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Noninvasive Three-dimensional Cardiac Activation Imaging on a Rabbit Model

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***Abstract*—Three-dimensional cardiac activation imaging (3-DCAI) aims at imaging the activation sequence throughout the 3-D myocardium. In the present study, the performance of 3-DCAI was validated through both *in vivo* animal experiments and computer simulations under a pacing protocol. The non-invasively imaged activation sequence from body surface potential maps (BSPMs) was quantitatively compared with the measured activation sequence obtained from the simultaneous intramural recording using a 3-D intra-cardiac mapping technique in a rabbit model. In addition, computer simulations were conducted to provide further assessment of the performance of the 3-DCAI algorithm in a realistic-geometry rabbit heart-torso model. The encouraging results suggest that 3-DCAI can non-invasively image the activation sequence and localize the origin of activation with good accuracy.**

I. Introduction

NONINVASIVE imaging of cardiac electrical activities is of enormous value both in basic cardiovascular research and clinical diagnosis of various cardiac disorders. For decades, investigations have been made to image and localize the cardiac electrical activities non-invasively from body surface potential maps (BSPMs), which is called the electrocardiography (ECG) inverse problem. These formations typically include equivalent moving dipole solutions [1], epicardial potential imaging [2], [3] and heart surface activation imaging [4]. Recently the ECG inverse problem has been extended to imaging the three-dimensional (3-D) cardiac electrical activity [5]-[9]. In addition to a heart cellular automaton model-based 3-D imaging approach [6]-[8], 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) [9].

In the present study, both *in vivo* experiments and computer simulations were conducted to evaluate the performance of the biophysical model-based 3-D cardiac activation imaging (3-DCAI) approach [9] in a rabbit model under a pacing protocol. Simultaneous measurements of body surface potentials and intra-cardiac bipolar recordings [10] were obtained in a closed-chest condition during rapid ventricular pacing. The 3-DCAI imaging results were quantitatively compared with intra-cardiac mapping results in order to assess imaging performance.

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II. Methods

A. Principles of 3-DCAI

The principle of 3-DCAI lies in the physical modeling of the cardiac electrical sources by 3-D distributed ECDs, which are proportional to the spatial gradient of the local transmembrane potentials (TMPs) throughout the ventricular myocardium. Based on bidomain theory [11], a boundary element method (BEM) is applied to characterize the linear relationship between the potentials over body surface and the 3-D ECD distribution, which is mathematically described as

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

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

The algorithm detailed in [9] was used to solve the inverse problem. In brief, a spatiotemporal regularization technique is used on the ECG data matrix to truncate the spatial components dominated by noise perturbation. The lead-field normalized weighted minimum norm (LFN-WMN) estimation is then applied to the remaining spatial components to reconstruct the time course of the local ECD at each myocardial site. The activation time at each myocardial site is determined as the instant when the time course of the estimated local ECD reaches its maximum magnitude.

B. Rabbit Model and In Vivo Mapping

A healthy New Zealand rabbit was studied using a protocol approved by the Institutional Animal Care and Use Committees of the University of Minnesota and the University of Alabama at Birmingham. The experimental protocol was detailed in [8]. In brief, before *in vivo* mapping study, two sets of Ultra Fast Computer Tomography (UFCT) images with and without intravenous (IV) contrast were obtained to construct a piecewise homogeneous rabbit heart-torso model. The isotropy of the conductivity was assumed within the myocardium. Plunge needles were placed in both left and right ventricles. The chest and skin were closed, and rapid right ventricular pacing was then performed (for 10-20 secs) via bipolar electrode-pairs on selected plunge needles. The bipolar electrograms were continuously recorded from electrode-pairs on all plunge needles together

with body surface potentials from BSPM electrodes on the anterior-lateral rabbit chest. 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.

Quantitative comparison was made between the invasively measured activation sequence via intra-cardiac mapping and the non-invasively imaged activation sequence. The relative error (RE) was computed to provide the difference between measured and 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.

C. Computer Simulation

In order to evaluate the performance of 3-DCAI comprehensively, computer simulations were conducted on a realistic geometry rabbit heart-torso model. Ventricular electrical activity, represented by ECDs, was simulated by a cellular automaton heart model [6]-[8] using both single-site and dual-site pacing protocols. BSPMs were generated by the forward computation in Eq. (1) with an additive 20 μV level Gaussian white noise (GWN) to simulate the realistic ECG measurement 3-DCAI was then applied tho the BSPM to inversely reconstruct the activation squence throughout the ventricular myocardium. Quantitative comparisons were made between the forward simulated and imaged activation sequences, and the RE and LE were calculated.

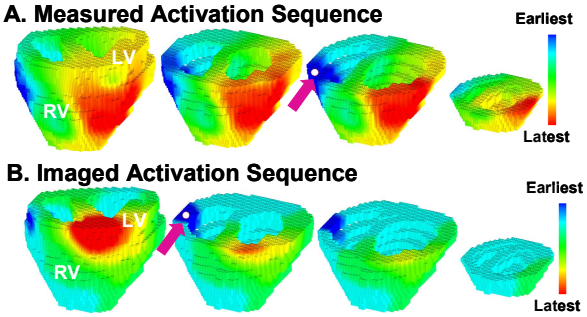

Fig. 1. Comparison between the 3-D activation sequence measured via 3-D intra-cardiac mapping (A) and the 3-D activation sequence imaged by using 3-DCAI (B) under single-site pacing during *in vivo* experiment. The pacing site and the estimated initial site of activation are marked by a red circle and a purple arrow. The progressive cut away views of the ventricles from basal to apex are displayed from left

III. Results

Fig. 1 shows an example of comparison between the measured and imaged activation under single-site pacing during the *in vivo* experiment. The rabbit was paced at the middle free wall of the right ventricle. The activation time distributions on four representative axial slices are displayed with the 3-D realistic heart geometry. The blue corresponds to early activation, while red corresponds to late activation. The imaged activation sequence (Fig. 1.B) was qualitatively consistent with the measured one (Fig. 1.A), and the origin of the activation was localized to be in close proximity to the true pacing site. The quantitative comparison returned a RE of 0.26 and a LE of 7.48 mm for this case.

In addition to the *in vivo* experiments, computer

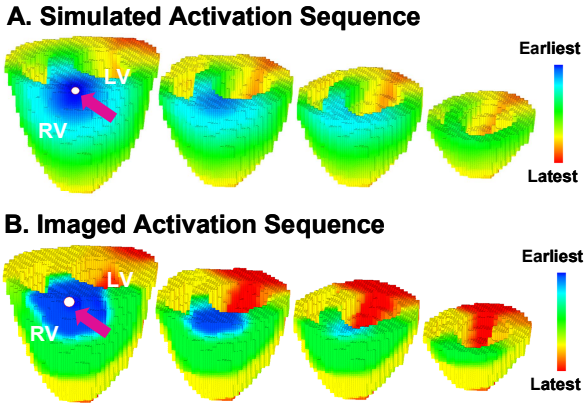

Fig. 2. Comparison between the simulated 3-D activation sequence (A) and the 3-D activation sequence imaged by using 3-DCAI (B) under single-site pacing during computer simulation.

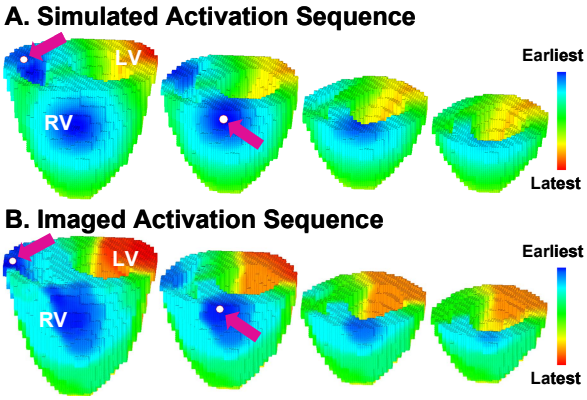

Fig. 3. Comparison between the simulated 3-D activation sequence (A) and the 3-D activation sequence imaged by using 3-DCAI (B) under dual-site pacing during computer simulation.

simulations were also conducted under single-site and dual-site pacing protocols, and the results are displayed in Fig. 2 and Fig. 3. As shown in Fig. 2, the rabbit ventricles are paced at the basal anterior wall, and the imaged activation sequence in Fig. 2.B correlates well with the forward simulated activation sequence, with a RE of 0.19 and a LE of 3.61 mm. Fig. 3 shows an example of dual-site pacing during computer simulation, in which the rabbit ventricles are simultaneously paced at the basal lateral wall of right ventricle and the middle anterior wall. The two origins of activation are well localized, and a quantitative comparison gives a RE of 0.23.

IV. Discussion

The present study validated the biophysical model-based 3-DCAI approach in imaging the 3-D ventricular activation sequence in a rabbit model under a pacing protocol, as assessed by the invasive 3-D intra-cardiac mapping. While the effect of open-chest surgery was neglected in the present

study, such surgery, as well as other experimental procedures (e.g., localization of body-surface electrodes and volume conductor modeling) might contribute to larger estimation errors, as compared with the computer simulation results. However, as shown in our previous study [8], the open-chest surgery procedure did not significantly alter the BSPM patterns on two rabbits. The present results obtained from both *in vivo* experimental studies and computer simulations 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 findings are encouraging and suggest that the 3-DCAI technique may have potential to become a useful means for imaging cardiac electrical activity non-invasively throughout the 3-D myocardium.

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