

## Assessment of ventricular mechanical dyssynchrony by short-axis MRI

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**Abstract**—Nowadays, patients with symptomatic heart failure and intraventricular conduction delay can be treated with a cardiac resynchronization therapy. Electrical dyssynchrony is typically adopted to represent myocardial dyssynchrony, to be compensated by cardiac resynchronization therapy. One third of the patients, however, does not respond to the therapy. Therefore, imaging modalities aimed at the mechanical dyssynchrony estimation have been recently proposed to improve patient selection criteria. This paper presents a novel fully-automated method for regional mechanical left-ventricular dyssynchrony quantification in short-axis magnetic resonance imaging. The endocardial movement is described by time-displacement curves with respect to an automatically-determined reference point. These curves are analyzed for the estimation of the regional contraction timings. Four methods are proposed and tested for the contraction timing estimation. They were evaluated in two groups of subjects with and without left bundle branch block. The standard deviation of the contraction timings showed a significant increase for left bundle branch block patients with all the methods. However, a novel method based on phase spectrum analysis shows a better specificity and sensitivity. This method may therefore provide a valuable prognostic indicator for heart failure patients with dyssynchronous ventricular contraction, adding new possibilities for regional timing analysis.

### I. INTRODUCTION

Almost two million people in the United States suffers from conduction system disease, i.e., the electrical depolarization signal that induces the muscle contraction is not properly conducted over the myocardium [1]. This problem, which is typically characterized by a prolongation of the QRS complex in the electrocardiographic measurement, leads to a dyssynchronous contraction of the left ventricle (LV). The major effects are a reduction of the cardiac efficiency and ejection fraction, which results in a progressive deterioration of the LV function.

Cardiac resynchronization therapy (CRT) is an established therapy for patients with symptomatic heart failure and prolonged QRS duration [2]. Nevertheless, not all patients respond to CRT and LV reverse remodeling is appreciated in slightly more than 50 % of patients [3]. This lack of response is typically attributed to inappropriate patient selection and, in particular, to the poor predictive value of QRS prolongation [4], [5]. Several studies on mechanical dyssynchrony

suggest that mechanical dyssynchrony is a better predictor for CRT response than electrical dyssynchrony [6], [7].

Mechanical dyssynchrony can be assessed using imaging modalities based on magnetic resonance imaging (MRI) or ultrasound echo-Doppler. In general, myocardial velocity timing can be evaluated by ultrasound tissue doppler imaging (TDI) [6], [7] and myocardial strain timing can be evaluated by MRI tagging [8]. However, TDI is limited by the acoustic windows through the ribs and the anisotropic sensitivity of the method (Doppler frequency shifts only occur for longitudinal motion), while MRI tagging requires extensive computation and shows a low sensitivity for reduced wall thickening (hypokinetic ventricle).

This paper presents a novel method for regional mechanical LV dyssynchrony quantification based on image analysis. The method is fully automated. Short-axis MRI cines are analyzed by an algorithm that is developed on the radial framework of the image segmentation approach proposed in [9], where the endocardium was detected by high-pass filtering and thresholding along a beam of rays originating in the ventricular center, referred to as seed point. The seed point was manually determined. The threshold was defined either manually or on the basis of the image histogram.

The proposed segmentation algorithm is based on dynamic morphology and radial multiscale analysis of the LV basal view [10], [11]. This results in a substantial advantage with respect to the method in [9] and several other methods proposed in the literature, as no user interaction or threshold definition is required.

MRI is chosen for the high contrast along the endocardium, which results in an increased segmentation robustness. A short axis basal view permits to assess the synchronicity of the basal segments, which is reported to be of prognostic value in CRT [5], [6]. This allows reducing the complexity of the diagnostic system from three to two dimensions.

In this study, segmentation is only a preprocessing step for the dyssynchrony analysis. Based on the endocardial tracking, the regional endocardial time-displacement curves (TDCs) are determined. Several methods can then be implemented to assess the contraction dyssynchrony along the endocardium. To this end, we have adapted and implemented the systolic time method [5], [12] and the inner product method [13], [14]. In the latter, the entire cardiac cycle is used to determine the local contraction timing. We also propose two alternative methods that are based on the cross correlation of the entire TDCs.

The developed dyssynchrony analysis was validated on two groups of patients with and without left bundle branch

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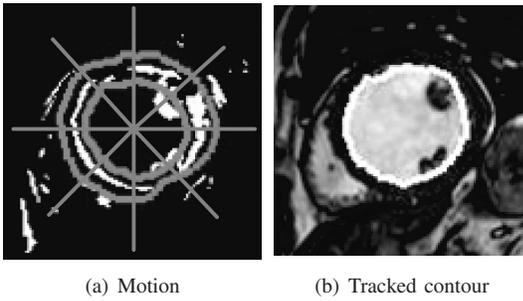


Fig. 1. A short-axis basal view of the left ventricle. The region of interest in the motion image (a) used for detecting and tracking the endocardium (b) is circumscribed by inner and outer borders on a beam of rays originating in the ventricular center, i.e., the seed point. For illustrative purpose the number of displayed rays is limited to 8.

block (LBBB). All the methods revealed a significant increase of the standard deviation of the contraction timings as a LBBB was present. However, one of the proposed cross correlation methods showed a better sensitivity and specificity for LBBB diagnosis.

## II. METHODOLOGY

### A. MRI cine acquisition and regularization

The MRI cines for the dyssynchrony analysis were acquired at high temporal resolution (one hundredth of the cardiac period) on a 1.5 T MRI scanner (Gyrosan Intera, Philips Medical Systems) equipped with a five-element phased array coil. A balanced steady-state free precession pulse sequence was adopted. Breath hold was used to avoid motion artifacts. Going from base to apex, the first slice that did not show the mitral valve structures was chosen for the dyssynchrony analysis (see Fig. 1). In order to avoid contour blurring, image regularization was performed by combination of morphological proper-closing and proper-opening operators with a nine element kernel [15].

### B. Contour detection

The detection of the endocardial contour in the selected MRI slice is fully automatic. The standard deviation of the pixel intensities during the cine is analyzed and a binary image generated by applying the threshold proposed by Otsu [16]. The resulting binary image facilitates the automatic detection of a region for the LV endocardium search, as this is the structure that shows the most of the movement and, therefore, the largest gray-level variations.

For the detection of the endocardial region, the Hough Transform (HT) is employed [17]. The HT is a method that tests the foreground pixels in a binary image against a defined curve equation, which in our case is a circle. In fact, the LV motion in a short axis view has a circular symmetry. The 21-HT implementation is adopted due to its efficient computation [18]. The results are the seed point coordinates and the average radius of the endocardial motion circle.

Based on the 21-HT results, a region of interest (ROI) for the endocardium search is defined as the endocardial range of motion, i.e., the inner and outer borders of the endocardium

in the binary motion image (see Fig. 1). The border coordinates are defined along the rays originating in the seed point. Possible outliers, e.g., due to the papillary structures, are corrected by means of a continuity condition on the border derivative in polar coordinates, which is bounded within the values assumed in case the seed point is located on the border itself (worst condition). Once the borders are defined, the seed point is relocated in the center of mass of the inner border to increase the localization accuracy of the following analysis. The defined ROI is expanded (20 % inwards and outwards) before the contour tracking.

### C. Contour tracking

Once a ROI for the contour detection in the original cine is defined, the endocardium could be tracked along the rays originating from the seed point by means of a high-pass filter and a threshold [9]. However, as the definition of a threshold is always critical, here we propose the replacement of the radial filter in [9] by a more elaborated algorithm, which does not require any threshold.

The multiscale analysis for edge detection proposed by Canny et al. [11] is modified and adapted to the proposed application [10]. A multiscale analysis with a Gaussian derivative mother wavelet is performed on each ray originating from the seed point with an angular resolution of 5 degrees and on each frame of the MRI cine. For each ray the multiscale analysis produces a scalogram  $W(n, s)$  where  $n$  is the distance (in pixels) from the seed point and  $s$  is the scale. A linear function of  $n$  is used to weigh  $W(n, s)$  and enhance the values at shorter distance from the seed point. This is performed to reduce the sensitivity of the algorithm to fatty structures at larger distance around the heart.

The edges (with negative slope) for each scale correspond to the (local) maxima of  $W(n, s)$  along a ray. Without the need for a threshold, the location  $\hat{n}$  along a ray of the dominant edge, i.e., the endocardium, can be defined as

$$\hat{n} = (n : \mu(n) > \mu(m), \forall n \neq m), \quad (1)$$

where  $\mu(n)$  is defined as the minimal value for all the scales  $s \in S$  of the normalized  $W(n, s)$ , i.e.,

$$\mu(n) = \min_S \left[ W(n, s) \left( \max_N [W(n, s)] \right)^{-1} \right]. \quad (2)$$

The solution of (1) results in an efficient compromise between localization accuracy and noise sensitivity.

In order to increase the robustness of the system, a temporal continuity constraint is integrated in the system by calculating  $\mu'(n)$  over the output scales of three subsequent frames together. The temporal continuity condition results from the use of high temporal resolution MRI scans.

### D. Dyssynchrony analysis

The result of the segmentation algorithm is a function  $r(\theta, k)$ , which defines the edge distance from the seed point along a  $\theta$  degree ray at the frame  $k$ . Dyssynchrony estimations result from the analysis of the TDCs  $r(\theta, k)$  for different rays.

To improve the accuracy of the timing analysis, the TDC time resolution is doubled by linear upsampling. The TDCs, which include both systole (contraction) and diastole (expansion), may resemble one period of a sinusoidal function. When no conduction system dysfunction is present, the ventricle contracts synchronously along its basal segments and  $r(\theta, k)$  shows a similar behavior in time for each angle. Instead, when a conduction system block is present, the TDCs for different rays are dyssynchronous.

Most segmentation-based methods for dyssynchrony evaluation are based on the estimation of the systolic time [12]. This approach might be more sensitive to noise as it focuses on one moment of the cardiac cycle (end systole). The analysis of the complete cardiac cycle was also proposed to compare lateral to septal phase differences [13], [14]. Under the assumption of a sinusoidal TDC, the mutual phase difference was defined as the arccosine of the inner product between the lateral and septal TDCs [14]. Another approach used the inner product with a reference sine and cosine curve (one cycle) to derive an absolute phase delay [13]. These methods are however based on the assumption of a sinusoidal TDC and they are therefore sensitive to TDC shape variations.

For a complete validation of the proposed methods, both the systolic time and the inner product approaches are adapted and integrated in our MRI short-axis-view analysis. The systolic time is defined as the time to the minimum value of the TDC. The inner product method provides a relative time delay (fraction of the cardiac period) between two TDCs corresponding to the angles  $\theta_i$  and  $\theta_j$  that is given as  $\arccos(\langle r(\theta_i, k), r(\theta_j, k) \rangle) / 2\pi$ , where  $\langle \cdot, \cdot \rangle$  represents the inner product. This delay is estimated for all the TDCs with respect to the TDC with the largest SNR.

Here we also propose the use cross correlation methods for the assessment of the mutual delays between TDCs from different angles. The same reference defined for the inner product method is also adopted for the cross correlation method and the regional contraction timing for each angle is defined as the time at which the cross correlation with the reference TDC shows its maximum. Typically 72 rays are employed to span the entire circle. Figure 2 shows a regional contraction timing plot for two subjects with and without a LBBB. The contraction timing in the presence of a LBBB shows increased variations.

The time resolution of this cross correlation method is limited by the sampling period of the signals. This problem can be overcome by phase spectrum analysis. If a Discrete Fourier Transform of two TDCs  $r(\theta_i, k)$  and  $r(\theta_j, k)$  is performed, the difference of the phase spectra results approximately in a line. This is due to the fact that  $r(\theta_i, k)$  and  $r(\theta_j, k)$  are time translations of the same curve. If the slope of the phase difference line is determined, then the delay between  $r(\theta_i, k)$  and  $r(\theta_j, k)$  can be estimated with no time resolution constraints.

The phase analysis is performed after the cross correlation re-alignment. As a result, the phase difference is bounded between  $-\pi$  and  $\pi$  with no phase wrapping issues. Ob-

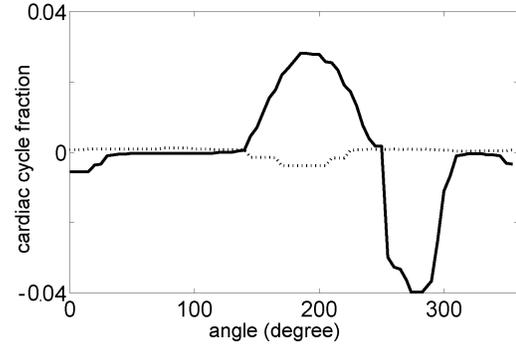


Fig. 2. The regional contraction timings for two subjects with (solid) and without (dashed) LBBB.

viously, the assumption of a pure temporal translation is not completely fulfilled, and the phase difference line may show a poor SNR. A least square error method is therefore employed for the interpolation of the phase difference line, whose slope can be estimated by a weighted linear regression. The weights for the linear regression are derived by the analysis of the amplitude of the frequency spectrum [19]. They are determined as the minimum value between the amplitudes of the spectra of the two TDCs. As a result, the higher energy components, which typically represent the myocardial movement, provide a larger contribution to the regression line determination.

### III. RESULTS

Ten subjects (five normals and five with LBBB) were tested for quantification of the regional contraction timings. LBBB was diagnosed by analysis of the QRS duration. The performance of the proposed segmentation method was validated on four evenly distributed image frames per cardiac cycle. A total number of 40 images was evaluated by measuring the percent area difference between manually and automatically delineated endocardial boundaries. The area was defined as the surface that was delimited by the delineated boundary and the absolute area difference (error) was defined as the area that was covered by only one of the two delineations. The manual segmentation was taken as the reference method since no gold standard for segmentation of cardiac images exist. The results show a correlation coefficient between the two methods  $R = 0.99$ . Bland-Altman [20] analysis resulted in an average area error equal to 9.8 % while the corresponding standard deviation was less than 3.8 %. Therefore, the segmentation algorithm is suitable for the following cardiac dyssynchrony analysis [9].

The validation of the dyssynchrony analysis was performed by estimating the standard deviation of the regional contraction timing assessed by the systolic time, inner product, cross correlation, and phase difference method for each subject. In Table I the population averages and standard deviations for the four indicators are given. All the values are reported as a fraction of the cardiac cycle. According to the results, separable ranges can be defined by each method for either population (with and without LBBB).

TABLE I  
MEAN AND STANDARD DEVIATION OF THE FOUR INDICATORS.

Method	LBBB	Normals
Systolic time	0.1500 ± 0.0365	0.0316 ± 0.0121
Inner product	0.1178 ± 0.0436	0.0436 ± 0.0275
Cross correlation	0.1422 ± 0.0317	0.0246 ± 0.0220
Phase difference	0.1468 ± 0.0191	0.0268 ± 0.0171

TABLE II  
SPECIFICITY AND SENSITIVITY OF THE FOUR INDICATORS.

Method	Specificity	Sensitivity
Systolic time	99.71 %	99.00 %
Inner product	90.68 %	89.28 %
Cross correlation	98.89 %	98.30 %
Phase difference	99.96 %	99.95 %

The evaluation of a diagnostic method is typically based on sensitivity and specificity analysis. To this end, a threshold must be defined that is used to decide whether a patient has a LBBB. Assuming our statistical samples to be well represented by Gaussian distributions defined by the means and standard deviations in Table I, inference by Bayes rule can be used to obtain the posterior class probability for each class (normals and LBBB) by each of the four methods. As a result, a threshold can be derived such that the posterior class probability is equal for the two classes. The thresholds for the systolic time, inner product, cross correlation, and phase difference method are 0.0650, 0.0800, 0.0749, and 0.0838, respectively. Based on these thresholds, specificity and sensitivity can be calculated for each method as given in Table II, where the phase difference method shows the best results.

#### IV. DISCUSSION AND CONCLUSION

A novel method is presented that permits the automatic evaluation of the intraventricular mechanical dyssynchrony based on high time-resolution MRI cines of a LV short-axis basal view. The analysis is fully automatic and does not require any user interaction.

It is known that the ventricular movement comprises a twist about its long axis. This twist is however limited to less than 5 degrees in the basal plane [21], and it is therefore negligible for the presented analysis. Ventricular translations due to respiration are also negligible since breath-hold MRI is performed.

Four algorithms have been implemented for the timing analysis. They are based respectively on systolic time, inner product, cross correlation, and phase difference analysis. Validation on ten patients showed that all methods are suitable for LBBB detection based on the standard deviation of the estimated regional contraction timings. The analysis of the entire cardiac cycle by phase difference analysis seems however to be the most promising in terms of sensitivity and specificity, although a more extensive validation is necessary.

The improved results obtained by the phase difference against the inner product and cross correlation methods were expected. In fact, the first one assumes the TDC to be fully

represented by a sinusoidal function while the second one has a limited time resolution. Compared to the systolic time method, the analysis of the complete cardiac cycle, also including diastole, represents a valid alternative, which might show interesting predictive value for the selection of CRT responders.

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