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Abstract. The paper presents a novel approach to assessment of ventricular dyssynchrony basing on multichannel electrical impedance measurements. Using a proper placement of electrodes, the sensitivity approach allows estimating time difference between chambers contraction from over determined nonlinear system of equations. The theoretical considerations which include Finite Element Method simulations were verified using measurements on healthy 28 year's old woman. The nonlinear least squares method was applied to obtain a time difference between heart chambers contraction. The obtained value was in a good agreement with theoretical values found in literature.

1. Introduction

Congestive heart failure (CHF) is nowadays one of the most frequent heart diseases in developed countries. Very promising treatment for patients with CHF is cardiac resynchronization therapy (CRT). Current criteria for CRT candidacy, as well as evaluation of the therapy effectiveness are not sufficient, as still 20-30% patients take no benefit from CRT [1]. The most popular marker of dyssynchrony, is based on electrocardiographic examination [2]-[3]. However, electrical dyssynchrony is not always linked to mechanical dyssynchrony and vice-versa [4], therefore examinations that can evaluate also mechanical activity of the heart are needed. The most popular supporting examination in CRT is echocardiography. Despite its many advantages correct diagnosis is strongly dependent on the chosen biomarker depicting pathology physiological substrate as well as physician interpretation of performed examination [5].

Our proposed method is a multichannel bioimpedance measurement. This technique has been introduced for the evaluation of cardiac function in the late 1930s [6] and is still used for stroke volume assessment [7]. Mechanical activity of the heart causes changes of internal organs volumes and placement, and changes of electrical properties of tissues (due to different blood contents). Thus, such measurements can be used to improve the evaluation of the mechanical work of heart. The measured impedance change, ΔZ, invoked by a conductivity change $\Delta\sigma$ can be evaluated using the relationship proposed by Geselowitz [8]

$$\Delta Z = -\int_V \Delta\sigma(x,y,z)\frac{\nabla\phi(\sigma,x,y,z)}{I_\phi}\cdot\frac{\nabla\psi(\sigma+\Delta\sigma,x,y,z)}{I_\psi}dv\,, \tag{1}$$

where ϕ represents the potential associated with current I_ϕ flowing between the "current" electrodes, ψ is the potential associated with hypothetical current I_ψ flowing between the "voltage" electrodes after the occurrence of the conductivity change $\Delta\sigma$; V is the volume of the region of changed conductivity,

and a dot stands for the scalar product. The local conductivity change is thus weighted by the scalar product of two gradients of potential normalized by corresponding currents I_ϕ and I_ψ. The gradient has to be calculated twice, before and after the conductivity change. The integral is calculated only in the region where the conductivity change, $\Delta\sigma$, is not equal to zero.

Using Geselowitz relationship the impedance change can be view as volume (in which $\Delta\sigma \neq 0$) multiplied by some constant

$$\Delta Z = aV\,, \tag{2}$$

where

$$a = \frac{-\int_V \Delta\sigma(x,y,z)\dfrac{\nabla\phi(\sigma,x,y,z)}{I_\phi}\cdot\dfrac{\nabla\psi(\sigma+\Delta\sigma,x,y,z)}{I_\psi}dv}{V}\,. \tag{3}$$

Assume that a body is divided into regions of different conductivity change, and conductivity change inside each of such regions is constant. Assuming that the potential gradients are constant in regions (which is poor near the boundaries of regions) one can approximate the coefficients a_i i=1,…,P, where P is the number of different regions

$$a_i = \Delta\sigma_i(x,y,z)\frac{\nabla\phi_i(\sigma,x,y,z)}{I_\phi}\cdot\frac{\nabla\psi_i(\sigma+\Delta\sigma,x,y,z)}{I_\psi}\,. \tag{4}$$

In fact it is enough that integral of the scalar product of potential gradients do not depend on conductivity change inside each region (local variations in potential can cancel each other).

In the resynchronization the main interest is into mechanical work of the heart. The blood volume changes inside the chest and blood movement caused impedance changes measured by impedance technique. If we consider only the systole the impedance changes will be caused mainly by blood volume changes in heart chambers and partially by blood flowing in aorta and lungs. However there are only two sources of the blood volume changes: right and left heart chamber. Thus our approach assumes that measured impedance change during systole can be approximated by some (unknown) coefficients and blood volume change in right and left heart chamber. Under the assumption of (almost) constant value of coefficients a_L and a_R the following system of equations is obtained

$$\Delta Z(t_k) = a_L\Delta V_L(t_k) + a_R\Delta V_R(t_k) \tag{5}$$

where t_k is time, k=1,…,N, $\Delta Z(t_k)$ is measured impedance change at time t_k, $\Delta V_L(t_k)$ is left chamber volume change at time t_k, $\Delta V_R(t_k)$ is right chamber volume change at time t_k. The constant value of coefficients a_L and a_R can be achieved by proper electrode configuration (so potential gradient almost do not vary with conductivity change). Such configuration also ensures that the influence of aorta and lungs can be neglected. Small changes in the coefficients' values can be treated as noise and removed by our method.

2. Material and Method

Basing on the periodicity and shape of measured impedance change signal, the source signals (blood volume changes) were approximated by sinusoidal signals. Although such approach suggest single period approximation due to the variations in RR interval in ECG another problem appears: that time of systole and diastole are no necessary equal. Thus two cases were considered. In the first case only the systole time was considered basing on ECG and impedance cardiogram (ΔZ) analysis. The analysis begun from the R point in ECG signal and the end time of analysis was valve closing time detected from ΔZ signal. In the second case whole impedance cardiogram between two successive R points in ECG was considered. For estimation of two chambers, two measurement channels are required at least. Thus the system of 2N equations is obtained

$$\begin{cases} \Delta Z_1(t_k) = a_{L,1}\Delta V_L(t_k) + a_{R,1}\Delta V_R(t_k) \\ \Delta Z_2(t_k) = a_{L,2}\Delta V_L(t_k) + a_{R,2}\Delta V_R(t_k) \end{cases} \tag{6}$$

According to our assumptions the blood volume change can be approximated by

$$\Delta V_i(t) = A_i \sin(2\pi f_i t + \phi_i), \quad i = L, R. \tag{7}$$

Since it is impossible to distinguish between magnitude of blood volume change signal A and mixing coefficients a_i the measured signal was normalized, as so we assume that A=1. Hence the problem is reduced to finding four unknown coefficients $a_{L,1}$, $a_{L,2}$ $a_{R,1}$ $a_{R,2}$, two phases ϕ_L, ϕ_R and two frequencies of the signal f_L and f_R. The working frequency of each chamber should be the same or almost the same due to physiological requirements. This mean that the number of parameters reduces to five (f_L=f_R). However weighted sum of two sinusoidal signals produces sinusoidal signal which phase depend not only on the phases of the source signals but also on weights. Hence our problem has no unique solution. However, there are two sources with normalized amplitudes thus it can be assumed that

$$a_{L,i} + a_{R,i} = 1, \quad i = 1, 2. \tag{8}$$

This assumption is valid if the phases of two signals are equal. Thus we have 2N+2 equations and only 5 unknowns. We use nonlinear least squares to solve this over-determined system of nonlinear equations. The advantage of least squares approach is that each equation has not to be satisfied accurately. Thus the strength of the last condition can be weighted

$$M(a_{L,i} + a_{R,i}) = M, \tag{9}$$

where M>0 was chosen on the base of N i.e. sampling frequency and length of time interval analysis. Our final system of equations consists of 2N equations from equation (6) with additional constrain (two equations – one from each measurement channel) generated by equation (9). Two values of M were considered during analysis, M=N/10 and M=N/2.

Data for analysis have been collected using a specially developed measurement system [9]. It consisted of a sinusoidal, 40 kHz, current source $I(\omega)$ and two identical measurement channels. The current was passing between electrodes I_+ and I_- while two pairs of electrodes $\{V_{1+},V_{1-}\}$ and $\{V_{2+},V_{2-}\}$ formed two measurement leads (figure 1). The sampling frequency was equal to 1 kHz. The measurements were done on healthy 28 years old woman.

3. Results

Example of the approximation results for M=N/2 for systole time is shown in figure 2. The obtained time difference between chamber contractions was equal to 35 ms while time delay between approximated signals was 21 ms. The approximations of measured signals were very good. RMS approximation error for the first measurement channel was equal to 0.0521 for systole period and 0.2428 for whole RR period analysis, while for the second measurement channel 0.0720 and 0.1689 respectively.

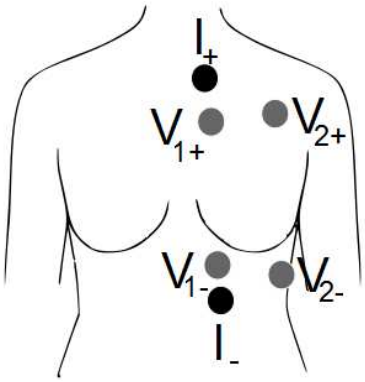

Figure 1. Measurement electrodes configuration.

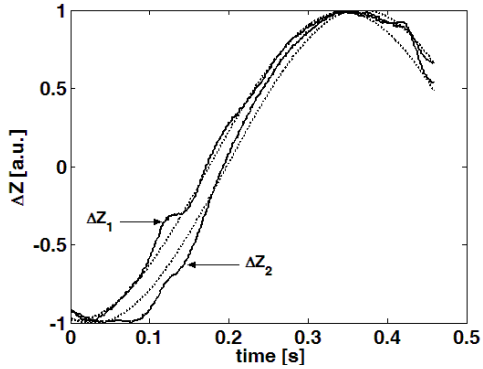

Figure 2. Measured impedance cardiograms (solid lines) and theirs approximations (dotted lines).

4. Discussion

The approximation of whole RR period does not give good results. The shape of this signal was too far from sinusoidal one, so for further analysis only systole interval was taken into account.

The obtained approximations of measured impedance cardiograms during systole time by sinusoidal signals were very good. The proposed algorithm does not allow indicating which signal comes from each chamber. This is due to symmetry of the problem (changing indexes *L* and *R* in equations produce the same approximation but different interpretation of sources). Also the indicated by our method domination chamber will depend not only on position of electrode but also on initial condition for least squares approximation (relation between *a* coefficients). This means that we can obtain time difference between chambers contraction without indicating the sequence. To do this anatomical placement of electrodes is required and support from FEM studies to estimate influence of each chamber, which allows setting proper initial conditions.

The weighting factor *M* should be chosen with care since even good approximation and small time difference for two chambers may be not correct. Its value should depend on difference of time contraction between chambers also, since the equation (9) is not exactly satisfied in general case. Better results were obtained for $M=N/2$ than for $M=N/10$.

The electrode should be placed according to the anatomy of the patient to ensure that chambers will dominate measured signals, and the placement should enable to dominate of each chamber for each measurement channel. However the last condition is not necessary to obtain proper results, but it can improve the quality of reconstruction of source signals.

Measurement system was verified by interchanging the measurement channels. Obtained results were the same. Approximated time difference (35 ms) was in good agreement with value given in literature for healthy people (about 20 ms). However, further studies include Doppler imaging as a reference method are under preparation.

5. Conclusions

The obtained results of time difference coincide with theoretical ones. Thus, the presented approach is a very promising in measuring mechanical dyssynchrony of heart chambers. The proposed method allows beat-to-beat evaluation of ventricles' synchrony. However, further studies including experimental one are needed.

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Corrigendum: Determination of time delay between ventricles contraction using impedance measurements

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