

Noninvasive Imaging of Three-dimensional Ventricular Activation Sequence in a Rabbit Model

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Abstract. Noninvasive imaging of ventricular activation is of great importance in cardiovascular research and clinical diagnosis of cardiac diseases. Three-dimensional (3-D) cardiac activation imaging (3-DCAI) is a biophysical model based approach that aims at imaging the activation sequence throughout the entire myocardium. In the present study, the performance of 3-DCAI was evaluated through *in vivo* pacing experiments in a rabbit model. The distributed cardiac equivalent current density (ECD) was estimated and the local activation time within myocardium was determined as the latency with the peak amplitude of local ECD estimates. To allow for a rigorous evaluation, intramural bipolar recordings were measured simultaneously with the body surface potentials in a closed-chest situation. The encouraging results suggest that 3-DCAI can non-invasively image the activation sequence and localize the origin of activation with good accuracy.

Keywords: Activation imaging, cardiac electrical imaging, intra-cardiac mapping, inverse problem, rabbit model.

1. Introduction

Noninvasive imaging of cardiac electrical activity is of importance for better understanding the mechanisms of cardiac physiology and pathology, and for guiding therapeutic treatments of cardiac disorders in clinical medicine. For decades, a number of efforts have been made to solve the inverse problem of electrocardiography (ECG) in order to estimate the equivalent cardiac sources from body surface potential maps (BSPMs) [Gulrajani et al., 1984; Oster et al., 1997; Greensite and Huiskamp, 1998; Tilg et al., 2002]. Recently the ECG inverse problem has been extended to imaging the three-dimensional (3-D) cardiac electrical activity [He and Wu, 2001; Li and He, 2001; He et al., 2003; Zhang et al., 2005; Liu et al., 2006]. In addition to a heart cellular automaton model based 3-D imaging approach [Li and He, 2001; He et al., 2003; Zhang et al., 2005], an alternative approach has been proposed to image the 3-D ventricular activation sequence by physically modeling the cardiac sources using equivalent current densities (ECDs) [Liu et al., 2006].

The purpose of the present study was to validate the performance of the biophysical model based 3-D cardiac activation imaging (3-DCAI) approach [Liu et al., 2006] using a 3-D intra-cardiac mapping procedure [Pogwizd, 1994] in a rabbit model. Healthy New Zealand white rabbits were studied during brief episodes of rapid ventricular pacing. Plunge-needle electrodes were placed in the ventricles, and the body surface potentials and intra-cardiac bipolar recordings were measured simultaneously in a closed-chest condition. The 3-DCAI imaging results were quantitatively compared with intra-cardiac mapping results in order to assess imaging performance.

2. Material and Methods

2.1. Rabbit Model and *In Vivo* Mapping

Two healthy New Zealand rabbits were studied using a protocol approved by the Institutional Animal Care and Use Committees of the University of Minnesota, the University of Illinois at Chicago and the University of Alabama at Birmingham. The experimental protocol was detailed in [Zhang et al.,

2005]. In brief, before *in vivo* mapping study, two sets of Ultra Fast Computer Tomography (UFCT) images were obtained for each rabbit. One without intravenous (IV) contrast was used to construct the rabbit torso model. Another one with IV contrast was obtained for construction of a detailed heart

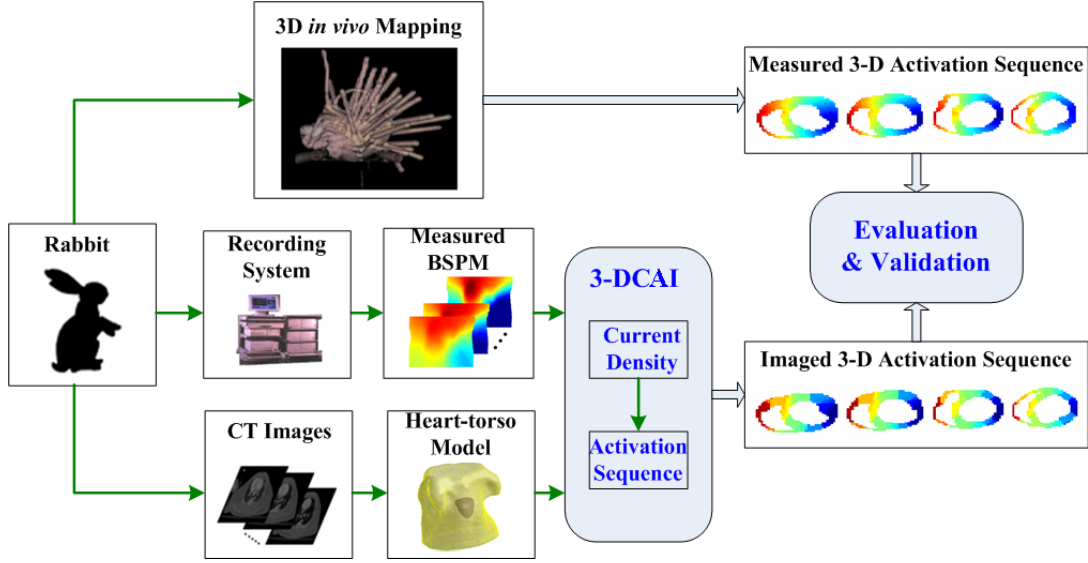


Figure 1. Schematic diagram of the experimental protocol and data analysis.

model. Up to 56 breathable BSPM electrodes were uniformly placed to cover the anterior-lateral rabbit chest up to the mid-axillary line. The heart was exposed via median sternotomy, and up to 22 transmural needles were inserted in the left and right ventricles of the rabbit. Each needle contains 8 bipolar electrode-pairs with an inter-electrode distance of 500 μm [Pogwizd, 1994]. The chest and skin were closed, and rapid ventricular pacing was then performed (for 10-20 secs) via bipolar electrode-pairs on selected plunge needles. The bipolar electrograms were continuously recorded from all plunge electrode-pairs together with body surface potentials from surface electrodes. At the completion of mapping, plunge needles were carefully localized by replacing each with a labeled pin. The heart was then excised, fixed in formalin, and underwent a post-operative UFCT scan to obtain precise 3-D localization of the transmural electrodes.

2.2. 3-DCAI and Data Analysis

In 3-DCAI, the cardiac electrical sources are represented by 3-D distributed ECDs throughout the ventricular myocardium. Based on the bidomain theory [Miller and Geselowitz, 1978], the potentials over body surface is linearly related to the 3-D ECD distribution, described as

$$\Phi(t) = LJ(t) \quad (1)$$

where $\Phi(t)$ and $J(t)$ are the vectors of body surface potential distribution and 3-D ECD distribution respectively, and L is the boundary element method (BEM) based lead field transfer matrix.

The algorithm detailed in [Liu et al., 2006] was used to solve the inverse problem. In brief, the singular value decomposition (SVD) is employed to decompose the spatiotemporal ECG data matrix into orthogonal spatial and temporal components. The spatial components that do not satisfy the discrete Picard condition [Hansen, 1990] are assumed to be dominated by noise perturbation, and thereby are truncated. The lead-field normalized weighted minimum norm (LFN-WMN) estimation is applied to each remaining spatial component. The LFN-WMN solutions multiplied with the corresponding singular values and temporal components are summed to obtain the spatiotemporal ECD estimates. The activation time at each myocardial site is then determined as the instant when the time course of the estimated local ECD reaches its maximum magnitude.

The activation sequence from the intra-cardiac data was taken as the golden standard to evaluate the performance of 3-DCAI. The relative error (RE) was computed to provide the difference between the invasively measured activation sequence and the non-invasively imaged activation sequence. The localization error (LE), which is defined as the distance from the pacing site to the center of mass of the myocardial region with the earliest imaged activation time, was computed to evaluate the performance of 3-DCAI in localizing the origin of activation in single-site pacing. Fig. 1 schematically depicts the experimental protocol and the flow of data analysis.

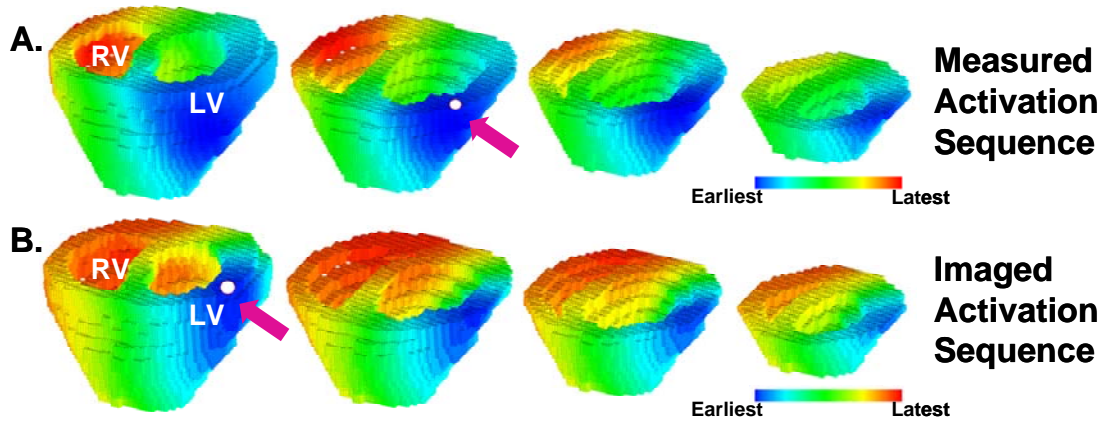


Figure 2. Comparison between the 3-D activation sequence measured via 3-D intra-cardiac mapping (A) and the 3-D activation sequence imaged by using 3-DCAI (B) under single-site pacing for the first rabbit. The pacing site and the estimated initial site of activation are marked by a red circle and a purple arrow. The progressive cut away views of the ventricles from basal to apex are displayed from left to right.

3. Results

Fig. 2 shows an example of comparison between the measured and imaged activation under single-site pacing for the first rabbit. The rabbit was paced at free wall of right ventricle. The activation time distributions on four representative axial slices were displayed with 3-D realistic heart geometry. The blue corresponds to early activation, while red corresponds to late activation. The imaged activation sequence (Fig. 2.B) was qualitatively consistent with the measured one (Fig. 2.A), and the origin of activation was localized to be around the true pacing site. The quantitative comparison returned a RE of 0.28 and a LE of 6.91 mm for this case. The second rabbit was paced at the anterior wall, and the comparison between the measured and imaged activation is shown in Fig. 3. It was observed from the imaged activation sequence that the origin of activation was located and the overall pattern was consistent with the measured activation sequence. The quantitative comparison returned a RE of 0.33 and a LE of 5.35mm.

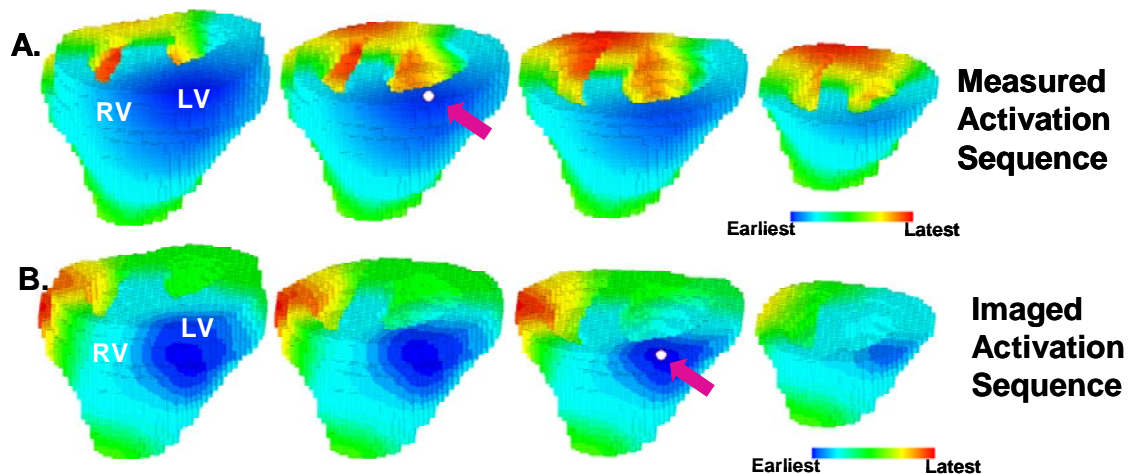


Figure 3. Comparison between the 3-D activation sequence measured via 3-D intra-cardiac mapping (A) and the 3-D activation sequence imaged by using 3-DCAI (B) for the second rabbit.

4. Discussion

The present study validated the biophysical model based 3-DCAI approach in imaging the 3-D ventricular activation sequence on a rabbit model under pacing protocol, as assessed by the invasive 3-D intra-cardiac mapping. The present results obtained from *in vivo* experimental studies indicate a

reasonable performance of the 3-DCAI algorithm in reconstructing the overall activation sequence and localizing the origin of activation under focal event. Such experimental finding is encouraging and suggests that the 3-DCAI technique may have potential to become a useful noninvasive imaging means for mapping cardiac electrical activity non-invasively throughout the 3-D myocardium.

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