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Comparison of two methods for mechanical activation detection using high frame rate ultrasound imaging

Kaja F. Kvåle
Center for Cardiological Innovation, Oslo University Hospital, University of Oslo, Oslo, Norway
GE Vingmed Ultrasound, Horten, Norway
kajakvale@gmail.com

Sebastien Salles
Norwegian University of Science and Technology, Trondheim, Norway
Univ Lyon, Inserm, Lyon, France
sebastien.salles@ntnu.no

Pål H. Brekke
Center for Cardiological Innovation, Oslo University Hospital, Oslo, Norway
ORCID: 0000-0003-4875-9633

Espen W. Remme
Institute for Surgical Research, Center for Cardiological Innovation, Oslo University Hospital, Oslo, Norway
espen.remme@medisin.uio.no

John M.Aalen
Institute for Surgical Research, Center for Cardiological Innovation, Oslo University Hospital, Oslo, Norway
john.aalen@rr-research.no

Thor Edvardsen
Center for Cardiological Innovation, Oslo University Hospital, *University of Oslo*, Oslo, Norway
thor.edvardsen@medisin.uio

Eigil Samset
Center for Cardiologial Innovation, Oslo University Hospital, Oslo, Norway
GE Vingmed Ultrasound, Horten, Norway
Eigil.samset@ge.com

***Abstract*— Noninvasive, clinical tools for detection of regional myocardial mechanical activation of the left ventricle are needed. The feasibility of using high frame rate echocardiography for this purpose has previously been investigated, and several methods are now published in the literature. In this study, we have evaluated two different methods for mechanical activation detection for feasibility, simplicity, time consumption and accuracy against two invasive reference standards. An animal model including three anesthetized, open chest dogs with implanted combined sonomicrometry and electromyography (EMG) crystals was used. Data was acquired while the animals were being paced from specified locations of the heart. The mechanical activation patterns were investigated using isochrone maps generated from the ultrasound data and manual measurements of the delay in mechanical activation from the septum to the lateral wall. The coefficients of determination between the activation delay measured with ultrasound vs EMG and sonomicrometry were all above $R^2 = 0.84$, indicating a strong correlation for both methods. This study shows that there are benefits and limitations to each method.**

Keywords— Electrical activation, high frame rate ultrasound, mechanical activation, pacing

I. Introduction

Information on regional timing of myocardial electrical activation is of clinical interest when diagnosing cardiac conduction abnormalities such as arrhythmic conditions, cardiomyopathies and dyssynchrony. Methods currently employed in the clinic to investigate electrical activity are non-invasive methods such as electrocardiography (ECG), which measures the electrical activity of the heart on the surface of the body, and invasive methods such as electrophysiology (EP) contact mapping, which measures electrical activity with a catheter from the inside. ECG has a very limited spatial resolution [1], and EP-mapping can be time-consuming, operator dependent and results in ionizing exposure for the patient [2] as it is performed under X-ray guidance. Because of this, a time effective, safe and non-invasive imaging method for electrical activation (EA) detection of the heart has been a long-term goal of researchers.

It is not possible to directly determine EA with imaging, but the EA pattern has previously been shown to correlate well with the mechanical activation (MA) pattern [3]. Thus, MA mapping has become a subject of much interest, especially due to the recent availability of high frame rate echocardiography as the MA wave propagates too rapidly through the heart to be detected with conventional ultrasound imaging [4].

Several methods for non-invasive spatiotemporal mapping of MA in the heart have been reported in the literature. One well known method is called electromechanical wave imaging (EWI) [5] and is based on estimating strain rate from ultrasound signal data to define MA in a spatiotemporal map called an isochrone map. Recently, a novel method using a clutter filter on the ultrasound data for the purpose of MA detection was introduced [6]. This method is based on clutter filter wave imaging (CFWI), a novel signal processing method that aims to detect and visualize mechanical waves propagation through the myocardium, but without using a conventional tissue motion estimator [7].

In this study, we aim to compare our implementation of a strain rate-based MA-mapping algorithm with the newly introduced CFWI-method in terms of accuracy against invasive reference standards, time consumption, feasibility and simplicity. Data was acquired during pacing from specified locations in the left ventricle (LV) in an animal model. MA determined by ultrasound was compared to EA and MA measured by combined electromyography and sonomicrometry crystals at several locations in the LV.

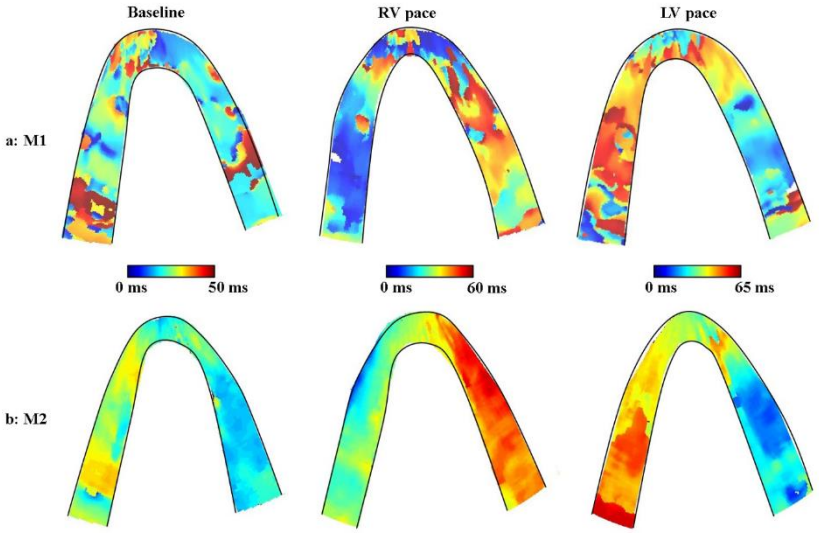

Fig. 1 Isochrone maps from M_{SR} (a) and M_{CF} (b) during baseline (left), RV (middle) and LV (right) pacing. (b) is partially reused @2019IEEE

II. Material and Method

All data analysis was performed off-line using MATLAB (The Mathworks, Natick, MA, USA).

A. Animal preparations

Three male, mongrel dogs of body weight 43±5.9 kg were under general anesthesia. The animals were surgically prepared with a partial splitting of the pericardium from apex to base. The ECG was monitored from limb leads. The National Animal Experimentation Board approved the study and the animals were supplied by the Center for Comparative Medicine (Oslo University Hospital, Rikshospitalet, Oslo, Norway).

B. Dimensions and electromyography

1) Data acquisition: 2 mm diameter crystals (Sonometrics Corporation, London, Ontario, Canada) were used to measure LV dimensions as longitudinal segment lengths. The ultrasonic crystals were combined with a bipolar electrode for recording of intramyocardial electromyograms (EMG). This enabled simultaneous assessment of myocardial EA and MA. Two crystal pairs were implanted for LV dimension recording. One crystal pair was placed in the mid and basal septum, and the other in the mid and basal lateral wall. The crystals in the mid-walls also recorded EMG. The pacing electrodes were placed in the mid-free wall in the right ventricle (RV) and the mid-lateral wall. Data were sampled at 200 Hz.

2) Data analysis: The EMG signal showed the timing and voltage of the depolarization wave as it arrived in the mid-septum and mid-lateral wall. The time point between the largest deflections in the EMG trace was defined as the time of EA [8, 9]. MA was found from the segment length measurements of the two sonomicrometry crystal pairs. Strain and strain rate were calculated from the myocardial segment lengths. The point of zero crossing for the strain rate curve was defined as the time of MA for a crystal pair segment [8]. The timing of EA and MA from the EMG and sonomicrometry recordings, respectively, was manually determined and averaged for at least three heart cycles per recording.

C. Echocardiography

1) Data acquisition: Apical 4-chamber views were acquired with a 2.8-MHz center frequency phased array probe connected to a modified GE Vivid E95 ultrasound system. Beamformed IQ-demodulated (IQ) data was acquired at 1000 to 1200 frames per second using plane wave imaging. 4 to 6 transmit beams per image were used. Surface ECG was acquired simultaneously and was monitored from limb leads. The protocol consisted of baseline sinus rhythm, RV pacing and LV pacing and was followed for all animals (n = 3). The acquisition lasted for about two seconds resulting in at least 2 heart cycles per acquisition as the animals had a heart rate of 100 to 120 bpm. The implanted crystals were not visible in the ultrasound image.

2) Data analysis: IQ data was extracted from the ultrasound scanner. For method 1 (M_{SR}), MA was defined as the first zero crossing of the strain rate curve after the onset of the Q-wave in the ECG [5, 8]. Strain rate was calculated from tissue velocity using a least squares algorithm [10] creating a strain rate map for the whole image. A 12 mm 1-D kernel was used for this. Tissue velocity was estimated using autocorrelation in the axial direction with temporal lag one [11]. MA was determined for every spatial point of the LV by an automatic zero-crossing detection algorithm.

The CFWI-method (M_{CF}), consisted of applying a high pass clutter filter on IQ-data to extract tissue velocities of interest. The filter used for this study was a 3rd order high pass-filter with a normalized cutoff frequency of 0.2. The CFWI acceleration was calculated as time derivative of the filter output, and MA was defined as the time of peak acceleration within a search area defined by the onset of the Q-wave in the ECG. The peak acceleration was found automatically.

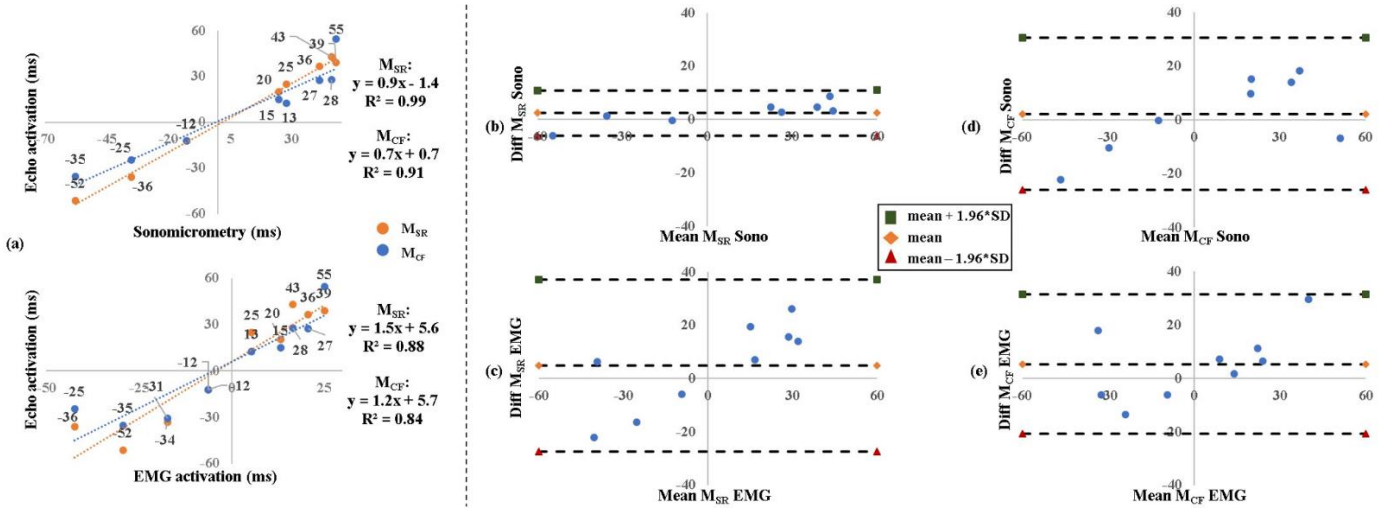

Fig. 2: Delay in activation of lateral wall relative to septum as measured by M_{SR} and M_{CF} and compared with sonomicrometry (sono) and electromyogram (EMG). Linear regression analyses are shown in (a) and Bland-Altman plots are shown in (b-e).

For both methods, the first output (tissue velocity for M_{SR} and CFWI filter output from M_{CF}) was smoothed by a moving average filter in space and time of 11 samples in the axial direction, 7 beams in the lateral direction and 10 frames in time. The images were segmented to only keep data from the LV walls and to reduce computing time for the MA detection. Isochrone maps were generated from the MA detections of M_{SR} and M_{CF} and smoothed by a moving average filter of sample size 2 in both spatial directions.

Additionally, MA detection was performed manually to determine the delay in activation between the septum and the lateral wall. Strain rate (M_{SR}) and acceleration (M_{CF}) curves from spatial areas corresponding to the locations of the EMG crystals were plotted and MA times were manually selected. The delays in activation between walls were compared with measurements from EMG and sonomicrometry.

III. Results

A. Isochrone maps

Automatically generated isochrone maps were used to visualize MA spatiotemporally. A blue to red color spectrum displayed early to late activation. Fig. 1 shows isochrone maps of MA in baseline sinus rhythm, RV and LV pacing for M_{SR} (a) and M_{CF} (b) for one animal. For baseline (left), the activation started slightly earlier in the lateral wall than in the septum for both methods. For M_{SR}, a region of relatively early activation in the apical lateral wall was observed, in addition to some noise in the basal septum and the mid-lateral wall, that was not visible for M_{CF}. For RV pacing (middle) both methods showed early activation in the septum and later activation in the lateral wall, however, a larger area of early activation in the septum was observed for M_{SR}. For LV pacing (right) early activation started in the mid lateral wall, spreading bilaterally towards the septum and the basal lateral wall for both methods. Some noise was observed in the apical and basal regions of the septum for M_{SR}.

B. Comparison against reference

Earlier activation of the septum relative to the lateral wall was defined as a positive activation delay. The EMG measurements were taken from the mid walls and the sonomicrometry measurements from the basal segments, while the ultrasound measurements were from areas corresponding to mid-wall locations in the image.

Fig. 2a shows a linear regression analysis of the MA delay calculated from the M_{SR} and M_{CF} measurements, correlated with the MA delay measured by sonomicrometry (upper) and the EA delay measured by EMG (lower). Resulting R^2-values were found to be 0.99 and 0.88 for M_{SR}, and 0.91 and 0.84 for M_{CF}, against sonomicrometry and EMG delays, respectively.

Fig. 2b, c, d and e show corresponding Bland-Altmann plots, where M_{SR} compared to sonomicrometry had the narrowest limits of variation and closely centered data points around the mean. For Fig. 2c and e an increasing slope was observed, which showed that for small activation delays the measured delays from ultrasound and EMGs were similar, while for increasing activation delays (positive and negative) the activation delays measured with M_{SR} and M_{CF} increased even more than the EA delay of the reference method.

C. Time consumption

Calculation of M_{SR} and M_{CF} included the same number of processing steps. The total processing time was 57.5 % longer for M_{SR} compared to M_{CF}. The main difference was in the autocorrelation estimation to calculate tissue velocity for M_{SR}.

IV. Discussion

Two methods for non-invasive assessment of regional MA of the LV myocardium using high frame rate echocardiography were developed and tested in this study. The MA patterns from 3 animals during baseline, RV and LV pacing were analyzed by automatically generated isochrone maps from the ultrasound data (Fig. 1) and by manual evaluation (Fig. 2).

The isochrone maps showed the approximate origins of the paced beats and the propagation of the activation through

the LV. The origins of pacing were consistent with the approximate locations of the pacing electrodes for all isochrones from M_{SR} and M_{CF}, and for both methods, there was a clear difference between baseline, RV and LV pacing. However, the isochrones from M_{SR} were significantly noisier than from M_{CF}. A reason for this was that the zero crossing of the strain rate curves was often noisy or ambiguous. The strain rate traces often had several zero crossings within the search window, even after spatial and time filtering, both due to noise and to natural tissue motion. The automatic zero-crossing detection algorithm was implemented to find the first positive to negative zero crossing in a search window, as described in [1]. Ideal strain rate traces follow a known pattern of a positive peak and then one single zero crossing during the time of the QRS-complex in the ECG, however, for our data, not all strain rate curves fitted this pattern. Thus, determining the correct zero crossing with an automatic detection algorithm proved difficult in some regions. Automatic generation of isochrone maps was therefore more feasible and simpler for M_{CF} than for M_{SR} for our data set. The difficulty of automatic interpretation led to manual MA delay measurements used for comparison with the invasive reference standards.

Correct activation sequences compared to the reference methods, in terms of septum to lateral wall activation, were found for all 9 cases. Furthermore, a good agreement between the activation delays measured with EMG and sonomicrometry and with M_{SR} and M_{CF} was found with all R^2-values above 0.84 (Fig. 2a). The Bland-Altman plots showed that the sonomicrometry and ultrasound measurements had little variation, especially for M_{SR}, while the EMG and ultrasound measurements showed a positive slope indicating that the time to onset shortening increased for late activated segments, consistent with previous studies [12]. For M_{CF}, fairly large limits of variation were found when compared to sonomicrometry (Fig. 2d). As the sonomicrometry also measured MA, we would have expected the comparison for M_{CF} with sonomicrometry to be similar in quality to the result for M_{SR} (Fig. 2b). Thus, these results indicated that M_{SR} had a better accuracy against the invasive MA measurements than M_{CF}. A reason for this could be that for M_{SR} and sonomicrometry, strain rate from ultrasound was compared to strain rate from crystals, while for M_{CF} CFWI acceleration was used to define MA.

An evaluation of the time consumption of the two methods was performed and the higher time consumption for M_{SR} over M_{CF} was found to be due to the autocorrelation estimation for M_{SR}. For research purposes this difference is insignificant, while in commercial systems this could be of importance and was found to be beneficial for M_{CF}.

There were several limitations to this study. The spatial resolution of the reference standards used for comparison was substantially poorer, as the ultrasound methods estimated MA for every spatial point of the LV, while only a few locations and segments were assessed for the crystals. Only 3 animals were included in this study, thus future work should include a larger study group to continue this work in determining the more suitable method for MA detection using high frame rate ultrasound.

V. Conclusions

The two methods for MA detection had different benefits and limitations. The automatic generation of isochrone maps was found to be more feasible with M_{CF} because of the difficulty interpreting the strain rate traces for M_{SR}. Additionally, M_{CF} was found to be less time consuming than M_{SR}. For the comparison against the reference standards, M_{SR} showed a slightly higher accuracy, especially against sonomicrometry. This preliminary study showed that both methods could potentially be useful for MA detection in a clinical setting, but further studies with larger study groups are needed to determine the more suitable method.

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