# On the Initial Estimate of Repolarization Times for Inverse Reconstruction Using the Equivalent Dipole Layer Source Model

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## Abstract

*The equivalent dipole layer (EDL) source model for noninvasive reconstruction of cardiac electrical activity applies a nonlinear parameter estimation procedure starting from an initial estimate of activation and repolarization times. In this paper, we compare two methods to determine the initial estimate for repolarization from that of activation: reversely (method 1) and directly (method 2). In a pig experiment, we found lower errors with higher correlation coefficients between measured and reconstructed repolarization times using method 2 as initial estimate for repolarization for both atrially and ventricularly paced beats. This corresponds with the linear positive relation between measured activation and repolarization time and the discordance of QRS complex and T-wave polarity on the body surface potentials in both atrially and ventricularly paced beats, indicating a similar sequence of activation and repolarization. In human data, there is a big difference in reconstructed repolarization pattern when using method 1 or 2 for initial estimate of repolarization. Here, there is a concordance in the majority of leads for a sinus beat and a discordance in the majority of leads for PVCs. We recommend using the relation of the QRS complex and T-wave to determine which method for initial estimate for the EDL method of the inverse solution is most suitable for each individual beat.*

## 1. Introduction

Noninvasive electrocardiographic imaging (ECGI) is a tool that estimates cardiac electrical activity from recorded body surface potential (BSP) measurements. Solving this inverse problem requires a patient-specific geometrical model and a model for the electrical source. Two frequently used source models are 1) the epicardial potential model, which estimates electrograms on the epicardial surface of the heart [1] and 2) the equivalent dipole layer (EDL) method, which directly estimates activation and repolarization times (AT and RT) on both epicardium and endocardium [2].

For the potential method, there is a linear relation between the BSPs and the epicardial voltages. Consequently, the associated inverse problem is linear, and the solution is relatively straightforward. With the EDL method, the relation between the BSPs and the model parameters (AT/RT) is nonlinear. It applies a nonlinear parameter estimation procedure starting from an initial estimate for activation and repolarization times.

While we can use propagating characteristics to determine the initial estimate for activation [3], this is not applicable for an initial estimate for repolarization since this process is not propagating from a single or small number of sites. We surmise that the polarity of the T-wave on the ECG can be used for an initial estimate of the repolarization process. In humans, the T-wave and QRS complex have the same polarities (concordant) in the standard 12-lead ECGs in sinus beats. This suggests that the overall repolarization process occurs in a sequence opposite to activation direction [4]. However, the T-wave and the QRS complex of a premature ventricular complex (PVC) are often discordant, indicating a similar sequence of activation and repolarization. The relation between the polarity of the QRS-complex and the T-wave is species dependent. In ungulates, the QRS-complex and the T-wave are commonly discordant. This is at least in part explained by the electrophysiological differences in His-Purkinje system between ungulates and humans [5]. Given these differences, inverse reconstruction with the EDL method might require a different approach for the initial estimate for pigs and humans, which is important since ECGI validation studies are often performed on pigs.

In this paper we test how different strategies for the initial estimate of the repolarization times can lead to different outcomes of the inverse problem, both in pig and human. We propose to use the relation between the polarity of the QRS-complex and the T-wave to determine the best method for an initial estimate.

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## 2. Methods

### 2.1. Experimental Data

Animal experiments were approved by the institutional review committee, and animal handling was in accordance with the Dutch Law on Animal Experimentation and the European Directive 2010/63/EU. Human data collection was approved by the local ethical committee and written informed consent was obtained.

Pig data. We recorded 60 lead BSPs and performed an MRI to determine the geometries. For validation on the epicardial surface, we opened the thorax, placed a 108-electrode sock around the heart and reclosed the thorax airtight. Furthermore, a venous and an arterial decapolar mapping catheter was placed for endocardial validation. Atrial pacing was performed from the venous catheter, placed in the right atrium, and ventricular pacing was performed through an epicardial pacing electrode on the LV free wall.

Human data. We recorded 67 lead BSPs and an MRI to determine heart geometry. The patient showed no structural abnormalities of the heart, but experienced frequent spontaneous PVCs. After recording the BSPs the patient underwent successful ablation in the right ventricular outflow tract (RVOT) to terminate the PVCs.

### 2.2. Initial Estimate

We investigated two methods to determine the initial estimate for repolarization. Both methods are based on the initial estimate for activation, which is determined by the fastest route algorithm, considering each node on the surface as initial focus and determining which resulting BSPs correlate best with the actual BSPs of the QRS-complex [3]. For ventricular activations, the initial estimate consisted of a single focus, while for atrial beats up to 3 additional foci are added to simulate multiple breakthrough points of activation in humans [6].

The first method of initial estimate for repolarization is described in a paper by van Dam *et al.* [3]. It assumes a long action potential duration (APD) for sites of early activation and a short APD for sites of late activation, representing a reversal of the pattern for activation, associated with a concordant T-wave. The second method of initial estimate for repolarization assumes a positive linear relation for activation and repolarization times. Therefore, the initial activation pattern was transformed to repolarization times by adding the fixed interval from QRS onset to the apex of the T-wave, as measured on the root-mean-square BSPs. This is associated with a discordant T-wave.

### 2.3. Data Analysis

RTs were determined as time of maximum dV/dt of T-wave on electrograms recorded at the heart surface. The mean absolute error (mean±SD) and the Pearson's R correlation coefficient (CC) between measured and calculated RT on the electrode recording sites were determined. The integral between QRS onset and J-point and between start of T-wave and end of T-wave (all determined manually on the root-mean-squared BSPs) were used to determine polarity of QRS complex and T-wave.

## 3. Results

### 3.1. Pig Data

BSPs maps indicate a concordance between QRS complex and T-wave of 8/60 leads (13%) in the atrially

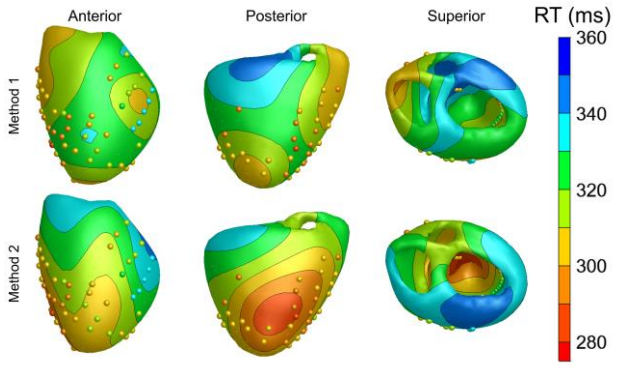


Figure 1. Three views of the heart, with surface color indicating the ECGI reconstructed repolarization pattern of the atrial paced beat, spheres indicating electrode measurement sites, and sphere color indicating the corresponding measured repolarization time (RT). Top part used method 1 as initial estimate, bottom part method 2.

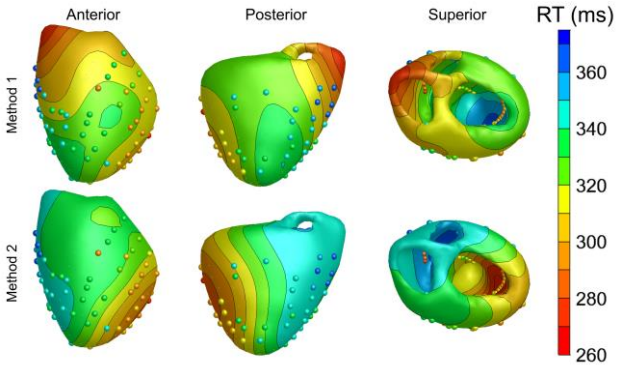


Figure 2. Three views of the heart, with reconstructed (surface) and measured (spheres) repolarization times of the ventricular paced beat. Top part used method 1 as initial estimate, bottom part method 2.

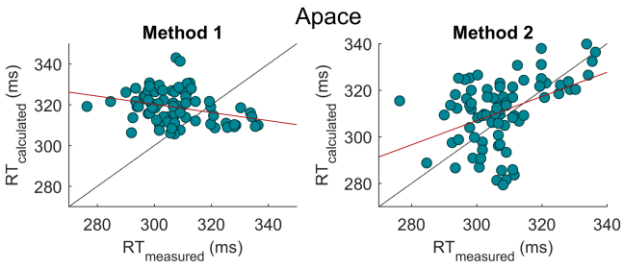


Figure 3. Scatterplot of measured versus calculated repolarization times at recording locations for an atrially paced beat, by using different methods for initial estimate of repolarization.

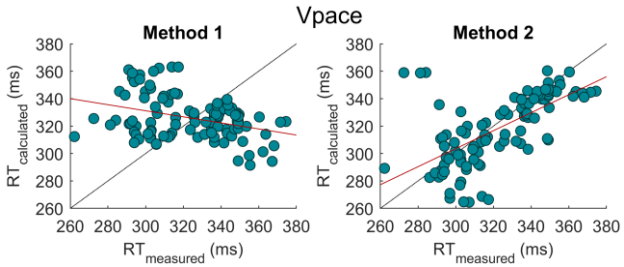


Figure 4. Scatterplot of measured versus calculated repolarization times at recording locations for an ventricularly paced beat, by using different methods for initial estimate of repolarization.

paced beat and 5/60 leads (8%) in the ventricularly paced beat. There was a linear positive correlation between measured AT and RT in both atrially and ventricularly paced beats (CC of 0.70 and 0.83 respectively, both $p<0.05$). Figure 1 shows the reconstructed repolarization patterns of the atrially paced beat with the spheres indicating the measured RT at that location. The reconstructed RTs calculated from an initial estimate constructed by method 2 fit the measured times better at most locations, as seen in the LV anterior view and near the apex in posterior view. The same is valid for the PVC in Figure 2. A big difference between reconstructed RT patterns is seen in the RV, with early reconstructed RT with method 1 and late reconstructed RT with method 2. A comparison between measured and calculated RTs is given in Figures 3 and 4. For the atrially paced beat (Figure 3), initial estimate method 1 resulted in a mean absolute error of 16.8±10.1 ms, and a correlation coefficient of -0.30 ($p<0.05$). Initial estimate method 2 resulted in a repolarization pattern with a mean absolute error of 11.4±8.8 ms, CC 0.44 ($p<0.05$) (N=79). For the ventricularly paced beat (Figure 4), initial estimate method 1 gave a mean absolute error of 27.3±19.6 ms, and a CC of -0.34 ($p<0.05$). Initial estimate method 2 resulted in a repolarization pattern with a mean absolute error of 14.5±16.2 ms, CC 0.64 ($p<0.05$) (N=105). For both beats, the differences in error between method 1 and method 2 are statistically significant ($p<0.05$).

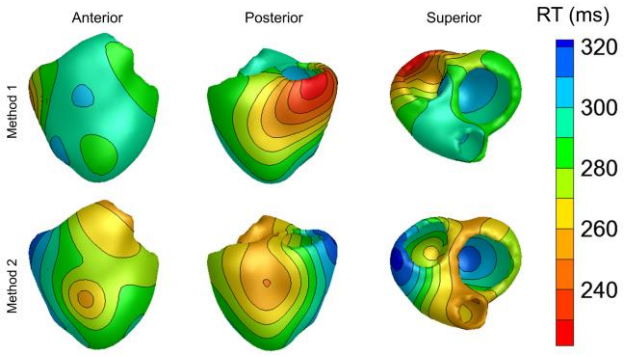


Figure 5. Three views of the heart showing final ECGI reconstructed repolarization patterns of a sinus beat. Top part used method 1 as initial estimate, bottom part method 2.

## 3.2. Human Data

BSPs maps indicate a concordance between QRS complex and T-wave of 49/67 leads (73%) in sinus beat and 5/67 leads (7%) in PVC. The results of the inverse for a sinus beat and a PVC are given in Figures 5 and 6 respectively, showing the heart in anterior, posterior and superior position with initial estimate method 1 at the top and initial estimate method 2 at the bottom. A large difference exists between the two reconstructed patterns using the two methods of initial estimate. RT was early in RV base with method 1 and late with method 2 in sinus beat (Figure 5) and late with method 1 and early with method 2 in RVOT for the PVC (which was the point of origin for this beat) (Figure 6).

## 4. Discussion & Conclusion

The results from this study show that the EDL method can estimate repolarization times, provided that the initial estimate of the repolarization times does not contradict the global direction of the spread of repolarization. It may still find the correct pattern of repolarization if the general

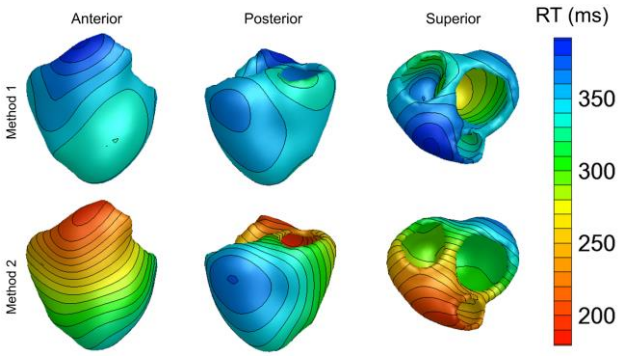


Figure 6. Three views of the heart showing final ECGI reconstructed repolarization patterns of a PVC. Top part used method 1 as initial estimate, bottom part method 2.

order of repolarization is incorrect, but that is not assured. This is a typical property of non-linear problems, where the solution is improved step by step starting at an initial estimate, akin to walking down a slope in order to end up in the valley; by starting at the other side of a mountain range, you end up in a different valley.

The pig data show an overestimation of RT at early and underestimation of RT at late repolarizing sites when using method 1 for initial estimate of repolarization. Given the predominant discordance in the recorded BSPs, this is likely a direct consequence of the method used for initial estimate of repolarization; early initial activation gives late initial repolarization. Method 2, a direct relation between AT and RT, gives better results. The positive linear relation between measured AT and RT fits with the discordance on the BSPs and explains the better fit with method 2.

In the human heart, both ECGI reconstructions resulted in a similar (good) fit of BSPs, despite the fact that the solutions differed significantly. This illustrates the difficulty of solving a nonlinear ill-posed problem and the importance of a good initial estimate. In these recorded BSPs, however, there was a clear difference in QRS-T relations between sinus beat and PVC. For sinus beats, the concordance of QRS and T-wave polarity suggests that the repolarization follows the opposite direction of the activation order. For ventricular premature beats, the activation and repolarization occur in more or less the same direction, leading to a QRS-T discordance. Thus, we argue that the morphology of the T-wave relative to that of the QRS-complex can serve to improve the inverse solution in the EDL method of ECGI. Even in one individual patient, the T wave may be concordant or discordant to the QRS-complex, depending on the origin of the PVC. For example, a PVC coming from an area close to Purkinje network might result in a QRS-T relation that more resembles that of a T-wave of a sinus beat. On the other hand, a PVC originating at a distance of the Purkinje system may generate a discordant T-wave (as in our pig and human experiment). Human in-vivo data about full repolarization patterns is scarce, but seems to corroborate the hypothesis that the AT/RT relation is linear in ventricular paced beats [7] and inverse in sinus beats [8].

We therefore recommend using the relation of the QRS complex and T-wave to determine which method for initial estimate for the EDL method of the inverse solution is most suitable for each individual beat. Implementing the QRS-T polarity relation in the initial estimate for repolarization would objectify the EDL method for ECGI.

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