Hemodynamic Improvement in Cardiac Resynchronization Does Not Require Improvement in Left Ventricular Rotation Mechanics: Three-Dimensional Tagged MRI Analysis

Running Title: Cardiac Resynchronization and Ventricular Rotation

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Abstract

Background: Earlier studies have yielded conflicting evidence whether cardiac resynchronization therapy (CRT) improves left ventricular (LV) rotation mechanics or not.

Methods and Results: In dogs with left bundle branch block and pacing-induced heart failure (LBBB+HF, n=7), we studied the effects of CRT on LV rotation mechanics in vivo using three-dimensional (3-D) tagged MRI with temporal resolution of 14msec. CRT significantly improved hemodynamic parameters, but did not significantly change the LV rotation or rotation rate. LV torsion, defined as LV rotation of each slice with respect to that of the most basal slice, was not significantly changed by CRT. CRT did not significantly change the LV torsion rate. There was no significant circumferential regional heterogeneity (anterior, lateral, inferior and septal) in the LV rotation mechanics in either LBBB+HF or CRT, but there was significant apex-base regional heterogeneity.

Conclusions: CRT acutely improves hemodynamic parameters without improving LV rotation mechanics. There is no significant circumferential regional heterogeneity of LV rotation mechanics in the mechanically dyssynchronous heart. These results suggest that the LV rotation mechanics is an index of global LV function which requires coordination of all regions of the LV, and improvement in the LV rotation mechanics appears to be a specific but not sensitive index of acute hemodynamic response to CRT.

Key Words: MRI, tagging, ventricular function, mechanics, torsional deformation
Introduction

Left ventricular (LV) rotation mechanics represents a critical link that converts one-dimensional (1-D) shortening of obliquely aligned myofibers into three-dimensional (3-D) ventricular contraction. LV torsion is an important index of cardiac function, which is known to decrease in heart failure.

Cardiac resynchronization therapy (CRT) improves hemodynamics, symptoms and decreases mortality in patients with moderate-to-severe heart failure associated with an intraventricular conduction delay, most commonly of a left bundle branch block (LBBB) type. Some evidence suggests that CRT may acutely improve LV rotation mechanics, and that improvement in LV rotation mechanics may be used to identify CRT responders. However, another line of evidence reports that CRT does not improve LV rotation mechanics at all, even in responders. This discrepancy may arise from technical and interpretative limitations of two-dimensional (2-D) echocardiography that was used in these studies. Correlation of LV rotation mechanics between 2-D echocardiography and 2-D tagged MRI has been well established, but 2-D imaging cannot assess through-plane motion of the heart chambers that is a part of dynamic rotation mechanics during the cardiac cycle. In addition, a recent large multicenter study demonstrated that no single echocardiographic parameter can accurately identify CRT responders primarily due to high levels of both interobserver and intraobserver variability.

In the present study, we sought to study the acute effects of CRT on LV rotation mechanics using 3-D tagged MRI in dogs with left bundle branch block (LBBB) and tachycardia-induced cardiomyopathy. Three-dimensional tagged MRI is the gold standard technique to measure myocardial motion in vivo, which allowed objective and extensive...
mapping of 3-D displacement field within the LV. We also evaluated for regional heterogeneities of LV rotation mechanics in both circumferential and apex-base directions.

Methods

All studies were performed according to the *Position of the American Heart Association on Research Animal Use*<sup>9</sup>. All protocols were approved by the Animal Care and Use Committee of the Johns Hopkins University School of Medicine and the National Heart, Lung, and Blood Institute. A subset of data included in this study has been presented previously in our reports<sup>10, 11</sup>, which analyzed mechanical dyssynchrony.

*Experimental protocol.* Experimental details have been described previously<sup>10</sup>. Briefly, seven adult mongrel dogs (20-30kg) underwent radiofrequency ablation of the left bundle branch and 3-4 weeks of rapid ventricular pacing (210-250bpm) to create pacing-induced heart failure (HF). The animals with mechanical dyssynchrony and heart failure were anesthetized, and MRI-compatible pacing leads were positioned in the right atrium (RA), epicardial mid-LV free wall (LV), and right ventricular anteroapex (RV) via median sternotomy. Chamber hemodynamics was measured with an MR-compatible micromanometer (Millar, SPC-350, 5F). Hearts were paced at the RA (LBBB+HF), or LV plus RV (CRT) at 20bpm above intrinsic sinus rate and with antrioventricular (AV) delay selected to maximize dP/dt<sub>max</sub> for each pacing configuration. Tagged cine MRI in 3 orthogonal directions (2 short-axis and 1 long-axis orientation) were acquired for each pacing protocol at the temporal resolution of 14.0-14.6 msec which were used to derive 3-D displacement field and finite strains (Figure 1A, Supplemental Movie 1 and 2).

*Data analysis.* Cartesian 3-D coordinates (x, y, z) of a total of 192 material points at LV midwall (= 24 points on an LV short-axis slice x 8 slices) at each time frame were derived from
the 3-D displacement field (Figure 1B). LV volume (LVV) at each time frame was defined as the sum of space-filling multiple tetrahedral volumes created by the LV midwall material points. End diastole (ED) and end systole (ES) were defined as the time of the maximum and minimum LVV, respectively.

At each time frame, all marker coordinates were transformed into a moving cylindrical coordinate system \((r, \theta, z)\) with the origin at the centroid of the material points of the most basal LV short-axis slice, the z-axis passing through the centroid of the material points defining the most apical short-axis LV plane. For each LV short-axis slice, overall rotation (in degrees) was defined at each time frame as the average angular displacement \((\theta)\) of the 24 material points on each LV short-axis slice, and rotation of each LV region (anterior, lateral, inferior, and septal) (Figure 1C) was calculated by averaging the corresponding six circumferential material points at those locations. Torsion (in degrees) was defined as LV rotation of each region of each slice with respect to that of the corresponding region of the most basal short-axis slice. Both rotation and torsion were defined as zero at ED, and positive rotation was defined as counterclockwise as viewed from apex to base (Figure 1C). During systole in normal hearts, the apex has a positive (counterclockwise) rotation and the base a negative (clockwise) rotation, resulting in a positive (counterclockwise) torsion. The time course of rotation and torsion was linearly interpolated over time to yield the same number of data points during the cardiac cycle in each animal.

**Statistical analysis.** Values are mean ± SD (n=7) unless otherwise specified. A Student’s t test was used to compare peak LV rotation, torsion, rotation rate and torsion rate with and without CRT. Two-factor repeated-measures (RM) ANOVA was used to evaluate regional heterogeneity of the LV rotation mechanics with respect to circumferential (anterior, lateral, inferior and septal) and apex-base (slice 1 through 8) directions. The results were also confirmed
by mixed effects models that treated the dogs as a random effect as opposed to a fixed effect. Statistics were performed using SigmaStat 3.0 (SPSS, Inc., Chicago, Illinois) and JMP 6 (SAS Institute, Inc., Cary, NC).

**Results**

Hemodynamic parameters are summarized in Table 1. CRT significantly improved peak LV pressure (P<0.001), LV end-diastolic pressure (LVEDP) (P<0.002), dP/dt_{max} (P<0.0002), dP/dt_{min} (P<0.01), LV end-systolic volume (LVESV) (P<0.001), stroke volume (SV) (P<0.04), and ejection fraction (EF) (P=0.02).

*LV rotation mechanics*. Overall, CRT did not significantly change the maximum or minimum rotation (Table 2). However, CRT significantly shortened the time to the maximum rotation, which came immediately prior to end systole. In addition, CRT significantly shortened the time to the minimum rotation. This indicates significant shortening of an initial large, brief negative (clockwise) rotation, which peaked at around 40 msec in the the mechanically dyssynchronous hearts (LBBB+HF) (Figure 2).

CRT did not significantly change the maximum or minimum rotation rate (Table 3). However, CRT significantly shortened the time to the maximum rotation rate, which came immediately following the initial large, brief negative (clockwise) rotation (Figure 2). CRT also significantly shortened the time to the minimum rotation rate in apical slices. This reflects a significant shift of the time of minimum rotation rate to immediately after end systole, which is likely in the isovolumic relaxation phase.

CRT did not significantly change the maximum or minimum torsion, or the time to the maximum or minimum torsion (Table 4). CRT did not significantly change the maximum or
minimum torsion rate (Table 5). However, CRT significantly shortened the time to the maximum torsion rate, which came at the beginning of contraction (Figure 2).

**Regional assessment of LV rotation mechanics.** Regional heterogeneity of LV rotation mechanics was evaluated in circumferential (anterior, lateral, inferior and septal) and apex-base (slice 1 through 8) directions (Supplemental Figure 1, 2). Overall, the mechanically dyssynchronous hearts (LBBB+HF) showed a similar time course in all four regions, characterized by an initial brief negative (clockwise) rotation followed by a long systolic counterclockwise rotation, which peaked beyond end systole at the base (slice 8).

In the mechanically dyssynchronous hearts (LBBB+HF), there was no significant circumferential regional heterogeneity in any indices of the LV rotation mechanics (Supplemental Table). However, as expected, there was significant apex-base regional heterogeneity in the maximum rotation, maximum torsion, maximum and minimum torsion rate (P<0.001), reflecting an incremental nature of LV rotation as a function of the distance from the base. CRT did not significantly change the circumferential regional heterogeneity, and there was no significant circumferential regional heterogeneity in any indices of the LV rotation mechanics (Supplemental Table).

In summary, there was no significant circumferential regional heterogeneity (anterior, lateral, inferior and septal) in the LV rotation mechanics in either LBBB+HF or CRT, but there was significant apex-base regional heterogeneity.

**Discussion**

The present study used 3-D tagged cine MRI to examine the effects of CRT on LV rotation mechanics. Our results indicate that CRT clearly improves hemodynamics, however,
CRT does not improve LV rotation mechanics. These results suggest that LV rotation mechanics may not be an essential component of LV function.

*Effects of CRT on LV rotation mechanics in the mechanically dyssynchronous heart.*

Normal LV torsional deformation begins with a brief clockwise torsion (untwisting or pre-twisting) during isovolumic contraction phase, resulting from basal counterclockwise rotation and apical clockwise rotation, because endocardially-located Purkinje fibers activate endocardial myofibers first\(^{15}\). Our results show that this brief clockwise torsion is absent in the mechanically dyssynchronous hearts (LBBB +HF), because the normal Purkinje conduction, or the normal endocardial-to-epicardial activation sequence, is disrupted. Instead, all slices make a relatively large and simultaneous clockwise rotation (Figure 2), which likely results from an early activation of inferoseptal LV which is the site of LBBB in this model. All slices then made a long counterclockwise rotation during systole, which peaked beyond end systole at the base (slice 1). This systolic counterclockwise rotation at the basal slice diminished the magnitude of peak instantaneous torsion.

CRT diminished the duration of the initial simultaneous clockwise rotation by synchronizing the RV and LV activation (Figure 2). However, CRT did not recover the brief clockwise torsion during isovolumic contraction which is seen in normal heart due to endocardial activation\(^{15}\). This is because both the RV and LV leads in CRT electrically stimulate the LV from the epicardium, or from the outer surface. Epicardial pacing reverses normal endocardial-to-epicardial activation sequence, and mechanical activation indeed begins in the epicardium\(^{16}\). The mechanical activation of the epicardium causes counterclockwise LV torsion because the epicardial fiber is directed to approximately -60 degrees with reference to the circumferential direction\(^{17}\).
CRT also recovered basal systolic clockwise rotation, as seen in normal heart. The combination of basal clockwise and apical counterclockwise rotation during systole appears to contribute to maximizing peak instantaneous torsion. However, CRT did not significantly change the maximum or minimum rotation in any slice (Table 2). The net effect is that CRT did not significantly change the maximum torsion (Table 4).

Although CRT did not significantly change the maximum or minimum rotation rate, CRT did significantly shift the time of the minimum rotation rate and the minimum torsion rate to the isovolumic relaxation phase in apical slices (P<0.001, Table 3). This could represent improvement of LV diastolic suction\(^1\), but because the minimum torsion rate is not significantly different (Table 5), its mechanical effect is unclear.

**Regional assessment of LV rotation mechanics with and without CRT.** In the mechanically dyssynchronous heart, regional heterogeneity of LV wall motion with presence of early- (septal) and late-activated (lateral) regions is easily recognized by clinical imaging modalities, such as echocardiogram and MRI. In addition, regional mechanics derived from wall motion is significantly different between early- and late-activated regions\(^1\). However, our results indicate that there is no significant circumferential (anterior, lateral, inferior and septal) regional heterogeneity in LV rotation mechanics of the mechanically dyssynchronous heart, even though LV rotation is also derived from wall motion.

Our results may simply reflect the fact that LV rotation is a global motion which results from coordination of all regions of the LV. This concept is supported by the fact that rotation mechanics correlates well with indices of global LV function rather than regional function\(^2\). In fact, our finding is consistent with a 3-D tagged MRI study by Sorger et al\(^1\) who found no
significant regional heterogeneity of LV rotation mechanics in normal dog hearts with mechanical dyssynchrony by RV pacing.

Effects of CRT on hemodynamics and LV rotation mechanics. Our results demonstrate that CRT significantly improves hemodynamics without improving LV rotation mechanics. This suggests that hemodynamic improvement in CRT does not require improvement of LV rotation mechanics.

To understand the relationship between hemodynamics and LV rotation mechanics, we need to consider what the primary hemodynamic effect of CRT is. In our data, CRT significantly decreased LVEDP, a clinical index of preload (Table 1). However, CRT does not typically change the LV end-diastolic volume (LVEDV), which reflects physiological preload more accurately. CRT significantly increased ejection fraction (EF), as clinically observed by echocardiography. EF can be increased in increased preload, decreased afterload or increased contractility, but in this case the primary cause of increased EF in CRT is increased stroke volume (SV) due to reduction in LV end-systolic volume (LVESV), which is clinically used to identify responders to CRT. CRT increased peak LV pressure, an index of afterload (Table 1), but this is secondary to an increase in SV. CRT also significantly increased dP/dt max, but this is also likely a dependent variable in response to increased afterload because mechanical synchronization does not change the end-systolic pressure-volume relationship (ESPVR), thus does not increase contractility, of the mechanically dyssynchronous heart. In summary, the primary hemodynamic effect of CRT is an increase in SV due to mechanical synchronization, and other apparent hemodynamic improvements (LVEDP, ESV, EF, peak LVP, dP/dt) are secondary effects.
Because LV rotation results from shortening of obliquely oriented myofibers, a change in LV chamber size, or SV when EDV is constant, should uniquely determine the extent of LV rotation. Earlier studies have shown that an increase in SV increases LV rotation and torsion when contractility is constant25.

An additional factor to consider is that CRT essentially uses epicardial pacing to stimulate the LV from both the septum and the lateral walls. As described above, epicardial pacing alters normal transmural activation sequence, and the reverse transmural mechanical activation sequence16 alone appears to reduce LV rotation and torsion. In a 3-D tagged MRI study, Sorger et al14 found that biventricular pacing in normal dog heart disrupts normal transmural gradient in rotation, and significantly reduces peak LV rotation and torsion without significant changes in hemodynamics compared to atrial pacing. This finding indicates that the normal endocardial-to-epicardial electrical activation sequence is critical in generating the normal LV rotation mechanics. However, in the studies by Sorger et al14 biventricular pacing was performed without any AV delay. This likely abolished atrial kick and decreased preload, which may have contributed to a decrease in LV rotation and torsion compared with those of normal AV conduction25.

In our data, these positive and negative effects of CRT on the LV rotation mechanics appear to cancel each other, therefore the net result is that CRT did not significantly change the LV rotation mechanics. The positive effect of CRT on the LV rotation mechanics is likely dependent on the magnitude of improvement in SV25. This concept is demonstrated by the fact that LV torsion was unchanged in CRT responders (defined as reduction of ESV >15%8), and worsened in non-responders7. The negative effect of CRT on the LV rotation mechanics by altering the normal transmural mechanical activation sequence may be relatively constant, due to
a local nature of electrical pacing effects. It may be possible to minimize or abolish the negative effect and improve the LV rotation mechanics by pacing the LV endocardium in CRT, i.e. septal endocardium and lateral endocardium. In fact, a recent report by Mills et al suggests that LV endocardial pacing tends to maintain regional and global cardiac mechanics26.

In summary, the presence of both the positive and the negative effects can explain the apparently conflicting effects of CRT on the LV rotation mechanics despite consistent hemodynamic improvements3, 7.

Clinical implications. Improvement in the LV rotation mechanics would identify CRT responders, because it appears to be associated with improvement in SV. However, because CRT inherently has a negative effect on the LV rotation mechanics by epicardial pacing, the LV rotation mechanics could only be marginally improved or not changed at all in some subsets of patients. Therefore, CRT responders could have no improvement in the LV rotation mechanics, as in our data set. In summary, the LV rotation mechanics is a specific but not sensitive index of identifying CRT responders.

Limitations. Because the animals in our study were not known to have coronary artery disease, by definition, this is a model of non-ischemic cardiomyopathy. There is a possibility that effects of CRT on LV rotation mechanics may be different between ischemic and non-ischemic cardiomyopathy. However, recent reports6, 7 suggest that the effects of CRT on LV rotation mechanics are not significantly different between ischemic and non-ischemic cardiomyopathy.

Because congestive heart failure in this model is reversible over 24-48 hours once the pacing is discontinued27, this animal model may not be suitable for evaluating the chronic effects of CRT on hemodynamic parameters and LV rotation mechanics. However, this is an excellent model to evaluate the acute effects of CRT on hemodynamic parameters and LV rotation
mechanics. In addition, this model recapitulates many biochemical, molecular, and structural features relevant to human heart failure, and its mechanical response to CRT is analogous to that in patients with dilated cardiomyopathy and conduction delay\textsuperscript{10}.

The 3D displacement that we measured in open-chest, anesthetized dogs may not accurately reflect that of closed-chest, conscious animals. Some of the LV rotation mechanics that we observed may be specific to this model. For example, LV rotation mechanics may be different at a different level of block of LBBB. This study examined LV rotation mechanics only acutely, and long-term effects of CRT on LV rotation mechanics was not assessed in this study.

In addition, acute hemodynamic improvement with CRT may not be a surrogate for long-term outcomes such as reverse remodeling and improvement in mortality. However, a recent report by Steendijk \textit{P et al}\textsuperscript{28} demonstrates that hemodynamic improvements shown in acute settings are maintained chronically, which suggests that hemodynamic improvements may contribute to the long-term clinical outcomes.

In conclusion, CRT significantly improves hemodynamics without improving LV rotation mechanics. There is no significant circumferential regional heterogeneity of LV rotation mechanics in the mechanically dyssynchronous heart. Therefore, the LV rotation mechanics is an index of global LV function which requires coordination of all regions of the LV, and improvement in the LV rotation mechanics appears to be a specific but not sensitive index of acute hemodynamic response.
Acknowledgement

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Funding Sources

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Disclosures

None.
References


### Table 1.

<table>
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<tr>
<th></th>
<th>LBBB+HF</th>
<th>CRT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>123±13</td>
<td>123±13</td>
<td>n.s.</td>
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<tr>
<td>AV delay (ms)</td>
<td>144±10</td>
<td>69±18</td>
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<td>Peak LV pressure (mmHg)</td>
<td>86.8±7.7</td>
<td>97.4±12.6</td>
<td>&lt;0.001</td>
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<td>LVEDP (mmHg)</td>
<td>14.0±4.5</td>
<td>11±3.2</td>
<td>&lt;0.002</td>
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<td>dP/dt&lt;sub&gt;max&lt;/sub&gt; (mmHg/s)</td>
<td>1048±242</td>
<td>1392±413</td>
<td>&lt;0.0002</td>
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<td>dP/dt&lt;sub&gt;min&lt;/sub&gt; (mmHg/s)</td>
<td>-960±162.2</td>
<td>-1152±250</td>
<td>&lt;0.01</td>
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<tr>
<td>LVEDV (mL)</td>
<td>62±26</td>
<td>60±26</td>
<td>0.07</td>
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<tr>
<td>LVESV (mL)</td>
<td>49±27</td>
<td>46±28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SV (mL)</td>
<td>13±6</td>
<td>15±6</td>
<td>&lt;0.04</td>
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<tr>
<td>EF (%)</td>
<td>23±12.7</td>
<td>27.5±16.2</td>
<td>0.02</td>
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</table>

**Hemodynamics.** LBBB+HF, left bundle branch block with heart failure; CRT, cardiac resynchronization therapy; AV, atrioventricular; LVEDP, left ventricular end-diastolic pressure; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; SV, stroke volume; EF, ejection fraction.

### Table 2.

<table>
<thead>
<tr>
<th>Rotation</th>
<th>Maximum</th>
<th>Minimum</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>LBBB+HF</td>
<td>CRT</td>
</tr>
<tr>
<td></td>
<td>Value (deg)</td>
<td>Time (ms)</td>
</tr>
<tr>
<td>Slice 1 (base)</td>
<td>2.0±7.5</td>
<td>355±40</td>
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<td>Slice 2</td>
<td>2.4±7.5</td>
<td>343±39</td>
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<tr>
<td>Slice 3</td>
<td>3.1±7.5</td>
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<tr>
<td>Slice 4</td>
<td>3.6±7.6</td>
<td>343±39</td>
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<tr>
<td>Slice 5</td>
<td>4.0±7.6</td>
<td>343±39</td>
</tr>
<tr>
<td>Slice 6</td>
<td>4.6±7.4</td>
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<tr>
<td>Slice 7</td>
<td>5.2±7.2</td>
<td>292±33</td>
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<tr>
<td>Slice 8 (apex)</td>
<td>5.6±7.5</td>
<td>292±33</td>
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</table>

**LV rotation.** Values are mean±SD. *: P<0.05 vs. LBBB+HF. Abbreviations as in Table 1.
### Table 3

<table>
<thead>
<tr>
<th>Rotation Rate (Value x10^{-5})</th>
<th>Maximum</th>
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<tbody>
<tr>
<td></td>
<td>LBBB+HF</td>
<td>CRT</td>
</tr>
<tr>
<td></td>
<td>Value (deg/s)</td>
<td>Time (ms)</td>
</tr>
<tr>
<td>Slice 1 (base)</td>
<td>3.3±9.5</td>
<td>51±6</td>
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<tr>
<td>Slice 2</td>
<td>3.3±9.2</td>
<td>51±6</td>
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<tr>
<td>Slice 3</td>
<td>3.6±8.9</td>
<td>51±6</td>
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<tr>
<td>Slice 4</td>
<td>3.8±8.9</td>
<td>51±6</td>
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<tr>
<td>Slice 5</td>
<td>4.4±8.2</td>
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<tr>
<td>Slice 6</td>
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<tr>
<td>Slice 7</td>
<td>5.1±7.8</td>
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<tr>
<td>Slice 8 (apex)</td>
<td>5.1±7.9</td>
<td>152±17</td>
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**LV rotation rate.** Values are mean±SD. *: P<0.05 vs. LBBB+HF. Abbreviations as in Table 1.

### Table 4

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<tr>
<th>Torsion</th>
<th>Maximum</th>
<th>Minimum</th>
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<tr>
<td></td>
<td>LBBB+HF</td>
<td>CRT</td>
</tr>
<tr>
<td></td>
<td>Value (deg)</td>
<td>Time (ms)</td>
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<tr>
<td>Slice 1 (base)</td>
<td>0.0±0.0</td>
<td>0±0</td>
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<tr>
<td>Slice 2</td>
<td>0.6±0.7</td>
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<td>Slice 3</td>
<td>1.6±1.1</td>
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<td>Slice 4</td>
<td>2.6±1.2</td>
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<td>Slice 5</td>
<td>3.5±1.4</td>
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<td>Slice 6</td>
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<td>Slice 7</td>
<td>4.7±1.6</td>
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<tr>
<td>Slice 8 (apex)</td>
<td>5.3±1.9</td>
<td>254±29</td>
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**LV torsion.** Values are mean±SD. *: P<0.05 vs. LBBB+HF. Abbreviations as in Table 1.
Table 5

<table>
<thead>
<tr>
<th>Torsion rate (Value x 10^-5)</th>
<th>Maximum</th>
<th>Minimum</th>
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<tbody>
<tr>
<td></td>
<td>LBBB+HF</td>
<td>CRT</td>
</tr>
<tr>
<td></td>
<td>Value (deg/s)</td>
<td>Time (ms)</td>
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<tr>
<td>Slice 1 (base)</td>
<td>0.0±0.0</td>
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<tr>
<td>Slice 2</td>
<td>0.90±1.4</td>
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<td>Slice 3</td>
<td>1.7±1.6</td>
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<td>Slice 4</td>
<td>2.2±1.5</td>
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<tr>
<td>Slice 8 (apex)</td>
<td>3.9±1.5</td>
<td>165±19</td>
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</table>

Values are mean±SD. *: P<0.05 vs. LBBB+HF. Abbreviations as in Table 1.
Figure Legends

Figure 1. A. Tagged cine MR images acquired in 3 orthogonal directions (horizontal, vertical short-axis and long-axis). B. 3-D displacement map derived from tagged MRI. Each arrow (red) on the mesh represents a displacement vector at a total of 192 material points at LV midwall (= 24 points on an LV short-axis slice x 8 slices), which points from end diastole (ED) to end systole (ES). Systolic rotation is clockwise at the basal slice and counterclockwise at the apical slice, as viewed from the apex. C. Left ventricular regions. Anterior, lateral, inferior and septal regions are shown as viewed from the apex. Both LV rotation and torsion were defined as zero at ED, and positive direction defined as counterclockwise as viewed from apex.

Figure 2. LV rotational mechanics with and without CRT on each slice. Values are mean (n=7). ES, end systole. Other abbreviations as in Table 1.
Figure 1

A

End diastole

End systole

B

RV

LV

slice 1 (base)

slice 2

slice 3

slice 4

slice 5

slice 6

slice 7

slice 8 (apex)

C

Anterior

Septum

RV

LV

Lateral

Inferior

Positive rotation

Short Axis

Long Axis
Figure 2

Rotation

LBBB+HF

CRT

Torsion

LBBB+HF

CRT

Angle (degree)

ES

Rate (deg/sec)

Time (msec)

slice 1 (base)

slice 2

slice 3

slice 4

slice 5

slice 6

slice 7

slice 8 (apex)
Hemodynamic Improvement in Cardiac Resynchronization Does Not Require Improvement in Left Ventricular Rotation Mechanics: Three-Dimensional Tagged MRI Analysis
Hiroshi Ashikaga, Christophe Leclercq, Jiangxia Wang, David Alan Kass and Elliot R. McVeigh

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# Supplemental Table

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<th>LBBB+HF Mixed Effects</th>
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Regional heterogeneity analysis. P values of regional heterogeneity analysis of indices of LV rotation mechanics with respect to circumferential (anterior, lateral, inferior and septal) and apex-base (slice 1 through 8) directions obtained from RMANOVA and a mixed effects model are shown.
Supplemental Figure 1. *LV rotation and torsion with and without CRT in each region.*

Values are mean (n=7). Abbreviations as in Figure 2.

Supplemental Figure 2. *LV rotation rate and torsion rate with and without CRT in each region.* Values are mean (n=7). Abbreviations as in Figure 2.

Supplemental Movie 1. *Sample tagged cine MRI for short-axis (left panel) and long-axis (right panel) slices during right atrial pacing in dogs with left bundle branch block and pacing-induced heart failure (LBBB+HF)* (Courtesy of Dr. Owen P. Faris).

Supplemental Movie 2. *Sample tagged cine MRI for short-axis (left panel) and long-axis (right panel) slices during biventricular pacing in dogs with left bundle branch block and pacing-induced heart failure (CRT)* (Courtesy of Dr. Owen P. Faris).