

# Noninvasive Three-dimensional Cardiac Activation Imaging of Ventricular Arrhythmias in the Rabbit Heart

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## Abstract

In the present study, a physical-model based three-dimensional (3-D) cardiac electrical imaging (3-DCEI) technique was evaluated with the aid of 3-D intra-cardiac mapping from 200 intramural sites during norepinephrine (NE) induced ventricular arrhythmias in the rabbit heart. Body surface potentials and intramural bipolar electrical recordings using plunge-needle electrodes were simultaneously measured in a closed-chest condition in a healthy rabbit. The non-invasively imaged activation sequence correlated well with invasively measured counterparts, with an averaged correlation coefficient of 0.70, and a relative error of 0.30. The sites of initial activation were well localized to be within ~5mm from the initiation sites determined from intra-cardiac mapping. The present experimental results suggest that the 3-DCEI approach can reconstruct 3-D ventricular global activation sequence and localize the origin of activation during focal ventricular arrhythmias.

## 1. Introduction

Ventricular arrhythmias claim nearly 400,000 deaths per year in United States alone. Noninvasive imaging of cardiac electrical activities during ventricular arrhythmias within a single cardiac cycle would therefore be of enormous value in helping define arrhythmia mechanisms and guide therapeutic treatments. A number of efforts have been made to obtain spatial information with regard to cardiac activation. In addition to body surface potential maps (BSPM), investigators have attempted to image electrical activities by solving the electrocardiographic (ECG) inverse problem, which usually includes moving dipole solution [1], epicardial potential imaging [2], and heart surface activation imaging [3]. While such heart surface imaging approaches provide useful information to help localize sites of origin of arrhythmias, the direct imaging of cardiac electrical activities within the 3-dimensional (3-D) volume of the heart is desirable since

ventricular arrhythmias typically arise within the myocardium [4]. Investigations have been made in imaging the 3-D cardiac electrical activities [5]-[9]. A feasibility study [10] in the rabbit heart using a 3-D intra-cardiac mapping procedure showed the potential application of the physical-model based 3-DCEI approach in localizing the origin of activation and imaging global activation sequence under single-site pacing.

The present study aims to evaluate the imaging performance of this 3-DCEI approach using a well-established 3-D intra-cardiac mapping procedure [11]-[12] during ventricular arrhythmias induced by norepinephrine (NE) in the normal rabbit heart. Plunge-needle electrodes were placed in the left ventricle (LV) and right ventricle (RV) of the rabbit, and the body surface potentials and intramural bipolar recordings were measured simultaneously in a closed-chest condition. The 3-DCEI imaging results were quantitatively compared with intra-cardiac mapping results and imaging performance was assessed.

## 2. Methods

### 2.1. Animal experimental procedures

A New Zealand white rabbit was studied based on a protocol of simultaneous body surface potential mapping and 3-D intra-cardiac mapping of ventricular electrical activities. After anesthetization, the torso and limbs of rabbit were shaved for placement of surface ECG electrodes, and 64 repositionable BSPM electrodes were uniformly placed to cover the anterior-lateral chest up to the mid-axillary line. The heart was exposed via median sternotomy, and 25 transmural plunge-needle electrodes were inserted in the left and right ventricles of the rabbit. Each plunge-needle electrode contains 8 bipolar electrode-pairs with an inter-electrode distance of 500  $\mu\text{m}$  [11], [12]. The chest and skin were then carefully closed with silk suture. NE was infused to induce ventricular arrhythmias including premature ventricular complexes

(PVCs) and ventricular tachycardias (VTs). Bipolar electrograms were continuously recorded from all electrode-pairs together with body surface potentials from surface electrodes. At the completion of the mapping study, two sets of ultra fast CT (UFCT) scans were performed on the living rabbit. One without intravenous (IV) contrast was used to construct the rabbit torso model and extract the location of BSPM electrodes. Another one with IV contrast was obtained for construction of a detailed heart model and 3-D localization of plunge-needle electrodes. At the completion of the above procedures, the rabbit was euthanized and the plunge-needle electrodes were carefully localized as described in [11], [12] by replacing each with a labeled pin. The heart was then excised and fixed in formalin; a post-operative UFCT scan was done to further facilitate precise 3-D localization of the transmural electrodes.

## 2.2. Principles of the 3-DCEI approach

The physical-model based 3-DCEI approach is developed by means of modeling 3-D cardiac electrical activities using equivalent current densities (ECDs) and by mathematically solving a spatial-temporal linear inverse problem from multiple-channel body surface ECGs [9]. A realistic geometry heart-torso model is constructed from computer tomography (CT) images of the individual subject. The ventricular myocardium is tessellated into thousands of grid points. A current density is assigned on each grid point within the ventricles to represent the equivalent cardiac electrical sources. Derived from bidomain theory [13], the extracellular potentials measurable over the body surface is linearly related to the 3-D ECD distribution, (given a tessellated geometrical heart-torso model and the prior knowledge of the electrical conductivity of relevant tissues and organs). The inverse problem is solved by using a spatial-temporal weighted minimum norm linear approach to estimate the current density within each grid point. The activation time at each point within the myocardium is determined as the instant when the time course of estimated current density reaches its maximum [9]. The activation sequence, which is the spatial distribution of the activation time throughout the 3-D ventricular myocardium, could then be derived to provide clinically important information regarding the cardiac excitation process.

## 2.3. Evaluation of 3-DCEI solutions

The performance of 3-DCEI was evaluated by comparing the non-invasively imaged activation sequence with the simultaneously direct measurements obtained from 3-D intra-cardiac mapping. The orientation and location of each needle within the 3-D ventricular myocardium was determined directly from the same CT

images used for constructing the detailed heart model after the mapping study. To facilitate the identification and localization of the needles, an alternative heart surface model was built from the post-operative CT images of the isolated heart with labeled pins (representing the sites of transmural needles). The corresponding activation time of each recording electrode was assigned on the basis of peak criteria [11]-[12], and then an interpolation algorithm as described in [7] was applied to obtain the complete 3-D measured activation sequence throughout the ventricular myocardium.

Quantitative comparison was made between non-invasively imaged activation sequence and the invasively measured activation sequence. The correlation coefficient (CC) and relative error (RE) were computed respectively to quantify the agreement of overall activation pattern and the consistency of the activation time between the invasively measured activation sequence and the non-invasively imaged activation sequence. The localization error (LE), which is defined as the distance between the site of the earliest activation (from the 3-D intra-cardiac measurements) and the center of mass of the myocardial region with the earliest imaged activation time, was computed to evaluate the performance of 3-DCEI in localizing the origin of activation.

## 3. Results

The realistic geometry rabbit heart-torso model was constructed from two sets of CT images obtained after the mapping study. Six PVCs were analyzed in the present study. The PVCs beats initiated by a focal, and what we believe to be a nonreentrant mechanism, based on the lack of intervening electrical activity between the preceding beat and the initiation of the ectopic beat in intramural recordings [11], [12]. Different activation patterns with different initiation sites were observed for the PVCs beats in this animal. The initiation sites covered both LV and RV, including basal right wall (BRW), basal lateral wall (BLW), middle right wall (MRW), and apex.

An example is shown in Figure 1 of a PVC beat. The activation time distributions on five representative axial slices were displayed with a 3-D realistic heart geometry. The red corresponds to early activation, while blue corresponds to late activation. The measured activation sequence shows that the PVC beat initiated at around the apex, with a total activation time of 40ms. The wavefront moved to the base, and terminated in the basal RV. The non-invasively imaged activation sequence closely approximated the measured one, with a CC of 0.72, and a RE of 0.32. The origin of activation was well localized within the myocardium, with a LE of 4.70mm for this beat.

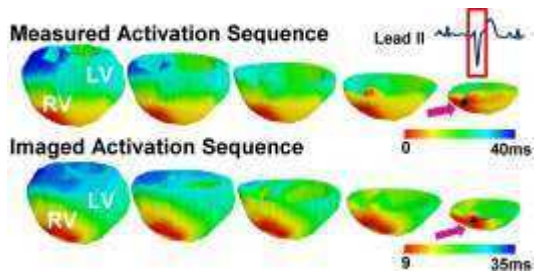


Figure 1. Comparison between the measured and the imaged activation sequence during a PVC beat. The initial sites of activation are marked by a black dot and a purple arrow. The progressive cut away views of the ventricles from basal to apex are displayed from left to right.

#### 4. Discussion and conclusion

The present study aims to assess the performance of the 3-DCEI technique in non-invasively reconstructing the 3-D ventricular activation sequence and localizing the origin of arrhythmia in the in vivo rabbit heart. The 3-DCEI approach was applied in imaging the activation sequence of NE-induced PVCs and in validating these data with the aid of invasive 3-D intra-cardiac mapping from 200 intramural sites in a rabbit. While VT was also induced in the experiment, no data analysis was performed so not included here. Our results showed a good agreement of the global activation pattern between the non-invasively imaged activation sequence and its directly measured counterpart, as quantified by a CC of 0.70 and RE of 0.30 averaged over the ectopic beats in the rabbit. The origins of the activation were reasonably localized to be within ~5mm from the sites of earliest activation detected by 3D intra-cardiac mapping. These findings imply that 3-DCEI is feasible in reconstructing spatial pattern of 3-D ventricular activation sequence, localizing the focal arrhythmogenic foci, and imaging dynamically changing arrhythmia on a beat-to-beat basis.

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