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Localization of the Origin of Premature Beats Using an Integral Method

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Abstract. A method to reconstruct integrals of transmembrane voltages in the heart from measured integrals of Body Surface Potential Maps (BSPM) is proposed. It is applied to localize the origin of premature beats in the heart (extrasystoles). In contrast to other proposals no specific assumption about the slope of the transmembrane voltage during depolarization is made, in particular it must not be a step function. This way the non-linear problem of localizing ectopic foci based on activation times is translated into a linear inverse problem. A Maximum-A-Posteriori (MAP) estimator is applied to solve the ill-posed linear inverse problem. Successful localization of ventricular extrasystoles is demonstrated using computer simulations. Even endocardial, midmyocardial and epicardial foci can be separated.

Keywords: inverse problem of ECG, premature beat, extrasystole, body-surface-potential-map BSPM, integral method

1. Introduction

Extrasystoles can initiate arrhythmias like atrial fibrillation (AF) or ventricular fibrillation (VF). In case of AF, extrasystoles often originate from the orifice of the pulmonary veins. Systematic isolation of the pulmonary veins using RF-ablation can reliably prevent initiation of AF. Non-invasive localization of the origin of these extrasystoles can support the cardiologist in selecting the suitable ablation strategy. In the ventricles, extrasystoles falling into a vulnerable window can initiate ventricular flutter that is likely to evolve into VF. If the frequency of ventricular extrasystoles becomes too high, they have to be treated with RF-ablation. A non-invasive localization of ectopic foci before the ablation can speed up the procedure in the catheter laboratory significantly. Especially a solid knowledge whether the origin is located endocardially, midmyocardially or epicardially is of utmost importance for the strategy of the cardiologist.

Various methods for solving the ill-posed inverse problem of ECG have been proposed [van Oosterom, 1997; MacLeod and Brooks, 1998; Gulrajani 1998; Dössel, 2000]. They are all aiming at imaging bioelectric sources in the heart from measured BSPMs. Activation time imaging is known to be a preferred approach to localize extrasystoles [Berger et al., 2006; He, Li and Zhang, 2002] or accessory pathways from the atria to the ventricles (WPW-syndrome) [Tilg et al., 2002, Modre et al., 2002]. The mathematical problem of activation time imaging is non-linear and only iterative solvers can handle the problem. Critical point theorem is used to find the location of the onset of the depolarization [Huiskamp and Greensite, 1997; Reimund at al. 2008]. Several model-based approaches to localize the origin of an ectopic beat have been presented [Li and He, 2001; Tilg et al., 2002, Farina et al., 2008; Farina et al., 2009; Liu, Liu and He, 2006].

Methods using the temporal integral of measured BSPM have been published before [Geselowitz, 1985]. Most of them use a strongly simplified model of the action potential: they assume the shape of a step function [Cuppen and van Oosterom, 1984] or an arctan-function [Modre et al. 2002]. The advantage of using temporal integrals is the fact, that the inverse problem to find the onset of a depolarization wave can be transferred into a linear problem.

In this article a method is proposed that exploits the advantage of the integral methods while allowing for any function of action potential, provided that it is continuously rising. Using this method the origin of an extrasystole can be localized with high accuracy.

2. Methods

This section describes the mathematics to transfer the non-linear inverse problem of finding the origin of an extrasystole into a linear problem by using integrals. Also the regularization method applied in this work to solve the final linear problem is presented. In addition a method for validation of the new approach is described briefly: a cellular automaton is applied to simulate realistic distributions of transmembrane voltages in the heart, and FEM is used to find the corresponding BSPMs. This way synthetic BSPMs of various ventricular extrasystoles with known origin are created. After adding noise the new integral method is employed to reconstruct the origin of the extrasystole. The result is compared with the true focus of the extrasystole.

2.1. Integral method and transfer to a linear problem

The forward problem of ECG is usually stated as:

$$Ax = b \tag{1}$$

with x being the source vector, A the leadfield matrix and b the vector of measured signals at the body surface. x could be a vector of impressed currents, of epi- and endocardial potentials or of transmembrane voltages. In this article the choice for transmembrane voltages has been made.

Obviously the equation is also valid, if on both sides temporal integrals are introduced o both sides:

$$A\tilde{x} = \tilde{b} \tag{2}$$

with

$$\tilde{x} = \sum_{i=k1}^{k2} x_i \quad and \quad \tilde{b} = \sum_{i=k1}^{k2} b_i \tag{3}$$

The clue is, that for any shape of action potential curves – provided it is continuously rising and nearly equal in all points around the origin – the temporal integral of transmembrane voltages will show a maximum at the point of first depolarization. All other points will depolarize with a delay so that the temporal sum can only be smaller. So an image of $\tilde{x}$ must show a clear maximum at the origin of the extrasystole.

Using a specific assumption about the slope of the action potential, e.g. based on cellular measurements or based on widely accepted computer models of heart cells, even a first approximation of the activation times can be calculated from the distribution of $\tilde{x}$. The slope of the action potential of atrial cells differs significantly from ventricular cells, but various atrial cells show a very similar onset of action potential, and the various ventricular cell types behave similarly as well.

The contrast of the image becomes better if the time window k1 to k2 in equation (3) is chosen as the time the depolarization wave needs to spread out across the heart, which is about 80ms for the ventricles. The time window must not be larger than the time, the action potential stays in the plateau phase. The specific choice of the length of the time window is not critical.

Taking more temporal points into account by increasing the temporal window will improve the signal-to-noise ratio of the solution. So there is a tradeoff between a long time window to reduce noise and a short time window to make sure that the falling slope of the action potential is not included into the integral. A downsampling of the temporal measuring points is an advantage concerning the signal to noise ratio, and in addition the upstroke of the action potential will give a stronger impact on the temporal sum as compared to the plateau phase contribution.

The beginning of the time window k1 should be chosen at the onset of the BSPM signal of the extrasystole. Also the precise choice of the right moment for k1 is not critical.

Obviously Eq. 2 is a linear problem. This way the non-linear problem of activation time imaging that aims at finding ectopic foci has been transferred into a linear problem. But it should be pointed out again, that the resulting distribution $\tilde{x}$ is not an activation time map. It can be used to find the onset of depolarization and it can be used to calculate a first approximation of the activation times.

2.2. Regularization technique for the linear problem

In this article a maximum-a-posteriori (MAP) estimator was employed to solve the linear inverse problem. It has been described before [Martin et al., 1975; van Oosterom, 1999; Farina et al., 2005; Serinagaoglu et al., 2005; Serinagaoglu et al., 2006; Jiang et al., 2007]. Equation (4) gives the details:

$$\hat{\tilde{x}} = C_x A^T \left(A C_x A^T + C_e \right)^{-1} \tilde{b} \tag{4}$$

where C_x and C_e are covariance matrices of the source distributions and errors respectively. The covariance matrix C_x is calculated by triggering extrasystoles in 81 segments of the left ventricle at 3 different depths (endocardial, midmyocardial and epicardial). This way a database of 243 extrasystoles is created which is then used to calculate a covariance matrix of the source distributions. This covariance matrix can easily be calculated for each individual patient. Calculation time is several hours but the calculation can be done beforehand without any user interaction.

C_e is estimated as λI where λ indicates the variance of the error and I is the identity matrix.

2.3 Method of validation

First a 3D dataset of a patient's thorax gained with MRI was selected (4mm*4mm*4mm) and segmented (heart, lung, intestines, liver). The heart was segmented and interpolated with 1mm*1mm*1mm resolution.

Next, a cellular automaton was used to create the time course of the transmembrane voltage after the onset of an extrasystole. The cellular automaton is a rule based automaton, where every voxel represents a patch of ventricular tissue. Every cell that is depolarized will initiate a depolarization in the neighboring cells. The time course of action potential was calculated beforehand using ten Tusscher's cardiac cell model [tenTusscher et al., 2004], embedded into a virtual wedge preparation. Transmural heterogeneity of the ventricular wall was taken into account.

After the calculation of the time course of all transmembrane voltages in all voxels of the left ventricle (saved with a time step of 4ms) the extracellular potentials were calculated using following equation:

$$\nabla \cdot \left(\left(\sigma_i + \sigma_e \right) \nabla \Phi_e \right) = -\nabla \cdot \left(\sigma_i \nabla V_m \right) \tag{5}$$

with σ_i and σ_e representing the intra- and extracellular conductivity tensors, Φ_e the extracellular potential and V_m the transmembrane voltage. FEM on a tetrahedral grid was used to solve the Poisson equation (5) using appropriate boundary conditions.

64 virtual electrodes were attached to the body surface and a simulated BSPM was created. Various levels of noise were added to the "measured" signals. For the temporal integrals 7 time steps of 4ms (8 time points) summing up to a time window of 28ms were selected.

These BSPM data were used to validate the method described in 2.1 and 2.3. This method of validation bears the disadvantage of not using real patient data. It has the advantage that the ground truth about the real origin of the extrasystole is known, which is often not the case in real patient data.

3. Results

3.1. Comparison of activation times and temporal integrals of transmembrane voltages

Figure 1 shows a comparison of activation times and sums of transmembrane voltages gained with the cellular automaton after initiating an extrasystole at the endocardium, midmyocardium and epicardium of the left ventricle. It can be recognized that the spread of depolarization and the sum of transmembrane voltages show a large similarity. In addition the sum of BSPM is depicted in Fig. 1. It also becomes obvious, that endocardial, midmyocardial and epicardial extrasystoles show a very different BSPM, so they can clearly be distinguished.

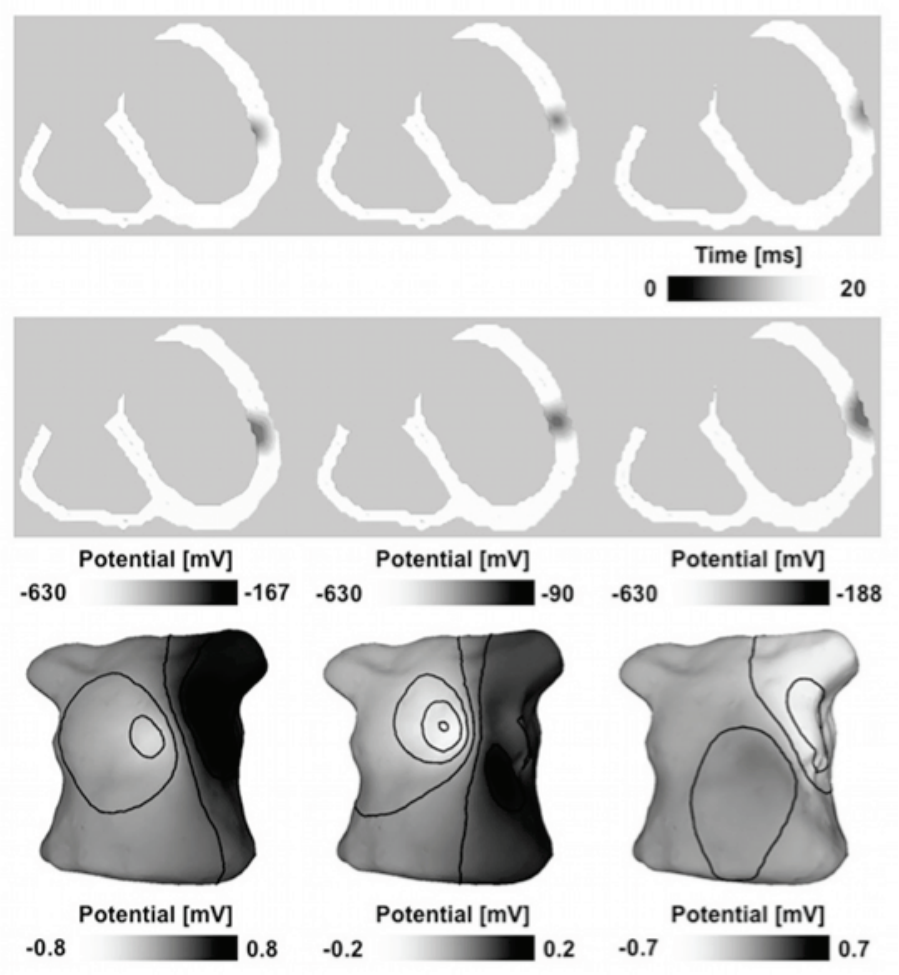

Figure 1. *upper row: activation times after initiating an extrasystole in the endocardium, midmyocardium and epicardium, middle row: sum of transmembrane voltages with 16 time steps and a total time window of 32ms, lower row: sum of BSPMs with 16 time steps and a total time window of 32ms.*

3.2. Localization of premature beats

Several ectopic beats (not belonging to the data base for the covariance matrix C_x, see Eq. 4) were first localized using conventional Tikhonov regularisation and MAP regularization for a single time instant near to the onset of the extrasystole. Next, the temporal integrals were used, and again conventional Tikhonov regularization and MAP regularization were applied. Figure 2 compares one of the results. In addition, the distance between the ground truth of the ectopic focus and the reconstructed focus is given in mm.

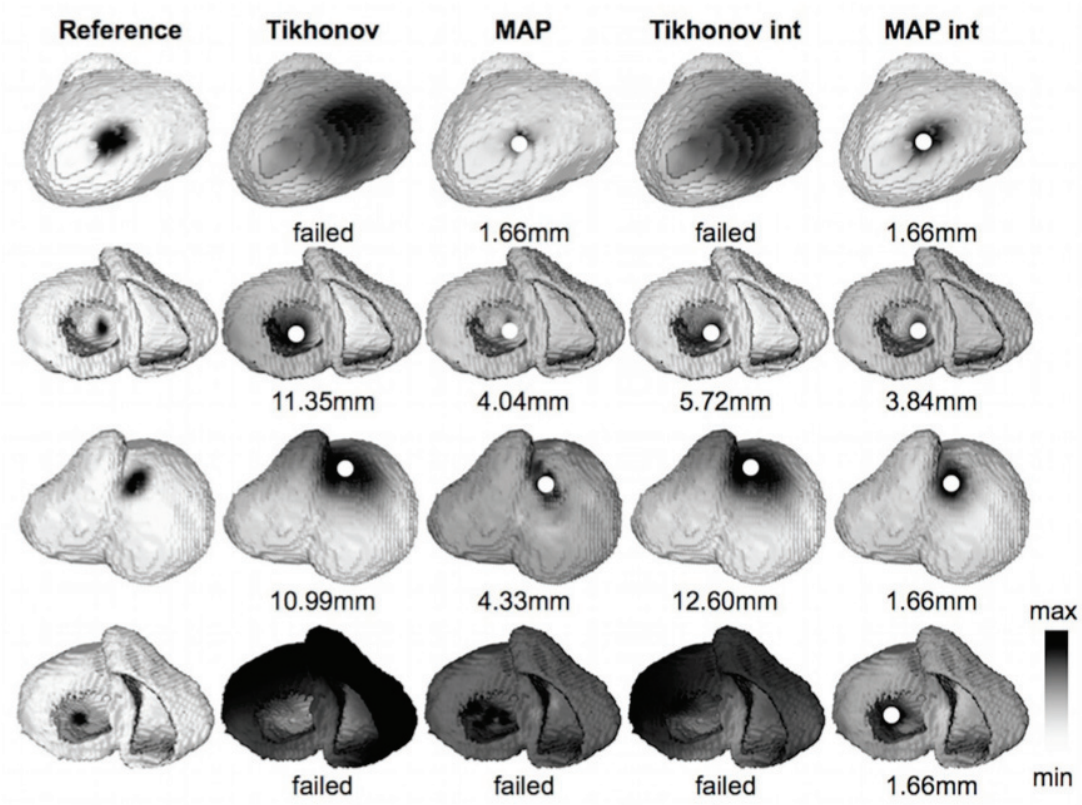

***Figure 2**. left column: 4 different simulated extrasystoles – ground truth,*
second column: reconstructed transmembrane voltages (TMVs) using conventional Tikhonov regularization for a single time instant near to the onset,
third column: reconstructed TMVs using MAP regularization for a single time instant near to the onset,
forth column: reconstructed integral of TMVs using conventional Tikhonov regularization,
fifth column: reconstructed integral of TMVs using MAP regularization.
In addition the distance between ground truth and reconstructed focus is given.

4. Discussion and conclusions

Whereas the conventional reconstruction techniques give only smeared out results with no clear answer to the localization of the ectopic focus, the integral method performs much better. Comparing Tikhonov and MAP based regularization, the MAP method performs significantly better.

The next step must be a test with clinical data, preferably with a clear knowledge of the ground truth based on intracardiac mapping data.

It has to be stated that the MAP based method relies on the input of the cardiologist, that the event is a ventricular extrasystole. If this input is wrong the method will fail. This is not a crucial disadvantage, because cardiologists can clearly distinguish ventricular extrasystoles from other events.

The proposed method might be tested with atrial extrasystoles as well. Reasonable results are expected even though the problem of reconstruction of atrial sources is significantly more ill-posed as compared to ventricular signals due to the larger distance between the electrodes and the sources.

It could be also worthwhile to test, whether the sum of transmembrane voltages can be translated into activation time maps. Figure 1 supports this idea, since activation times and sums of transmembrane voltages show a very similar distribution. These estimated activation times could be used as a first approximation for an iterative solver to reconstruct activation time maps.

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