Contents lists available at ScienceDirect



Journal of Cardiovascular Computed Tomography

journal homepage: www.JournalofCardiovascularCT.com



Research paper

Motion correction of wide-detector 4DCT images for cardiac resynchronization therapy planning



Ashish Manohar^{a,b,c}, James Yang^d, Jed D. Pack^e, Gordon Ho^f, Elliot R. McVeigh^{d,f,g,*}

^a Division of Cardiovascular Medicine, Department of Medicine, Stanford University, Stanford, CA, USA

^b Department of Radiology, Stanford University, Stanford, CA, USA

^c Cardiovascular Institute, Stanford University, Stanford, CA, USA

^d Department of Bioengineering, University of California San Diego, La Jolla, CA, USA

^e Radiation Systems Lab, GE Global Research, Niskayuna, New York, USA

^f Department of Medicine, Division of Cardiology, University of California San Diego, La Jolla, CA, USA

⁸ Department of Radiology, University of California San Diego, La Jolla, CA, USA

ARTICLE INFO

Keywords: Cardiac 4DCT Motion correction LV mechanical activation Cardiac resynchronization therapy

ABSTRACT

Background: Lead placement at the latest mechanically activated left ventricle (LV) segments is strongly correlated with response to cardiac resynchronization therapy (CRT). We demonstrate the feasibility of a cardiac 4DCT motion correction algorithm (ResyncCT) in estimating LV mechanical activation for guiding lead placement in CRT.

Methods: Subjects with full cardiac cycle 4DCT images acquired using a wide-detector CT scanner for CRT planning/upgrade were included. 4DCT images exhibited motion artifact-induced false-dyssynchrony, hindering LV mechanical activation time estimation. Motion-corrupted images were processed with ResyncCT to yield motion-corrected images. Time to onset of shortening (TOS) was estimated in each of 72 endocardial segments. A false-dyssynchrony index (FDI) was used to quantify the extent of motion artifacts in the uncorrected and the ResyncCT images. After motion correction, the change in classification of LV free-wall segments as optimal target sites for lead placement was investigated.

Results: Twenty subjects (70.7 \pm 13.9 years, 6 female) were analyzed. Motion artifacts in the ResyncCT-processed images were significantly reduced (FDI: 28.9 \pm 9.3 % vs 47.0 \pm 6.0 %, p < 0.001). In 10 (50 %) subjects, ResyncCT motion correction yielded statistically different TOS estimates (p < 0.05). Additionally, 43 % of LV freewall segments were reclassified as optimal target sites for lead placement after motion correction.

Conclusions: ResyncCT significantly reduced motion artifacts in wide-detector cardiac 4DCT images, yielded statistically different time to onset of shortening estimates, and changed the location of optimal target sites for lead placement. These results highlight the potential utility of ResyncCT motion correction in CRT planning when using wide-detector 4DCT imaging.

1. Introduction

Cardiac resynchronization therapy (CRT) is an effective treatment for patients in heart failure and with left ventricular (LV) dyssynchrony.¹ However, 30–50 % of patients selected for CRT do not respond to the treatment.² Efforts to reduce the non-responder rate through better patient selection and optimal lead placement, primarily with echocardiography, have had limited success.^{3–5}

Cardiac magnetic resonance (CMR) strain imaging is an excellent modality for accurately and precisely estimating the timing of LV Modern four-dimensional x-ray computed tomography (4DCT) has immense potential for CRT planning. High spatial resolution 3D

https://doi.org/10.1016/j.jcct.2024.01.007

Received 16 October 2023; Received in revised form 11 December 2023; Accepted 7 January 2024 Available online 11 January 2024 1934-5925/© 2024 Society of Cardiovascular Computed Tomography. Published by Elsevier Inc. All rights reserved.

mechanical activation.^{6–8} Lead placement at LV sites with the latest mechanical activation, as determined by CMR, strongly correlates with CRT response.^{9–11} Thus, LV mechanical activation is established as an important parameter for guiding optimal lead placement. However, the complexity and limited availability of highly skilled CMR centers has hindered its routine clinical use for CRT planning. Additionally, 28 % of patients under consideration for CRT already have existing right ventricular pacing systems in place, serving as a contraindication for CMR imaging in many of these patients.¹²

^{*} Corresponding author. 9452 Medical Center Drive, La Jolla, CA 92037, USA. *E-mail address:* emcveigh@ucsd.edu (E.R. McVeigh).

Nomenclature				
CRT LV CMR 4DCT TOS UCSD FDI RS _{CT} LPS	cardiac resynchronization therapy left ventricle cardiac magnetic resonance four-dimensional computed tomography time to onset of shortening University of California San Diego false dyssynchrony index endocardial regional shortening lead placement score			
	F			

volumetric images of the heart can be acquired across the entire cardiac cycle using routine FDA approved scanning protocols with low radiation dose.^{13,14} Previous studies have investigated the use of 4DCT for LV dyssynchrony assessment and CRT planning. The Rinaldi lab^{15,16} demonstrated that leads placed at sites determined optimal by cardiac CT resulted in greater clinical response rates¹⁵ and superior acute hemodynamic responses.¹⁶ Truong et al.¹⁷ found that leads placed at sites detire major adverse cardiac events, defined as a composite end point of death, LV assist device, heart failure hospitalization, and cardiac transplantation. Fyenbo et al.¹⁸ reported that myocardial scar burden and proximity of scar to the LV pacing site were associated with CRT nonresponse.

These previous studies used either dual-source or wide-detector CT scanners, both having their advantages and disadvantages. Dual-source scanners offer higher temporal resolution which is beneficial for estimating timing of LV mechanical activation. However, due to their limited z-axis detector coverage, they can suffer from step-artifacts that arise during acquisition of the superior-to-inferior extent of the heart over multiple irregular heartbeats. It was previously reported that out of 147 subjects recruited for a retrospective CRT study using dualsource scanners, 37 subjects (25 %) had severe step-artifacts preventing the precise estimation of LV mechanics.¹⁹ Wide-detector scanners permit single-heartbeat single-table position acquisitions which is beneficial for imaging patients with arrythmias but have poorer temporal resolution and suffer from gantry-induced motion artifacts.²⁰ These motion artifacts affect the fidelity of edge locations; hence, impeding the precise measurement of timing of LV mechanical activation.²¹

Recent advances in motion correction technology²² have improved the temporal resolution of 4DCT images.²³ This is especially advantageous for wide-detector CT scanners: the enhanced temporal resolution, combined with the benefits of single-heartbeat and single-table position acquisitions, makes them promising imaging systems for CRT planning. Thus, the objective of this study was to demonstrate the feasibility of a validated cardiac CT motion correction algorithm, called ResyncCT,^{21,24} on clinically acquired 4DCT images of subjects under consideration for CRT. Using this cohort, we investigate the effect of ResyncCT on reducing motion artifacts in the 4DCT images and on estimating LV mechanical activation times for guiding lead placement in CRT.

2. Methods

2.1. Subjects

Twenty consecutive subjects with 4DCT images acquired for CRT planning/upgrade were included in this study. The scans were acquired and read by radiologists at the University of California San Diego (UCSD). Neither subject enrollment, image acquisition, image reconstruction, nor clinical diagnosis was modified for this study; the subjects were scanned, and images read as per routine clinical protocols established at UCSD for CRT evaluation. This retrospective study was approved by the

institutional review board at UCSD and adhered to the Declaration of Helsinki guidelines.

2.2. 4DCT imaging and left ventricle segmentation

All subjects were scanned with a 256-detector row scanner (Revolution CT, General Electric Healthcare, Chicago, IL) under established clinical imaging protocols for CRT planning at UCSD. The protocols included retrospective ECG-gated single-heartbeat full cardiac cycle imaging with no modulation of the x-ray tube current. The 256-detector row scanner had a z-axis coverage of 16 cm, permitting full heart volume imaging from a single table position. The gantry revolution time was 280 ms. The scans were acquired with tube voltages of 80 kVp (n = 3), 100 kVP (n = 16), and 120 kVp (n = 1) and a median tube current of 600 mA (interquartile range 430–720 mA). The images were reconstructed at 70 ms intervals (90° of rotation for a gantry revolution time of 280 ms) using the 'Standard' reconstruction kernel of the Revolution CT into 512 × 512 x 256 voxels. The median in-plane pixel spacing was 0.47 mm (interquartile range 0.45–0.48 mm) with a slice thickness of 0.625 mm for all images.

The reconstructed 4DCT images of each subject exhibited motion artifacts that were dependent on the direction of motion of the endocardial walls with respect to gantry position. These artifacts rotated synchronously with the orientation of the gantry, giving a false impression of dyssynchronous contraction.²⁰ The motion corrupted images are referred to hereafter as the uncorrected images. The uncorrected images were processed with a validated cardiac CT motion correction algorithm called ResyncCT^{21,24} to yield motion corrected images. ResyncCT works directly on a series of reconstructed DICOM images and leverages the power of conjugate pairs of partial angle reconstruction images for motion estimation and motion compensation. A version of ResyncCT called SnapShot Freeze 2 (General Electric Healthcare, Chicago, IL), is FDA approved and currently available on the Revolution CT (General Electric Healthcare, Chicago, IL) clinical scanner. The motion corrected images are referred to hereafter as the ResyncCT images.

For each subject, the LV blood volume was segmented from each time frame of the uncorrected and the ResyncCT images using a procedure previously described in detail.²⁵ The volume of the LV for each time frame was computed by summing the segmented 3D voxels. Meshes delineating the surface of the LV endocardium were then extracted from the segmented LV volumes.

2.3. False dyssynchrony index

All scans were acquired with a gantry revolution time of 280 ms. Individual time frames in the 4DCT image series were reconstructed at 70 ms intervals, with each time frame using $\sim 90^{\circ}$ of new projection views while the remaining views were old views shared with the previous time frame. This view sharing between consecutive reconstructed time frames means that only edges parallel to the central acquired views have their position sampled once, while edges sampled by the newest and oldest acquired views can be in two possible configurations. As a result, motion artifacts exist in 4DCT images that are dependent on the direction of wall motion with respect to the position of the gantry.^{20,24} These artifacts lead to erroneous estimates of LV mechanical activation because of the uncertainty in endocardial wall positions in the images (Fig. 1); hence, the artifact name "false dyssynchrony".²¹ The magnitude of the false dyssynchrony artifacts were quantified using a false dyssynchrony index (FDI); the derivation of the FDI is described in detail in the Supplemental Material (Figs. S1, S2).

2.4. LV mechanical activation time: time to onset of shortening (TOS)

LV mechanical activation was estimated as the 'time to onset of shortening' (TOS), computed from high-resolution endocardial regional



Fig. 1. Effect of ResyncCT motion correction on reduction of gantry induced motion artifacts. (a-b) Pronounced "double-wall" motion artifact in an example subject highlighted by the red ellipse in (**a**) the uncorrected images. In (**b**), ResyncCT improves the edge fidelity of the endocardial wall. (**c-d**) Difference images between two consecutive systolic time frames highlighting regions of LV wall motion derived from the (**c**) uncorrected and (**d**) ResyncCT images in an example subject. In (**c**), due to gantry-induced motion artifact, only one pair of LV walls parallel to each other (highlighted by the red arrows) move between the consecutive time frames. ResyncCT recovers motion of the walls uniformly over all LV regions as shown in (**d**). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

shortening $(RS_{CT})^{26,27}$ data (detailed information on the calculation of RS_{CT} and TOS from RS_{CT} can be found in the Supplemental Material, Fig. S3). The LV was divided into 72 endocardial segments: 18 in the circumferential direction (a segment every 20°) for each of 4 slices from apex to base along the LV long axis. The TOS was estimated for each of the 72 LV segments for both the uncorrected and the ResyncCT images for all subjects. The TOS is an important parameter in CRT planning; lead placement on the latest mechanically activated segments (highest TOS values) is strongly correlated with CRT response.^{10,19,28} Hence, understanding the effect of motion correction of 4DCT images on the fidelity of the TOS estimates is necessary.

2.5. Effect of ResyncCT on optimal lead placement for achieving CRT response

The previously published 'Lead Placement Score' (LPS) model was used to identify regions for optimal LV lead placement that yield the highest probability of achieving positive CRT response.¹⁹ The LPS model

provides a map of scores for all LV free-wall segments. The classification of LV segments as target sites for lead placement is as follows:

$$LV \text{ segment classification for lead placement} = \begin{cases} Poor & LPS \le -1\\ Good & -1 < LPS < 1\\ Best & LPS \ge 1 \end{cases}$$
(1)

Forty-eight of the total 72 LV segments were defined as free-wall segments. The dependence of LPS values on motion correction was tested by evaluating the LPS scores for all free-wall segments of all subjects independently from both the uncorrected and the ResyncCT images.

2.6. Statistical analysis

Continuous variables were expressed as their mean with standard deviation, unless otherwise specified. The FDI and TOS estimates between the uncorrected and ResyncCT images were tested for statistically significant differences using the two-sample *t*-test; a p-value <0.05 was

considered statistically significant. A reclassification table was used to examine the change in classifications (as listed in Eq. (1)) of the free-wall LV segments as target sites for lead placement before and after motion correction with ResyncCT.

3. Results

3.1. Subject characteristics

Six subjects were female (30 %), and the average age of the cohort was 70.7 \pm 13.9 years (median: 75 years; interquartile range: 62–79 years). The average dose length product across the 20 4DCT scans was 362.5 \pm 94.1 mGy-cm. Fourteen of the 20 subjects had existing pacing systems, demonstrating the utility of ResyncCT on images with metallic lead artifacts. Table 1 lists the subject characteristics.

3.2. False dyssynchrony

Fig. 2 highlights the pronounced effect of motion correction with ResyncCT on the position of the LV walls across the cardiac cycle. Fig. 2(a) and (b) show data derived from the uncorrected and ResyncCT images, respectively, in an example subject. The first rows in both Fig. 2(a) and (b) show central axial CT images from five consecutive systolic time frames. To highlight differences in the effect of heart wall motion, the second rows in both Fig. 2(a) and (b) show difference images between the consecutive time frames. In Fig. 2(a), only those walls moving perpendicular to the x-ray beam direction were updated between consecutive frames of the uncorrected images, leading to significant HU differences, as indicated by the red arrows. In contrast, those moving parallel to the x-rays were not updated and showed virtually no HU difference. As a result, pairs of walls were updated every other time frame in a series of 4DCT images reconstructed at time intervals corresponding to 90° of gantry rotation. The artifact seen in these images hinders the precise estimation of LV mechanical activation at various locations of the endocardial wall. Fig. 2(b) demonstrates the motion field recovered uniformly over all regions of the LV by ResyncCT. The reduction in falsedyssynchrony artifacts was quantified by the significantly lower FDI for the ResyncCT images (28.9 \pm 9.3 % vs 47.0 \pm 6.0 %, p < 0.001).

3.3. Effect of ResyncCT on LV mechanical activation: estimates of time to onset of shortening

Fig. 3(a) and (b) show two example subjects and the effect of ResyncCT on their TOS estimates. For each subject, the first row shows bullseye maps of TOS for the 72 LV segments, the second row shows short-axis slices for three consecutive systolic time frames (t1 = 70 ms, t2

Table 1

Subject	characteristics.
5	

	All subjects ($n = 20$)
Age, years	70.7 ± 13.9
Female, n (%)	6 (30)
Heartrate, bpm	69.1 ± 10.9
4DCT-derived EF, %	36.3 ± 17.8
4DCT-derived EDV, mL	273.8 ± 109.4
4DCT-derived ESV, mL	183.9 ± 107.3
CTDIvol, mGy	22.6 ± 5.9
DLP, mGy-cm	362.5 ± 94.1
Effective dose, mSv	5.1 ± 1.3
FDI, %	
Uncorrected	$47.0\pm6.0^{\rm a}$
ResyncCT	$28.9 \pm \mathbf{9.3^a}$

bpm: beats per minute; EF: ejection fraction; EDV: end diastolic volume; ESV: end systolic volume; CTDIvol: CT dose index; DLP: dose length product; FDI: false dyssynchrony index.

^a Denotes statistically significant differences.

= 140 ms, t3 = 210 ms), and the third row shows difference images of the short-axis slices between the three time frames (t2-t1 and t3-t2). The figures on the left are derived from the uncorrected images and the figures on the right are derived from the ResyncCT images for each subject. Fig. 3(a) shows a subject whose TOS map derived from the uncorrected images had higher values on the inferoseptal and anterolateral walls compared with those obtained from the ResyncCT images. Due to gantryinduced artifacts, the motion of these walls between time frames t2 and t1 was lost in the uncorrected images (red arrows; bottom left), leading to artifactually high TOS values representing an incorrect delay in the onset of contraction. ResyncCT recovered the motion field and improved the TOS estimates. Similarly, Fig. 3(b) shows a subject whose TOS map derived from the uncorrected images had higher values on the septum. Again, due to gantry-induced motion artifacts, the septum did not move between time frames t2 and t1 (red arrow; bottom left), producing the higher TOS estimates. As discussed in Sec 3.4, accurate TOS estimates are a key parameter for classifying LV myocardial tissue as "delayed".

Fig. 4 shows bullseye maps of the significant differences in TOS estimates between the uncorrected and the ResyncCT images over many of the 72 endocardial segments for all 20 subjects. In 10 (50 %) subjects, the differences in TOS values were statistically significant (p < 0.05). Fig. 4 also highlights the heterogenous subject-specific differences in the TOS estimates between the uncorrected and the ResyncCT images implying that individual motion correction is needed for each scan. The degree of motion correction achieved depends on the direction of motion of the endocardial walls with respect to the position of the gantry; thus, the effect of ResyncCT will vary between scans.

3.4. Effect of ResyncCT on guiding optimal lead placement

The change in classification of the LV free-wall segments before and after motion correction as either poor, good, or best target sites for lead placement is shown in Table 2. The rows correspond to the LV segment classes estimated from the uncorrected images and the columns correspond to those estimated from the ResyncCT images. There was a total of 960 segments, i.e., 20 subjects and 48 free-wall segments per subject. Ninety-six (10.0 %) segments were downgraded from good to poor target lead placement sites, and 11 (1.1 %) from best to poor after motion correction. Additionally, 85 (8.9 %) segments were upgraded from poor to good target lead placement sites, and 31 (3.2 %) from poor to best after motion correction. Overall, 43.4 % of all LV free-wall segments were reclassified after motion correction with ResyncCT.

4. Discussion

The main findings of this study demonstrate the necessity of motion artifact correction in cardiac 4DCT images acquired using single-source wide-detector scanners. The effect of a validated motion correction algorithm (ResyncCT) on the estimation of LV mechanical activation, measured as its 'time to onset of shortening', was investigated. This is especially important because LV lead placement on the latest mechanically activated segments is strongly correlated with CRT response. Motion correction with ResyncCT^{21,24} significantly reduced motion artifacts in the cardiac 4DCT images, leading to significantly different TOS estimates in half the subjects, and reclassification of 43 % of LV free-wall segments as optimal target sites for lead placement. These results highlight the potential utility of motion corrected wide-detector cardiac 4DCT imaging in estimating LV mechanical activation for CRT guidance.

4.1. CRT planning with 4DCT

Significant effort has been made to improve the CRT non-responder rate with echocardiography.²⁹ However, quantitative results with echocardiography are operator and vendor dependent leading to poor reproducibility.³⁰ CMR is an excellent modality to identify regions of scar and late activated LV segments to guide lead placement.^{9,11} Despite its



Fig. 2. False dyssynchrony and recovery of motion field with ResyncCT in an example subject. Data are presented for (**a**) the uncorrected images and (**b**) the ResyncCT images. For both (**a**) the uncorrected and (**b**) the ResyncCT images, the first rows display central axial CT images for five consecutive systolic time frames (t1 through t5), while the second rows show the corresponding difference images between these consecutive time frames. In (**a**), it is evident from the uncorrected images that pairs of endocardial walls perpendicular to each other are updated every other time frame (indicated by the red arrows, showing wall positions that have moved between consecutive time frames). In contrast, ResyncCT recovers a continuous motion field across all LV regions at each time frame, as demonstrated in (b). Also note the clarity of the right coronary artery in the ResyncCT motion-corrected images across all time frames. HU limits were set to [-100,600] and [-300,300] for the grayscale and difference images, respectively. LV: left ventricle; RCA: right coronary artery. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

advantages, it is primarily used in a research setting, mainly due to challenges in imaging patients with non-MRI compatible medical devices. However, both these modalities offer significantly higher temporal resolution than current 4DCT scanners. Thus, it is imperative to develop effective technologies to minimize motion artifacts and improve 4DCT temporal resolution. Previous studies have successfully used CT to estimate LV dyssynchrony and mechanical activation,^{16,17} correlating these parameters with clinical outcomes. The use of advanced technologies to

enhance 4DCT temporal resolution will further improve the fidelity and precision of these estimates.

Dual-source CT scanners yield images with higher temporal resolution (\sim 2x) than their single wide-detector counterparts. While this presents a significant advantage, the limited z-axis coverage of the current detectors (\sim 5 cm) on dual-source scanners poses difficulties for obtaining full-heart volume imaging, particularly in patients with irregular heartbeats and/or arrythmias. The patients must be scanned in helical or



Fig. 3. Effect of ResyncCT motion correction on the estimation of time to onset of shortening (TOS) in two example subjects (a) and (b). For each subject, the left column shows data from the uncorrected images, and the right column shows data from the ResyncCT images. Within each column for both subjects, the first row shows bullseye maps of TOS over all 72 segments of the LV, the second row shows short-axis slices for three consecutive systolic time frames, and the last row shows difference images of the short-axis slices between the three time frames. The bullseye plots are oriented according to the traditional American Heart Association 17-segment model. Red arrows show regions of the endocardium in which motion is not evident due to false dyssynchrony. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)



Fig. 4. Differences in time to onset of shortening (TOS) estimates between the uncorrected and ResyncCT images for all 20 subjects. Bullseye maps of the difference in TOS estimates across all 72 LV segments between the uncorrected and the ResyncCT images for all 20 subjects. For each subject, a bullseye map oriented according to the traditional American Heart Association 17-segment model is shown.

Table 2

Reclassification table for all 960 LV free-wall segments across all 20 subjects before and after motion correction. Each LV segment was classified as either a poor, good, or best target site for optimal lead placement. The rows correspond to LV segment classifications estimated from the uncorrected images, and the columns correspond to the classifications estimated from the ResyncCT motion corrected images. Percentages are given in parentheses.

		Re-classification of LV segments after ResyncCT motion correction		
		Poor target site for lead placement	Good target site for lead placement	Best target site for lead placement
Classification of LV segments prior to motion correction	Poor target site for lead placement Good target site for lead placement Best target site for lead placement	141 (14.7) 96 (10.0) 11 (1.1)	85 (8.9) 243 (25.3) 58 (6.0)	31 (3.2) 136 (14.2) 159 (16.7)

"step and shoot" axial mode over multiple heartbeats which may then yield step-artifacts, often rendering the images unanalyzable for the estimation of timing of mechanical events. Wider detector scanners (256or 320-detector rows) with effective motion estimation and motion compensation technologies are better suited for applications that require single heartbeat imaging.

4.2. Motion correction with ResyncCT

ResyncCT has previously been validated under controlled phantom experiments,²¹ the results from which highlight the high accuracy and precision of ResyncCT-derived TOS estimates of LV wall motion. The work reported here expands that validation of ResyncCT to clinically acquired human 4DCT studies in CRT patients. Another important

finding from the previous phantom studies was that the accuracy and precision of the TOS estimates were higher when measured on the constant motion profile of LV wall motion during systole vs. measuring the peak of pre-stretch; previous studies with tagged MRI used the peak of the strain curves to characterize mechanical activation delays.^{7,31,32} For this reason, the TOS in this study was defined as the time of the cardiac cycle when the LV endocardium shortened by 10 % during systolic contraction.

This study and previous work^{21,24} highlight the heterogenous effect of gantry-induced motion artifact on the TOS estimates. LV orientation, heart rate, LV systolic motion profile (velocity and acceleration), and gantry position with respect to LV wall motion during systole are some of the factors that make the corrections of ResyncCT specific to each scan. In some cases, the gantry and relative motion of the wall are aligned; hence, d ResyncCT will Appendix A. Supplementary data

Supplementary data to this article can be found online at https://do i.org/10.1016/j.jcct.2024.01.007.

References

- Prinzen FW, Vernooy K, Auricchio A. Cardiac resynchronization therapy. *Circulation*. 2013;128(22):2407–2418. https://doi.org/10.1161/ CIRCULATIONAHA.112.000112.
- Vernooy K, van Deursen CJM, Strik M, Prinzen FW. Strategies to improve cardiac resynchronization therapy. Nat Rev Cardiol. 2014;11(8):481–493. https://doi.org/ 10.1038/nrcardio.2014.67.
- Delgado V, Bax JJ. Assessment of systolic dyssynchrony for cardiac resynchronization therapy is clinically useful. *Circulation*. 2011;123(6):640–655. https://doi.org/10.1161/CIRCULATIONAHA.110.954404.
- Sung RK, Foster E. Assessment of systolic dyssynchrony for cardiac resynchronization therapy is not clinically useful. *Circulation*. 2011;123(6):656–662. https://doi.org/ 10.1161/CIRCULATIONAHA.110.954420.
- Heydari B, Jerosch-Herold M, Kwong RY. Imaging for planning of cardiac resynchronization therapy. JACC (J Am Coll Cardiol): Cardiovas Imag. 2012;5(1): 93–110. https://doi.org/10.1016/j.jcmg.2011.11.006.
- McVeigh ER, Prinzen FW, Wyman BT, Tsitlik JE, Halperin HR, Hunter WC. Imaging asynchronous mechanical activation of the paced heart with tagged MRI. Magn Reson Med. 1998;39(4):507–513. https://doi.org/10.1002/mrm.1910390402.
- Wyman BT, Hunter WC, Prinzen FW, McVeigh ER. Mapping propagation of mechanical activation in the paced heart with MRI tagging. Am J Physiol Heart Circ Physiol. 1999;276(3):881–891. https://doi.org/10.1152/ajpheart.1999.276.3.H881.
- Wyman BT, Hunter WC, Prinzen FW, Faris OP, McVeigh ER. Effects of single- and biventricular pacing on temporal and spatial dynamics of ventricular contraction. *Am J Physiol Heart Circ Physiol*. 2002;282(1):372–379. https://doi.org/10.1152/ ajpheart.2002.282.1.H372.
- Auger DA, Bilchick KC, Gonzalez JA, et al. Imaging left-ventricular mechanical activation in heart failure patients using cine DENSE MRI: validation and implications for cardiac resynchronization therapy. J Magn Reson Imag. 2017;46(3): 887–896. https://doi.org/10.1002/jmri.25613.
- Bilchick KC, Kuruvilla S, Hamirani YS, et al. Impact of mechanical activation, scar, and electrical timing on cardiac resynchronization therapy response and clinical outcomes. J Am Coll Cardiol. 2014;63(16):1657–1666. https://doi.org/10.1016/ j.jacc.2014.02.533.
- Taylor RJ, Umar F, Panting JR, Stegemann B, Leyva F. Left ventricular lead position, mechanical activation, and myocardial scar in relation to left ventricular reverse remodeling and clinical outcomes after cardiac resynchronization therapy: a featuretracking and contrast-enhanced cardiovascular magnetic r. *Heart Rhythm.* 2016; 13(2):481–489. https://doi.org/10.1016/j.hrthm.2015.10.024.
- Daubert JC, Saxon L, Adamson PB, et al. EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management: a registered branch of the European Society of Cardiology (ESC), and the Heart Rhythm Society; and in col. *Europace*. 2012;14(9): 1236–1286. https://doi.org/10.1093/europace/eus222, 2012.
- Chen MY, Shanbhag SM, Arai AE. Submillisievert median radiation dose for coronary angiography with a second-generation 320-detector row CT scanner in 107 consecutive patients. *Radiology*. 2013;267(1):76–85. https://doi.org/10.1148/ radiol.13122621.
- Manohar A, Colvert GM, Ortuño JE, et al. Regional left ventricular endocardial strains estimated from low-dose 4DCT: comparison with cardiac magnetic resonance feature tracking. *Med Phys.* 2022;49(9):5841–5854. https://doi.org/10.1002/ mp.15818.
- Behar JM, Rajani R, Pourmorteza A, et al. Comprehensive use of cardiac computed tomography to guide left ventricular lead placement in cardiac resynchronization therapy. *Heart Rhythm.* 2017;14(9):1364–1372. https://doi.org/10.1016/ i.hrthm.2017.04.041.
- Gould J, Sidhu BS, Sieniewicz BJ, et al. Feasibility of intraprocedural integration of cardiac CT to guide left ventricular lead implantation for CRT upgrades. J Cardiovasc Electrophysiol. 2021;32(3):802–812. https://doi.org/10.1111/jce.14896.
- Truong QA, Szymonifka J, Picard MH, et al. Utility of dual-source computed tomography in cardiac resynchronization therapy—DIRECT study. *Heart Rhythm.* 2018;15(8):1206–1213. https://doi.org/10.1016/j.hrthm.2018.03.020.
- Fyenbo DB, Sommer A, Kühl JT, et al. Transmural myocardial scar assessed by cardiac computed tomography. J Comput Assist Tomogr. 2019;43(2):312–316. https://doi.org/10.1097/RCT.0000000000824.
- Manohar A, Colvert GM, Yang J, et al. Prediction of cardiac resynchronization therapy response using a lead placement score derived from 4-dimensional computed tomography. *Circulation: Cardiovas Imag.* 2022;15(8):603–613. https://doi.org/ 10.1161/CIRCIMAGING.122.014165.
- Kidoh M, Shen Z, Suzuki Y, et al. False dyssynchrony: problem with image-based cardiac functional analysis using x-ray computed tomography. In: Flohr TG, Lo JY, Gilat Schmidt T, eds. *Medical Imaging 2017: Physics of Medical Imaging.* 2017: 101321U. https://doi.org/10.1117/12.2250257.
- Manohar A, Pack JD, Schluchter AJ, McVeigh ER. Four-dimensional computed tomography of the left ventricle, Part II: estimation of mechanical activation times. *Med Phys.* 2022;49(4):2309–2323. https://doi.org/10.1002/mp.15550.
- Kyme AZ, Fulton RR. Motion estimation and correction in SPECT, PET and CT. Phys Med Biol. 2021;66(18):18TR02. https://doi.org/10.1088/1361-6560/ac093b.

motion artifacts in the CT images are not pronounced and ResyncCT will have minimal effect. This is reflected by the segments in Fig. 4 in which ResyncCT did not bring about an appreciable change in the TOS estimates. However, it is impossible to predict the interaction of wall motion with gantry orientation, so ResyncCT is needed in case there are profound motion artifacts. Detailed information on gantry-induced motion artifacts and their dependence on gantry orientation and wall motion can be found in Pack et al.²⁴ and Manohar et al.²¹

4.3. Limitations

While we successfully demonstrated the feasibility of a previously validated motion correction algorithm, ground-truth values of TOS to validate the accuracy of the motion-corrected 4DCT-derived estimates were not available for the CRT patients.

The 4DCT images of all 20 subjects were acquired at a single center with the same CT scanner. The imaging protocol at the center did not include any tube-current modulation across the cardiac cycle. While this was beneficial in estimating TOS values that weren't subject to image quality differences across the cardiac cycle, future studies could investigate the effect of tube current modulation and ultra-low-dose scan protocols on the computed TOS estimates.

Lastly, the retrospective single-center nature of the study, together with the relatively small number of CRT subjects could affect the robustness of the reported results. Additionally, while prior work has established the importance of TOS in predicting CRT outcomes, ¹⁹ we did not have clinical outcomes for the subjects used in this study; thus, were not able to investigate the effect of ResyncCT on CRT outcomes. The results reported here motivate the use of motion corrected data for future prospectively recruited multi-center studies with larger cohorts of CRT patients to investigate the effect of 4DCT and motion correction on predicting patient responses to CRT.

5. Conclusions

A novel cardiac 4DCT motion correction algorithm called ResyncCT was shown to significantly reduce motion artifacts on the endocardial wall in 4DCT images clinically acquired for CRT planning/upgrade. Timing of LV mechanical activation, a parameter shown to be a strong predictor of CRT response, was significantly changed after motion correction with ResyncCT. Additionally, ResyncCT reclassified 43 % of all free-wall LV segments, determining their suitability as optimal target sites for LV lead placement.

Sources of funding

Research reported in this publication was supported by NHLBI of the National Institutes of Health under award number R01 HL144678. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

This work was done during the term of an award from the American Heart Association (AHA 20PRE35210261).

Disclosures

Dr. Ho received research grants from NIH (2KL2TR001444), AHA (19CDA34760021), holds founder shares in Vektor Medical Inc. (unrelated to this study) and consulting for Kestra Medical.

Dr. McVeigh holds founder shares in Clearpoint Neuro Inc. and receives research funding from GE Healthcare, Abbott Medical, and Pacesetter Inc.

Declaration of competing interest

The authors declare no conflicts of interest.

A. Manohar et al.

- Kim S, Chang Y, Ra JB. Cardiac motion correction based on partial angle reconstructed images in x-ray CT. *Med Phys.* 2015;42(5):2560–2571. https://doi.org/ 10.1118/1.4918580.
- Pack JD, Manohar A, Ramani S, et al. Four-dimensional computed tomography of the left ventricle, Part I: motion artifact reduction. *Med Phys.* 2022;49(7):4404–4418. https://doi.org/10.1002/mp.15709.
- Colvert GM, Manohar A, Contijoch FJ, et al. Novel 4DCT method to measure regional left ventricular endocardial shortening before and after transcatheter mitral valve implantation. *Structural Heart*. 2021;5(4):410–419. https://doi.org/10.1080/ 24748706.2021.1934617.
- McVeigh ER, Pourmorteza A, Guttman M, et al. Regional myocardial strain measurements from 4DCT in patients with normal LV function. J Cardiovas Comp Tomog. 2018;12(5):372–378. https://doi.org/10.1016/j.jcct.2018.05.002.
- Manohar A, Colvert GM, Schluchter A, Contijoch F, McVeigh ER. Anthropomorphic left ventricular mesh phantom: a framework to investigate the accuracy of SQUEEZ using Coherent Point Drift for the detection of regional wall motion abnormalities. *J Med Imag.* 2019;6(4):1–14. https://doi.org/10.1117/1.JMI.6.4.045001.
- Borgquist R, Barrington WR, Bakos Z, Werther-Evaldsson A, Saba S. Targeting the latest site of left ventricular mechanical activation is associated with improved longterm outcomes for recipients of cardiac resynchronization therapy. *Heart Rhythm O2*. 2022;3(4):377–384. https://doi.org/10.1016/j.hroo.2022.05.003.
- Marek J, Gandalovičová J, Kejřová E, Pšenička M, Linhart A, Paleček T. Echocardiography and cardiac resynchronization therapy. *Cor Vasa*. 2016;58(3): 340–351. https://doi.org/10.1016/j.crvasa.2015.08.001.
- Chung ES, Leon AR, Tavazzi L, et al. Results of the predictors of response to CRT (PROSPECT) trial. *Circulation*. 2008;117(20):2608–2616. https://doi.org/10.1161/ CIRCULATIONAHA.107.743120.
- Prinzen FW, Hunter WC, Wyman BT, McVeigh ER. Mapping of regional myocardial strain and work during ventricular pacing: experimental study using magnetic resonance imaging tagging. J Am Coll Cardiol. 1999;33(6):1735–1742. https:// doi.org/10.1016/S0735-1097(99)00068-6.
- Faris OP, Evans FJ, Ennis DB, et al. Novel technique for cardiac electromechanical mapping with magnetic resonance imaging tagging and an epicardial electrode sock. *Ann Biomed Eng.* 2003;31(4):430–440. https://doi.org/10.1114/1.1560618.