Optimizing Cardiac Source Model Accuracy by Incorporating Endocardial Electro-Anatomical Structures

Machteld J Boonstra[1], Rob W Roudijk[1], Peter Loh[1], Peter M van Dam[1]

[1]UMC Utrecht, Utrecht, the Netherlands

Abstract

Non-invasive estimation of the cardiac activation sequence by solving the inverse problem of electrocardiography based on the equivalent double layer is appropriate for premature ventricular beats. However, the method has to be improved to simulate sinus rhythm because the His-Purkinje system is involved. Therefore, a correct anatomical representation of the complete cardiac surface including endocardial electro-anatomical structures may be relevant. Comparing models with and without these electro-anatomical structures, the initial estimation of the cardiac activation sequence was often similar. However, the estimation of initial foci in the extensive model was more similar to initial foci known from in vitro and invasive mapping studies. Therefore, incorporation of electro-anatomical structures may improve robustness of modeling cardiac activation sequences with His-Purkinje involvement.

1. Introduction

Solving the inverse problem in electrocardiography (*i*ECG) is used to non-invasively estimate the cardiac activation sequence. The most complex cardiac activation sequence is when the His-Purkinje system is involved, leading to multiple initial activation sites of the myocardium. In vitro studies and invasive mapping studies described healthy left ventricular and right ventricular activation [1,2]. Initial foci are often associated with distinct anatomical structures like the papillary muscles and the moderator band.

In our previous research we have been using a 64 leads body surface potential map (BSPM) recording and a geometry derived from medical imaging. The non-invasive imaging method used is based on an equivalent double layer (EDL) which is modeled at the myocardial surface as the equivalent source of cardiac activity [3,4]. The EDL based *i*ECG method gives an appropriate estimation of the electrical activation sequence of premature ventricular beats. However, when simulating His-Purkinje involved rhythms, this method is less accurate. In research to date as well as our EDL based *i*ECG method, electro-anatomical structures associated with His-Purkinje activation, like papillary muscles or the moderator band, were neglected.

A correct anatomical representation of the complete cardiac surface is relevant [5,6] to reduce simulation error. Incorporation of these electro-anatomical structures is relevant to improve sinus rhythm simulation in the EDL based *i*ECG method.

In this pilot study we evaluated the influence of the incorporation of endocardial electro-anatomical structures like the papillary muscles and the moderator band on the estimated endocardial and epicardial activation sequence.

2. Methods

2.1 Materials

Patient specific models were constructed using GeomPeacs (Peacs BV, Nieuwerbrug, The Netherlands) and either cardiac CT or cardiac MRI. Per patient two anatomical models were created: 1) without electro-anatomical structures (fundamental model) and 2) with electro-anatomical structures (extensive model). Additional surface meshes of blood cavities, lungs and torso were created. After creating the fundamental model, electro-anatomical structures were added and saved as the extensive model.

Sinus beats of a 64 lead BSPM measurement were used for the *i*ECG procedure. Three initial foci were estimated based on the *first come-first served* principle [3]; the initial activation sequence was estimated and simulated BSPM

 ISSN: 2325-887X DOI: 10.22489/CinC.2019.263

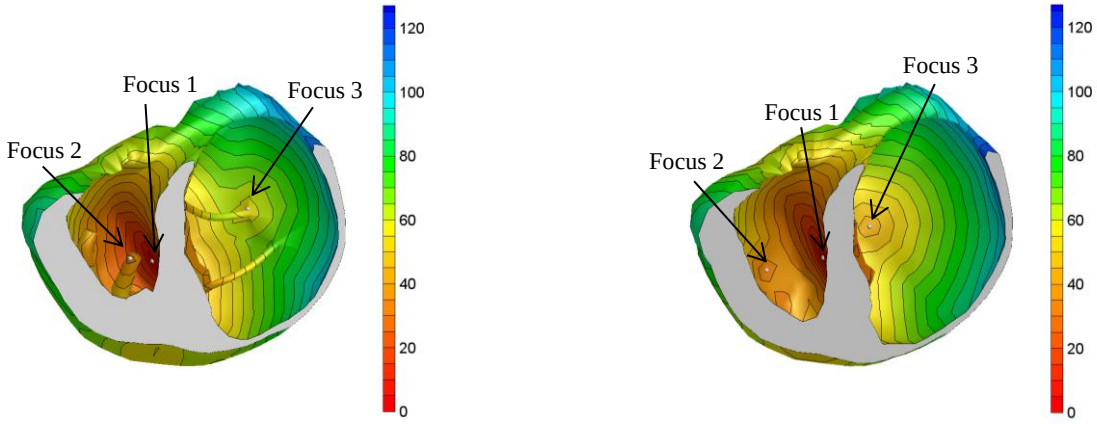

Figure 1: Initial estimation of the endocardial electrical activation sequence of a sinus beat (QRS 127 ms) in an extensive (left, correlation = 0,65, relative difference = 0,77) and fundamental (right, correlation = 0,65, relative difference = 0,77) model. White dots (black arrow) indicate initial foci in order of estimation. The activation sequence was plotted using isochrones 5 ms apart from red (0 ms) to blue (127 ms).

were compared to the recorded BSPM.

The initial estimation algorithm was tuned to search for three initial activation foci only on the endocardium. The algorithm was further modulated to find the first two initial foci on the left ventricular endocardium and the third on the right ventricular endocardium. Nodes within a range of 30 mm from valvular nodes were excluded as possible foci. Except for the valvular constrains, the algorithm was free to determine the initial foci on the rest of the endocardium.

The first initial focus was always determined at QRS onset. For each tested node, initial timing of the second and third foci was set earlier in steps of 10 ms than the depolarization time of the node as estimated by the first focus. The final activation sequence was the combination of the individual sequence of the other selected node(s) For each activation sequence the correlation and relative difference of the simulated BSPM and recorded BSPM was compared.

The activation sequence which had the highest correlation or lowest relative difference values was selected as an (additional) initial focus. As the EDL based *i*ECG procedure largely depends on the initial estimation, only the initial estimation of activation points was performed in this study.

2.2 Data analysis

Per subject, 4 beats were simulated on the cardiac anatomical model. Isochronal maps were compared based on initial focus sites, mean correlation values and mean relative difference values. Initial activation sites were scored based on whether they were located in the anatomically correct position. Three initial foci were defined as physiologically expected and correct based on in vitro and invasive mapping studies. Based on anatomical landmarks, three sites were scored: (1) Located at the left interventricular septum within a range of 4 cm from the left ventricular apex, (2) located at or nearby papillary muscles in a region with radius 4 cm from the point located between the insertion of the papillary muscles at the left ventricular free wall and (3) within a region with radius 4 cm from the insertion of the moderator band on the right ventricular free wall. Per simulated activation sequence, the initial locations were scored in vicinity of an anatomical structure or at the mid left septal wall.

Mean correlation values and mean relative difference values between recorded BSM and simulated BSM of the initial estimation were evaluated per added focus.

Table 1: Score of the location of initial foci in the fundamental (F) and extensive (E) models. Scoring was based on whether initial foci were located at the left ventricular septum, left ventricular free wall or right ventricular free wall and whether the initial activation points lay within a range of 4 cm from these anatomical landmarks. Four beats were analyzed and scored; values were determined as scores of initial points of activation in the predefined expected area.

	Left ventricular septum Location, n (range, n)		Left ventricular papillary muscle insertion at LV free wall Location, n (range, n)		Moderator band insertion at RV free wall Location, n (range, n)	
Subject	Fundamental	Extensive	Fundamental	Extensive	Fundamental	Extensive
1	4 (1)	4 (3)	4 (4)	4 (2)	4 (2)	4 (2)
2	4 (0)	4 (4)	4 (0)	4 (4)	1 (1)	4 (2)
3	4 (4)	4 (4)	0 (0)	3 (3)	3 (1)	3 (3)
4	4 (0)	4 (0)	4 (0)	4 (0)	4 (0)	4 (4)
5	4 (4)	4 (4)	2 (0)	4 (4)	4 (2)	4 (3)
6	4 (2)	4 (3)	4 (2)	4 (3)	4 (2)	3 (2)

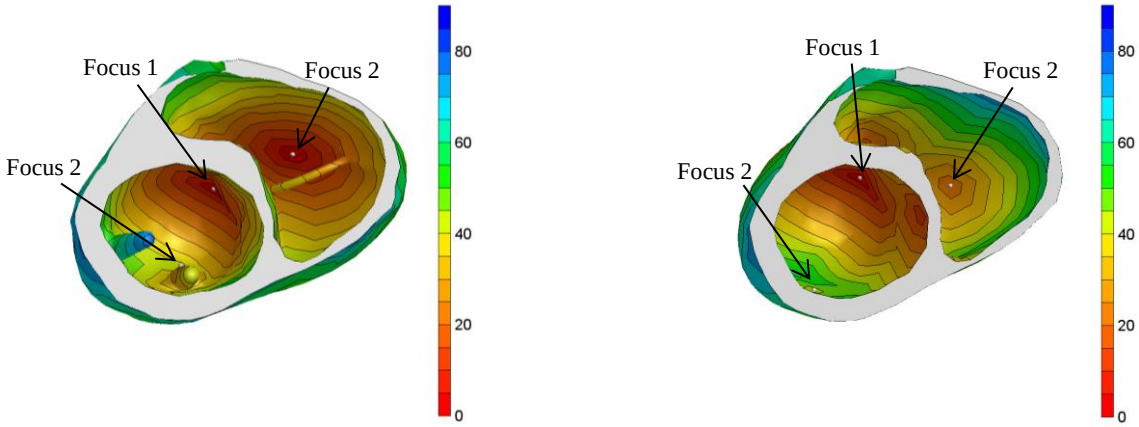

Figure 2: Initial estimation of the endocardial electrical activation sequence of a sinus beat (QRS 99 ms) in an extensive (left, correlation = 0,70, relative difference = 0,78) and fundamental (right, correlation = 0,66, relative difference = 0,79) model. White dots (black arrow) indicate initial foci in order of estimation. The activation sequence was plotted using isochrones 5 ms apart from red (0 ms) to blue (99 ms).

3. Results

In six subjects, cardiac activation sequences were estimated using the fundamental and extensive model. Three subjects (1-3) were patients diagnosed with arrhythmogenic cardiomyopathy (ARVC) and had a QRS duration of 96-124 milliseconds. The other three subjects (4-6) were healthy controls and had had a mean QRS duration of 84-98 milliseconds. The initial estimate of the cardiac activation sequence changed when electro-anatomical structures were added to the anatomical model. Figure 1 and 2 show some examples of the differences found in initial activation estimation using the fundamental and extensive model.

Three initial foci were determined per QRS using the constrained algorithm. The first initial focus was determined at QRS onset. The second and third initial foci differed in onset from 10-50 milliseconds after QRS onset. In five subjects, the first focus found was located on the lower 1/3 of the interventricular septum on the left ventricular endocardium in fundamental models as well as in extensive models. In the extensive models, activation maps showed the effect of the incorporation of the moderator band most prominently; initial activation at the lower part of the left ventricular septum affected right ventricular free wall activation. As can be observed in Table 2, papillary muscles and the moderator band were involved in the first half phase of QRS duration. Initial foci were determined in expected regions in the fundamental and extensive models. As observed in activation maps, the first initial focus located on the left ventricular septum already affected right ventricular wall activation via the moderator band. Initial sited of activation in fundamental models were nearby these structures, as can be observed in Figure 1-4. In Table 1 anatomical resemblance of multiple foci is stated. For the fundamental model, 45% of all foci were found at the lower 1/3 of the left ventricular septum, 25% nearby papillary muscles at the left ventricular free wall and 33% nearby the moderator band insertion at the right ventricular free wall. For extensive models, percentages were 75%, 67% and 67% respectively.

Correlation and relative difference between simulated and recorded BSPM for each added focus is stated in Table 2 and Table 3. Correlation and relative difference values increased respectively decreased by increasing the amount of foci, indicating a better fit. Correlation of the fundamental and extensive model were about the same in the initial estimation of the cardiac activation sequence comparing the extensive model to the fundamental model.

*Table 2: Mean correlation (standard deviation ≤0,02, values presented with * ≤0,06) between recorded BSP and simulated BSP with increasing initial foci in a fundamental (F) and extensive (E) model.*

Subj	Focus 1		Focus 2		Focus 3	
	F	E	F	E	F	E
1	0,45	0,47	0,55	0,55	0,61	0,58*
2	0,60	0,59	0,61	0,60	0,64	0,63
3	0,49	0,49	0,58*	0,54	0,59	0,55
4	0,55	0,56	0,63	0,61	0,63	0,62
5	0,63	0,61	0,67	0,64	0,70*	0,69
6	0,52*	0,52*	0,55*	0,56*	0,59*	0,61*

*Table 3: Mean relative difference (standard deviation ≤0,02, values presented with * ≤0,06) between recorded BSP and simulated BSP with increasing initial foci in a fundamental (F) and extensive (E) model.*

Subj	Focus 1		Focus 2		Focus 3	
	F	E	F	E	F	E
1	0,89	0,89	0,84	0,84	0,80	0,81
2	0,80	0,81	0,79	0,80	0,77	0,78
3	0,89	0,89	0,84	0,87	0,83	0,86
4	0,86	0,86	0,81	0,82	0,81	0,82
5	0,82	0,83	0,79	0,82	0,77	0,78*
6	0,86*	0,86*	0,83*	0,84	0,82*	0,83*

4. Discussion

This study shows that cardiac electrical activation is affected by the incorporation of endocardial electro-anatomical structures. The incorporation of the moderator band affects right ventricular wall activation timing when only defining one initial focus placed on the left ventricular septum, at it creates a connection between septum and right ventricular free wall. In five subjects, initial activation of the left ventricular free wall was located at or nearby papillary muscles. In fundamental models, the initial focus was found near the origin of the papillary muscles, more apically or more basally compared to the origin of the papillary muscles. These left ventricular activation points are known and expected from the anatomy of the His-Purkinje system [1,2], initial activation points estimated in this study resembled these points. In the fundamental model, the initial focus on the right ventricular free wall was located near to the insertion of the moderator band and on the left ventricular free wall near or between the insertion of both papillary muscles. These findings and initial activations points found around or onto papillary muscles or the insertion of the moderator band indicate a strong influence of these electro-anatomical structures on the estimation of sinus rhythm. This is further anticipated due to earlier studies showing the effect of segmentation error and incorporation of the atrial myocardial surface on the *i*ECG procedure [5,6]. Incorporation of the endocardial electro-anatomical structures is expected to similarly affect the robustness of cardiac activation sequences and decrease modelling error. Moreover, incorporating endocardial electro-anatomical structures provides the physician with anatomical landmarks which can be taken into account during clinical decision making.

Comparison of these maps with invasive measured epicardial and endocardial activation maps is required to determine which simulated cardiac activation sequence most adequately resembles the invasively measured cardiac activation sequence. As both the fundamental and extensive model resemble healthy activation sequences as determined during in vitro and endocardial mapping studies, differences with ground truth should be determined. As the dataset used in this study contained three cases of ARVC, comparison is even more necessary. As ARVC is a cardiac disease in which healthy myocardial tissue is replaced by fibrofatty tissue due desmosomal dysfunction, the cardiac activation sequence alters due to changing conduction velocity [7]. EDL based *i*ECG assumes equal conduction velocity throughout the complete myocardium, therefore physiological truth is violated in case of ARVC and other pathogenic states affecting conduction velocity. Therefore, further studies will focus on the effects of incorporating fibrofatty tissue on accuracy of the estimated sequence.

Further improvement of the initial estimation in the extensive anatomical model is based on improving physiological robustness, for example by incorporating conduction velocity of the moderator band in the procedure. Another option to improve the initial estimation is to use the papillary muscles and moderator band as predefined initial foci.

5. Conclusion

Overall, cardiac activation sequence in models with and without endocardial electro-anatomical structures behave similar to physiologically expected cardiac activation sequence. However, the estimation of initial foci in the extensive model were more similar to initial foci known from in vitro and invasive mapping studies. Incorporation of electro-anatomical structures is expected to improve the robustness of modeling cardiac activation sequences using an EDL based *i*ECG method.

References

[1] Durrer D, Van Dam RT, Freud GE, Janse MJ, Meijler FL, Arzbaecher RC. Total excitation of the isolated human heart. Circulation. 1970 Jun;41(6):899-912.

[2] Cassidy DM, Vassallo JA, Marchlinski FE, Buxton AE, Untereker WJ, Josephson ME. Endocardial mapping in humans in sinus rhythm with normal left ventricles: activation patterns and characteristics of electrograms. Circulation. 1984 Jul;70(1):37-42.

[3] van Dam PM, Oostendorp TF, Linnenbank AC, van Oosterom A. Non-invasive imaging of cardiac activation and recovery. Ann Biomed Eng. 2009 Sep;37(9):1739-56.

[4] van Oosterom, A. Genesis of the T wave as based on an equivalent surface source model. Journal of Electrocardiography 2001; 34 (Supplement): 217-227.

[5] Tate, J., Gillette, K., Burton, B., Good, W., Zenger, B., Coll-Font, J., & MacLeod, R. (2018). Reducing error in ECG forward simulations with improved source sampling. Frontiers in physiology, 9.

[6] Tate, J., Zemzemi, N., Good, W., Van Dam, P., Brooks, H., MacLeod, R. (2018). Effect of segmentation variation on ECG imaging. Computing in Cardiology conference papers, 45.

[7] Riley MP, Zado E, Bala R, Callans DJ, Cooper J, Dixit S, Garcia F, Gerstenfeld EP, Hutchinson MD, Lin D, Patel V. Lack of uniform progression of endocardial scar in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy and ventricular tachycardia. Circulation: Arrhythmia and Electrophysiology. 2010 Aug;3(4):332-8.

Address for correspondence.
Machteld Boonstra
The Netherlands
E-mail address: M.J.Boonstra-3@umcutrecht.nl