Differences in Non-Invasive Imaging of Atrial and Ventricular Recovery

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Abstract

Non-invasive imaging of cardiac activation and recovery based on the equivalent double layer source model is a non-linear and ill-posed problem. The problem involved is cast in the form of a non-linear parameter estimation, requiring an initial estimate and regularized minimization.

While focusing on the estimation of the timing of repolarization, we compared the effect of applying the regularization to either the timing of recovery or to the activation recovery interval (ARI). The results suggest that regularizing the ARI is to be preferred in the estimation of the timing of recovery of the atria as well as of the ventricles.

1. Introduction

Recently we have reported on progress made in a non-invasive method for imaging the timing of activation (depolarization) and recovery (repolarization) [1]. The method uses an equivalent double layer at the surface bounding the myocardium having a strength proportional to the local transmembrane potentials (TMP). The TMP is parameterized by the clinical relevant timing of depolarization and repolarization. These parameters are found by minimizing the difference between measured body surface potentials and those based on the source description.

The parameter estimation procedure involved is non-linear and thus requires the specification of initial estimates for the timing of depolarization (δ) and repolarization (ρ) [1]. The subsequent iterative estimation procedure alternated between improving the estimates of the timing of depolarization and repolarization. The surface Laplacian was applied as the regularization operator.

The quality of the resulting estimated timing of depolarization was in qualitative agreement with reports in the literature. However, for the timing of repolarization, no complete set of experimental data is available. In fact, widely different models for the genesis of the T wave, the expression of repolarization in the ECG, can be found in the literature. While scrutinizing our results the idea arose of testing the quality of estimation of the timing of repolarization of applying regularization to the activation recovery interval (ARI), i.e., $\alpha = \rho - \delta$ instead of the timing of repolarization itself.

In this report we compare the estimation of the timing of repolarization, while regularizing either the ARI values or the timing of repolarization, both for the atria and ventricles.

2. Materials

Body surface potentials (64-lead ECG) were recorded on a healthy subject, a 22-year old human male. The fiducial points: onset P, onset QRS, J-point and end T wave were derived from the root mean square signal of the ECG signals. The signals were sampled at 1 ms intervals. The resulting data were stored in a matrix of size ($64 \times T$), with T the number of samples used; for the atrial activity T=169 samples taken from onset P wave till onset QRS, and T=350 from the complete QRST interval. The atrial signals do not cover the compete atrial repolarization, the remaining part is hidden in the QRS complex.

On this subject, MRI-based geometry data were recorded, from which the individualized volume conductor model was constructed, incorporating the effect of major inhomogeneities in the conductive properties of the thorax, *i.e.* the lungs, the blood-filled cavities and the myocardium on the transfer between the electric sources and body surface potentials. The geometries of the atria and ventricles were reconstructed from the data at the P wave onset.

3. Methods

The inverse procedure used is based on the equivalent double layer (EDL) source model. The local source strength is the transmembrane potential (TMP) at the surface of the myocardium. The TMP waveform is described analytically by a parameterization that includes the local timing of depolarization (δ) and repolarization (ρ) [2] over the myocardial surface. The latter is described by two triangular meshes, one for the atrium and one for the ventricles, each comprising N=1500 nodes. The

problem involved deals with the estimation of vectors **δ** and **ρ**, each of size *N*=1500, specifying the timing of depolarization and repolarization, respectively.

The estimation problem was carried out by minimizing in the least squares sense with respect to the parameters **δ** and **ρ**, the difference between the matrix of simulated potentials, Φ(**δ, ρ**), and the matrix **V** of corresponding body surface potentials observed on the subjects studied. Since the source strength depends non-linearly on the **δ** and **ρ**, the minimization procedure needs to be carried out iteratively, for which we used a dedicated version of the Levenberg-Marquardt algorithm [1].

The non-linearity of the problem requires the specification of an initial estimate. For the timing of depolarization, **δ,** this was derived by using the fastest route algorithm, which takes into account the anisotropic nature of the propagation of cardiac activation (van Dam *et al*. [1]). In short, *N* activation sequences are generated at all nodes on the myocardial surface, one for each node acting as a focus. Next the node is identified for which the activation sequence results in simulated ECGs that correlate best with the measured one. Subsequent breakthroughs are added to the activation sequence until no further improvement of the correlation between the elements of the simulated and measured data is obtained.

The initial estimate for **ρ** takes into account electrotonic effects: with longer ARIs (**α** = **ρ** – **δ**) values at local minima of **δ** and shorter ones at local maxima of **δ** [3].

The subsequent iteration steps alternate between updating **δ** and **ρ**, carried out by solving

$$\arg\min_{\delta,\rho} \| \mathbf{V} - \mathbf{\Phi}(\boldsymbol{\delta},\boldsymbol{\rho}) \|_F^2 + \mu_\sigma^2 \| \mathbf{L}\boldsymbol{\sigma} \|^2 . \qquad (8)$$

Matrix **L** represents the surface Laplacian operator, which serves to regularize the solution by guarding its (spatial) smoothness, μ^2_σ the weight for the regularizing any of the parameters, denoted by **σ,** tested and $\| \ \|_F$ the Frobenius norm. A larger μ_σ creates a smoother spatial pattern and a reduced dispersion of the elements of solution vector, generally reducing their standard deviation and range.

The differences between simulated and recorded ECGs were quantified by using the *rd* measure: the root mean square value of the differences between all matrix elements relative to that of the recorded data.

4. Results

Based on our previous experience [1] the regularization weight, μ_δ was fixed at 1.5e-4, which resulted in a stable solution at subsequent iteration steps, having a value for $\|\mathbf{L}\boldsymbol{\delta}\|$ of ±24-25 and a range for **δ** of ±95 ms. Subsequently, three values for μ_ρ and μ_α were used in the optimization procedure (Table 1).

Table 1. Ventricular activity; ranges of **ρ** *and* **α** *found by regularizing either* **α** *or* **ρ** *for different values of* $\mu_\alpha = \mu_\rho$. *Regularization values of* $\|L\sigma\|$, *as listed.*

μ_α and μ_ρ × *1e-6*	$\|\mathbf{L}\cdot\boldsymbol{\alpha}\|$ $s\cdot m^{-1}$	**ρ** range *ms*	**α** range *ms*	$\|\mathbf{L}\cdot\boldsymbol{\rho}\|$ $s\cdot m^{-1}$	**ρ** range *ms*	**α** range *ms*
15	62.3	144	175	61.1	148	181
150	23.3	59	95	7.0	37	108
1500	21.2	57	68	0.9	22	105

The final value of $\|\mathbf{L}\boldsymbol{\sigma}\|$ was more stable for larger values of μ when using the ARI values (**α**) instead of the repolarization values (**ρ**) as the regularization parameter. The number of iterations needed to obtain a stable solution ranged from 8 (μ=1.5e-6) to 25 (μ=1.5e-4). When using μ (1.5e-6) the solutions were nearly identical for both regularization parameters. For larger values of μ smoother patterns are obtained, having a smaller range.

For the estimation of the depolarization of the atria less regularization is required, because the sinus node activation is far less complex than the ventricular activation, influenced as it is by the His-Purkinje system. On the other hand the range of the ARI values is expected to be smaller [3], requiring more regularization. Accordingly, μ_δ was set at to *1e-6* and μ_ρ and μ_α to 3e-5. These values resulted in a depolarization range of 125 ms for the **ρ**-regularized procedure (18 iterations) and 119 ms for the **α**-regularized one(15 iterations).

The *rd* values for the atria were 0.22 for either of the regularized parameters. The estimated activation sequences were almost the same: their difference in timing was 0.01 ± 0.28 ms

For the ventricles the *rd* was 0.11 when using ARI regularization as well as when regularizing using the repolarization times; the difference for the ventricles -0.02 ± 0.63 ms (see also Figure 1 and 3).

Table 2. Ranges of **α** *and* **ρ** *found by using either* **α-** *and* **ρ-** *based regularization. Numbers in brackets indicate the range. All values are given in ms.*

		regularized parameter	
		ARI	**repolarization**
atria	**α**	75 (44) 119	106 (117) 223
	ρ	52 (92) 144	139 (43) 182
ventricles	**α**	186 (95) 281	268 (59) 327
	ρ	181 (108) 289	277 (37) 314

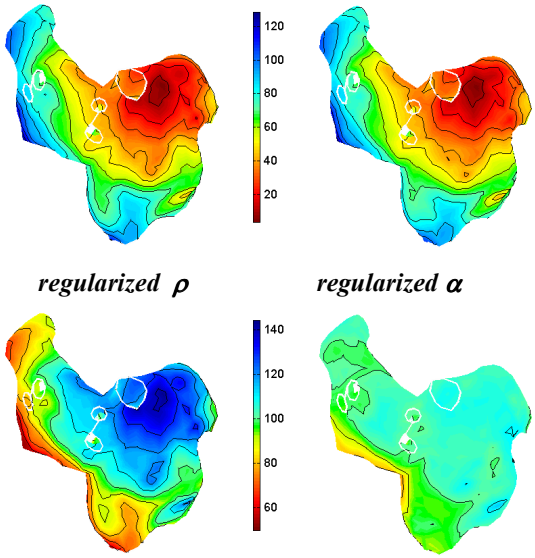

Figure 1. Upper panels: timing of atrial depolarization δ*. Lower panels: ARI values* α*. Regularization applied to the timing of repolarization* ρ *(left panels) or* α *(right panels). (μ_δ=1e-6, μ_ρ =μ_α =3e-5). Timing in ms; posterior view.*

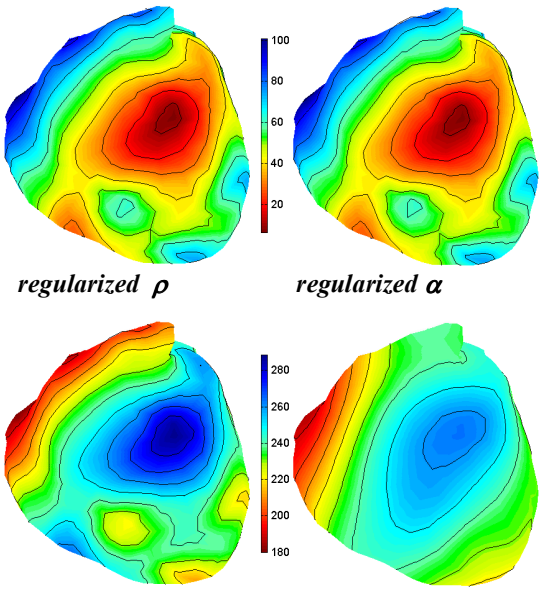

Figure 3. Upper panels: timing of ventricular depolarization δ*. Lower panels: ARI values. Regularization applied to the timing of repolarization* ρ *(left panels) or* α *(right panels). (μ_σ=1.5e-5). Timing in ms; natural, anterior view.*

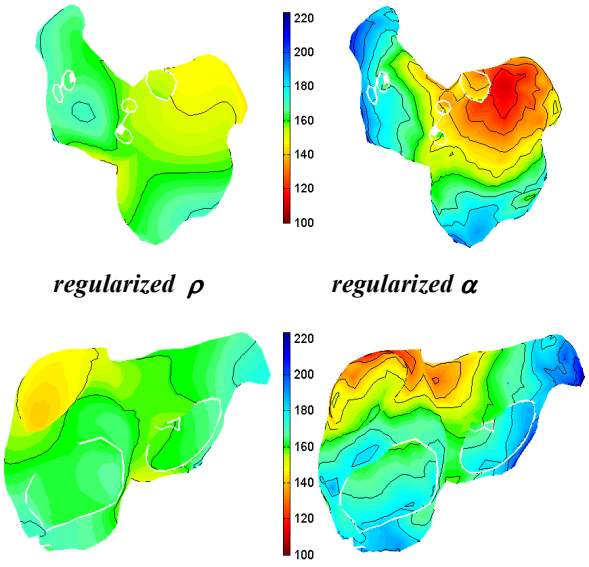

Figure 2. Timing of atrial repolarization found while regularizing either ρ *(left panels) or* α *(right panels). Upper panels: posterior view. Lower panels: natural, anterior view. (μ_δ=1e-6, μ_ρ =μ_α =3e-5). Timing in ms.*

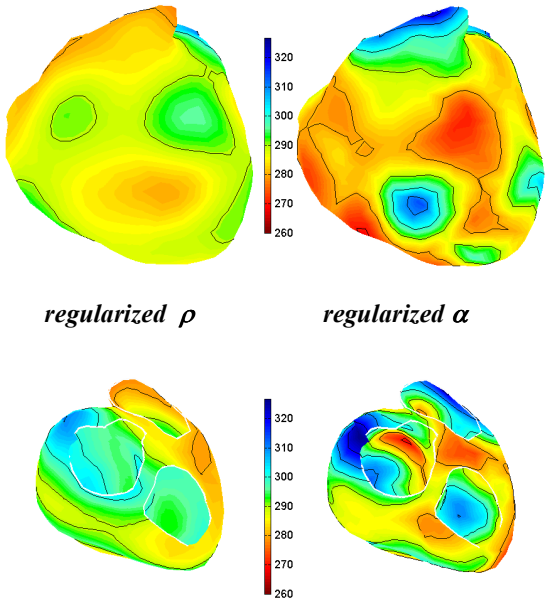

Figure 4. Timing of ventricular repolarization found while regularizing either ρ *(left panels) or* α *(right panels). Upper panels: natural, anterior view. Lower panels: posterior view.(μ_σ=1.5e-5). Timing in ms.*

The ranges of ARI and repolarization times for the atria and ventricles are listed in Table 2. The range and distribution of the atrial repolarization times is similar to the distribution in depolarization times when regularizing $\boldsymbol{\alpha}$. The range of $\boldsymbol{\alpha}$ is limited, having a smooth distribution. When using $\boldsymbol{\rho}$-based regularization the patterns and ranges of the solutions for $\boldsymbol{\rho}$ and $\boldsymbol{\alpha}$ are almost opposite to the ones obtained from using $\boldsymbol{\alpha}$-based regularization (Figures 1 and 2).

For the ventricles a similar phenomenon is observed, i.e. a smooth pattern in $\boldsymbol{\alpha}$ for $\boldsymbol{\alpha}$-based regularization and a smooth pattern in $\boldsymbol{\rho}$ for $\boldsymbol{\rho}$-based regularization. Consequently, the resulting pattern in the unregularized parameter is less smooth (Figures 3 and 4).

5. Discussion

The results presented indicate that the ARI is the preferred parameter to be used in the optimization procedure. Using the ARI as the regularization parameter results in a reduced range in the ARI values, which is in accordance with the literature [3,7].

The results also confirm the quality of the fastest route algorithm-based initial activation sequences [1]. The estimated atrial and ventricular depolarization sequences were almost the same, irrespective of the value of the μ used in regularization of either ARI or repolarization times. The quality of the initial atrial activation estimate is furthermore confirmed by the fact that hardly any regularization needed to be applied (μ_δ=1e-6).

The estimation of the atrial repolarization is hampered by the fact that the last part of the atrial repolarization occurs within the QRS complex. The first part, however, is clearly visible, mainly in leads in close proximity to the atria (e.g. V1 and V2) [6]. Despite this limited availability of data the optimization procedure was able to estimate ARI values in agreement with large-scale ion-kinetics modeling of the myocardium [3]. The range in ARI values can be further reduced by increasing the μ_α. For μ_α 1e-4 the range in ARI was reduced to ±22 ms.

The dispersion in ventricular ARI values is larger than those of atria due to the differences in wall thickness, involvement of the Purkinje system and the intrinsic differences of ion kinetics of left and right ventricle. For the ventricles the range in ARI and repolarization times are found to be in the same range, which is in accordance with data available in the literature [4,5]. When the ARI values are used in the regularization, the relation between the depolarization times and the ARI solution found is also in greater accordance with results shown in the literature [7].

The patterns of the timing of $\boldsymbol{\rho}$ and $\boldsymbol{\alpha}$ found using either repolarization- or ARI-based regularization show local maxima and minima in the same areas for the unregularized parameter. For the ventricle this can be observed on the epicardium of the right ventricle (Figure 3), where a local maximum can be found in the repolarization time when the ARI is regularized and a local minimum in the ARI pattern when the repolarization times are regularized (figure 4). This can also be observed in the atria in the sinus node area (Figure 1,2). Consequently, ARI-based regularization is perceived to be the preferred procedure.

6. Conclusions

Although this study is limited to a single case, the ARI-based regularization seems to be the appropriate choice, both for the atria and the ventricles. The dispersion and resulting spatial distribution in repolarization times and ARIs are in better accordance with literature. Furthermore the results confirm the high quality of the fastest route based initial activation estimate and its inclusion in the initial estimate of the timing of repolarization based on isotonic interaction.

References

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