Estimation of Activation Sequence from Time Course of Equivalent Current Density in Pathological Hearts - A Simulation Study

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***Abstract*— The equivalent current density (ECD) model has been previously used in the cardiac electrical imaging technique for non-invasively reconstructing the global activation sequence (AS) in the normal heart. However, its performance in estimating AS in the heart with structural defects remains uncertain. This study aims to evaluate its feasibility in two common cardiac structure diseases--ischemia and infarction, by performing forward simulation using a cellular automaton heart model. The AS was derived from ECD and quantitatively compared to the true AS simulated with the heart model by calculating correlation coefficient (CC) and relative error (RE). In ischemia condition, the ECD model returns a CC (0.97) and RE (0.13), comparable with those of normal heart. In infarction condition, it is also able to identify area of infarction and reconstruct global AS at the excitable myocardium with CC of 0.97 and RE of 0.12. The present pilot simulation results suggest the feasibility of applying ECD model in the pathological heart, which would help the investigation of pathology mechanism and clinical management of cardiac diseases.**

Keywords - Ischemia; Infarction; Equivalent Current Density; Activation Sequence; Cellular Automaton Heart Model

I. INTRODUCTION

Noninvasive 3-dimensional (3-D) imaging of cardiac electrical activities is important for facilitating basic cardiovascular research and management of cardiac diseases [1-5]. The equivalent current density (ECD) model based 3-D cardiac electrical imaging (3-DCEI) approach has been proposed for the inverse reconstruction of 3-D ventricular activation [5]. It is based on the principle that the activation time of normal heart tissue is corresponding to the instant when the time course of ECD reaches maximum at every myocardial site [5]. This method has been evaluated in a healthy animal model [6], but it remains unclear that whether it is applicable to heart tissues with structural defects.

The purpose of the present study is to test the feasibility of estimating activation sequence (AS) from the time course of ECD in hearts with ischemia and infarction, by means of forward simulation. The ventricular activation was simulated by a cellular automaton heart model and defined as the 'true' activation sequence. The current density at every myocardial unit was constructed accordingly and the activation time for each cellular unit was determined by picking up the time instant corresponding to the peak magnitude of ECD. The estimated AS from ECD time course was then quantitatively compared with the 'true' AS from the cellular automaton heart model.

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II. METHOD

A. Cellular Automaton Heart Model

The forward simulation was performed using a cellular automaton heart model as in our previous studies [2-3]. The geometry of the heart was reconstructed from CT images from a human subject. The entire ventricular model contains over 30,000 myocardial cellular units with a spatial resolution of 1.5mm. The action potential (AP) of each unit was defined based on knowledge of cardiac anatomy and electrophysiology. The myocardial fiber orientations revolved counterclockwise from the epicardium (-60 degree) to endocardium (+ 60 degree). The conduction velocity of each cellular unit was set to be 0.2 m/s and 0.6 m/s along the transverse and longitudinal fiber directions, respectively. The electrical conductivity was set to be 0.05 S/m and 0.15 S/m along the transverse and longitudinal fiber directions. The ventricular activation during sinus rhythm was simulated and defined as the 'true' activation sequence. The ECD was derived as the product of the myocardial conductivity tensor and the gradient of transmembrane potential. Subsequently, the activation time at each myocardial unit was determined by picking up the time instant of which ECD corresponds to the maximum peak magnitude [5]. The AS derived from the ECD time course is defined as the 'estimated' one. The schematic diagram is shown in Figure 1.

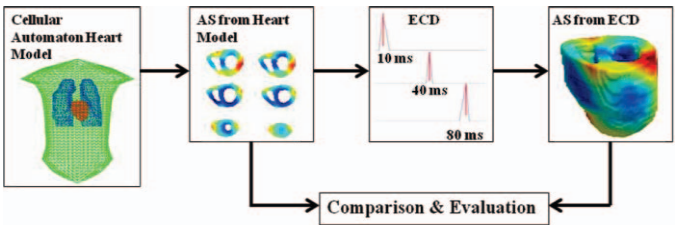

Figure 1. Schematic diagram of the present computer simulation study.

B. Pathological Heart Models

Two common cardiac pathologies were simulated, ischemia and infarction. In the simulation of each disease, the myocardial units are divided into four zones: the normal zone, the outer border zone, the inner border zone and the central

pathological zone. Each zone is marked with different color and number (Figure 2.a) with AP in the same color (Figure 2.b). The first zone, marked with dark blue, corresponds to normal cardiac tissue with an action potential pattern of blue. The second region, marked with yellow, represents all myocardial units in the outer border of the central pathological zone, with an action potential shape displayed in yellow. The third region, marked with green, indicates the inner border zone with an action potential of green. The forth area, marked with dark red, represents the central pathological zone, which could be either central ischemia or central infarction, with an action potential shape of red. The central pathological zone is located at the anterior wall with a volume of 3.4cm^3, surrounded by the 3mm-thick inner border zone. They are encircled by the outer border zone, which constitutes the outermost pathological layer with a thickness of 3mm.

Compared with action potential in normal tissue, the action potentials in ischemia and infarction area including the border zones are characterized by higher resting potential, shorter duration, lower amplitude and slower upstroke velocity [7-8]. In the simulation, the resting membrane potentials, action potential durations and amplitudes are set within the range of experimental data for ischemia and infarction [7-8]. The maximum upstroke velocity and conduction velocities are predetermined based on the dependence on resting potentials [9-10]. The overall shapes are also in accordance with the experimental results from human subject [11]. Figure 2.b illustrates the details of action potentials in the two pathological models.

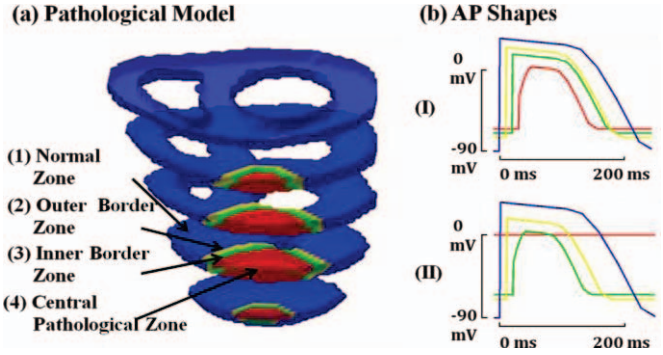

Figure 2: Pathological heart model and corresponding action potentials. (a) Blue, yellow, green and red colors represent (1) normal zone, (2) outer border zone, (3) inner border zone and (4) central pathological zone, respectively. (b) Action potentials coded with color. Blue, yellow, green and red represent AP at (1) normal zone, (2) outer border zone, (3) inner border zone and (4) central pathological zone, respectively. (I) shows details of AP morphologies in the simulation of ischemia, and (II) shows details of AP used for the simulation of infarction.

C. *Evaluation Method*

The performance of ECD model was quantitatively evaluated using correlation coefficient (CC) and relative error (RE). The CC is defined as:

$$CC = \frac{\mathrm{cov}(AS^E, AS^T)}{\sigma_E \sigma_T} \quad (1)$$

where AS^E denotes the estimated AS and AS^T the true AS. cov(AS^E , AS^T) is the corresponding covariance. σ_E and σ_T are the standard deviation of AS^E and AS^T , respectively. RE is expressed as:

$$RE = \sqrt{\frac{\sum_{i=1}^{n}(AS_i^E - AS_i^T)^2}{\sum_{i=1}^{n}(AS_i^T)^2}} \quad (2)$$

where the n is the total number of myocardial cellular units, AS_i^E and AS_i^T are respectively the estimated and true activation time of the i^{th} cellular unit.

III. RESULTS

The activation sequences of sinus rhythm from healthy heart, ischemic heart and infarcted heart were reconstructed respectively. The performance of ECD model is quantitatively evaluated by calculating the CC and RE between true AS and estimated AS, as summaried in Table I. In the healthy heart, the CC is as high as 0.99 and RE is as low as 0.078, suggesting that the ECD model is able to determine global AS with high accuracy under healthy condition.

TABLE I. EVALUATION OF ECD MODEL

	Healthy Heart	Ischemia	Infarction
CC	0.99	0.97	0.97
RE	0.078	0.13	0.12

Under ischemia condition, the AS from ECD time course is well consistent with the true one, with a CC of 0.97 and a RE of 0.13, comparable to those of healthy heart. In the central ischemia area (Figure 2.a, red zone), due to a significantly low action potential upstroke velocity (Figure 2.b (I), AP in red), the magnitude of current density curve is much lower than that in both the normal zone and border zone. Nevertheless, the ECD at border zone and central ischemic zone still presents a peak whose time instant corresponds to the activation time, producing nearly identical AS with the true one.

In the infarction model, the ECD model is able to identify the area of infarction (Figure 3, black area) and reconstruct AS in the exitable zones with a high CC (0.97) and low RE (0.12). Under infarcted condition, the area of infarction is defined as where the time course of ECD does not show a peak magnitude, indicating no actual activation presenting at the corresponding location. The simulation results show that the ECD model recognizes such infarcted area (Figure 3.(2), black area) with high consistency comparing with the true one (Figure 3.(1), black area). Figure 3 also shows that the ECD model is able to reconstruct global AS in the excitable zones with a high CC (0.97) and low RE (0.12). All the results suggest that, in this pathological condition, the ECD model is able to identify the infarcted area and reconstruct a consistent global AS.

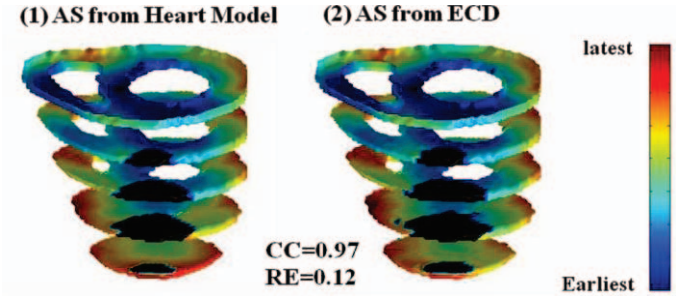

Figure 3: Activation sequences. The black region represents area of infarction. The blue color represents the earliest activation and the red color denotes the lastest activation. (1) shows the true AS from heart model and (2) shows the estimated AS from ECD.

IV. DISCUSSION

The present pilot simulation study suggests that the ECD model is able to reconstruct global activation sequence in the heart with pathological conditions. In the simulation of cardiac ischemia, the CC and RE are still high, demonstrating its applicability in such cardiac pathology. In the infarction condition, the ECD model is capable to identify area of infarction and obtain consistent global AS. Our pilot computer simulation results suggest that the method of determining activation times from the local equivalent current densities can be applied in hearts with structure defects.

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