Results of performing or not cardiac resynchronization therapy for live assessment of LV function and mechanical systole synchrony using gated myocardial perfusion imaging and real-time three-dimensional echocardiography. Seven months follow-up

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Abstract

We studied a 50 years old male patient who underwent cardiac resynchronization therapy on and off (CRT-on and CRT-off) for assessment of left ventricular (LV) function and mechanical systole synchrony using gated myocardial perfusion imaging (GMPI) and real-time three-dimensional echocardiography (RT3DE). The patient was reexamined after seven months. The comparison of these two modalities showed consistent results on assessing both the CRT-on and CRT-off conditions. This result may indicate that an immediate synchronization parameter change during CRT-on may be valuable for predicting response to CRT surgery.

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Introduction

Cardiac resynchronization therapy (CRT) is an effective regimen for heart failure (HF) in patients with wide QRS in the electrocardiogram (ECG). Traditional ECG has been used to predict response to this therapy. Unfortunately, not all patients respond. Furthermore, there has been ongoing discussion on complexity of ECG selection criteria [1-3]. Assessment of LV dyssynchronization in patients selection before CRT remains a challenge. Real-time three-dimensional echocardiography (RT3DE) and gated myocardial perfusion imaging (GMPI) are other useful options for assessing mechanical dyssynchronization. However, there is lack of studies on the usefulness of GMPI. After a thorough literature search, we found there simply had been no large-scale clinical trials done on GMPI.

Case Report

A 50 years old male patient was admitted on May 4, 2015 with recurrent shortness of breath and chest pain for more than one year. The ECG indicated complete left bundle branch block with QRS of 189ms and serum B-type Natriuretic Peptide (BNP) of 277ng/mL. The transesophageal echocardiogram (TEE) found decreased LV systolic function, with LV ejection fraction (LVEF) of 29%, and mild to moderate mitral valve regurgitation. Coronary angiogram demonstrated a 30% stenosis in the middle segment of the left circumflex coronary artery and a 95% stenosis in the middle segment of the right ventricular branch of the right coronary artery (arterial diameter less than 2mm). The clinical diagnosis was diastolic cardiomyopathy with clinical cardiac function class III according to New York Heart Association (NYHA) functional classification class III. The patient had been receiving heart failure treatment for more than one year without significant improvement prior to admission. Based on patient's symptoms, physical examination, ECG, and other imaging results, the treating physician recommended pacemaker implant and CRT according to the European Society of Cardiology standards [4]. On May 14, 2015, a Medtronic PXJ 606450S CRT/D LV pacemaker wire was inserted into the coronary vein sinus branch. As shown in Figure 1, the pacemaker wire reached the lower lateral wall of the LV in the LAO 45° view (pacemaker threshold 0.8V, resistance 534Ω).

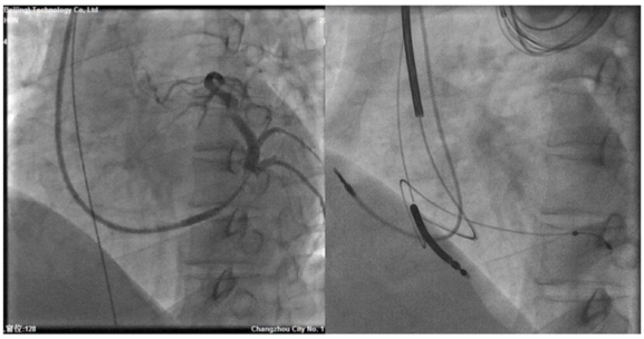

Figure 1. Left: LAO 45°coronary angiogram; right: LAO45° view after the electrode was implanted. White arrow: electrode implant at the left inferolateral wall.

After procedure, the patient experienced significant improvement of symptoms and increase of cardiac function to NYHA class I or II. In the regular follow-ups, the pacemaker parameters were optimized according to the echocardiogram results. During a 7 months follow-up, RT3DE and GMPI were used to further evaluate LV and synchronization of the LV. The patient was under ECG monitor after he gave his written consent. Emergency medication including nitroglycerin oral pills and intravenous steroids were available at his bedside.

The Philips EPIQ 7C machine, equipped with Qlab 10.0 quantitative analysis software, was used for the RT3DE. In RT3DE, time to minimum systolic volume (Tmsv) was calculated. Several dyssynchrony indices were then decided: a) Tmsv-16 SD (the SD of Tmsv in 16 of 17 segments based on the American Heart Association, a 17-segment model, excluding the apical cap), b) Tmsv-12 SD (the SD of Tmsv of 6 basal and 6 middle segments). Tmsv-Dif (Tmsv16-Dif, and Tmsv12-Dif) stood for maximal difference between the segments.

The RT3DE results (Figure 2A and 2B) demonstrated that: 1) during CRT-on, the LV end diastolic volume (LVEDV) and LV end systolic volume (LVESV) both decreased from CRT-off, (LVEDV: 149.2mL vs. 177mL, LVESV: 81.1mL vs. 110mL), while LVEF increased (45.6% vs. 37.9%), indicating improvement of LV function; and 2) during CRT-off, irregular arrangements and morphological changes in the time-volume curves (Figure 2A). In contrast, the curves turn into parabolic and regular order during CRT-on (Figure 2B). Furthermore, Tmsv-16SD (19 vs.74ms), Tmsv-12SD (21 vs. 66ms), Tmsv16-Dif (86 vs. 256ms), and Tmsv12-Dif (86 vs. 256ms) all decreased during CRT-on, indicating an improvement in systolic synchronization or a decrease in ventricular dyssynchrony.

We used for the GMPI the Siemens Symbia T16 dual-head, single photon emission tomography/computed tomography (SPET/CT) camera. The 99m-technetium sestamibi was used as a tracer, with a radionuclide purity of more than 95%, and a dose of 925MBq. For methods and techniques of image acquisition and reconstruction, please refer to our previous work. Briefly, images of GMPI were acquired using a matrix of 128x128, magnification of 1.45, and 20% window centered on the 140keV peak energy. Reconstruction was performed using the filtered back projection (RBP) method (Butterworth filter with cutoff frequency of 0.35 and order of 5 [5]. By using the Emory (explain ECT) ECToolbox software, we obtained phase histograms and synchronization analysis charts. The histogram bandwidth (BW) represents the range of 95% phase distribution, while the SD of the histogram represents the variations in the LV contraction phase. These two parameters are inversely proportional to ventricular synchronization. The smaller these two parameters, the better the synchronization of the LV is the segment with the largest mean phase value is, by default, the latest activated site [6].

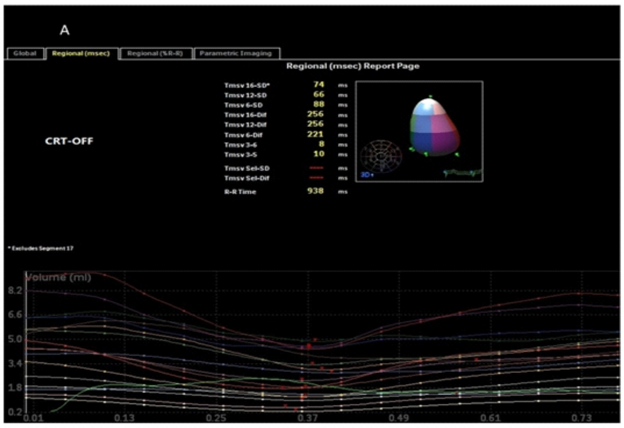

Figure 2A. Real-time time-volume curve during CRT-off, the curves are in irregular arrangements with morphological changes.

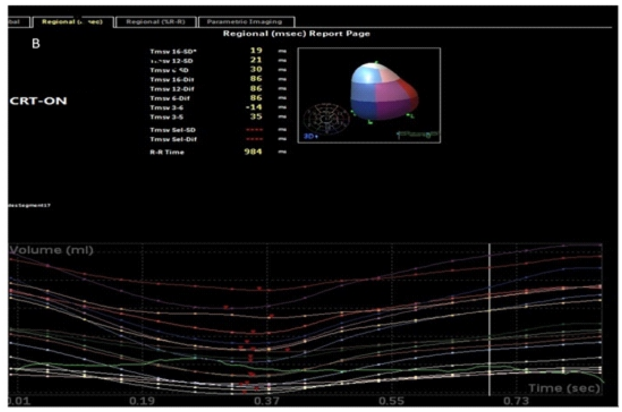

Figure 2B. Real-time time-volume curve during CRT-on, the curves are parabolic and in regular order. The end-systolic volumes of 17 segments almost occur simultaneously as illustrated.

The viability of the myocardium is decided by tracer uptake intensity. Segments with less than 50% uptake of the mean value are considered non-viable [7]. The quantitative analysis results of GMPI included the left ventricular contractile function and synchronization parameters. These results are parallel to the RT3DE results. The perfusion study results indicated that during CRT-on, LVEDV and LVESV both decreased (LVEDV: 120 vs. 142mL; LVESV: 67 vs. 99mL), while LVEF increased (44% vs. 30%). The synchronization parameters, inclu ding BW and SD of phase analysis, also decreased (BW: 48° vs 104°, SD: 15° vs 38°) (Figure 3). The polar plot of the phase image demonstrated that the latest activated segment was in the left basal inferolateral segment, which made it an ideal place for pacemaker electrode placement (Figure 4), and 75% of this segment was viable according to the intensity of tracer uptake. Finally, the latest activated segment position and pacemaker electrode placement was consistent and confirmed by X-ray imaging findings.

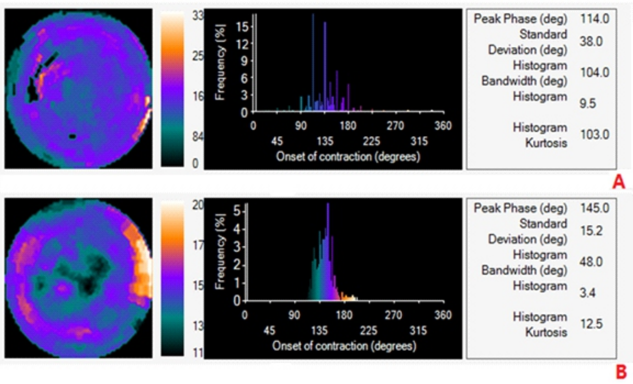

Figure 3. A: CRT-off phase polar plot and histogram; B: CRT-on phase polar plot and histogram. Narrower phase distribution of CRT-on is obvious in contrast to CRT-off.

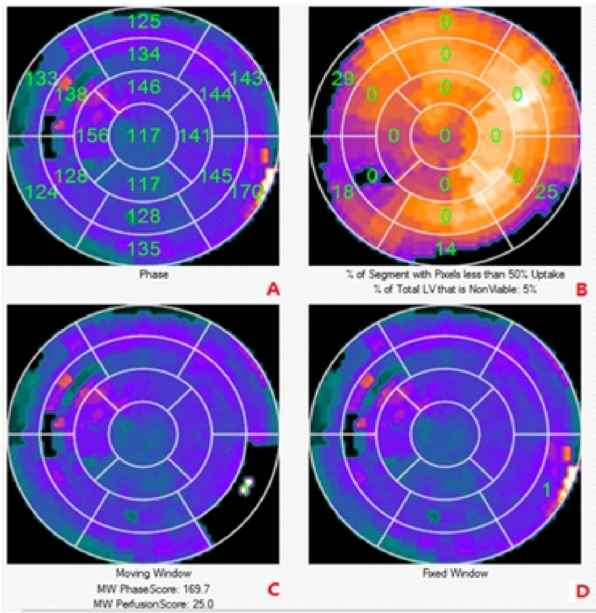

Figure 4. During CRT-off, A: 17 segments phase polar plot, the larger the phase degree, the later of excitation. The basal inferolateral segment phase mean 170° was the latest activated segment, B: perfusion polar plot, values as percentage difference below the well-perfused segments. With the basal inferolateral segment 25% lower than normal area, or 75% viability. C& D. The basal inferolateral segment evaluated through superposition of phase and perfusion polar plot results was the most ideally segment for electrode implant.

Discussion

One of the most effective methods to mitigate heart failure is CRT. The mechanism relies on improved synchronization, which results in increased contractility, symptom improvement, increased exercise susceptibility, and decreased mortality. The current standard CRT response criteria include: a) Improvement of cardiovascular function from class III of NYHA, to class I or II, b) At least 10% improvement in six-minute walking distance and c) LVEF; and LVESD decrease of at least 15% [8]. The super response to CRT must meet all of the following criteria: NYHA function improvement to class I; LVEF increase of at least 20%; and LVESV decrease of at least 20% [8]. With advancements in implant technology, instrument, and updates of the guidelines, more patients are benefiting from CRT. However, a multi-center study found that approximately 20%-30% of patients have little or no response to CRT [9]. Several studies have shown that crucial factors impacting response include the improvement of synchronization after surgery and correct location of the CRT electrode placement (at the latest activated segment) [10-12]. Ypenburg et al. (2007) showed that immediately after CRT surgery, the mitral valve regurgitation decreased, along with synchronization and LV contractility [13]. This result indicated that an immediate synchronization parameter change during CRT-on may be valuable for predicting response to CRT surgery. Reports on cardiac perfusion studies to evaluate LV synchronization are scarce and therefore the value of these studies remains unclear. This case report focuses on the possible relationship between immediate synchronization improvement during CRT-on and response to CRT surgery in regular follow-up exams. This study used the studies of RT3DE and GMPI study simultaneously.

Currently, ECG is the standard method of assessing CRT surgery response. Indicators of poor response include the presence of LBBB and QRS width increase [14]. Another common practice is using echocardiogram to assess synchronization improvement. According to the literature, there is a linear correlation between improved synchronization and decrease in LVEDV, decrease in LVESV, and increase in LVEF six months after CRT surgery [15]. As mentioned above in the results, the synchronization changes we observed during CRT-on seven months after CRT surgery by RT3DE are consistent with other published findings. The RT3DE bears several advantages including: a) real-time automatic calculation of the LV time-volume, time-phase curves in the same cardiac cycle simultaneously. b) Imaging not relying on any anatomic assumption of the LV. c) Not affected by cardiac muscle morphology. Therefore, it has the potential to serve as a useful tool for assessing the cardiac function after the CRT treatment.

The 2008 PROSPECT research identified potential limitations of the echocardiogram to predict the response to CRT [16], but the result itself was influenced by the non-random design, differences in equipment, and differences in surgery technique [17]. We also observed a few limitations of the RT3DE, which was reconstructed from 2D images obtained during four cardiac cycles. The 3-D image reconstruction caused slight delays and thus cannot be strictly used as real-time image assessment. Furthermore, it can easily be affected by the patient's respiratory movements.

Another useful way to assess synchronization and contractility is GMPI. During our study, the phase distribution parameters (BW, SD), and the hemodynamic values (LVEDV, LVESV and LVEF) were reliably achieved during CRT-on. The values are parallel to the RT3DE results, although mildly lower. Previous study showed that the parameters were slightly affected by GMPI software types with emory cardiac toolbox (ECTb) but not quantitative gated SPET (QGS) analysis results closer to cardiac catheterization [18].

The latest activated segment can be determined by phase value. The viability of the myocardium can be determined by the intensity of tracer uptake. As described in the literature, the electrode placement in the scarred myocardium or in a non-viable segment can significantly decrease the response to CRT. The comprehensive superposition of these two analyses will help determine the optimal site of pacemaker electrode implant (Figures 4C&D).

Overall, our case report indicates the value of assessing immediate synchronization parameters change to predict CRT response by comparing CRT-on and CRT-off conditions through a nuclear medicine cardiac perfusion study and RT3DE. In addition, the GMPI study can help assess the viability of the myocardium and the latest activated segment to determine where to place the pacemaker electrode implant. We will try using both GMPI and RT3DE in the future studies of initial CRT planning.

In conclusion,our study uniquely indicated that an immediate synchronization parameter changes during CRT-on in comparison to CRT-off may be valuable for predicting response to CRT surgery using either GMPI over RT3DE. We prefer GMPI as it provides additional useful information like myocardium viability

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The authors of this study declare no conflicts of interest

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