system. The variable limits can leave more space for the pacing rate to vary accordingly to the body’s demand.

It is important to underline that the energy supply of the patient’s organism (body) and the heart (myocardium) has the primary importance, not the heart rate itself. The pacing rate $PR$ is just a parameter (the only one, by the way), which is available to control the heart by the means of a pacemaker.

The current values of limits must be calculated and set up automatically. It is difficult to imagine that the pacemaker patient itself or a doctor could regulate the limits currently using online programming of the pacemaker.

2.2 The Upper Pacing Rate Limit (PRL)

Calculation is based on keeping the balance between the energy consumption and energy supply of myocardium (Fig.3) at the higher workloads of patients [3, 5]. The demanded energy consumption (myocardium’s work) can be find from the volume-pressure loop area $S_{dem}$ (Fig.4 a):

$$ W = S_{dem} \approx \Delta P \cdot SV, $$

where $\Delta P$ is the mean value of the ventricular pressure variations, and $SV$ is the stroke volume.

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![Figure 3. Block diagram of the pacemaker with automatically adjustable pacing rate limits.](image-url)
A graphical-analytical approach:

The energy supply of the myocardium can be derived graphically from the time response curve of the ventricular pressure in Fig. 4b. The area $S_{\text{supp}}$ is proportional to energy supply ($E \sim S_{\text{supp}}$). To get the physical energy dimension for the geometrical area $S_{\text{supp}}$ a formal energetical coefficient $K$ is introduced:

$$E = S_{\text{supp}} \cdot K = (\Delta P \cdot t_{\text{diast}}) \cdot K.$$  

(2)

The formal coefficient $K$ has the physical tractation too. The coefficient $K$ represents a conductance for energy influx into the myocardium, and $K$ can be expressed as

$$K = \frac{\Delta CO_2 \cdot kO_2}{R},$$  

(3)

where

$\Delta CO_2$ is the difference of the blood oxygen concentration in the artery and vein (oxygen uptake),

$kO_2$ is an energy productivity of blood oxygen, and

$R$ is a hydraulic resistance of the coronary arterial system.

The balance $W = E$ gives

$$\frac{SV}{t_{\text{diast}}} = K,$$  

(4)

and if

$$\frac{SV}{t_{\text{diast}}} > K,$$  

(5)

then the $PR$ must be reduced (limited), because the myocardium does not get sufficient amount of energy $E$, though the patient’s organism (body) can demand even increasing of the $PR$.

A medical-physical explanation:

The myocardium energy supply $E$ can be expressed as follows:

$$E = V_{mc} \cdot AVD \cdot kO_2,$$  

(6)

where $V_{mc}$ is the blood volume flowing through the myocardium during one heart cycle, and $AVD$ is arteriovenous difference (exactly the same blood oxygen uptake as $\Delta CO_2$).

Knowing that

$$V_{mc} = \int_{0}^{t_{\text{diast}}} f_c(t) \cdot dt = f_c \cdot t_{\text{diast}},$$  

(7)

we can obtain the equation

$$E = f_c \cdot AVD \cdot kO_2 \cdot t_{\text{diast}},$$  

(8)

where $f_c$ is the blood flow through the myocardium, and $f_c$ is its mean value.

Whereas

$$f_c = \frac{\Delta P}{R},$$  

(9)

we can derive the next equation for energy supply:

$$E = \frac{\Delta P}{R} \cdot (AVD \cdot kO_2 \cdot t_{\text{diast}}),$$  

(10)

and the coronary hydraulic resistance is equal to

$$R = \frac{AVD \cdot kO_2 \cdot t_{\text{diast}}}{SV},$$  

(11)

when keeping energy balance ($E = W$).

A well known parameter expressing the potential work ability of heart is the coronary reserve $CR$:  

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Figure 4. Ventricular pressure-volume loop (a) and variation of arterial pressure (b).

1. $HR = HR_{\text{initial}}$ (e.g. 60 bpm)
2. $HR = 2 \cdot HR_{\text{initial}}$ (e.g. 120 bpm)
The current value of the ratio \( R_{\text{rest}}/R \) is called coronary resistance ratio CRR:

\[
CRR = \frac{t_{\text{diast,rest}} \cdot AVD_{\text{rest}} \cdot kO_2 \cdot SV}{t_{\text{diast}} \cdot AVD \cdot kO_{2,\text{rest}} \cdot SV_{\text{rest}}},
\]

where \( R_{\text{rest}} \) characterises the hydraulic coronary resistance in the rest conditions of a patient. Knowing that \( kO_{2,\text{rest}} = kO_2 \), and denoting

\[
\frac{AVD_{\text{rest}}}{AVD} = q,
\]

(where \( q \) can vary from 1.0 to 0.5, declining lower the unite value only in the case of anaerobic work of the myocardium), we can get

\[
CRR = \frac{t_{\text{diast,rest}} \cdot SV}{t_{\text{diast}} \cdot SV_{\text{rest}}} \cdot q.
\]

As a matter of fact, the CRR expresses the degree of utilisation of the potential coronary reserve \( CR \).

When \( CRR = CR \), then all the coronary reserve is utilised, which means that the energy consumption reaches to the boarder of balance \( E = W \).

If the CRR gets bigger than \( CR \), we should limit and even reduce the pacing rate \( PR \). That is, we must avoid

\[
\frac{t_{\text{diast,rest}} \cdot AVD_{\text{rest}} \cdot kO_2 \cdot SV}{t_{\text{diast}} \cdot AVD \cdot kO_{2,\text{rest}} \cdot SV_{\text{rest}}} \cdot q > CR,
\]

or

\[
\frac{SV}{SV_{\text{rest}}} \cdot \frac{1}{q} > CR \cdot \frac{t_{\text{diast,rest}}}{t_{\text{diast}}}. \quad (17)
\]

Comparing (16) with (5) one can find the energy coefficient

\[
K = CR \cdot \frac{SV_{\text{rest}}}{t_{\text{diast,rest}}} \cdot \frac{1}{q}. \quad (18)
\]

Using \( q = 1 \), there is no over pacing danger, and a careful \( PR \) limiting takes place, avoiding even the anaerobic operation of the myocardium. The following simple inequality could be used as the criterion for \( PR \) limiting:

\[
t_{\text{diast}} > \frac{t_{\text{diast,rest}} \cdot SV}{CR \cdot SV_{\text{rest}}}.
\]

The value of \( CR \) is obtainable from the standard physical stress test using a velo-ergometer or a tread-mill, knowing that \( W = S_{\text{dem}} = AP \cdot SV \) is a mechanical work of the myocardium, and \( E = S_{\text{supp}} \cdot K = (AP \cdot t_{\text{diast}}) \cdot K \) describes the myocardium’s energy supply.

The actual value of \( upperPRL \) can be calculated from the measured relative stroke volume \( SV/SV_{\text{rest}} \) and \( t_{\text{diast}} \), knowing the values of \( HR_{\text{rest}}, SV_{\text{rest}} \) and \( CR \).

### 2.3 The Lower PRL

Too low pacing rate causes too slow influx of blood enriched with oxygen. Also a dangerous ventricle over-loading (expansion or stretching out) may occur.

So the lower \( PRL \) limit must be high enough to avoid myocardium’s hypoxia, which can appear due to slow influx of the blood, and to prevent ventricle overloading. But its value should be low enough not to disturb a peaceful sleep.

The balance between energy consumption (work) and energy supply \( E \) of the heart was proposed for determination of upper pacing rate limit (PRL) [3, 5], but the lower PRL must always ensure the minimal energy supply of the patient’s organism (body). This means that the current cardiac output \( CO = SV \times HR \) should never be lower than the rest state value \( CO_{\text{rest}} \):

\[
lowerPRL = \frac{CO_{\text{rest}}}{SV}, \quad (20)
\]

because

\[
CO_{\text{rest}} = HR_{\text{rest}} \times SV_{\text{rest}}, \quad (21)
\]

and

\[
lower PRL = HR_{\text{rest}} \cdot \frac{SV_{\text{rest}}}{SV}. \quad (22)
\]

In addition, the maximal value of the stroke volume must be also limited to avoid stretching out the ventricle, e.g.

\[
\text{max} SV < 1.5 \cdot SV_{\text{rest}} \quad (23)
\]

These two conditions must be fulfilled simultaneously for ensuring physiologically well-founded heart work management at low workloads, must be higher than the lower limit:

\[
PR > HR_{\text{rest}} \cdot \frac{SV_{\text{rest}}}{SV} \quad (24)
\]

\[
\frac{SV}{SV_{\text{rest}}} < \lambda. \quad (25)
\]

where \( \lambda = 1.2 \) to 1.5, typically, and depends on the myocardium’s health.

In the best cases \( lowerPRL < HR_{\text{rest}} \) (here \( HR_{\text{rest}} \) is typical heart rate in rest condition). So the pacemaker adapts to needs of the sleeping patient. The \( lower PRL \) is calculated currently measuring the actual relative stroke volume \( SV/SV_{\text{rest}} \), knowing the values of \( SV_{\text{rest}}, HR_{\text{rest}} \) and \( \lambda \).
3. Bioimpedance based solution

The intracardiac measurement of electrical bioimpedance is often used in the rate adaptive implantable pacemakers as a main means for sensing energy consumption of the body, because its respiratory component $Z_R(t)$ (lung impedance) reflects the minute volume $MV$ adequately. The intracardiac bioimpedance is measured by the aid of electrodes on the pacing lead, which is placed inside the heart, whereas the lungs have relatively strong effect upon the electrical impedance between the pacemaker’s metallic case and the tip electrode placed to the apex of ventricle (Fig. 5).

The respiratory component $Z_R(t)$ can be filtered out from the complex impedance response signal and used as an information on amount and character of respiration, reflecting so the minute ventilation $MV$ and physical activity, which are in a good correlation with aerobic energy consumption of the body $W_{body}$.

The means for calculating of the pacing rate limits ($PRL$) operates on the basis of information, what is acquired from the same impedance response signal as the variation of cardiac component $\Delta Z_C(t)$ changing together with the heart beating, as is given in Fig. 5 [4]. Additionally, the ventricular impedance $Z_V(t)$ is measured for better determination of the basic parameters as stroke volume $SV$ [8] and diastolic time $t_{dias}$, needed for calculation of the $PRL$.

Practical implementation:

The solution proposed can be applied in different kind of rate adaptive pacemakers in a straight way (Fig. 6). Of course, after more confident medical approvals than still has been done in this field [9]. For digital devices, an application of the method can be implemented algorithmically, that means in software.

For mixed analog/digital devices, the solution is not so easy to implement because the rate limiting unit with the limit setting means has to be added, as well as the means for computing the limit values of the $PR$ (Fig.6).

Nevertheless, the on-chip hardware realisation does not make complications. The controllable limiting can be accomplished without significant increasing the chip complexity and without raising the current consumption.

Several cardiac impedance measurement means and methods have been developed [1, 2, and 10]. The new approach is described in [11]. This method is specially elaborated for applications in such implantable devices as cardiac monitors and pacemakers.

The pacing rate controller in Fig. 6 uses variations $\Delta Z_R(t)$ of the respiratory component of bioimpedance $Z(t)$ for the direct feed-forward control of the $PR$, and the limiter uses variations $\Delta Z_C(t)$ of the cardiac component for the feedback correction of the directly elaborated $PR$ value through the changing of $PR$ limits ($PRL$).

4. Discussion and Conclusion

The proposed solution has several advantages in flexible pacing rate control (limiting) methods without affecting on the traditional $PR$ control according to the physical needs of patients.
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