Ultrasound in Med. & Biol., Vol. 00, No. 00, pp. 1–9, 2018

0301-5629/$ - see front matter

https://doi.org/10.1016/j.ultrasmedbio.2018.06.006

● *Original Contribution*

NON-INVASIVE CHARACTERIZATION OF FOCAL ARRHYTHMIA WITH ELECTROMECHANICAL WAVE IMAGING *IN VIVO*

Alexandre Costet,* Elaine Wan,† Lea Melki,* Ethan Bunting,* Julien Grondin,* Hasan Garan,† and Elisa Konofagou*,‡

* Department of Biomedical Engineering, Columbia University, New York, New York, USA; † Department of Medicine—Cardiology, Columbia University, New York, New York, USA; and ‡ Department of Radiology, Columbia University, New York, New York, USA

(*Received* 18 *November* 2017; *revised* 5 *June* 2018; *in final from* 11 *June* 2018)

Abstract—There is currently no established method for the non-invasive characterization of arrhythmia and differentiation between endocardial and epicardial triggers at the point of care. Electromechanical wave imaging (EWI) is a novel ultrasound-based imaging technique based on time-domain transient strain estimation that can map and characterize electromechanical activation in the heart *in vivo*. The objectives of this initial feasibility study were to determine that EWI is capable of differentiating between endocardial and epicardial sources of focal rhythm and, as a proof-of-concept, that EWI could characterize focal arrhythmia in one patient with premature ventricular contractions (PVCs) before radiofrequency (RF) ablation treatment. First, validation of EWI for differentiation of surface of origin was performed in seven (n = 7) adult dogs using four epicardial and four endocardial pacing protocols. Second, one (n = 1) adult patient diagnosed with PVC was imaged with EWI before the scheduled RF ablation procedure, and EWI results were compared with mapping procedure results. In dogs, EWI was capable of detecting whether pacing was of endocardial or epicardial origin in six of seven cases (86% success rate). In the PVC patient, EWI correctly identified both regions and surface of origin, as confirmed by results from the electrical mapping obtained from the RF ablation procedure. These results reveal that EWI can map the electromechanical activation across the myocardium and indicate that EWI could serve as a valuable pre-treatment planning tool in the clinic. (E-mail: ek2191@columbia.edu) **© 2018 Socity**

Key Words: **Arrhythmias, Electromechanical activation, Electromechanical wave imaging, Non-invasive imaging, Premature ventricular contraction, Strain, Ultrasound.**

INTRODUCTION

Sources of focal ventricular arrhythmia may be located in the left or right ventricle, on the endocardium, in mid-myocardium or on the epicardium (Kaltenbrunner et al. 1991). For example, the prevalence of epicardial focal ventricular tachycardia (VT) is around 7%–13% of all focal VTs (Sacher et al. 2008; Tada et al. 2001). Radiofrequency (RF) catheter ablation for the treatment of VT, introduced in the early 1980s, has become one of the main options available to treat VT, and successful ablation hinges on correctly determining the site of origin of the arrhythmia (Njeim and Bogun 2015). The 12-lead electrocardiogram (ECG) is used for initial diagnostics and may reveal characteristics that enable physicians to infer the location of the origin, although the criteria seem to be limited (Bazan et al. 2007; Berruezo et al. 2004). The methods most commonly used to determine the origin of an arrhythmia are invasive catheterization techniques, such as activation sequence mapping and pace mapping (Moreno et al. 2005; Nademanee and Kosar 1998). Endocardial and epicardial mapping approaches differ, and because there is currently no non-invasive imaging technique capable of differentiating between endocardial and epicardial origin, an ablation procedure often consists of an electrophysiology study during which endocardial catheter mapping is performed and which may be followed by epicardial catheter mapping when endocardial mapping fails to identify an origin (Sosa et al. 1998).

Electromechanical wave imaging (EWI) is a non-invasive, non-ionizing, ultrasound-based imaging modality that can map the electromechanical activity of

Address correspondence to: Elisa Konofagou, 1210 Amsterdam Avenue, ET351, MC 8904, New York, NY, 10027. E-mail: ek2191@columbia.edu

the heart in all four chambers at high spatial and temporal resolution, with real-time feedback capabilities (Costet et al. 2014; Konofagou et al. 2010; Provost et al. 2010, 2011a, 2011b, 2013). At the tissue level, the depolarization of the myocardium triggers the electromechanical activation, that is, the first time at which the muscle transitions from a relaxation to a contraction state, and the spatial propagation of the electromechanical activation forms the electromechanical wave (EW) that follows the pattern of propagation of the electrical activation sequence. Unlike tissue Doppler methods, which rely on the use of frequency domain technique to estimate velocity and strain (Koyama et al. 2003; Uematsu et al. 1995), EWI relies on speckle-tracking techniques to estimate minute displacements and incremental (or inter-frame) strains in the time domain at a sufficiently high frame rate to enable tracking the EW through systole.

Electromechanical activation times rely on the onset of the mechanical activation and are essentially a surrogate for the electrical activation. Indeed, previous studies have found that EW propagation is highly correlated with the underlying electrical activation in all four chambers of the heart in normal canine hearts during sinus rhythm and various pacing protocols *in vivo* and *in silico* (Costet et al. 2016; Provost et al. 2011a, 2011b). Additionally, EWI has been reported to be capable of mapping the electromechanical activation sequence in both human (Provost et al. 2013, 2015) and canine (Costet et al. 2014, 2015; Provost et al. 2010, 2011a, 2011b) models, during sinus rhythm, pacing and both focal and re-entrant arrhythmias. EWI is not limited to the endocardial or epicardial surface and is capable of mapping the EW transmurally, but whether EWI is capable of differentiating between endocardial and epicardial origins has not yet been determined. If EWI had the potential not only to identify the region of the heart responsible for a focal ventricular arrhythmia, but also to distinguish between endocardial and epicardial origins, it would be a particularly useful clinical tool for planning treatment with RF catheter ablation as it could eliminate unnecessary endocardial mapping when the origin of the arrhythmia is located at the epicardial level.

We hypothesized that EWI is capable of differentiating between endocardial and epicardial sources of focal arrhythmia and that it could be used to plan intracardiac mapping and RF ablation procedures. To test this hypothesis, we first aimed to illustrate that EWI is capable of differentiating between endocardial and epicardial sources of focal rhythm, and second, we presented a proof-of-concept that EWI is capable of characterizing focal arrhythmia and predicting its origin noninvasively before mapping and ablation. To reach that goal, we first performed a feasibility study in a paced animal model in which we attempted to simulate focal ventricular arrhythmia by pacing the hearts of adult mongrel dogs from the epicardium and the endocardium. Then, we acquired EWI in one patient diagnosed with premature ventricular contraction (PVC) before their scheduled mapping and RF ablation procedures. PVCs are additional, abnormal heartbeats originating in either ventricle that can be treated by ablating the region from which they originate. Pseudo-3-D maps of the PVC patient's electromechanical activation, as well as videos of the activation, were generated. These were used to determine that EWI is capable of identifying the earliest region of activation and correctly differentiating between endocardial and epicardial foci, and, as a proof-of-concept in one patient, EWI results were compared with the findings of the electrophysiology mapping procedures to confirm the accuracy of the prediction.

METHODS

Experimental animal protocol

This study complied with the Public Health Service Policy on Humane Care and Use of Laboratory Animals and was approved by the Institutional Animal Care and Use Committee of Columbia University. Seven adult mongrel dogs (N = 7) were used in this study. After lateral thoracotomy, the pericardium was removed, and a pericardial cradle was formed to exclude the lungs and support the heart to expose the apex. Epicardial pacing was performed in four animals (n = 4). A bipolar electrode of an ablation catheter (TactiCath, St. Jude Medical, Secaucus, NJ, USA) was used in two dogs (n = 2) for epicardial pacing by manually placing the electrode at the mid-level, slightly toward the apex. In two other dogs, epicardial pacing was performed through pacing electrodes sutured to the lateral wall near the base (n = 1) or to the posterior-lateral wall at the mid-level (n = 1). Endocardial pacing was performed on four animals (n = 4) by placing a 64-electrode basket catheter (Constellation, Boston Scientific, Natick, MA, USA) in the left ventricle (LV) and pacing using two of its adjacent electrodes. For endocardial pacing with the basket catheter, we chose electrodes located at the mid-level providing good contact with the endocardium. Please note that of the 7 animals, 1 was used for both epicardial and endocardial pacing. The pacing rate was chosen just high enough to overdrive the intrinsic sinus rhythm, and the voltage output was set at 10 V. For this validation study, EWI acquisition was performed open chest by placing the probe coated with ultrasound gel directly at the apex. Pacing locations are summarized in Table 1. EWI was acquired while pacing open-chest canines in the standard apical echocardiographic views (4-, 2- and 3-chamber), with the addition of a view taken in between