Physiology-based Regularization Improves Noninvasive Reconstruction and Localization of Cardiac Electrical Activity

Matthijs JM Cluitmans[1,2], Monique MJ de Jong[1], Paul GA Volders[1],
Ralf LM Peeters[2], Ronald L Westra[2]

[1] Cardiovascular Research Institute Maastricht, Maastricht, The Netherlands
[2] Department of Knowledge Engineering, Maastricht University, Maastricht, The Netherlands

Abstract

The objective of the inverse problem of electrocardiography is to noninvasively reconstruct information about electrical activity at the heart surface (epicardium), from electrical measurements on the body surface and a patient-specific torso-heart geometry. This is complicated by the ill-posedness of the inverse problem. Previously, we have shown that a realistic basis can be created from (simulated) epicardial training potentials. Potentials reconstructed with traditional methods can be projected onto this basis, improving the quality of reconstructions. Here, we propose a novel superior method called 'physiology-based regularization' that renders traditional reconstruction and projection unnecessary. Instead, reconstruction of epicardial electrograms is achieved directly, by pursuing a sparse representation in terms of this realistic basis. We validate this method by invasive epicardial electrogram recordings in a canine experiment. We further demonstrate that by creating a realistic basis for a specific purpose, this method can answer clinical questions with improved accuracy. Ultimately, physiology-based regularization would improve patient care by yielding patient-specific results, inspired by electrophysiological knowledge and optimized to answer clinically relevant questions.

1. Introduction

Electrocardiographic imaging (ECGI) aims at noninvasively reconstructing the electrical activity of the heart, based on body-surface potential measurements and a patient-specific torso-heart geometry. [1, 2] This is achieved by solving the inverse problem of electrocardiography. In the last decades, much progress has been made in ECGI and clinical applications occur with increasing frequency. [3, 4] However, the accuracy of the reconstructed electrical heart activity is still suboptimal.

Previously, we have introduced a method that utilizes a 'realistic basis' to improve reconstruction of epicardial (heart surface) electrograms. [5] This realistic basis is constructed by simulating beats on the patient-specific epicardium and spans the space of those simulated training potentials. We showed that traditional reconstructions (such as Tikhonov-regularized solutions) become more accurate when projected onto this realistic basis. In this paper, we improve this method by removing the need for traditional regularization methods. We will show that it is possible to solve the inverse problem directly in terms of the most prominent elements of the realistic basis, thereby taking advantage of the electrophysiological knowledge that is present in that basis. This approach creates the possibility to focus the inverse solution on the type of pathology at hand by creating a specific basis. We will show that cardiac beats that originate from a specific part of the heart are reconstructed more accurately when using a basis that is trained for beats originating from that side of the heart. These improvements will be illustrated and validated by unique *in vivo* data.

2. Physiology-based regularization

Physiology-based regularization of electrical heart activity is based on (see Figure 1):

1. An inverse model, relating epicardial and body-surface potentials;
2. A realistic epicardial potential basis, based on some form of 'electrophysiological knowledge';
3. Regularization of epicardial potentials in terms of this basis.

2.1. The inverse model

In this study, we use a potential-based formulation to reconstruct epicardial potentials. This is described by the following forward problem:

$$Y_B = AY_H \qquad (1)$$

in which Y_B represents the vectorized body-surface potentials, Y_H the vectorized heart-surface (epicardial) poten-

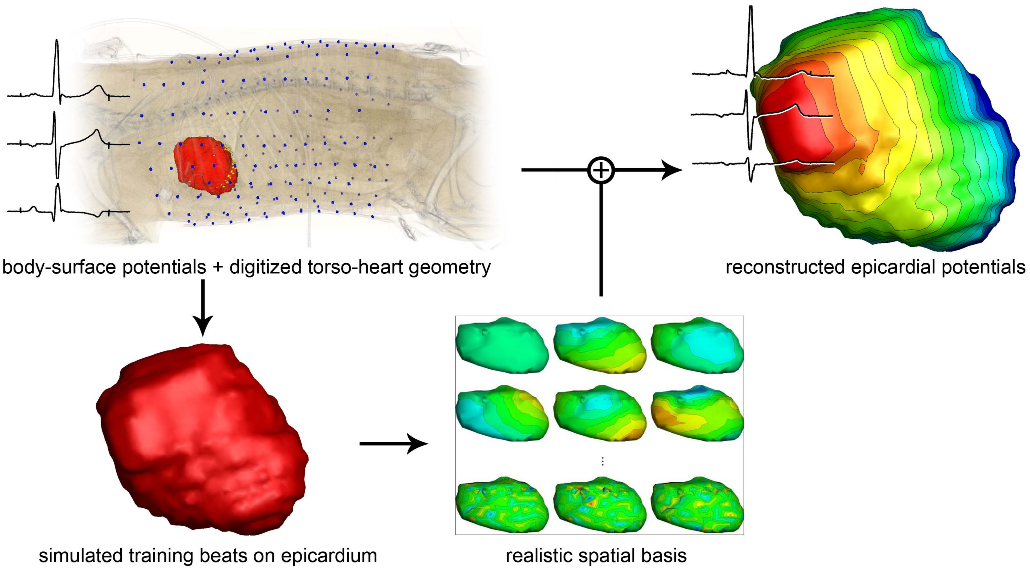

Figure 1. Physiology-based inverse reconstruction of electrical heart activity in a dog. Body-surface potentials were recorded with 192 electrodes. A CT scan was performed to localize the electrodes and epicardial surface. The digitized epicardial surface was used to simulate electrical activity of a diverse set of beats, creating a physiologically realistic basis. Subsequently, epicardial electrical activity was reconstructed in terms of this simulated realistic basis. In the specific experimental setup shown here, also 99 epicardial electrodes were implanted, providing validation electrograms to which the reconstructed electrograms could be compared.

tials, and A the transfer matrix that contains the electromagnetic relation between those potential vectors. [1] In the inverse problem, the body-surface potentials Y_B and the transfer matrix A are known, and the epicardial potentials Y_H unknown.

2.2. The realistic epicardial basis

The realistic epicardial basis will provide the building blocks that will be used to reconstruct epicardial potentials from measured body-surface potentials. Therefore, this basis should include some kind of physiological knowledge. This is achieved by simulating a few dozen electrical beats on the digitized patient-specific epicardium, using the FitzHugh-Nagumo action potential model. [5, 6] The beats are chosen to originate from different locations on the epicardium as to generate diversity. We decompose the simulated FitzHugh-Nagumo simulated potentials $Y_H^{\#}$ by applying singular value decomposition:

$$Y_H^{\#} = USV^{\mathrm{T}} \tag{2}$$

which will yield U and V containing the left and right singular vectors, respectively, and S containing the singular values σ_i. [7] The columns of U represent a spatial basis for the set of simulated realistic epicardial potentials, and V the temporal basis. Whereas the time series of FitzHugh-Nagumo potentials does not resemble real epicardial electrograms much, the spatial distribution of potentials over the epicardium that originates from those action potentials is much like the spatial distribution of true epicardial potentials. Therefore, we assume that U can be used as a realistic spatial basis for potentials over a (patient-specific) epicardial surface.

Due to the descending ordering of singular values, the first columns of U are more important for representing the simulated data, and truncation may be applied to arrive at a smaller spatial basis. A condensed basis will be beneficial as it leaves fewer possibilities for ill-posed influences that could result in unrealistic solutions. Therefore, we truncate U to a suitably small basis U_t consisting of only the first t components.

2.3. Regularization in terms of the realistic basis

Due to the ill-posed nature of the inverse problem, it is very sensitive to noise. Additional information is needed to arrive at a realistic solution, which is called regularization. [3] Usually, mathematical or physical constraints are added to the problem as method of regularization. In this paper, we propose to use the realistic basis U_t as a constraint, thereby using physiological knowledge as regularization constraint. If we assume that U_t is a realistic basis for the epicardial potentials, there should be a vector β

such that we can define the (to be reconstructed) epicardial potentials in terms of this basis:

$$Y_H = U_t \beta \tag{3}$$

and our forward problem becomes:

$$Y_B = A U_t \beta \tag{4}$$

Reconstruction of epicardial potentials in terms of this new basis can then be achieved by lasso regularization. This is a form of least squares approximation, that minimizes the least squares error of the direct solution $||Y_B - AU_t\beta||_2$ while at the same time requiring $||\beta||_1$ to be smaller than a given parameter λ. [8] Constraining the L_1-norm of the parameter vector β tends to produce only a few nonzero coefficients in β, pursuing sparsity. This results in only the most important elements of the realistic basis being used for reconstruction of the epicardial potentials. As the realistic basis only consists of well-defined spatial potential patterns, we expect that this approach drastically reduces the influence of ill-posedness on reconstructed epicardial potentials.

3. Experimental validation

To test the proposed method, validation data was acquired in a dog experiment. In a healthy dog, electrodes were implanted around the epicardium via a thoracotomy and body-surface electrodes were attached to the torso. A homogeneous geometry was digitized from a CT scan and consisted of the body-surface electrodes and the epicardial surface. Potential recordings were obtained simultaneously on the body-surface and on the epicardium. The transfer matrix A, relating the electrical activity at the heart-surface to the body-surface, was computed with methods available from the SCIrun software repository. [9]

Reconstruction of epicardial potentials was achieved by physiological regularization as explained in the previous section. For comparison, also traditional zeroth order Tikhonov regularization was performed. Regularization parameters were determined automatically (L-curve method for Tikhonov regularization) or manually (in the case of physiological regularization). A local electrogram was reconstructed for each node of the digitized epicardial surface. Of all implanted epicardial electrodes, 67 electrodes recorded a good signal. Those electrograms (the ground truth) were compared to the reconstructed electrograms from the corresponding (closest) virtual epicardial node. Selected epicardial electrodes were also used for pacing. In that case, reconstructed epicardial electrograms were used to determine the location of first activation (defined by the earliest maximum $-dV/dt$) and compared to the known pacing location.

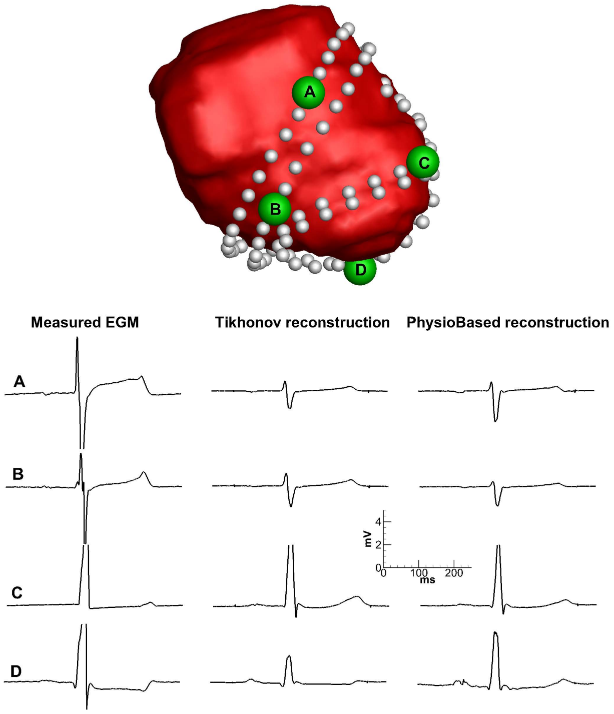

Figure 2. A sinus beat was reconstructed on the epicardial surface of this test animal, based on measured body-surface potentials and the digitized torso-heart geometry. On selected epicardial locations, electrograms (EGM) are shown: measured (left), Tikhonov-reconstructed (middle) and physiology-based reconstructed (right).

4. Results I: using a general basis

Selected measured and reconstructed local epicardial electrograms are shown in Figure 2 for a sinus beat. Overall, the Pearson correlation coefficient between the Tikhonov-reconstructed electrograms and the 67 measured electrograms was on average 0.59; for the physiology-based reconstructed potentials, the correlation with the measurements was 0.60. Thus, physiology-based regularization yields electrograms of equal quality as those reconstructed with Tikhonov regularization.

5. Results II: using a specific basis

An advantage of using simulations to create a realistic basis, is that these simulations can be tuned to create a basis that is specific for a certain type of electrical activity. By simulating beats originating only from the right ventricle or only from the left ventricle, we created two different bases and hypothesized that these are tuned to detect beats paced on the right or left ventricle, respectively.

For six beats paced on the right ventricle and six paced on the left ventricle, we reconstructed the local epicardial

	Tikh	PhysGen	PhysLe	PhysRi
Left paced	42±26	68±18	31±22	66±12
Right paced	40±24	46±29	53±33	35±30

Table 1. Mean localization error (mm ± standard deviation) for beats reconstructed with zeroth order Tikhonov regularization (Tikh), physiology-based nonspecific regularization (PhysGen), and physiology-based left-specific and right-specific regularization (PhysLe and PhysRi, respectively). The results are given separately for beats paced on the left (n=6) and right (n=6) ventricle.

electrograms based on the general (non-specific) basis, or from the left- or right-specific bases and determined the location of earliest activation. This location was then compared with the known location of pacing (Table 1). When left- or right-specific bases are used, the localization error decreases compared to a non-specific basis (significantly for left-paced beats (p=0.02), nonsignificantly for right-paced beats). This suggests that physiology-based regularization indeed can be used to focus on a specific region of beat origin.

6. Discussion

We have shown that it is possible to noninvasively reconstruct electrical heart activity in terms of a realistic basis. This approach differs radically from the traditional regularization methods in the inverse problem of electrocardiography, which apply mathematical or physical constraints. By using a realistic epicardial basis, it is possible to include electrophysiological knowledge as constraints. The correlation between reconstructed and *in vivo* measured electrograms is similar to those of traditional reconstruction methods. We have also shown that it is possible to create a basis that is optimized to answer a distinct question, such as the location of first activation on the epicardium. This approach might give clinicians the opportunity to pick a basis that is designed for a certain pathology, improving reconstruction quality for that purpose.

We expect that these results will be more pronounced when methods are developed to automatically determine a suitable basis size t and constraining parameter λ. Another improvement would be to simulate beats using an action potential model that is more cardiac-specific then the FitzHugh-Nagumo model; however, this will come at a substantial computational cost.

Although we validated this method in just one animal experiment, the high quality of the validation data is unique. To our knowledge, this is the first time in the field of the inverse problem of electrocardiography that these type of data have been acquired *in vivo*: extensive epicardial electrograms that are measured simultaneously to the body-surface potentials, in a closed chest in a healthy animal. Continuation of these experiments will help these and other inverse algorithms to reach their full potential.

Ultimately, physiology-based regularization would improve patient care by yielding noninvasive patient-specific results, inspired by electrophysiological knowledge and optimized to answer clinically relevant questions.

Acknowledgements

The animal experiment would have not been possible without the support of Frits Prinzen, Lars van Middendorp, Marc Strik, Marion Kuiper, Sophie Bosch, Rob Wiegerinck, Marco Das, Bas Kietselaer, Joël Karel and Pietro Bonizzi.

References

[1] Rudy Y, Messinger-Rapport BJ. The inverse problem in electrocardiography: solutions in terms of epicardial potentials. Crit Rev Biomed Eng 1988;16:215–68.

[2] Ramanathan C, Ghanem RN, Jia P, Ryu K, Rudy Y. Noninvasive electrocardiographic imaging for cardiac electrophysiology and arrhythmia. Nat Med 2004;10:422–8.

[3] MacLeod RS, Brooks DH. Recent progress in inverse problems in electrocardiology. IEEE Eng Med Biol Mag 1998; 17:73–83.

[4] Rudy Y. Noninvasive electrocardiographic imaging of arrhythmogenic substrates in humans. Circ Res 2013;112:863–874.

[5] Cluitmans M, Peeters R, Volders P, Westra R. Realistic training data improve noninvasive reconstruction of heart-surface potentials. In Conf Proc IEEE Eng Med Biol Soc. IEEE, 2012; 6373–6376.

[6] Fitzhugh R. Impulses and physiological states in theoretical models of nerve membrane. Biophys J Jul 1961;1:445–466.

[7] Golub G, Reinsch C. Singular value decomposition and least squares solutions. Numerische Mathematik 1970;14:403–420.

[8] Tibshirani R. Regression shrinkage and selection via the lasso. Journal of the Royal Statistical Society Series B Methodological 1996;267–288.

[9] Burton BM, Tate JD, Erem B, Swenson DJ, Wang DF, Steffen M, Brooks DH, van Dam PM, Macleod RS. A toolkit for forward/inverse problems in electrocardiography within the scirun problem solving environment. Conf Proc IEEE Eng Med Biol Soc 2011;2011:267–270.

Address for correspondence:

Matthijs JM Cluitmans
Department of Knowledge Engineering, Maastricht University,
P.O. Box 616, 6200 MD Maastricht, The Netherlands
m.cluitmans@maastrichtuniversity.nl