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Three-Dimensional Ventricular Activation Imaging by Means of Equivalent Current Source Modeling and Estimation

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***Abstract*—This paper presents a novel electrocardiographic inverse approach for imaging the 3-D ventricular activation sequence based on the modeling and estimation of the equivalent current density throughout the entire myocardial volume. The spatio-temporal coherence of the ventricular excitation process is utilized to derive the activation time from the estimated time course of the equivalent current density. At each time instant during the period of ventricular activation, the distributed equivalent current density is noninvasively estimated from body surface potential maps (BSPM) using a weighted minimum norm approach with a spatio-temporal regularization strategy based on the singular value decomposition of the BSPMs. The activation time at any given location within the ventricular myocardium is determined as the time point with the maximum local current density estimate. Computer simulation has been performed to evaluate the capability of this approach to image the 3-D ventricular activation sequence initiated from a single pacing site in a physiologically realistic cellular automaton heart model. The simulation results demonstrate that the simulated "true" activation sequence can be accurately reconstructed with an average correlation coefficient of 0.90, relative error of 0.19, and the origin of ventricular excitation can be localized with an average localization error of 5.5 mm for 12 different pacing sites distributed throughout the ventricles.**

I. INTRODUCTION

The heart functions as two side-by-side blood pumps that periodically pump the oxygen-poor blood to the lung or the oxygen-rich blood to the rest of the body. The mechanical function of the heart is triggered and coordinated by cardiac electrical events due to the intimate and causal linkage between the electrical and mechanical behaviors of myocardial cells. Therefore, measuring the cardiac electrical activity is of practical importance to study the heart function and to diagnose a variety of heart diseases.

A type of noninvasive cardiac electrical measurements is the recording of electrical potentials through an array of electrodes placed on a subject's chest and limbs. The instantaneous distribution of electrical potentials at all of the electrodes is usually referred to as the body surface potential map (BSPM), and the waveform recorded at any specific electrode is commonly known as electrocardiogram (ECG). However, neither BSPM nor ECG is able to provide enough specificity regarding where the electrical sources are located within the heart or how the cardiac electrical activity evolves over time. This is simply because the measured electrical activity is registered to the body surface instead of the anatomy of the heart, and the electrical signal arising from the heart is considerably attenuated and smeared after traveling through the volume conductor that separates the heart from the body surface.

To overcome such limitations, the ECG inverse imaging has been posed to extract from the BSPM important features of cardiac electrophysiology, such as the origin and the propagation of cardiac excitation. For example, efforts have been made to image the distribution of the activation time (the time of arrival of the upstroke of activation potentials) over the surface of the heart [1]. Heart-surface based activation imaging techniques can provide the information on when the excitation wavefront breakthrough the heart surface; however they are insufficient to image the entire activation sequence throughout the three-dimensional (3-D) volume of myocardium. Recently, He *et al.* proposed an indirect approach utilizing a parameterized cellular automaton heart model [2-3]. The model parameters were optimized by minimizing a multi-objective function that assessed the dissimilarity between the measured and the heart-model generated BSPMs. The 3-D myocardial activation sequence can subsequently be obtained through the optimized heart model in a well-posed manner [2-3]. Similarly, Ohyu *et al.* also used a ventricular excitation model including a template step function of the activation potential amplitude (APA) and the activation time to approximately describe the transmembrane potentials. They inversely reconstructed the distributions of APA and activation time from the MCG data in a simulation study by using the maximum *a posteriori* (MAP) estimation and the simulated annealing method [4].

These existing 3-D activation imaging techniques rely on the physiological information (such as the conduction velocity or the template function of transmembrane potentials). However, such information may be difficult to obtain in practice, or be inaccurate during pathological conditions. To overcome such limitations, we propose an alternative approach to image the 3-D ventricular activation sequence based on the physical modeling of the heart-torso volume conductor and the 3-D distributed equivalent current

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sources. In brief, the equivalent current source distribution is estimated from the BSPM at every time instant during the period of the ventricular depolarization. The activation time at a given myocardial location is determined as the time point when the estimated local current density reaches its maximum amplitude. Fig. 1 illustrates the proposed imaging strategy.

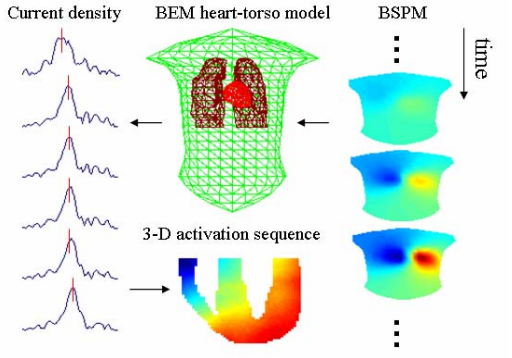

Fig. 1. The illustration of the proposed 3-D activation imaging. See the text for details.

Computer simulations were conducted to quantitatively evaluate the performance of our proposed approach. We employed a previously developed cellular automaton heart model [5-6] to simulate the ventricular excitation using a single-site pacing protocol. By means of the boundary element method (BEM) [7], the BSPMs were generated by the simulated cardiac electrical activity in the physiological heart model embedded in a realistic-geometry heart-torso volume conductor. The proposed imaging algorithm was applied to reconstruct the 3-D distributed activation sequence from the BSPMs with additive noise. The reconstructed activation sequence was finally quantitatively compared with the simulated "true" activation sequence.

II. Methods

A. From 3-D Equivalent Current Density to BSPM

Deriving from the bidomain theory [8-9], the electrical field within a heart-torso volume conductor is governed by Eq. (1)

$$\nabla\cdot\left[(G_i+G_e)\nabla\phi_e\right]=\nabla\cdot\left(-G_i\nabla\phi_m\right) \qquad (1)$$

where G_i and G_e are the intracellular and extracellular effective conductivity tensors, ϕ_e is the extracellular potential, and ϕ_m is the transmembrane potential confined to the 3-D myocardial volume, respectively.

By defining equivalent current density $\vec{j}_{eq}=-G_i\nabla\phi_m$, Eq. (1) can be re-written as Eq. (2)

$$\nabla\cdot\left[(G_i+G_e)\nabla\phi_e\right]=\nabla\cdot\vec{j}_{eq} \qquad (2)$$

Eq. (2) suggests that $\vec{j}_{eq}$ can serve as equivalent current sources for computing the potential field generated by cardiac electrical activity. Thus, at any instant *t*, the electrical potential ϕ_b at an observation point r_b over the torso surface is a linear superimposition of the instantaneous potential fields generated by the equivalent sources $\vec{j}_{eq}$ at every possible source location r_s inside the heart volume *V*, as expressed by Eq. (3)

$$\phi_b(r_b,t)=\int_{r_s\in V}\vec{\Psi}(r_b,r_s)\cdot\vec{j}_{eq}(r_s,t)dr_s^3 \qquad (3)$$

where $\vec{\Psi}(r_b,r_s)$ is the impedance transfer function dependent on the conductivities and the shape of the heart-torso volume conductor [10].

To model the distributed equivalent current sources, the whole ventricular myocardium is divided into *N* grid points. An orthogonal triple of dipoles is placed at each grid point. Applying the BEM [7], a discrete matrix equation can be obtained in place of Eq. (3), written as Eq. (4).

$$\Phi_b(t)=LJ(t) \qquad (4)$$

where $\Phi_b(t)$ is a vector of the instantaneous BSPM at *M* electrode positions, $J(t)$ is a vector of equivalent current sources at *N* known myocardial sites, $L=(L_1,L_2,...,L_N)$ is an *M*-by-*3N* transfer matrix, and L_i is an *M*-by-*3* matrix that represents the electric lead field of the three source components at the *i*-th grid point.

B. From equivalent current density to activation time

By definition, the amplitude of equivalent current density $\vec{j}_{eq}(r_s,t)$ is proportional to the spatial gradient of transmembrane potential $\nabla\phi_m(r_s,t)$. During the ventricular activation, the spatial distribution of $\vec{j}_{eq}(r_s,t)$ is dominated by its values at the interface between the depolarized and non-depolarized myocardium (known as the *excitation wavefront*), where the myocardial cells are undergoing rapid depolarization. Owing to the steepness of depolarization, the excitation wavefront is expected to propagate by a given myocardial site only at its activation time. As a result, when one looks at the time-varying equivalent current density $\vec{j}_{eq}(r_k,t)$ at a fixed location r_k, its amplitude $\left|\vec{j}_{eq}(r_k,t)\right|$ reaches the maximum exactly at its activation time $\tau(r_k)$ for the entire duration *T* of the ventricular depolarization. This concept is mathematically expressed by Eq. (5).

$$\arg\max_{t\in T}\left(\left|\vec{j}_{eq}(r_k,t)\right|\right)=\tau(r_k) \qquad (5)$$

C. Noninvasive activation imaging

Eq. (5) implies a key concept that the activation sequence throughout the 3-D ventricular volume can be determined by evaluating the time course of local equivalent current density at every myocardial site. Therefore, the noninvasive estimation of activation sequence from the BSPM consists of solving the inverse problem of (4), and detecting the temporal "marker" at which the inversely calculated source magnitude arrives at its maximal peak.

Applying the weighted minimum norm (WMN) approach to solve the inverse problem, the inverse solution $\hat{J}(t)$ can be written as (6)

$$\arg\min_{J(t)}\left(\left\|\Phi_b(t)-LJ(t)\right\|_2^2+\lambda\left\|WJ(t)\right\|_2^2\right) \qquad (6)$$

where $W=\Omega\otimes I$ ($\otimes$ denotes the Kronecker product, I is the identity matrix, and Ω is a N-by-N diagonal matrix). Ω provides a single lead field normalization factor for all three dipole components at each grid point.

The solution of (6) can be obtained by a linear inverse matrix as a function of the regularization parameter.

$$T(\lambda)=\left(W^TW\right)^{-1}L^T\left(L\left(W^TW\right)^{-1}L^T+\lambda I\right)^{-1} \qquad (7)$$

The regularization parameter λ can be chosen for all the time points simultaneously, using a method proposed in [11]. The singular value decomposition (SVD) of the ECG matrix $\Phi_b=[\Phi_b(1),\Phi_b(2),\ldots,\Phi_b(T)]$ is written as Eq. (8)

$$\Phi_b=U\Sigma V^T=\sum_{k=1}^{\min(T,M)}u_k\sigma_k v_k^T \qquad (8)$$

where $\{u_k\}$ represents a group of spatial components of the BSPMs, and $\{v_k\}$ represents their corresponding time courses. The spatial components that do not satisfy the discrete Picard condition should be truncated. The spatial distribution of the sources that account for each of the P remaining BSPM components can be obtained by Eq. (9),

$$\hat{J}_k=T(\lambda_k)u_k \qquad (9)$$

where λ_k is chosen by the "L-curve" method [12].

The entire spatiotemporal current source distribution $\hat{J}=[\hat{J}(1),\hat{J}(2),\ldots,\hat{J}(T)]$ can be obtained by Eq. (10)

$$\hat{J}=\sum_{k=1}^{P}\hat{J}_k\sigma_k v_k \qquad (10)$$

Once the above inverse problem is solved, the activation time is subsequently determined by detecting the time instant with the occurrence of the maximum current source estimate for each 3-D grid point.

D. Computer Simulation

The proposed 3-D activation imaging method was evaluated in a computer simulation. A cellular automaton heart model was employed to realistically simulate the cardiac electrical activity initiated from a single pacing site. The geometry of the heart was extracted from the CT images of a normal human subject. The detail description of the heart model can be found in [6].

The heart model was then embedded into a piece-wise homogeneous heart-torso model built from the same set of CT images. The whole 3-D ventricular myocardial volume was discretized into 36,709 grid points evenly spaced by 1.5 mm. Two hundred ECG electrode locations were selected to cover the anterior and posterior chests. The BSPMs was simulated by a BEM-based forward model with additive Gaussian white noise.

The correlation coefficient (CC) and relative error (RE) were calculated to measure the overall agreement or disagreement between the inversely estimated activation sequence and the "true" activation sequence simulated by the cellular automaton heart model. The capability of localizing the origin of excitation was measured by the localization error (LE), defined as the distance from the true pacing location(s) to the center(s) of mass of locations with the earliest activation time in the imaged activation sequence.

III. Results

Fig. 2 shows an example of the imaged 3-D ventricular activation sequence. The simulated ventricular activation was initiated from the basal anterior wall of LV. The activation sequences were inversely estimated from the simulated BSPM with 20 μV additive noise. For both the forward-simulated and the reconstructed activation sequences, five representative axial slices were selected from a total of 50 slices for illustration purpose. Apparently, the propagation of excitation can be clearly observed from the estimated activation sequence with a high accuracy (CC=0.9446, RE=0.1833). However, we can also observe that the earliest activation time in the inverse results was 18 ms later than the true activation time of the pacing site. The imaged earliest activation involved a region of myocardium instead of a single point, indicating the reduced spatial resolution in terms of localizing the origin of excitation. Nevertheless, the center of the myocardial region with the earliest activation time was close to the true initial site, with a LE as small as 2.6 mm.

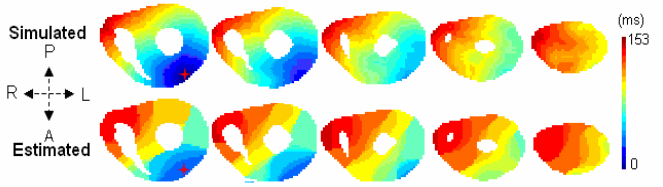

Fig. 2 Comparison between the simulated "true" (upper row) and imaged (bottom row) 3-D activation sequences under 20 μV noise. The images from the left to the right correspond to the axial slices from the base to the apex of the ventricles.

Fig. 3 shows the comparison between the estimated current density waveforms under different noise levels and the true current density waveforms. We intentionally selected three locations, whose true activation times were 20 ms, 80 ms and 120 ms respectively, as representative myocardial sites activated during the early, middle and late stage of the ventricular depolarization. For the locations of the middle and late activation, the "peaks" of the estimated current density arrived at about the same time as those of the simulated current density (with their difference in time as small as 3~6 ms). This estimation error did not further deteriorate with increasing noise levels (up to 60 μV). In contrast, a considerable delay of the estimated activation time can be observed for the early activated location. Also note that the shape of the estimated current density time

courses were less "steep" than the shape of "delta function" that appeared in the simulated current density waveforms. This phenomenon demonstrated the inherent ill-posedness of the ECG inverse problem.

We deployed the pacing site to 12 representative locations throughout the entire ventricles. Under a 20 μV noise level, the mean CC was 0.90 with a standard deviation of 0.06; the mean RE was 0.19 with a standard deviation of 0.07; and the mean localization error is 5.49 mm with a standard deviation of 1.17 mm.

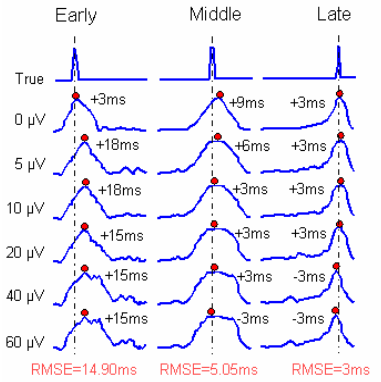

Fig. 3 Comparison between the "true" and the estimated current density time courses (under different noise levels) at three representative myocardial sites respectively activated during the early, middle or late stage of the ventricular depolarization. All the estimated and the "true" time courses were normalized into (0, 1). The time differences in the occurrence of the peak values (marked by the red circle) between the estimated and "true" time courses are shown by each of the estimated waveforms. The root mean squared error (RMSE) is calculated with respect to all noise levels.

IV. Discussion

The important distinctions of the present method from other existing activation time imaging methods lie in 1) the *3-D* activation sequence instead of the 2-D heart-surface activation sequence [1] is imaged; 2) it does not require the assumption of isotropic or equally anisotropic conductivity of the entire myocardial medium in order to formulate the inverse solver; and 3) it is a physical-model-based approach, without incorporating physiological assumptions [2].The present study proposed, *for the first time*, a physical-model-based approach for the 3-D ventricular activation sequence reconstruction from the BSPM.

The promising results in the present study also suggest the feasibility of extracting physiologically useful information (i.e. the 3-D distribution of activation time) from the considerably ill-posed inverse solution of the instantaneous current density estimation from the BSPM. The 3-D distributed source reconstruction from a limited number of remote measurements is challenging and troublesome; however, in terms of the 3-D activation sequence imaging, the useful information is not carried by the spatial distribution of the instantaneous current source reconstruction but the time course of equivalent current density estimates at each spatial location. Our results clearly show that by shifting our view of inspecting the ECG inverse solution from the spatial domain to the spatio-temporal domains, a physiologically reasonable activation sequence reconstruction can be obtained regardless of the complication and difficulty associated with the estimation of a huge number of dipole sources.

In summary, we have developed a 3-D cardiac activation imaging algorithm based on the inverse solution of equivalent current density from the BSPM. Through computer simulation, it has been demonstrated that the present technique is able to reconstruct the ventricular activation sequence well consistent with the true activation sequence, and to localize the initial site of excitation with a small localization error. The present promising results suggest that the newly developed method provides an important alternative approach to the 3-D cardiac electrical imaging and merits further investigation.

References

[1] B. Tilg, G. Fischer, R. Modre, F. Hanser, B. Messnarz, M. Schocke, C. Kremser, T. Berger, F. Hintringer and F.X. Roithinger, "Model-based imaging of cardiac electrical excitation in humans," *IEEE Trans. Medical. Imaging*, vol. 21, pp.1031-1039, Sep. 2002.

[2] B. He, G. Li and X. Zhang, "Noninvasive three-dimensional activation time imaging of ventricular excitation by means of a heart-excitation model," *Phys. Med. Biol.,* vol. 47, pp. 4063-4078, Nov. 2002.

[3] X. Zhang, I. Ramachandra, Z. Liu, B. Muneer, S. M. Pogwizd and B. He, "Noninvasive three-dimensional electrocardiographic imaging of ventricular activation sequence," *AJP – Heart Circ. Physiol.*, vol. 289, pp. H2724-H2732, Nov. 2005.

[4] S. Ohyu, Y. Okamoto and S. Kuriki, "Use of the ventricular propagated excitation model in the magnetocardiographic inverse problem for reconstruction of electrophysiological properties," *IEEE Trans. Biomed. Eng.,* vol. 49, pp. 509-519, Jun. 2002.

[5] G. Li and B. He, "Localization of the site of origin of cardiac activation by means of a heart-model-based electrocardiographic imaging approach," *IEEE Trans. Biomed. Eng.,* vol. 48, pp. 660-669, Jun. 2001.

[6] B. He, G. Li and X. Zhang, "Noninvasive imaging of ventricular transmembrane potentials within three-dimensional myocardium by means of a realistic geometry anisotropic heart model," *IEEE Trans. Biomed. Eng.*, vol. 50, pp. 1190-1202, Oct. 2003.

[7] R. C. Barr, T. C. Pilkington, J. P. Boineau and M. S. Spach, "Determining surface potentials from current dipoles, with application to electrocardiography," IEEE Trans. Biomed. Eng., vol. 13, pp. 88-92, Apr. 1966.

[8] W. T. Miller and D. B. Geselowitz, "Simulation studies of the electrocardiogram. I. The normal heart," *Circ. Res.,* vol. 43, pp. 301-315, Aug. 1978.

[9] L. Tung, "A bidomain model for describing ischemic myocardial D.C. potentials," *Ph.D Dissertation,* 1978.

[10] Y. Yamashita and D. B. Geselowitz, "Source-field relationships for cardiac generators on the heart surface based on their transfer coefficients," IEEE Trans. Biomed. Eng., vol. BME-32, 964-970, 1985.

[11] F. Greensite and G. Huiskamp, "An improved method for estimating epicardial potentials from the body surface," *IEEE Trans. Biomed. Eng.,* vol. 45, pp. 98-104, Jan. 1998.

[12] P.C. Hansen, "Analysis of discrete ill-posed problems by means of the L-curve," *SIAM Review*, vol. 34, pp. 561-580, Dec. 1992.