

Noninvasive electromechanical wave imaging and conduction velocity estimation *in vivo*

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Abstract— Electromechanical imaging is a novel technique for the noninvasive mapping of electrical conduction waves in the left ventricle through the combination of ECG gating, high frame rate and RF-based displacement estimation techniques. In this paper, we identify and separate the electromechanical waves from the hemodynamically induced waves and determine the dependence of the wave direction and velocity at different pacing scenarios. In vivo imaging (30 MHz) was performed on anesthetized wildtype mice (n=12) at high frame rates (Vevo 770, Visualsonics, Inc.) in order to better explore the electromechanical coupling within the heart muscle. The acquisition was triggered on the mouse electrocardiogram (ECG) and yielded a high frame rate of 8000 fps. RF frames from long-axis views were digitized at 160 MHz. Axial, frame-to-frame displacements were estimated using 1D cross-correlation (window size of 240 microns, overlapping at 90%). Three pacing protocols were applied in each mouse: 1) sinus rhythm (SR) (natural pacing), 2) right-atrial (RA) pacing and 3) right-ventricular (RV) pacing. Pacing was achieved using a nine-electrode catheter and catheterization through the right side of the heart, with each separately activated for varying the pacing location. Throughout the entire cardiac cycle, several waves were shown on the electromechanical images that propagated transmurally and/or from base to apex (septum) or apex to base (posterior wall). Through comparison of the ciné-loop images obtained at different pacing protocols, we were able to identify and separate the electrically induced, or contraction, wave from the hemodynamic (or, blood-wall coupling) waves. The contraction wave was best observed along the posterior wall starting at the S-wave of the ECG, which occurs after Purkinje and during myocardial activation. Only the contraction wave changed direction when the pacing origin changed, i.e., it propagated from apex to base at SR and RA pacing and from base to apex at RV pacing. This reversal in the wave propagation direction was found to be consistent in all mice scanned and the wave velocities were found to be within the reported conduction wave range with statistically significant differences between SR/RA pacing (0.8496 +/- 0.2214 m/s and 0.8379 +/- 0.1967 m/s), respectively and RV pacing (0.5213 +/- 0.3125 m/s). This pacing study demonstrates that electromechanical imaging may constitute the sole noninvasive method for conduction mapping of the entire left ventricle and thus diagnosis and treatment of dyssynchrony, arrhythmia or other conduction abnormalities.

Keywords— *Conduction; Contraction; Displacement; Electromechanical; Motion; Myocardium; Velocity; Wave.*

I. INTRODUCTION

Cardiovascular disease remains American's No. 1 killer for both men and women, still claiming more lives than the rest of major causes of death, according to the American Heart Association's Heart Disease and Stroke Statistics. Early detection of myocardial abnormality is the key to treating cardiovascular disease early and thus reducing the associated high death toll. However, there is currently no real-time, or near real-time, reliable imaging technique providing quantitative information on the extent and location of an infarct or the electrical viability of the affected muscle tissue. The heart, being an inherently dynamically moving organ, changes its mechanical properties as a result of disease. Therefore, current assessment of cardiac wall motion by routinely used echocardiography in the clinic, relies on qualitative estimation of endocardial wall motion excursion, but is both insensitive and subject to low inter- and intra-observer reproducibility.

Furthermore, the heart is an electrically-driven organ. The path of electrical activation in the heart originates at the sinoatrial node propagating to the atrioventricular node, along the Bundle of His until it activates both ventricles starting from the apex and along the Purkinje fibers (Fig. 1). The propagation of the conduction wave has been determined to have a speed of 0.5-5 m/s depending on the animal model and the presence of disease.

Heart failure can result from insufficient contraction among other causes. Patients with cardiac arrhythmias can be treated, depending on the site and degree, with Radiofrequency (RF) ablation or Cardiac Resynchronization Therapy (CRT). However, currently, there are no noninvasive (i.e., transthoracic) electrical conduction mapping techniques of the heart. Conventional echocardiography [1] using Tissue Doppler, 3D or other conventional methods offers can assess dyssynchrony but cannot map the electrical signal or observe the propagation of the conduction during systole or diastole. The only imaging technique for directly mapping the conduction signal is optical imaging, but can only be applied

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after open-heart surgery and only on the epicardium. Therefore, it cannot be used as a diagnostic technique. 2D mapping of the wave has thus been restricted to invasive techniques that entail the use of epicardial electrode measurements. The main reason for the lack of noninvasive techniques for accurate electrical mapping is the fact that standard imaging modalities are either limited by the penetration depth (i.e., optical techniques) or by the frame rate required (ultrasound or MRI). The only technique that can directly map the contraction wave during propagation is our electromechanical imaging technique that we have recently demonstrated in mice [2-5], dogs [2-3] and humans [4]. Our group has also shown how the contraction wave can be separated from hemodynamic or vibration (e.g., from valves; [6]) waves through pacing of the heart from different origins and tracking the wave that depend on the change of pacing only [5]. Waves that emanated from the apex of the heart were the only ones considered in order to avoid interference from vibration waves, typically propagating from the root of the mitral or aortic valves (i.e., from the base) towards the apex [6].

In this paper, we aim at evaluating the reproducibility of electromechanical imaging in mapping the contraction wave at the beginning of systole and quantifying its properties, such as its propagation speed, at three different pacing scenarios in 12 mice.

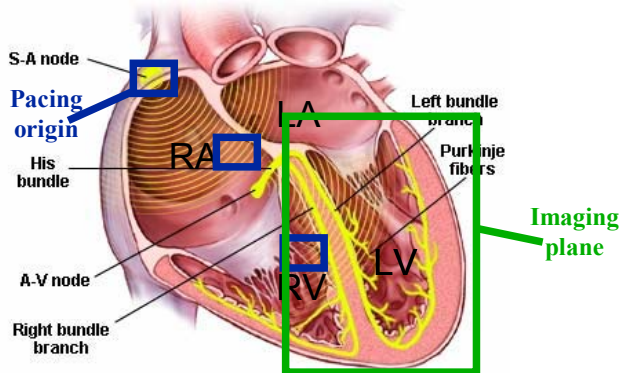


Figure 1. The cardiac conduction system of the heart. The three separate pacing origins and imaging plane used in the study are also shown. The transducer was placed on the left side relative to the imaging plane shown in all cases. The imaging plane was chosen in order to align it with the path of propagation of the contraction wave of the heart (in yellow) for better visualization.

II. METHODS

A. Animal Preparation

Twelve wild-type mice were anesthetized with 125 mg/kg intraperitoneal injection of tribromoethanol. The ultrasound probe was placed on the mouse chest using degassed ultrasound gel (Aquasonic 100, Parker Laboratories, Inc., Orange, Fairfield, NJ) as a coupling medium. Each mouse was placed supine on an ECG platform and the ECG was acquired simultaneously while imaging.

B. Data Acquisition

The high frame-rate data acquisition system developed previously [2] was used in this study. A 30-MHz ultrasound probe (VisualSonics Inc., Toronto, ON, Canada) was placed on the mouse chest in the parasternal position to obtain a longitudinal (long-axis) view of the LV of the heart. The field of view is 12 mm \times 12 mm, the axial resolution was equal to 50 μ m, and the lateral resolution was equal to 115 μ m.

In the EKVTM (ECG-based kilohertz visualization) mode provided by the imaging system, the transducer operated on a line-by-line basis. The ultrasound echo signals were recorded at a pulse-repetition frequency (PRF) of 8 kHz at each position of the transducer. A two-channel, 14-bit waveform digitizer (CompuScope 14200, Gage Applied Technologies, Inc., Lachine, QC, Canada) was used to simultaneously acquire the RF signals of the ultrasound scanner and the associated ECG at 160 MS/s. After data acquisition, the acquired RF signals were gated between two consecutive R-waves in the ECG to reconstruct the RF image sequence for a complete heart cycle at the extremely high frame rate of 8 kHz [2]. This allowed for a maximum wave speed calculation of approximately 96 m/s, which is well beyond the contraction speeds measured in the mouse heart (0.5-5 m/s) [7] and thus aliasing can be successfully avoided. RF signals from long-axis views (Fig. 1) were digitized and stored in real-time at the same sampling rate for off-line processing.

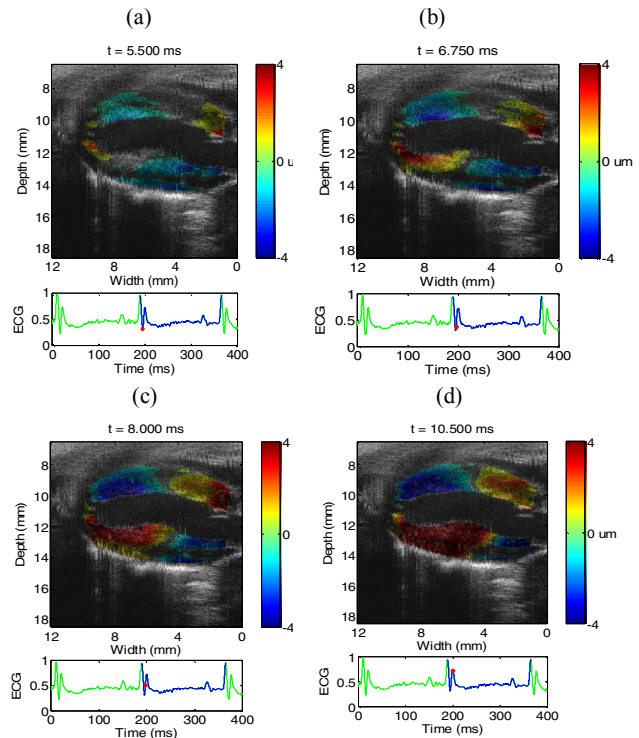


Figure 2. Sinus rhythm (SR; 120 ms): Red denotes motion upwards while blue denotes motion downwards, indicating contraction of the myocardium from a) to d). Note that the contraction (i.e., the “red wave”) starts at the apex (left, center edge) in (a) and propagates along the posterior wall finally covering the entire wall in (d) so that contraction can start. The septum is the top colored region and the posterior wall is the diametrically opposite (or bottom) colored region. The time above each image denotes the time lapsing after the R-wave and the time to which the image below it corresponds to. The ECG is shown below each image as a reference and the red dot denotes the phase in the cardiac cycle, at which the image above it corresponds to.

C. Animal Pacing

The mice were imaged during sinus rhythm (i.e., at the natural pacing of the heart (120 ms period)), right-atrial pacing (at 100 ms) and right-ventricular pacing (at 100 ms). Pacing was achieved using catheterization through the right side of the heart (Fig.1), where the catheter carried eight electrodes that could be separately activated for varying the pacing location.

D. Data Processing

The axial displacement was estimated off-line using the normalized cross-correlation function [2]. The RF window size was equal to 480 μm , while the window overlap was equal to 95%, deemed high enough to retain the high axial resolution needed. The aforementioned displacements were the instantaneous or incremental displacements occurring between two consecutive frames, i.e., 0.125 ms apart. Ciné-loops of the incremental displacements were generated to monitor the wave propagation as shown at the presentation of this paper.

III. RESULTS AND DISCUSSION

In all mice scanned, as indicated before [5], the most pronounced wave propagating during sinus rhythm (SR) (Fig. 2) and atrial (RA) pacing (Fig. 3) was the contraction wave, or wave originating at or after the isovolumic contraction phase, that propagated along the longitudinal direction of the myocardium initiating radial motion or thickening in its path. The contraction wave originated at the apex right at the QRS wave (Fig. 2(a) or 3(a)) and then propagated along the posterior wall (Fig. 2(b)-(d) or 3(b)-(d)). Therefore, in a long-axis view, the wave propagation was shown to be counter-clockwise (Figs. 2 and 3). Right-ventricular (RV) pacing (Fig. 5) induced a reversal in the direction of the contraction wave with a wave propagating from base to apex and along the posterior wall. A similar wave with the same speed and direction but inducing opposite motion in its path can also be visualized along the septum (top). The opposite motion at the level of the septum could also be visualized in the SR and RA pacing cases. Finally, imaging in 12 mice, where each mouse underwent all three pacing scenarios, allowed for estimation of the wave velocity that was found to be equal to 0.85 ± 0.22 m/s, 0.84 ± 0.20 m/s and -0.52 ± 0.31 m/s in SR, RA and RV pacing, respectively (Fig. 5). The SR wave velocity was of the same amplitude as reported in existent literature regarding conduction velocities in murine myocytes (0.84 m/s; [7]). More importantly, the SR and RA pacing induced waves were thus concluded to be statistically similar while the RV wave velocity was concluded to be statistically different ($p < 0.0001$). Therefore, the electromechanical imaging technique can reliably detect and quantify abnormal patterns in the heart in a noninvasive fashion.

IV. CONCLUSION

In summary, strong contraction waves were imaged at 8 kHz frame rate in the posterior wall (from apex to base) that changed direction when an abnormal pacing scheme was induced. Through comparison of the ciné-loop images obtained at different pacing protocols, we were able to identify and separate the electrically induced, or contraction, wave from the

hemodynamic (or, blood-wall coupling) waves. The contraction wave was best observed along the posterior wall starting at the S-wave of the ECG, which occurs after Purkinje and during myocardial activation. Only the contraction wave changed direction when the pacing origin changed, i.e., it propagated from apex to base at SR and RA pacing and from base to apex at RV pacing. These preliminary results indicate that through electromechanical coupling, noninvasive mapping of the contraction waves can help detect, analyze and quantify normal or abnormal activation patterns, yield thus a novel non-invasive method for conduction mapping of the live myocardium and diagnosis of related diseases. Finally, we have recently shown feasibility of this technique in humans [8] and will determine its applicability for the detection of abnormalities in a clinical setting.

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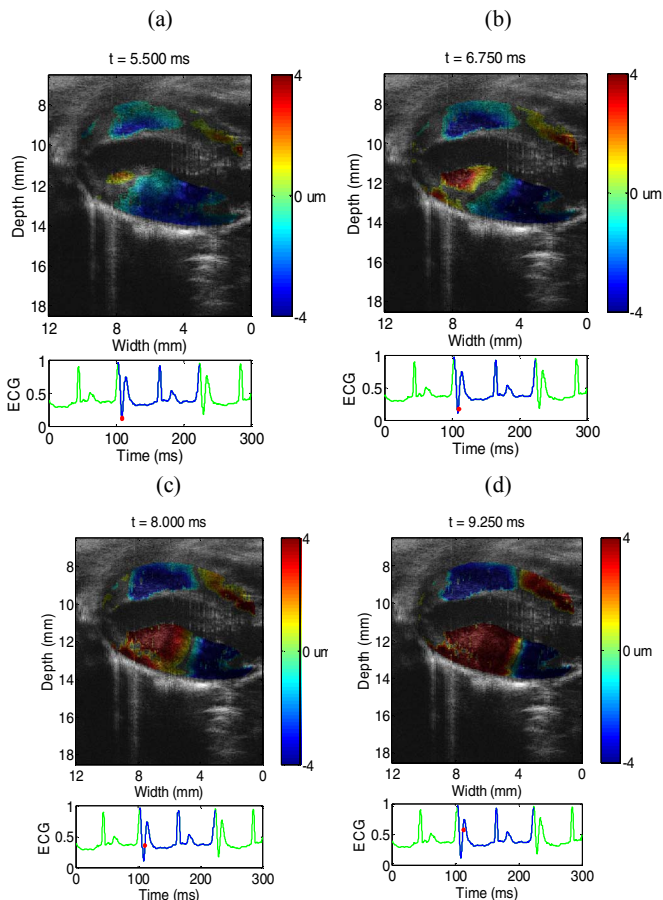


Figure 3. Right-atrial (RA) pacing at 100 ms: Note the slight difference in the propagation due to the change of origin (pacing now is from a region closer to the middle of the right atrium, i.e., below the sinoatrial node) and the field of view. A similar wave to that seen

propagating along the posterior wall in Fig. 2 can also be seen from (a) to (d), indicating that the origin is similar to the case in Fig. 2.

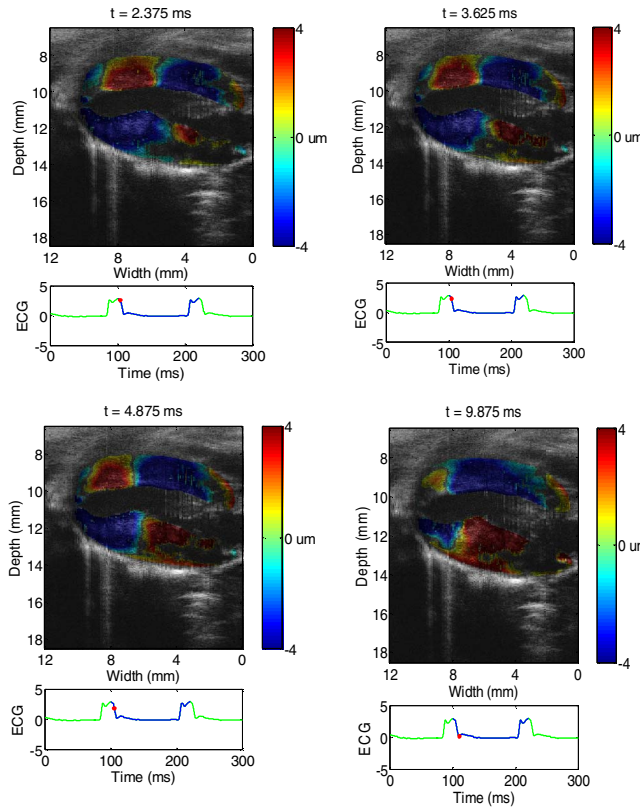


Figure 4. Right-ventricular pacing at 100 ms in mouse 2: Note the reversal in the direction of propagation in the posterior wall due to the change of origin (pacing now is performed from the right ventricle) and the field of view. The wave propagates from the base to the apex, i.e., clockwise, indicating that the wave mapped is electrically induced.

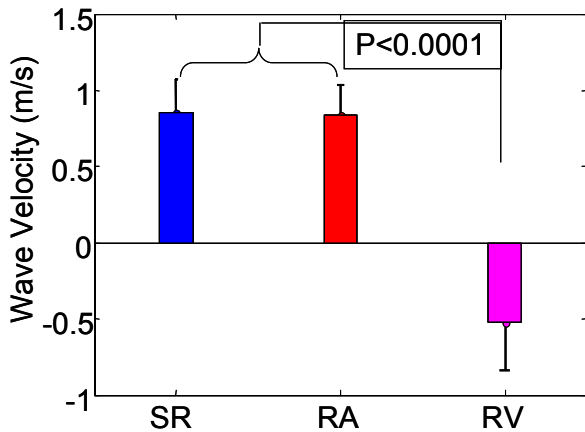


Figure 5. Statistical analysis in all mice (n=12) for the contraction wave velocity measurements under the three different pacing scenarios.

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