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Imaging or imagination of cardiac mechanics?

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Abstract—**Ultrasound and MRI systems allow to measure many variables related to cardiac motion and deformation. These imaging modalities have the advantage to be non-invasive, thereby facilitating measurements in man. Many custom available parameters are, however, not useful for proper analysis of cardiac mechanics and can yield confusing results. This is especially relevant if important decisions for the patient have to be made and if complicated mechanical abnormalities are investigated, such as abnormal electrical activation of the ventricles. Recent developments in ultrasound technology and data analysis provide novel opportunities for better mechanical analysis and, presumably, better diagnosis.**

I. Introduction

For decades the main focus of measurements on cardiac mechanics was the effect of ischemia and infarction. In the clinical situation the majority of the measurements was focused on quantifying the extent of reduction of contraction (dyskinesis, akinesis) and the size of the area affected. In recent years interest is increasing in another topic: the mechanical abnormalities as a consequence of abnormal electrical activation of the ventricles, as induced by ventricular pacing or bundle branch block. These conditions give rise to far more complicated mechanical behavior than during ischemia, because local deformation is often multiphasic and because also information on timing of onset and peak of contraction is desired. Over the last decade several indices have been proposed for better prediction of response of patients to Cardiac Resynchronization Therapy (CRT) [1] [2]. While several single center studies provided an optimistic view on the possible contribution of "mechanical dyssynchrony" to the prediction of CRT response, a few recent multicenter studies showed that this idea is not valid [3] [4]. It has been suggested that the poor performance of indices of "mechanical dyssynchrony" is due to technical limitations of the technology, inadequate interpretation of the signals or an incorrect concept about prediction of CRT response. [5] Because the experienced observer recognizes a dyssynchronous wall motion by eye [5], it is even possible that some observers adjusted the image analysis using their "imagination" in order to achieve "sensible" values of mechanical dyssynchrony.

This paper will briefly review the physical background of various "mechanical" indices provided by imaging modalities, like echocardiography and MRI, and discuss to what extent technical limitations of these techniques can explain the confusing results on the reliability of dyssynchrony indices. Finally, novel developments are discussed, which could result in better prediction of CRT response.

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II. Measuring Cardiac Mechanics Using Imaging Modalities

In the clinical setting echocardiography is the most commonly used modality. Beside the measurement of valve opening and closing times using Doppler studies, mechanical behavior of the cardiac walls can be measured using conventional echocardiography (wall motion, usually endocardial wall motion), velocity (Tissue Doppler Velocity Imaging (TDI) and strain analysis. The latter can be performed using comparison of tissue velocity in adjacent regions or using the novel speckle tracking analysis. MRI basically offers the same opportunities, using velocity gradient imaging, cine-imaging and tagged imaging, respectively. Over the last decade various techniques and approaches have been used to determine mechanical dyssynchrony (for extensive review see [6]).

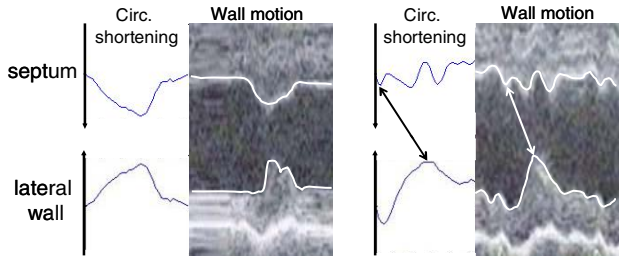


Figure 1. Example of M-mode echocardiographic determination of SPWMD (double arrows) and related circumferential strain recordings (inverted for the lateral wall, in order to facilitate comparison of shape with wall motion).

A. *Measures relying on displacement of tissue.*

These methods measure displacement of tissue with respect to a certain reference point. The septal-to-posterior wall motion delay (SPWMD) is measured using conventional M-mode echocardiography and is defined as the delay between the maximal inward movement of the septum and the LV lateral wall (*Fig. 1*). An SPWMD >130 ms has been shown to predict clinical and echocardiographic response to CRT [7]. The figure shows that the endocardial wall motion pattern looks similar to that of circumferential strain, as measured using MRI tagging (see below). A problem with interpreting the septal motion pattern is that it is often multiphasic and that the time of inward motion of the septum is dependent on which peak is chosen. Based on comparison of septal wall motion and strain measurements

(see below) most likely the first inward motion provides the best estimation of the onset of septal activation. Interpreting the origin of the paradoxical septal motion and septal strain pattern is complicated, because it can be influenced by both early rise of RV cavity pressure and early onset of septal muscle fiber contraction. It is almost impossible to dissect these two factors. On the other hand, a dissociation between each of the two factors with LV cavity pressure and LV free wall contraction, respectively, is probably disadvantageous [8] [9].

The novel 3D echocardiography technology allows to measure endocardial wall motion in many LV wall segments. From this motion regional ejection fraction is derived, as calculated using a central cavitary reference point.[6] The regional differences in peak endocardial wall motion are then used to describe ventricular dyssynchrony.

Tissue tracking (TT) measures the displacement of segments of myocardium with respect to the ultrasound transducer. Dyssynchrony is assessed by determining the location and the number of wall segments with delayed longitudinal displacement (i.e., after aortic valve closure) and by measuring the magnitude of the time delay for each segment.[6]

B. *Measures relying on tissue velocity*

TDI measures the velocity of myocardial displacement and, consequently, results in noisier signals than displacement measurements *(Figure 2)*. Commonly measured parameters include the time from end-diastole to onset and/or peak systolic velocity. Regional differences in these times are the most commonly used indicators of mechanical dyssynchrony. Examples are the septal-to-lateral wall delay in peak systolic velocity and the standard deviation of the time to peak systolic velocity for 12 LV wall segments (Ts-SD-12).[6]

TDI has theoretical and technical limitations, part of which were demonstrated in a recent study[5]. TDI measures velocity in the direction of the ultrasound beam, rather than along the muscle fibers. Moreover, local movement of a point in the heart is a function of the motion of the entire heart and of local deformation. Motion of the entire heart motion consists of longitudinal and lateral displacement as well as rotation along its long-axis. Deformation consists of circumferential, longitudinal and radial strain as well as shear strains and torsion. Therefore, TDI measures a limited part of local deformation and also depends on factors other than deformation [10]. Accordingly, TDI can make significant errors in estimating local myocardial behavior when wall segments are not aligned with the ultrasound beam [5]. Even slight changes in the position of the sample volume also change the shape of the velocity tracings, thereby also changing the timing of peak velocities [5](*Fig.* 5).

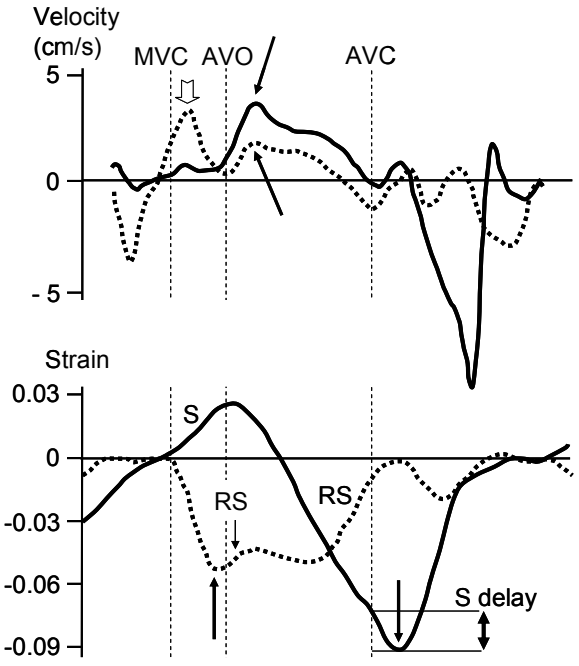
Moreover, While these problems appear to be well coped with in single center studies, the PROSPECT multicenter trial showed disappointing predictions of CRT success by echocardiographic indices of mechanical dyssynchrony. [4] Moreover, in patients with narrow QRS complex, the presence of mechanical dyssynchrony did not lead to a beneficial affect of CRT [3]. A recent consensus paper concludes therefore, that no single measure of mechanical dyssynchrony can be recommended to further improve patient selection beyond the current guidelines [11].

C. *Measures relying on deformation, strain.*

Strain represents the extent of deformation of a tissue segment over time and is expressed as the percentage of segmental shortening or lengthening in relation to its original dimension. Thus, strain describes mechanical behavior of a specific myocardial region. As shown in Figure 2, strain signals are easier to analyze than velocity signals, because they contain less peaks and are less noisy.

The first measurements on strain-based indices of "mechanical dyssynchrony" with imaging techniques were performed using magnetic resonance imaging (MRI) tagging.[12]

Figure 2: Recordings of TDI (upper) and speckle tracking strain (lower) in the septum (dotted) and LV lateral wall (drawn) of a CRT candidate. Arrows indicate time of peak velocity and strain. Note that no dyssynchrony is observed using TDI, but a clear dyssynchrony using strain analysis. Small open arrow in top panel indicates peak velocity during isovolumic contraction phase, often not used for dyssynchrony analysis. S and RS indicate Stretch and Rebound



Tags are temporarily applied changes in the magnetic field, creating planes of saturation, leading to a family of lines, usually imposed at end diastole. These lines stick to the myocardium and move during subsequent phases of the cardiac cycle. Strain is calculated by measuring the difference in displacement between adjacent sites. Various indices of mechanical dyssynchrony have been calculated from strain information.[13] MRI tagging is regarded as the gold standard for strain imaging, but it is expensive and time-consuming. Therefore, it is primarily a research tool.

Strain can also be determined by post processing of TDI velocities on two adjacent regions to strain rate and subsequently strain (Fig. 5). Doing so, Breithardt et al[14] showed that, in describing dyssynchrony and its changes due to CRT, the thus calculated strain yielded more reliable information than tissue Doppler velocities. However, strain analysis from TDI is problematic, because all errors of TDI, as mentioned above, make subtraction of two of such signals cumbersome, time-consuming and operator dependent.[6]

A novel approach to quantify myocardial strain from echocardiographic data is speckle-tracking [15]. The gray scale echo image consists of a speckled pattern. Speckle-tracking software tracks the frame-to-frame movement of these acoustic markers throughout the myocardium, similar to the analysis of MRI tagging. De Boeck et al[5] showed that dyssynchrony based on speckle tracking strains provides a more reliable prediction of CRT response than TDI. Figure 2 shows an example of a patient where nearly synchronous TDI velocities coincide with highly dyssynchronous strains.

III. DYSSYNCHRONY VS. DISCOORDINATION.

While the use of 2D-strain is clearly an improvement, yet using this measurement to determine dyssynchrony may still not be optimal. In a small study Kirn et al investigated prediction of CRT response using mechanical dyssynchrony, derived from MRI tagging, the gold-standard of deformation measurements [16]. They found that MRI tagging derived mechanical dyssynchrony also poorly predicted CRT response. As an alternative to mechanical dyssynchrony, they proposed mechanical discoordination to predict CRT response. Discoordination was quantified as the ratio of the amount of stretch (indicated by S and RS in figure 2) and shortening, integrated over the systolic period. The idea behind this new index is that stretching segments absorb shortening energy from contracting segments, thus leading to reduced cardiac function and that CRT can recoordinate the motion of the different segment. The TUS (or CURE) index also includes information about coordination[13]. This index is calculated with Fourier analysis of strain in LV regions in space. The TUS index reflects the relative first-order Fourier power within the LV wall. In doing so, TUS assumes a sine wave spatial variation in strains and it does not express the amount of stretch. ISF is calculated without any assumption on distribution of strain in space and time.

Preliminary data also point to another interesting new index for CRT response: septal rebound stretch. This is defined as the stretch (lengthening) in the septum following initial shortening (indicated by RS in figure 2; De Boeck, personal communication). Yet another index of discoordination is "strain delay", being the amount of shortening after the end of the systolic period (and therefore "wasted"; figure 2) [17]. Therefore, the problematic prediction of CRT response by mechanical dyssynchrony could be primarily due to the fact that dyssynchrony (timing differences in onset or peak of shortening) have only a poor relation with pump function. Moreover, timing differences can also be caused by abnormalities not amenable to CRT [18]. Therefore, analysis of discoordination may offer new hope that non-invasive analysis of cardiac mechanics can predict the benefit of CRT,

IV. CONCLUSIONS

Good mechanical analysis of the heart requires a critical view on the potential and limitations of imaging modalities. Analysis of discoordination may provide a valuable addition to existing diagnosis of heart failure in general and CRT in particular.

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