Noninvasive detection of epicardial and endocardial activity of the heart

T. F. Oostendorp · P. F. H. M. van Dessel · R. Coronel · C. Belterman ·
A. C. Linnenbank · I. H. van Schie · A. van Oosterom · P. Oosterhoff ·
P. M. van Dam · J. M. T. de Bakker

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Abstract Determining electrical activation of the heart in a noninvasive way is one of the challenges in cardiac electrophysiology. The ECG provides some, but limited information about the electrical status of the heart. This article describes a method to determine both endocardial and epicardial activation of the heart of an individual patient from 64 electrograms recorded from the body surface. Information obtained in this way might be helpful for the treatment of arrhythmias, to assess the effect of drugs on conduction in the heart and to assess electrical stability of the heart.

Keywords ECG · Inverse problem · Forward problem · Electrophysiology · Body surface mapping

Background

The global electrical condition of the heart can be viewed by the 12-lead surface electrocardiogram (ECG). The standard ECG, however, provides insufficient information on the actual

activation sequence of the heart and its electrical stability. The development of a technique that enables estimation of the electrical activity on the epicardium and endocardium of the heart in a non-invasive way from multiple surface electrocardiograms may have great clinical potential. It may help to establish the electrical stability of the heart of an individual patient and help to guide ablation procedures by locating important arrhythmogenic areas prior to the procedure. Moreover, in patients prone to arrhythmias, noninvasive assessment of the pro-arrhythmic effect of cardiac and noncardiac medication would be of great value.

Forward and inverse problem

Morphology of the surface ECG is determined by the activation and recovery sequence of the heart. If the electrical activity of the heart and the heart-torso geometry and their conductive properties are known, potentials on the body surface can be calculated. This procedure is known as the *forward problem* in electrocardiography [1]. Although interesting, the *inverse problem* is clinically the more relevant problem and scientifically the more challenging. The *inverse problem* involves determination of the electrical activity of the heart from recorded body surface signals and the geometry of heart and thorax. These geometric parameters can be tailored to the individual patient.

To solve the *forward problem*, the potentials at the body surface that result from electric currents generated by the heart need to be calculated. For this, a realistic description of the volume conductor of the patients is needed, incorporating the shape and conductivity of all relevant tissues within the thorax. The standard procedure to obtain such a volume conductor model is to image the torso and different organs of a subject with magnetic resonance (MR)

A. C. Linnenbank · P. Oosterhoff · J. M. T. de Bakker (✉)
Interuniversity Cardiology Institute of the Netherlands,
Utrecht, the Netherlands
e-mail: j.m.debakker@amc.uva.nl

T. F. Oostendorp · I. H. van Schie · A. van Oosterom ·
P. M. van Dam
The Donders Institute for Brain, Cognition and Behaviour,
Centre for Neuroscience, Radboud University Nijmegen,
Nijmegen, the Netherlands

P. F. H. M. van Dessel · R. Coronel · C. Belterman ·
A. C. Linnenbank · P. Oosterhoff · J. M. T. de Bakker
Department of Clinical and Experimental Cardiology,
Academic Medical Center,
Amsterdam, the Netherlands

and compose a so-called triangulated computer model of the tissues and organs [2, 3]. In the volume conductor model, the geometry of the blood-filled cavities within the heart, the lungs, and the remaining parts of the torso is reconstructed and specific values of their electric conductivity assigned. Based on this volume conductor model, we use the boundary element method to compute the transfer function that relates the source activity on the heart surface to the potentials at the body surface. The main advantage of the boundary element method is its unique ability to provide a complete solution in terms of the potentials on the boundaries, with substantial savings in modelling effort (and computer time).

Although retrieving information on electrical activity on the heart from surface ECGs refers to solving an inverse problem, it is in fact a forward problem that is being solved. Starting with a suitable, dedicated model of the electrical activity of the heart, the surface ECGs are calculated using the volume conductor model of the patient and the calculated ECGs are compared with the recorded ones. The difference between calculated and recorded ECGs is used to adapt the source parameters in the model and to start a new calculation. This iterative process continues until a predefined similarity between calculated and recorded ECGs is reached.

Highly sophisticated computer models for conduction of the electrical activity in the heart are available. These models may contain tens of millions of ‘myocardial cells’ in which each cell harbours tens of different ion currents on the basis of which the body surface ECGs can be calculated [4]. However, despite very fast computers with parallel processing modalities, the time needed to carry out the simulation of a single heart beat with such a model is far too long to be of value for direct clinical use.

To be of clinical interest, reduction of the complexity of the forward model is mandatory. Two models that are most widely used for inverse electrocardiography use source descriptions at the surface of the heart. Solving the inverse problem with these models may be viewed as a type of functional imaging, which has led to their characterisation as ‘noninvasive electrocardiographic imaging’ [5] or ‘myocardial activation imaging’ [6].

A major complication of the inverse problem is that it is ill-posed, which means that the number of solutions is theoretically infinite. However, virtually all solutions are physiologically impossible and therefore adding prior physiological knowledge into the model is needed to force the solution into the right direction.

The source model implied in the noninvasive electrocardiographic imaging is the potential field on a surface closely surrounding the heart, such as the epicardium. This is based on the assumption that a unique relation exists between the potentials on either of two nested surfaces

bounding an electrically passive medium, one being the body surface, the other the epicardium. This model was first proposed by Martin and Pilkington at Duke in 1972 [7] and has subsequently been developed by several other groups [8]. A limitation of this model is that only the electrical activity at the epicardium can be assessed.

In contrast, the myocardial activation imaging model we use permits one to assess both epicardial and endocardial activity. Here, the electrical source is based on the macroscopic equivalent double layer model [9], applicable to the entire electrical activity of atria and ventricles, at any time instant. This source model is based on the classic model of the double layer as an equivalent source of the currents generated at the cellular membrane during depolarisation, as described by Wilson et al. [10]. The current dipole layer model describes the activity of a depolarisation front during propagation through the myocardium [11]. Geselowitz [12] showed that the actual *current* source distribution within the heart is equivalent to a double layer at the surface bounding the myocardium with a strength that is proportional to the local transmembrane potential [13]. The waveform of the transmembrane potential at each location on the myocardial surface is described by two parameters: the local activation and recovery time. The values of these times at about 1500 locations (nodes) on the surface bounding the myocardium act as the source parameters. These are found by using a standard parameter estimation method, minimising the difference between observed body surface potentials and those based on the source description. Since the body surface potentials depend non-linearly on these parameters, a non-linear parameter estimation technique is required, which demands the specification of initial estimates.

An initial estimate for activation is obtained by modelling the propagation of electrical activation in the heart based on the Huygens principle. For the activation sequences initiated at all of the 1500 nodes produced in such a propagation model, the resulting ECGs are computed. The activation sequence whose computed ECG matches the actual ECG the best is used as the initial estimate.

Key objective of the current study and collaboration

The key objective of this ICIN project is to establish new technology that allows the estimation of the electrical activity and status of the heart muscle non-invasively using 64 surface electrodes. This number is based on a study by Lux and co-workers who showed that 32 well-positioned leads are required to fully capture all body surface potential details [14]. This was done by starting with 196 electrodes and repeatedly removing electrodes and testing whether the original ECGs could be reconstructed from those recorded

at the remaining electrodes. The project requires a multi-disciplinary approach that involves expertise of signal acquisition and analysis techniques, knowledge of the inverse problem of electrocardiography, knowledge of animal experiments and clinical electrophysiology. To meet these requirements a collaboration between the departments of clinical and experimental cardiology at the AMC and the Centre for Neuroscience of the Radboud University at Nijmegen was initiated. At the AMC extensive electrophysiological knowledge is available, and the cardiology clinic is a referral centre for various genetically determined electrical diseases of the heart, such as the Brugada (BS) and long-QT (LQT) syndrome. Preliminary data obtained from Brugada patients have already revealed the strength of

our procedure to discriminate between electrical defects at the epicardium or endocardium. The Nijmegen group has outstanding knowledge and experience with the inverse procedure technique. Previous studies from the Nijmegen group have shown that the inverse procedure is well able to detect aberrant connections between atrium and ventricle in the Wolff-Parkinson-White syndrome [Fig. 1]. Financial support for the study is given by STW (Stichting Technische Wetenschappen). This funding agency demands that industry participates in the ‘gebruikerscommissie’ (user’s committee) and industrial partners are indeed involved. Utilisation is an important component of STW projects. Scientifically the project is supported and controlled by the ICIN scientific council.

Fig. 1 Upper panel: Epicardial and endocardial activation times computed from 64 body surface ECGs for a Wolff-Parkinson-White patient during a fusion beat. Activation times are in ms from onset QRS; red indicates early and blue indicates late activated areas. The location of successful ablation of the aberrant bundle is marked by a sphere. Note that both the normal, early activation at the septum and the one at the basal part of the left ventricular free wall are identified by the inverse procedure. LV: left ventricle, RV: right ventricle, RVOT: right ventricular outflow tract. Lower panel: Tracings are the 12 lead ECG of the fusion beat

Project outline

For patient-tailored estimation of the electrical activity and status of the heart muscle from surface ECGs, the following steps have to be taken. Heart-torso geometry will be determined by magnetic resonance imaging. Signals from 64 sites on the body surface will be recorded.

The non-invasive myocardial activation imaging technique is used to derive electrical activity at the outside (epicardium) and inside (endocardium) of the heart. For the ‘inverse solution’ the model originally developed by Van Oosterom, Huiskamp and Oostendorp in Nijmegen, which is based on the equivalent double layer source model, will be continued and extended. Importantly, this method allows estimation of maps of both the endocardial and the epicardial activity. Other inverse techniques are only able to assess (pseudo) epicardial activity.

For a further validation of the inverse procedure an in situ animal model is being used. A computer tomography (CT) scan is used to determine heart-torso geometry and the position of the body surface electrodes. Epicardial mapping with a sock electrode and endocardial mapping with a basket electrode will be performed. The animal model is closely true-to-life and allows various interventions such as electrical stimulation and the application of drugs.

Expected results

The combination of the proposed experiments will provide a non-invasive means (inverse technique) to obtain detailed information on: 1) The origin of ventricular tachyarrhythmias to guide treatment by catheter ablation; the technique is able to distinguish between epicardial and endocardial locations, information, which is crucial for this treatment modality, 2) local areas with impaired conduction and/or abnormal repolarisation; both parameters are related to arrhythmia vulnerability, 3) optimal positions of the stimulus electrodes used in resynchronisation therapy (CRT) in patients with heart failure, 4) the effect of cardiac and non-cardiac medication on conduction and electrical stability of the heart, 5) activation patterns that are related to fractionated surface ECGs; these ECGs are associated with arrhythmias, but their origin is unknown, 6) conduction velocity and action potential duration

restitution; these parameters are a measure of the electrical stability of the heart.

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