Mapping of cardiac electrical activation with electromechanical wave imaging: An in silico–in vivo reciprocity study

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BACKGROUND Electromechanical wave imaging (EWI) is an entirely noninvasive, ultrasound-based imaging method capable of mapping the electromechanical activation sequence of the ventricles in vivo. Given the broad accessibility of ultrasound scanners in the clinic, the application of EWI could constitute a flexible surrogate for the 3-dimensional electrical activation.

OBJECTIVE The purpose of this report is to reproduce the electromechanical wave (EW) using an anatomically realistic electromechanical model, and establish the capability of EWI to map the electrical activation sequence in vivo when pacing from different locations.

METHODS EWI was performed in 1 canine during pacing from 3 different sites. A high-resolution dynamic model of coupled cardiac electromechanics of the canine heart was used to predict the experimentally recorded electromechanical wave. The simulated 3-dimensional electrical activation sequence was then compared with the experimental EW.

RESULTS The electrical activation sequence and the EW were highly correlated for all pacing sites. The relationship between the electrical activation and the EW onset was found to be linear, with a slope of 1.01 to 1.17 for different pacing schemes and imaging angles.

CONCLUSION The accurate reproduction of the EW in simulations indicates that the model framework is capable of accurately representing the cardiac electromechanics and thus testing new hypotheses. The one-to-one correspondence between the electrical activation and the EW sequences indicates that EWI could be used to map the cardiac electrical activity. This opens the door for further exploration of the technique in assisting in the early detection, diagnosis, and treatment monitoring of rhythm dysfunction.

KEYWORDS Electrical activation sequence; Electromechanical wave imaging; Electromechanical model of the heart; High frame-rate echocardiography; Image-based computational modeling; Ventricular contraction

ABBREVIATIONS **3D** = three dimensional; **DTMR** = diffusion tensor magnetic resonance; **EW** = electromechanical wave; **EWI** = electromechanical wave imaging; **LV** = left ventricle; **LVa** = apex of the left ventricle; **LVb** = basal region of the lateral wall; **MR** = magnetic resonance; **MRI** = magnetic resonance imaging; **RF** = radiofrequency; **RV** = right ventricle; **RVa** = apex of the right ventricle

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Introduction

Disturbances in the electrical activation of the heart constitute a major cause of death and disability, affecting millions of people worldwide. However, no imaging method is currently capable of mapping the three-dimensional (3D) electrical activation sequence in the heart for clinical use. Currently available clinical methods are all catheter based, and are thus limited to mapping the endocardial or epicardial activation sequence; they are also time consuming and costly. Newly developed electrocardiographic imaging methods based on high-density body surface potential maps hold high promise for reconstruction of the 3D activation sequence in the heart[1,2] and have demonstrated clinical relevance.[3,4] However, these methods rely on either ionizing exposure, i.e., 3D computed tomography, or magnetic resonance imaging (MRI), which can be contraindicated for patients with pacemakers or stents. Even in a laboratory setting, mapping the 3D electrical activation sequence of the heart can be a daunting task.[5] Studies of transmural electrical activation usually require usage of a large number of plunge electrodes to attain sufficient resolution,[6–8] or are applied to small regions of interest in vivo,[9] or to small animals, e.g., the rabbit.[2] Optical imaging methods can map

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the activation sequence of ex vivo tissue on the endocardial and epicardial surfaces[10–12] and transmurally.[13–16]

Recently, we have developed a novel imaging technique termed electromechanical wave imaging (EWI), which is an entirely noninvasive, nonionizing, ultrasound-based imaging method capable of mapping along various echocardiographic planes in vivo[17] the electromechanical activation sequence, i.e., the sequence of first instants at which the muscle transitions from a relaxation to a contraction state following the electrical activation of the heart. Spatially, this electromechanical activation forms a wavefront, i.e., the electromechanical wave (EW), that follows a propagation pattern similar to the electrical activation sequence. EWI maps the EW with high accuracy by using a frame rate up to 7 times higher than that of standard echocardiography. In its essence, EWI uses cross-correlation of the radiofrequency (RF) signals to estimate the minute, electromechanically induced, interframe axial strains at an accuracy and spatial resolution never achieved before in a full view of the heart within a 2- to 3-millisecond-long time interval. Using these interframe axial strains, the timings at which a region in the heart transitions from a relaxing to a contracting state of the heart can be mapped.

EWI has previously been performed in mice,[18] dogs,[19] and humans.[20] These reports have demonstrated correlation of the EW with the pacing protocol and the conduction velocity of the electrical wave,[18] and have shown that EWI can be used to determine the location of the pacing site[21] and map the presence of ischemic regions.[17] Because the only required equipment to perform EWI is a clinical ultrasound scanner,[20] the application of EWI as a surrogate for the 3D electrical activation in the ventricles can be flexible and broad, at the doctor's office or point of care, to identify patients at risk, inform caregivers, or plan, monitor, and assist with follow-up of therapeutic interventions such as cardiac resynchronization therapy and ablation. However, to exploit the full potential of EWI in the clinic, it is of paramount importance that the degree to which EWI adequately represents the pattern of 3D electrical activation in the ventricles is explicitly determined.

To perform such an evaluation, the propagation of the EW needs to be compared with the 3D electrical activation in the ventricles, preferably in a large animal heart, such as the canine one. However, currently available experimental methods do not allow for simultaneous mapping of both the EW and the 3D (and in particular, the transmural) electrical activation sequence. Indeed, the spatial resolution of plunge needle recordings is insufficient for the adequate comparison with the EW sequence; moreover, because the strains associated with the EW are minute,[17] the insertion of needle electrodes is likely to significantly alter the normal EW.

Because of the limitations in current experimental techniques for mapping the 3D electrical activation sequence with high spatiotemporal resolution, an anatomically realistic modeling approach to cardiac function appears to be an attractive alternative in providing the 3D electrical activation sequence in the ventricles. We developed a high-resolution dynamic model of coupled cardiac electromechanics in the rabbit heart[22] and used it to ascertain the mechanisms of spontaneously induced arrhythmias in acute regional ischemia.[23] The model was recently extended to the canine heart, where the geometry and structure of the canine heart was reconstructed from MRI and diffusion tensor magnetic resonance (DTMR) imaging scans.[24] In this study, we use this novel electromechanics model of the canine heart for the first time and apply it, after optimizing it, to fully assess the utility of EWI in mapping the electrical activation sequence in the canine ventricles.

To achieve this goal, we simulate the EW in the model of the normal canine ventricles and compare the results to the in vivo experimental EW in the canine. Once the match between simulated and experimental EWs is obtained and the predictive capabilities of the canine electromechanics model are established, the EW is compared with the electrical activation sequence obtained from the model, providing the desired relationship between the EW and the 3D electrical activation maps in the canine ventricles, thus assessing the utility of EWI in mapping the electrical activation.

Methods

Experimental protocol

In this study, approved by the Institutional Animal Care and Use Committee of Columbia University, 1 male mongrel dog of 28 kg in weight was anesthetized with an intravenous injection of thiopental (10 to 17 mg/kg). The animal was mechanically ventilated with a rate- and volume-regulated ventilator on a mixture of oxygen and titrated isoflurane (0.5% to 5.0%). Morphine (0.15 mg/kg, epidural) was administered before surgery, and lidocaine (50 micrograms/kg/h, intravenous) was used during the procedure. To maintain blood volume, 0.9% saline solution was administered intravenously at 5 ml/kg/h. Solid-state pressure transducer catheters (Millar Instruments, Houston, Texas) were inserted into the left-ventricular (LV) cavity via the right carotid artery and the aorta. The chest was opened by lateral thoracotomy using electrocautery. After removal of the pericardium, 3 crystals of 2 mm in diameter combined with bipolar pacing electrodes were sutured onto the epicardium at the following locations: (1) basal region of the lateral wall (LVb), (2) LV apex (LVa) and (3) right ventricular (RV) apex (RVa), and used to pace the ventricles.

Electromechanical wave imaging

An Ultrasonix RP (Ultrasonix Medical Corp., Burnaby, BC, Canada) system with a 3.3-MHz phased array was used to acquire RF frames at 370 frames/s using an automated composite technique[20] (Figure 1A). Briefly, this method involves increasing the frame rate by dividing the image into partially overlapping sectors corresponding to separate cardiac cycles. The probe was attached to a stabilizer (Medtronic Corp., Minneapolis, MN), and the respirator was interrupted for 6 to 20 seconds during ultrasound ac-