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Electromechanical Wave Imaging for Arrhythmias

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Abstract

Electromechanical Wave Imaging (EWI) is a novel ultrasound-based imaging modality for the mapping of the electromechanical wave (EW), i.e., the transient deformations occurring in immediate response to the electrical activation. The correlation between the EW and the electrical activation has been established in previous studies. However, the methods used previously to map the EW required the reconstruction of images over multiple cardiac cycle, precluding the application of EWI for non-periodic arrhythmia such as fibrillation. In this study, we develop new imaging sequences based on flash and wide-beam emissions to image the entire heart at very high frame rate (2000 fps) during free breathing in a single heartbeat. The methods are first validated by imaging the heart of an open-chest canine while simultaneously mapping the electrical activation using a 64-electrode basket catheter. Feasibility is then assessed by imaging the atria and ventricles of closed-chest, conscious canines during sinus rhythm and during right-ventricular pacing following atrioventricular dissociation, i.e., a non-periodic rhythm. The EW was validated against electrode measurements in the open-chest case, and followed the expected electrical propagation pattern in the closed-chest setting. These results indicate that EWI can be used for the characterization of non-periodic arrhythmia in conditions close to the clinical setting, in a single heartbeat, and during free-breathing.

Keywords

Electromechanical Wave Imaging; ultrasound imaging sequences; flash sequence; wide beams; arrhythmia; pacing; atrio-ventricular dissociation; sinus node; non-periodic arrhythmias; free breathing; single heartbeat; electrical cardiac mapping; basket catheter

1. Introduction

The heart is an electromechanical pump that requires to be first electrically activated in a specific sequence to efficiently contract. Cardiac conduction abnormalities are a major cause of death and disability worldwide and their prevalence is expected to rise with the aging of

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the population. For example, the number of individuals with atrial fibrillation (AF) in the United States is expected to reach 12 million by 2050 (Lloyd-Jones et al., 2009). AF is the most common arrhythmia (Fuster et al., 2006), is responsible for 15–20% of strokes (Lloyd-Jones et al., 2009) and costs \$6.65 billion per year in treatment (Coyne et al. 2006). However, no non-invasive imaging method is currently available to the physician at the point of care to characterize arrhythmias for better diagnosis or for treatment planning, monitoring, optimization, and follow-up. Electromechanical Wave Imaging (Provost et al., 2011b, 2011a, 2010; Konofagou et al., 2010; Pernot et al., 2007) is an ultrasound-based imaging modality that maps the electromechanical wave (EW), i.e., the transient deformations occurring in immediate response to the electrical activation. The EW and electrical activation maps have been shown to be closely correlated both in vivo (Provost et al., 2011b) and in silico (Provost et al., 2011a), therefore indicating that EWI could become a low-cost, non-invasive, and real-time modality for the characterization of arrhythmias. To date, EWI has only been used to observe periodic cardiac rhythms, e.g., sinus rhythm and pacing (Provost et al., 2011b), over multiple heartbeats (Wang et al., 2008) in order to achieve high spatial and temporal resolution to accurately map the EW. However, this approach becomes limited when applied to non-periodic arrhythmias such as fibrillation.

In EWI, inter-frame motion (or, displacement) is estimated axially via cross-correlation of consecutive RF frames. From the displacements, one can then obtain the inter-frame strains (or, strains) depicting the EW by applying gradient operators on the displacement field. However, the heart is an organ that undergoes significant three-dimensional motion and large deformations, which both lead to the decorrelation of the RF signals and thus to the degradation of the motion and deformation estimation accuracy. Increasing the imaging frame rate reduces these effects. However, imaging at high frame rates over a large field of view and at high resolution constitutes a technical challenge. Standard echocardiography is based on focused insonification and the frame rate is therefore determined by the number of beams acquired per frame. Reducing the number of beams to increase the frame rate consequently results either in a smaller field of view (Konofagou et al., 2002; D'hooge et al., 2002) or in sparse-sector scans (Kanai et al., 1993). A number of different approaches have been suggested to increase the frame rate, with different tradeoffs. By acquiring over multiple heartbeats, automatic composite imaging techniques (ACT) can achieve very high effective frame rates in a full field of view with high beam density (Wang et al., 2008), but, as indicated previously, are difficult to use on arrhythmic cases or in patients who are unable to hold their breath. Modulated-Excitation and synthetic-aperture methods have also been developed (Misaridis and Jensen, 2005). In conventional pulsed Doppler imaging, a single scan beam is acquired repeatedly at high pulse repetition frequency (Jensen, 1996). Sector-based sequencing consists of dividing the image into sectors, which are then acquired multiple times before acquiring the next. This method is widely used for blood flow estimation, strain-rate imaging (Heimdal et al., 1998) and, more recently, for the estimation of the tissue motion for steady-state periodic excitations (Baghani et al., 2010; Azar et al., 2010). However, it remains limited in terms of frame rate when imaging in a full field of view of the heart.

On the other hand, modern scanners can be used to gather additional information. More specifically, to form an image, an ultrasound scanner emits a wave and records the returning

echoes by applying delay and apodization functions to the elements of the ultrasound probe both in transmit and receive modes. In a conventional scanner, these functions are typically identical in transmit and receive modes, resulting in one image line per transmit. They are also designed to minimize the width of the transmitted beam to maximize the lateral resolution. In modern scanners, it is possible to sample individual transducer elements; this feature allows to apply, in post processing, an infinity of delay and apodization functions in receive mode. For example, it becomes possible to reconstruct an entire image, focused in receive for each pixel (rather than for each line conventionally), per transmit. The resulting trade-off is that outside of the focal region of the transmitted wave, the SNR of such an image drops drastically. To increase the frame rate, approaches used in the literature consists thus in widening the transmit beam (Shattuck et al., 1984), sending multiple beams (Madore et al., 2009) or by sending plane waves (Tanter et al., 2002). Wide beams and multi-beams approaches are mostly used in the reconstruction of three-dimensional B-modes images and are currently available in clinical systems. Plane waves are most known for their use in supersonic shear imaging (Bercoff et al., 2004; Montaldo et al., 2009) where they are used for the estimation of one-dimensional (Montaldo et al., 2009) and two-dimensional motion (Tanter et al., 2002). In the heart, motion estimation was performed only recently using wide beams (Honjo et al., 2010).

In theory, widened transmit beams have the potential to eliminate the trade-off between beam density, field of view, and frame rate, and would thus allow high-resolution, single-heartbeat EWI. Currently, it is not known whether plane wave or wide beams approaches can successfully track the EWI in a clinical setting.

In this paper, we demonstrate the feasibility of flash- and wide-beam EWI in a full view of the heart. Experiments were first conducted in open-chest canines to allow for simultaneous cardiac electrical mapping using a basket catheter and confirming that a high correlation between EWI and cardiac mapping is maintained when using new transmit sequences. Then, experiments were conducted in a closed-chest setting. In these canines, EWI was performed both during sinus rhythm and during right-ventricular pacing following atrioventricular dissociation, i.e., a non-periodic rhythm. EWI performed in a closed-chest setting while respecting the Food and Drug Administration standards is more prone to artifacts originating from reflections, e.g., from the rib cage, and thus similar to the clinical setting. Therefore, this study indicates that flash- and wide-beam EWI can be applied in humans and thus paves the way to the study of irregular arrhythmias in patients.

2. Methods

We developed customized imaging sequences using a Verasonics system (Verasonics, Redmond, WA) to sample the 64 elements of an ATL P4-2 phased array probe using flash and wide transmit beams. A flash beam is a transmit mode in which every transducer element fires with the same amplitude but with delays such that the wavefront generated propagates as if it were emitted from a single point at the probe position. This mode is similar to plane wave imaging, but the circular shape of the wave allows the probing of regions in the front and on the side of the probe. Therefore, the entire field of view is probed at each transmit, but the divergent nature of this transmit makes it more sensitive to artifacts

originating, for example, from high impedance tissues such as the rib cage. A wide beam (Fig 1B) can be generated by reducing the transmit aperture, i.e., the number of elements used in transmit, and using apodization, i.e., the modulation of the transmit amplitudes of elements. In that case, only a portion of the image is probed at each transmit. This approach is also less prone to artifacts, as shown from its use in clinical systems to generate high quality three-dimensional images. RF signals were reconstructed from the elements data in a pixel-wise fashion described as follows. Assuming a constant sound velocity, the element signal over time can be converted to a distance. The value of the RF signal at each pixel of the resulting image was then obtained by summing the 64 element data samples corresponding to time required for the emitted wave to travel to the pixel location, be reflected and reach a given element. In the case of the flash sequence, images were acquired at 2000 fps during 2s, followed immediately by the acquisition of a 128-lines, 30-fps, B-mode during 1.5s. The electrocardiogram (ECG) was acquired simultaneously. In the case of the wide beam sequence, a transmit sequence was developed to transmit 12 beams twice at a rate of 137 Hz (motion-sampling rate) such that the repetition rate of these beams was 500 Hz (motion-estimation rate); no B-mode was acquired in wide beam acquisitions. More specifically, in the wide beam sequence, the amount of data acquired per frame was 12 times larger in comparison with the flash sequence. This led to longer data transfer times and thus reduced the frame rate to levels insufficient for EWI. For example, 12-beam frames at a 12-cm depth are acquired at approximately 180 Hz, which is too low to perform EWI accurately. To palliate this issue, we used an interweaving approach and acquired a group of two frames before this data transfer. This led to the following: frames 1 and 2, 3 and 4, 5 and 6, etc., were separated by 2 ms, while frames 2 and 3, 4 and 5, 6 and 7, etc., were separated by 7.3 ms. One motion map was generated via RF cross-correlation of a pair, i.e., at 500 Hz (motion-estimation rate). Since pairs were acquired every 7.3 ms, motion was sampled at 137 Hz (motion-sampling rate).

In this study, approved by the Columbia University Institutional Animal Care and Use Committee, one male mongrel dog was anesthetized with an intravenous injection of Diazepam 0.5–1.0 mg/kg IV as premedication, and Methohexital 4–11 mg/kg IV as induction anesthetic. It was mechanically ventilated with a rate- and volume-regulated ventilator on a mixture of oxygen and titrated isoflurane (0.5%–5.0%). Morphine (0.15 mg/kg, epidural) was administered before surgery, and heparin (100,000 IU/h, intravenous) was used during the entire procedure. The chest was opened by lateral thoracotomy using electrocautery. A pulmonary vein was canulated with a 9F sheath and guided, using ultrasound, to the left ventricle. A basket catheter was then introduced by aligning a marked spline of the basket catheter (Constellation, Boston Scientific, Natick, MA) along the anterior wall of the left ventricle. This basket catheter contains 64 electrodes that were used to generate 3D endocardial maps of the electrical activation. Custom-built acquisition boards which contains 64 channels were used to measure 57 bipolar electrograms and three ECG leads. The multiplexed outputs of the individual boards were then sampled by a low-cost, USB data acquisition system (USB-6259, National Instruments, Austin, TX) controlled via a LabView interface. Pacing can also be performed from any electrode, thus allowing multiple, simultaneous (up to a 2-ms resolution) pacing sites. A separate, open-source Arduino Mega board (www.arduino.cc) containing a micro-controller was used to send

pacing stimulus through transmit multiplexers and is controlled via a C-based algorithm. Images in the four-chamber view were acquired using wide beams during pacing from the apical region of the lateral wall.

In addition, four normal, conscious, shaved, mongrel canines of 20–25 kg in weight, were imaged before and after the implantation of a pacemaker in the right ventricle and ablation of the atrio-ventricular node in a closed-chest setting. These canines were conscious and drug-free and were gently held on a table by two people during the ultrasound scan. Images were acquired using the flash sequence.

Axial displacements were estimated at a 500-Hz motion-estimation rate in both cases and at a 2000-Hz and 137-Hz motion-sampling rates in flash and wide beams sequences, respectively. A 1D cross-correlation algorithm (Luo and Konofagou, 2010) on RF signals reconstructed at 20 MHz in a phased array configuration was used as in the previous implementation of EWI (Provost et al., 2010). The window size was 4.60 mm and the overlap 90%. The heart was segmented using an automated contour tracking technique (Luo and Konofagou, 2008). The incremental axial strains were estimated with a least-squares method (Kallel and Ophir, 1997) and a kernel size of 10.7 mm. The strains were then overlaid onto the B-mode image acquired immediately following the flash sequence. Finally, isochrones were constructed as in previous studies (Provost et al., 2010, 2011b).

3. Results

The wide beam sequence was first used in the open-chest animal and correlated with the electrical activation sequence during pacing from the apical region of the lateral wall. The heart was imaged in the four-chamber view, but with the ultrasound probe positioned parasternally. In that view, activation results mostly in thickening of the tissue (since the ultrasound beam is aligned with the radial direction of the heart, (Provost et al., 2010)). EWI shows activation (red) originating from the apical region of the lateral wall (Fig. 2A, B), followed by the activation of the right-ventricular wall (Fig. 2C) and finally by the septum (Fig. 2D). The corresponding EWI isochrones reflect this behavior (Fig. 2E). The EW and the electrical activation mapped using the basket catheter (Fig. 2F) were highly correlated (Fig 2G). A slope of 1.31 ($R^2 = 0.99$) was obtained between the electrical activation and the EW onset.

EWI at 2000 fps was then performed in a standard apical four-chamber view in a normal, conscious canine during sinus rhythm using the flash sequence. In that view, the EW is expected to mostly result in shortening (negative strains) of the tissue, since the ultrasound beam is aligned with the longitudinal direction of the heart. During sinus rhythm, the natural pacemaker is the sinus node, located in the right atrium. Signals are generated spontaneously at the node, travel through the atrium (during the P-wave), to the atrio-ventricular node, the bundle of His and finally the Purkinje fiber network and the ventricular myocardium (during the QRS complex). Complex activation patterns are expected when imaging the ventricles, since activation will originate from multiple locations following the Purkinje fiber network. Fig. 3 shows that the EW follows such a pattern. The EW (shortening, blue) originated from the right atrium and propagated towards the left atrium. Between the P- and the Q-wave on

the ECG, little or no propagation is observed. During the QRS complex, activation originating from multiple sources, located for example at the mid-level of the septum, high on the lateral wall and near the right apex are observed. These results are in accordance with previous studies of the normal electrical activation of the heart (Scher and Young, 1956; Durrer et al., 1970) and with previous studies using EWI with ACT (Provost et al., 2010, 2011b).

The same animal was then imaged during pacing from the right ventricle after the ablation of the atrio-ventricular node. In that case, the electrical activation of the atria and the ventricles are dissociated, i.e., the activation of the sinus node do not necessarily results in the activation of the ventricles. This phenomenon can be observed on the ECG trace, where multiple P-waves without a following QRS complex can be observed (Fig. 4A). During the P-wave, the EW (shortening, blue) is initiated from the right atrium and propagates in the left atrium (Fig. 4B). This is expected, since the atria are still driven by the sino-atrial node as during sinus rhythm (Fig. 3). During the QRS complex however, activation was triggered by the pacemaker located near the apex of the right ventricle. Therefore, the EW was expected to propagate from the right ventricle near the apex towards the other regions of the heart. EWI displays such a pattern (Fig. 4C): the EW (shortening, blue) originated near the right ventricular apex and propagated towards the septum and the lateral wall.

4. Discussion

In this study, we have demonstrated the feasibility of performing EWI using flash- and wide-beam imaging sequences. The possibility of using these techniques in a clinical setting expands the field of application of EWI. For example, it allows the study of irregular rhythms such as atrial fibrillation, atrial flutter, or ectopic beats. An example of such non-periodic rhythm was provided in the form of atrio-ventricular dissociation. Moreover, the total acquisition time is reduced to 3.5 s in comparison to acquisition times of 15–20 s using ACT. This makes free-breathing acquisition possible and limits potential artifacts due to the motion of the hand of the operator.

Ultrafast EWI as presented here is within the FDA limits both in terms of spatial-peak-temporal-average intensity (I_{spta}), and mechanical index (MI) for human use. The depths used in canines were 15 cm which are sufficient in most human cases. Therefore, the approach is highly translational and can be applied to patients. However, in larger subjects, it is often necessary to achieve larger depths (e.g., 20 to 22 cm). Due to the divergent nature of the emitted wave, the energy transmitted to these larger depths decays rapidly and could lead to lower image quality. To palliate this issue, wide beam sequence was also implemented (Fig. 2A, B, C, D) and shown to be highly correlated with the electrical activation (Fig. 2F). The slope of 1.31 obtained is expected, as is in the same range as what has been reported by other groups using a different methodology (Badke et al., 1980; Wyman et al., 1999; Faris et al., 2003) and similar to the slope predicted in simulations (Provost et al., 2011a).

When imaging in a closed-chest settings (Fig. 3 and 4), the EW obtained using the flash beam sequence were similar to the EW mapped in open-chest canines using methods relying

on multiple heartbeats (Wang et al., 2008; Provost et al., 2010) during sinus rhythm (Provost et al., 2010, 2011b). Since EWI using flash- or wide-beam sequences can image the entire heart within a single heartbeat, it was also possible to image the EW during a non-periodic rhythm, i.e., during atrio-ventricular dissociation. It was possible to map the location of earliest activation in the right atrium, which correlates with the expected location of the sino-atrial node, and did not propagate in the ventricles. In the ventricles, the origin of the EW was located at the pacing lead, and did not propagate in the atria.

Flash and wide-beam forming produce additional artifacts due to the divergent nature of the transmitted wave, and are thus more prone to generate reflections on high impedance materials such as the rib cage or on the pacemaker leads. Indeed, since the transmitted wave insonifies the entire field of view, artifacts generated by high impedance materials affect the entire image rather than only the focused region of insonification in ACT. This is especially true when generating B-mode images from the same sequences (Fig 2A–D). However, the results presented here tend to show that the speckle signature used for motion estimation remains sufficiently good to estimate motion and strains with high accuracy. Indeed, strain maps obtained subsequently with ACT in the same canine were qualitatively similar. Therefore, a simple strategy consisting of overlaying motion or strains onto a standard B-mode image acquired immediately following the flash- (Fig 3, 4) or the wide-beam sequence provides the best tradeoff: a high quality B-mode image for segmentation of the anatomic structures overlaid with high quality motion and strain maps obtained at extremely high frame rates.

5. Conclusion

Most invasive electrical mapping techniques currently used in the clinic rely on the periodicity of the arrhythmia studied to generate maps of the activation time. Such an approach is limited in many cases where the arrhythmia is not periodic, such as in atrial fibrillation. Flash and wide-beam EWI do not require the propagation pattern studied to remain periodic and is thus suitable for the study of non-periodic arrhythmias, i.e., it could be employed for the study of atrial fibrillation, atrial flutter, or ectopic beats. In summary, EWI may constitute a unique tool for evaluating the cardiac electromechanical function of an arrhythmic patient at the point of care and in real time for diagnosis and treatment planning, monitoring, and follow-up.

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Figure 1. Beam profiles of **A** a full-aperture, conventional imaging beam, and **B** a reduced-aperture 'wide beam'.

Figure 2.

The EW in a canine during pacing from the apical region of the lateral wall. A. Activation (red) originates from the endocardium and B. propagates both towards the apex (in blue, due to the orientation of the probe) and the base. C. The RV wall is then activated, D. followed by the septum. E. Corresponding EW isochrones. F. Electrical isochrones, depicting the activation on the 3-D endocardial surface of the heart. The symbols %, & and \$ indicate corresponding regions between E and F. G. Using the electrical activation times measured using the basket catheter, the electrical activation times can be compared to the EW onset time. Since no ECG was acquired during this acquisition, the intercept was fixed to 0 ms.

Figure 3.

EWI during sinus rhythm in a closed-chest canine. Activation is first observed in the right atrium (30 ms) followed by the left atrium (90 ms). Activation is then mapped in the ventricles, from multiple origins located on the endocardium of the septum, in the right ventricular wall and near the apex in the lateral wall (150–160 ms) until complete activation (190 ms).

Figure 4.

EWI during pacing from the right ventricle in a closed-chest canine. **A** ECG during atrioventricular dissociation. P-waves do not result to QRS complexes, since the atria and ventricles are electrically isolated. A total of five P-waves can be observed, while only 2 QRS complex are present. **B** EWI during the first P-wave (circled). Activation (blue) is initiated in the right atrium (276 ms) and propagates towards the left atrium (300, 320 ms). **C** EWI during the first QRS complex (circled). Activation (blue) is first observed in the right-ventricular wall (650 ms). The septum is then activated (670 ms), followed by the

lateral wall (690 ms). Activation does not propagate to the atria, since the atrio-ventricular node was ablated.