

# Estimation of the Myocardial Activation Sequence Based on B-Mode Ultrasound Cine-Images

D Adam, D Rappaport, A Landesberg, E Konyukhov,  
N Smirin, P Lysyansky, Z Friedman

Technion - Israel Institute of Technology, Haifa, Israel

## Abstract

*Non-invasive estimation of the mechanical activation sequence provides valuable diagnostic information on myocardial function. Here, an attempt is made to retrieve it from longitudinal strains calculated from B-mode echocardiographic loops in 3 sheep, paced at 2 sites – lateral and septal, and compare it to normal sequences. B-mode LV basal short-axis images were acquired followed by off-line analysis of Speckle Tracking Imaging by 2D Strain, a customized software application that calculates regional strains. Mechanical activation times were assessed as onset times of circumferential shortening measured from strain profiles, and quantified by the segmental propagation vector (SDV). The time of 90% activation within the ROI of the LV was  $\sim 60 \pm 5$ ms for lateral pacing,  $\sim 65 \pm 5$ ms for septal pacing vs.  $\sim 40 \pm 5$ ms for no-pacing, showing degradation of synchrony. The directivity of the propagation pattern was significantly higher (lower variance) of the SDV in the paced modes.*

## 1. Introduction

The normal heart is characterized by a nearly synchronous activation of the ventricles, governed by the special conduction system. The failing heart (HF), though, is usually characterized by asynchronous LV activation, caused by enlargement of the cardiac walls, inhomogeneity of the tissue conduction properties and disturbances of the electrical conduction system. The conduction delays produce ineffective LV contraction, which decreases systolic function.

Cardiac Resynchronization Therapy (CRT) is intended to recover the normal conduction delay, in an attempt to improve systolic function [1]. CRT systems are similar to pacemakers, and are implanted as pacemakers under the skin, but usually use 2 electrodes – one advanced to the RV apex, and the second through the coronary venous system to the LV epicardium. The placement of the electrodes and the timing of the pulses delivered through them provide the CRT, usually by attempting to reduce

the QRS width to less than 120ms. CRT has produced good results, decreasing the number of hospitalizations to 1/7 and days of hospitalization due to HF are decreased by 77% [2], but a very significant percentage of HF patients do not benefit from CRT. This may be due to non-optimal lead placement and erroneous criterion of optimization, since QRS duration shortening is related only to the electrical activation sequence, while optimizing the total systolic function is also related to the mechanical activation sequence and the individual time-dependant contributions of the different myocardial segments.

Physicians today usually lack the tools that would enable them to explore the LV electrical and mechanical excitation sequence and that would enable them to optimize the placement of the pacemakers accordingly, thus lead placement is mostly done at the more accessible locations of the coronary venous tree. It seems quite evident, therefore, that once non-invasive tools will be available for obtaining regional information regarding the timing of activation (electrical and mechanical), a significant improvement the criterion for optimization of the CRT treatment will be achieved, leading to a substantial enhancement of the CRT efficacy.

The regional electrical activity is measured non-invasively by ECG or by Body Surface Potential Mapping: The former is the most common measurement but provides only a gross, very low resolution estimation of the myocardial activity, while the latter provides better spatial resolution but at a much higher cost and complexity. The regional mechanical activity may be estimated by several imaging modalities – ultrasound (US) [3], MRI [4], cine-CT. Only the former modality is widely available, employs non-ionizing radiation and may provide the required spatial and temporal resolution. US may provide non-invasive determination of regions of pathological activation and real-time testing and evaluation of optional pacing sites, thus significantly improving patient prognosis.

US imaging currently provides mostly anatomical information and the ability to observe cardiac shape changes during the cardiac cycle. Many of the

echocardiographic systems today have Tissue Velocity Imaging (TVI or TDI) capabilities, which are Doppler based, facilitating measurements of local tissue motion along the ultrasonic beam direction [5-8]. These methods have gained limited clinical acceptance due to the fact that they allow evaluation of the strain in one direction in a limited number of views, while the motion of the entire heart produces undesired Doppler gate instabilities. This modality allowed various researchers to characterize cardiac asynchrony by measuring the time delay between mechanical activation in the basal septum and the lateral base [9]. Alternatively, in the current study, high rate B-mode US cine-images of LV 2D cross-sections are used for frame-by-frame analysis of the distribution of reflectors in small regions (50x50 pixels), thus enabling tissue tracking (2D Strain) and estimation of local tissue velocities and function. This method is not limited by the directional calculations of the Doppler based techniques.

In this study it was demonstrated that 2D Strain can be used to assess the sequence of activation in a two dimensional plane by detecting the origin of electrical stimulation as well as defining the direction of propagation and by quantifying the degree of synchronous activation.

## 2. Methods

High frame rate B-mode US cine-loops of LV 2D cross-sections were used for frame-by-frame analysis of the distribution of reflectors in small regions (e.g. 50x50 pixels), thus enabling tracking and estimation of local tissue velocities. The tracking method and its validation have been described elsewhere [10]. After 2D Spline filtration, local strain and strain-rate are estimated. Since the data is noisy, due to loss of tracking, movement and rotation of the LV, and execution of a divergence operator as part of the calculations, spatial curve-fitting is required. Therefore, longitudinal and transverse (radial) strain and strain-rate have been calculated for ~48 'knots' along the LV cross section, each calculated by processing the velocities of 'tracking points' that have properties calculated by the frame-by-frame analysis. Following the alterations of these 2 indices over time during the cardiac cycle allows estimation of the sequence of activation during systole and properties of relaxation and filling during diastole.

Animal experiments (sheep, n=3) were performed to verify the feasibility of this approach. The heart was exposed by thoracotomy, sonocrystals, pressure (LV and LA) and flow (aorta) transducers, and epicardial electrodes (7) were implanted to measure the local myocardial contraction, global pressures and flow, and local electrical activation, respectively. Pacing electrodes were implanted at the LV epicardium, ~15mm from the base, one at the lateral free-wall and one near the septum.

These measurements together with ECG were acquired at 1 kHz. The LV was activated either normally or by pacing at the septum or the lateral wall. Short axis B-mode cine-images (>40 FPS) were acquired (GE-Vivid 7, M3S probe) during each of the 3 pacing options.

The strain and strain-rate changes over time, at the 8 segments of the LV cross section, were post-processed to allow estimation of the sequences of activation. The activation time of each segment was defined as the time at which the segment begins its shortening at systole. These were then quantified by defining an activation delay vector (ADV) and a segmental delay vector (SDV) that were compared to the electrical activation sequence, estimated from the electrograms. The ability of the magnitude and angle of the vectors to differentiate between the different pacing protocols (at significance level >95%) was tested. The degree of synchronous activation was quantified by calculating the time duration from the moment the earliest section within the cross-section was initially activated until 90% of the myocardium was activated [1], derived from the cumulative mechanical activation plots.

## 3. Results

The sequences of activation were quantified by defining activation delay vector (ADV) and segmental propagation vector (SDV), which were compared to the electrical activation sequence, estimated from the electrograms. The ability of the magnitude and angle of the vectors to differentiate between the different pacing protocols (at significance level >95%) was tested. The magnitude of SDV was significantly different in all cases except for separating between lateral and septal pacing in one of the animals, while the SDV angle performed just as good, except for separating between septal and normal pacing in the same animal. ADV was somewhat more vulnerable to the tracking quality.

The US images acquired during the experiments were post-processed off-line. Each cardiac sequence, of a full cardiac cycle, whether normally, laterally or septally paced, was processed to produce LV short-axis view, superimposed with 2D Strain display (Fig. 1). The display includes the 48 'knots', and the strain profiles of 6 of the 'knots' (segments) are also displayed on the right-hand side of each frame. Color 'floating anatomical' M-mode display (bottom left in each frame) allows different presentation of the data. The upper frame of Fig. 1 displays the circumferential Strain, while the lower frame displays the circumferential Strain Rate. The data of all 'knots' is displayed in Fig. 2 during systole, together with the global Strain and the QRS-T complex of the ECG. There are small changes between the lateral pacing (left panel) and the septal pacing (right panel). When these curves are further processed to display the 'time of

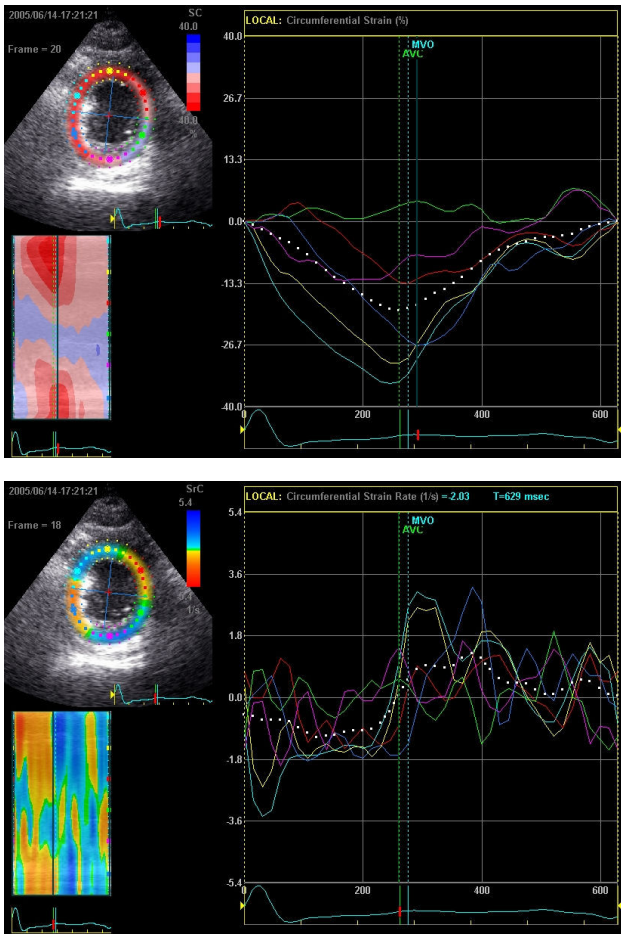


Fig. 1: LV Short-axis view, superimposed with 2D Strain display 36 'knots', of which 6 are also displayed on the right-hand side of each frame. Color M-mode display allows different presentation of the data. Upper frame: Circumferential Strain; Lower frame: Circumferential Strain Rate.

activation', as marked (by green dots) in Fig. 3 (same curves are displayed, but at a different scale and vertically shift), the sequence of activation can be estimated. In these figures, the sequence of activation during lateral pacing (left panels) is compared to that of septal pacing (right panels). The septal pacing causes a slower activation than the lateral pacing, and the location of the earliest time of activation is at a different 'knot' (34 vs. 14).

The results of all the data processed for the 3 controlled experiments are displayed in Fig.4. The mean and SD of the activation delay vector (ADV) and segmental propagation vector (SDV), are displayed for 3 pacing protocols: the amplitudes of these vectors are displayed in the upper panel, and the angles are displayed in the lower panel.

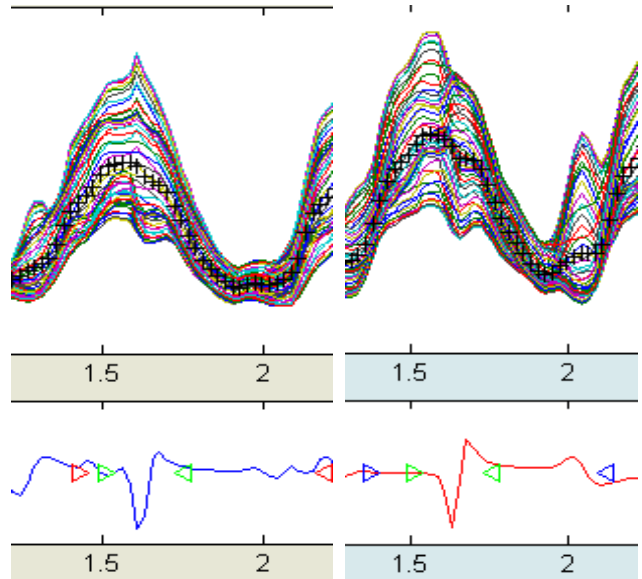


Fig. 2: Circumferential Strain, as measured at the 'knots', displayed during systole, together with the QRS-T complex of the ECG. Left panel: lateral pacing; Right panel: septal pacing.

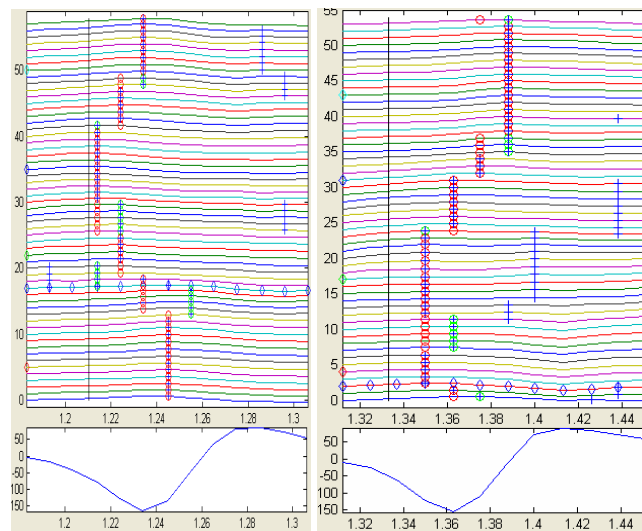


Fig. 3: 'Time of activation', marked by red dots, calculated from the circumferential Strain curves (same curves as in Fig. 2, but at a different scale and vertically shifted). Left panel: lateral pacing; Right: septal pacing. (Y-axis: 'knot' #; X-axis: time (s)). Lateral pacing close to 'knot' 5; Septal pacing close to 'knot' 35.

#### 4. Discussion and conclusions

The measurements in these studies were performed on normal hearts with high heart rate, caused by the surgical manipulations. The activation times were short. Thus, no large differences were expected in the measurements of 'times of activation' among the different pacing

protocols. The spatial distance between the lateral pacing electrode and the septal pacing electrode was about 5 cm. In spite of the small dissimilarity between the imposed conditions, the magnitude of SDV was significantly different in all cases except for separating between lateral and septal pacing in one of the animals, while the SDV angle performed just as good, except for separating between septal and normal pacing in the same animal. ADV was somewhat more vulnerable to the tracking quality. It is concluded that despite regional deviations of the tracking that interfere with calculations of local activation times, when global parameters are used, at the resolution of myocardial segments, differentiation among pacing sites is possible, as well as identification of the propagation synchrony and its direction.

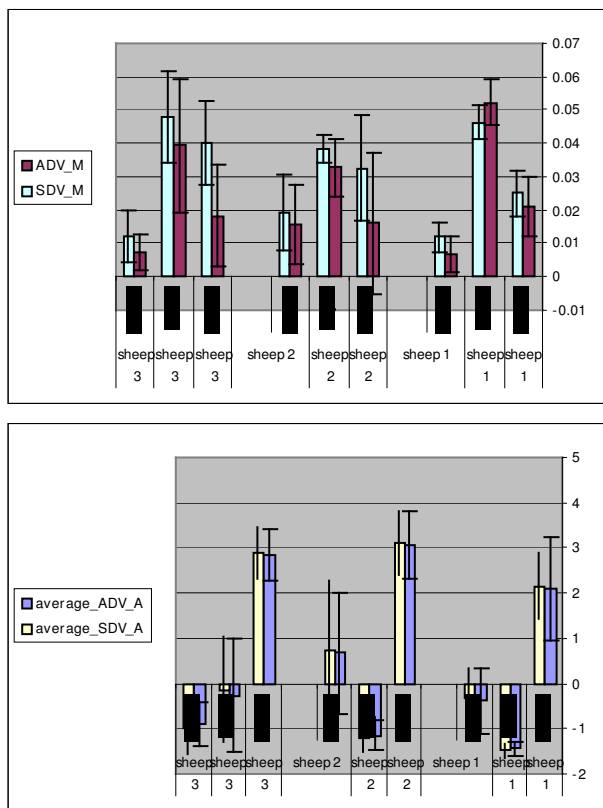


Fig. 4: The mean and SD of the activation delay vector (ADV) and segmental propagation vector (SDV), for 3 pacing protocols. Upper panel: amplitudes of the vectors; Lower panel: angles of the vectors.

## Acknowledgements

The authors are grateful for the help and assistance provided by Ms. Levy and Mr. Shenhav. This research was funded by the Magnetron program of the Chief Scientist, Israel Ministry of Industry, Trade & Labor.

## References

- [1] Wyman B. T., Hunter W.C., Prinzen F.W., Faris O.P., McVeigh E.R. effects of single- and biventricular pacing on temporal and spatial dynamics of ventricular contraction. *Am J Physiol Heart Circ Physiol*, 2002; **282**: 372-379.
- [2] Young JB, Abraham WT, Smith AL, et al., for the Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD) Trial Investigators. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: The MIRACLE ICD Trial. *JAMA*. 2003;**289**:2685-2694.
- [3] Heger JJ, Weyman AE, Wann LS, Dillon JC, Feigenbaum H. Cross-sectional echocardiography in acute myocardial infarction: detection and localization of regional left ventricular asynergy. *Circulation* 1979; **60**: 531-538.
- [4] Beyar R, Shapiro EP, Graves WL, Rogers WJ, Guier WH, Carey RL, Soulen EA, Zerhouni ML, Weisfeldt ML, Weiss JL. Quantification and validation of left ventricular wall thickening by a three-dimensional volume element magnetic resonance imaging approach. *Circulation* 1990; **81**: 297-307.
- [5] Pislaru C, Belohlavek M, Bae RY, Abraham TP, Greenleaf JF, Seward JB. Regional asynchrony during acute myocardial ischemia quantified by ultrasound strain rate imaging. *J Am Coll Cardiol*. 2001 Mar 15;37(4):1141-8.
- [6] McDicken WM, Sutherland GR, Moran CM, Gordon LN. Colour doppler velocity imaging of the myocardium. *Ultrasound Med Biol* 1992; **18**: 651-654.
- [7] Sutherland GR, StewartMJ, Groundstroem WE, Moran CM, Fleming A, Guell-Peris FJ, Riemersma RA, Fenn LN, Fox KAA, McDicken WN. Color doppler myocardial imaging: a new technique for the assessment of myocardial function. *J Am Soc Echocardiol* 1994; **7**: 441-458.
- [8] Tsutsui H, Uematsu M, Shimizu H, Yamagishi M, Tanaka N, Matsuda H, Miyatake K. Comparative usefulness of myocardial velocity gradient in detecting ischemic myocardium by a dobutamine challenge. *J Am Coll Cardiol* 1998; **31**: 89-93.
- [9] Guth B, Savage R, White F, Hagan A, Samtoy L, Bloor C. Detection of ischemic wall dysfunction: comparison between m-mode echocardiography and sonomicrometry. *Am Heart J* 1984; **107**: 449-457.
- [10] Adam D, Landesberg A, Konyukhov E, Lysyansky P, Lichtenstein O, Smirin N, Friedman Z. Ultrasonographic Quantification of Local Cardiac Dynamics by Tracking Real Reflectors: Algorithm Development and Experimental Validation. *Computers in Cardiology* 2004; **31**: 337-340.

Address for correspondence

Prof. Dan Adam  
Dept. of Biomedical Engineering, Technion, Haifa, Israel  
E-mail: dan@bm.technion.ac.il