Correction of hysteretic respiratory motion in SPECT myocardial perfusion imaging: Simulation and patient studies

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Purpose: Amplitude-based respiratory gating is known to capture the extent of respiratory motion (RM) accurately but results in residual motion in the presence of respiratory hysteresis. In our previous study, we proposed and developed a novel approach to account for respiratory hysteresis by applying the Bouc–Wen (BW) model of hysteresis to external surrogate signals of anterior/posterior motion of the abdomen and chest with respiration. In this work, using simulated and clinical SPECT myocardial perfusion imaging (MPI) studies, we investigate the effects of respiratory hysteresis and evaluate the benefit of correcting it using the proposed BW model in comparison with the abdomen signal typically employed clinically.

Methods: The MRI navigator data acquired in free-breathing human volunteers were used in the specially modified 4D NCAT phantoms to allow simulating three types of respiratory patterns: monotonic, mild hysteresis, and strong hysteresis with normal myocardial uptake, and perfusion defects in the anterior, lateral, inferior, and septal locations of the mid-ventricular wall. Clinical scans were performed using a Tc-99m sestamibi MPI protocol while recording respiratory signals from thoracic and abdomen regions using a visual tracking system (VTS). The performance of the correction using the respiratory signals was assessed through polar map analysis in phantom and 10 clinical studies selected on the basis of having substantial RM.

Results: In phantom studies, simulations illustrating normal myocardial uptake showed significant differences ($P < 0.001$) in the uniformity of the polar maps between the RM uncorrected and corrected. No significant differences were seen in the polar map uniformity across the RM corrections. Studies simulating perfusion defects showed significantly decreased errors ($P < 0.001$) in defect severity and extent for the RM corrected compared to the uncorrected. Only for the strong hysteretic pattern, there was a significant difference ($P < 0.001$) among the RM corrections. The errors in defect severity and extent for the RM correction using abdomen signal were significantly higher compared to that of the BW (severity = -4.0% , $P < 0.001$; extent = -65.4% , $P < 0.01$) and chest (severity = -4.1% , $P < 0.001$; extent = -52.5% , $P < 0.01$) signals. In clinical studies, the quantitative analysis of the polar maps demonstrated qualitative and quantitative but not statistically significant differences ($P = 0.73$) between the correction methods that used the BW signal and the abdominal signal.

Conclusions: This study shows that hysteresis in respiration affects the extent of residual motion left in the RM-binned data, which can impact wall uniformity and the visualization of defects. Thus, there appears to be the potential for improved accuracy in reconstruction in the presence of hysteretic RM with the BW model method providing a possible step in the direction of improvement. © 2016 American Association of Physicists in Medicine [<https://doi.org/10.1002/mp.12072>]

Key words: cardiac imaging, hysteresis, respiratory motion, SPECT

Abbreviations

AP	anterior-posterior
BW	Bouc–Wen
CT	computed tomography
DOF	degree-of-freedom
EKG	electrocardiogram
LEHR	low-energy high-resolution
LPO	left posterior-oblique
MPI	myocardial perfusion imaging
MRI	magnetic resonance imaging
NCAT	NURBS-based cardiac-torso
OSEM	ordered subset expectation maximization
PET	positron emission tomography
RAO	right anterior-oblique
RM	respiratory motion
ROI	region-of-interest
SI	superior-inferior
SNR	signal-to-noise ratio
SPECT	single photon emission computed tomography
VTS	visual tracking system

1. INTRODUCTION

Respiratory motion (RM) during image acquisition causes artifacts that can affect the clinical diagnosis in myocardial SPECT images. Conventional respiratory correction methods in SPECT make use of respiratory signals from external surrogates (e.g., tracking an external marker, a pneumatic bellow on the abdomen, or a spirometer)^{1–3} based on the assumption that there exists a consistent relationship between the external signals and internal heart motion. However, MRI studies have demonstrated that patients can exhibit respiratory hysteresis, wherein the heart takes different trajectories during the inspiratory and the expiratory phases of the respiratory cycle.^{4–7} Such internal behavior suggests that prediction of the heart motion from a single parameter (such as the respiratory signal related to the abdominal motion) may not sufficiently provide the information about the true motion trajectory of the heart. Motion correction methods used in RM compensation essentially bin the emission data according to the respiratory signal from the external tracking device. Binning can be performed in one of the two ways: phase-based or amplitude-based. The amplitude-based RM correction methods have been determined to perform better than the phase-based methods by capturing variation in the depth of breathing.^{8–12} However, both binning methods fail to account for respiratory hysteresis leading to inherent residual blurring in the final image.

We have previously investigated the correlation between the internal organs and the external markers with respiration.⁶ Results from this study indicate that the hysteretic behavior of the heart may be predicted using a model based on more than one source of external respiratory information. Current methods accounting for hysteresis include separating the respiratory signal into inspiration and expiration phases,^{11,13} fitting ellipses,^{4,7} or state augmentation techniques.¹⁴ These methods have been primarily used in estimating lung tumor

motions. However, employing the aforementioned methods often requires either a shape prior, short pre-scans, or phase-offsets to construct an accurate model to predict the internal position. These methods are limited in application for extended imaging times due to changes in the subject's respiratory pattern in terms of phase and magnitude within and between the respiratory cycles. Furthermore, the efficiency of the motion correction method in estimating the extent of respiratory motion can be limited when separately done on the inspiration and expiration data due to low counts, hence resulting in images with poorer signal-to-noise ratio (SNR). In PET, exciting research has shown the possibility of tracking the motion of individual structures with respiration.^{15–18} These methods avoid the disadvantages of using external surrogates such as the costs of the devices, the added time and effort for setting them up and using them, and the possibility of a lack of agreement between the surrogate signal and the actual motion within the patient. However, SPECT data-driven tracking is difficult because of the rotation of two camera heads, low count rates, and variations in structure overlap and attenuation with angle.^{19,20}

In our previous work,²¹ we investigated a method for correcting respiratory hysteresis by applying the Bouc–Wen (BW) model without the need for shape prior, pre-scans, or phase-offsets. The model uses first-order nonlinear differential equations to account for the hysteretic motion occurring between the inspiration and expiration phases.^{22,23} It also accounts for the variations within and between the respiratory cycles. The effects of RM on uniformity of the left ventricular wall and defect detection have been previously comprehensively investigated through simulations^{12,24–26} and in clinical settings^{27,28} in myocardial perfusion imaging (MPI) studies. However, to the best of our knowledge, there is no previous report in the literature on the effects of respiratory hysteresis on wall uniformity and defect representation in MPI studies. Thus, the objectives of this study were as follows: first, to evaluate the impact of respiratory hysteresis on MPI images when amplitude-based motion correction is performed, and second, to evaluate the performance of the amplitude-based motion correction when the BW model is employed.

2. MATERIALS AND METHODS

2.A. Overview

The impact of respiratory hysteresis and its correction on MPI images were evaluated using both anthropomorphic digital phantom simulations and clinical studies. RM in the simulation studies was based on navigator measurements of the internal motion of the heart and diaphragm in the superior-inferior (SI) direction in free-breathing volunteers during MRI acquisition.⁶ MRI data collection was temporally synchronized with acquisition of the motion in the anterior-posterior (AP) direction of external markers on the chest and abdomen measured via a visual tracking system (VTS).⁶ The internal motions measured by MRI were used to create MPI simulations with known truth as to the axial location of the

internal organs (heart, liver, and spleen). From these simulations, we determined the impact of hysteresis on respiratory motion correction strategies for various levels of hysteresis. An overview of the simulation process is illustrated in Fig. 1. Polar map based quantitative analysis of the RM correction methods was then performed on both the phantom and clinical reconstructions to evaluate the impact on the left-ventricular uniformity and the perfusion defect detection.

2.B. Respiratory signals and their acquisitions

Table I summarizes the list of respiratory signals and the manner they are used in this study. The MR navigator technique²⁹ was employed to measure the SI respiratory motion of the heart and the diaphragm over 300 EKG-gated cardiac cycles during free breathing by volunteers conducted with informed consent and Institutional Review Board approval. Details of the acquisition of these signals can be found in our previous publication.⁶ The measured internal respiratory motion acquired using MR navigators served two purposes in our investigations. First, they were used as the basis for generating simulated RM of the heart, liver, and spleen. Second, they served as the “truth” through which the performance of the RM correction using the external respiratory signals

(from abdomen, chest, and BW) was evaluated. The external respiratory signals employed in these investigations refer to the anterior-posterior RM of markers placed on the abdomen and chest regions of the volunteers that were simultaneously tracked with the MRI acquisitions using the VTS.³¹ The BW signal here represents the respiratory signal derived from the BW model applied to the VTS data as described in section 2.C.

2.C. Bouc–Wen model of hysteresis and compensation of hysteresis

The RM signals acquired from the chest and the abdomen regions tracked via the VTS were input to a modified BW model to estimate a signal, which accounts for hysteresis when employed to bin list-mode MPI acquisitions. The modified BW model is expressed as³¹

$$\dot{w} = \rho(\dot{x} + \delta x|\dot{w}| - \sigma|\dot{x}|w - \gamma w|\dot{w}|) \quad (1)$$

where $x(t)$ and $w(t)$ are the AP displacements of the abdomen and chest markers, respectively, $|\dot{w}| = \text{abs}(\dot{w})$, $|\dot{x}| = \text{abs}(\dot{x})$, $\dot{w} = dw/dt$, $\dot{x} = dx/dt$ and ρ , δ , σ , and γ are parameters that determine the shape and extent of hysteresis in the modified BW model.

FIG. 1. Schematic diagram illustrates the signal acquisitions and their usage in the simulation process. Simultaneous acquisition of internal (MRI navigator) and external (VTS) motion data from free-breathing volunteers were employed to generate realistic organ RM in NCAT phantoms simulating SPECT MPI, and correct for this motion by employing the external respiratory signals in amplitude-based motion correction strategies. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE I. Respiratory signals and their usage.

Source	Respiratory signal	Usage
MRI navigators ^a	Heart, right and left diaphragm	Creating phantom organ motion, and true motion correction of heart
VTS ^b	Chest and abdomen ^b regions	Motion correction
BW Model ^b	BW signal	Motion correction

^aUsed in simulation studies only.^bUsed in both simulation and clinical studies.

We are interested in the variation of RM determined by comparing that of the chest with that of the abdomen regions. Thus, we employ dw/dx to bin the list-mode data. We will call this term w_{EST} . It is derived by rearranging Eq. (1) and dividing it by the respiratory rate dx/dt to yield:

$$w_{EST} = dw/dx = \rho(1 - \sigma w \operatorname{sgn}(\dot{x})) / (1 - \rho \delta x \operatorname{sgn}(\dot{w}) + \rho \gamma w \operatorname{sgn}(\dot{w})) \quad (2)$$

More details on the BW model, such as how we used a set of human volunteer simultaneous MRI and VTS studies to determine the initial parameters of the model, and how these parameters were used with the VTS signal to estimate w_{EST} , can be found in.²¹

2.D. Digital phantoms simulating source and attenuation distributions for MPI with RM

To assess the impact of respiratory hysteresis on MPI SPECT studies and its correction under controlled conditions, we performed analytical simulations of Tc-99m sestamibi cardiac-perfusion SPECT imaging using the 4D NURBS-based cardiac-torso (NCAT) digital anthropomorphic phantom for humans.³² The RM of the heart is known to vary in magnitude from that of the diaphragm.^{5,6,33} Furthermore, in the presence of hysteresis, the RM of the organs exhibits differences between inspiration and expiration.^{5,6} Thus, the standard NCAT phantom was specifically modified to allow

more complex SI motion of the heart and diaphragm as determined by the navigator measurements over the 300 cardiac cycles acquired in three of our volunteers.⁶ The limited data available on MRI imaging^{5,21} documents the presence and variability in magnitude of hysteresis of heart motion in humans with respiration but does not allow us to predict the frequency of its occurrence with clinical cardiac SPECT imaging. Thus, to assess the impact of hysteresis, we selected three studies from our data pool to represent respiratory patterns ranging from no hysteresis to maximum hysteresis, which we call (a) monotonic; (b) mild hysteresis; and; (c) strong hysteresis. However, we do not know the relative abundance of these three levels of hysteresis. The maximum extent of measured heart motion in each was 1.5 cm, 1.3 cm, and 2.3 cm, respectively, as determined by the MRI navigator signal on the volunteers' heart. Figure 2 shows the three respiratory patterns used for simulating RM in NCAT phantoms generated at a matrix size of $256 \times 256 \times 256$ and voxel size of 0.234 cm. The phantoms were created to represent source and attenuation distributions for Tc-99m sestamibi MPI imaging for each of the 300 time points (relative locations of diaphragm and heart). That is, each phantom was unique in that its organ displacements match the navigator measured organ movements of a given volunteer at each of the 300-measured time points. Thus, in total, they create a "breathing" phantom mimicking the organ motion in each volunteer. In addition, for each of the NCAT phantom, the cardiac motion due to the beating heart was modeled as an average of 16 frames per one cardiac cycle. Except for the motion, the anatomy of the phantoms used for the three different patterns remained the same.

For each of the three RM patterns, the phantom data were created for both normal (no perfusion defect) and with perfusion defects at four different locations in the left ventricular wall to investigate the impact of RM and several RM correction strategies on apparent wall perfusion agent localization. The perfusion defects were not associated with corresponding regional motion defect. Normal phantoms represent the healthy condition of heart. They were used in comparing the effects of hysteresis and its correction by examining the RM estimates obtained from the motion correction algorithm and

FIG. 2. Plots for the MRI navigator measured internal motion on the heart and diaphragm for the monotonic, mild, and strong hysteresis respiratory patterns simulated in the phantom studies. Plotted data portray individual navigator measurements of the heart and diaphragm position for each of the 300 measured time points. Notice that as the extent of hysteresis increased the heart takes on increasingly different positions during inspiration (red points online) and expiration (blue points online) for the same diaphragm location. [Color figure can be viewed at wileyonlinelibrary.com]

the mean uniformity of the short-axis slices of the myocardial wall. Perfusion defect phantoms were created by defining myocardial perfusion defects as independent volumes, which were then subtracted from normal NCAT phantoms. Myocardial perfusion defect locations were in the anterior (a), lateral (b), inferior (c), and septal (d) regions of the left ventricle wall. The defects spanned 60° in short axis and extended 3 cm in long axis with a contrast of 50% uptake reduction compared to normal wall uptake. Figure 3 shows the schematics illustrating the defect locations in left-ventricular short-axis and long-axis slices. These phantoms with perfusion defects were used to evaluate how accurately the defects were represented in the presence of respiratory hysteresis. Figure 4 summarizes the ways in which the phantoms were simulated to evaluate the effect of respiratory hysteresis and its correction.

2.E. SPECT simulation of 4D NCAT phantoms

Projections of the NCAT phantoms were obtained using an analytical projector³⁴ modeling attenuation (without scatter) and distance-dependent collimator blur (low-energy high-resolution, LEHR). In all, 60 projections (circular

FIG. 3. Schematic illustrations show the short-axis (left) and long-axis (right) views of the left ventricle wall. The shaded areas represent the locations of the perfusion defects simulated on the anterior ($\theta_{\text{center}} = 0^\circ$), lateral ($\theta_{\text{center}} = 90^\circ$), inferior ($\theta_{\text{center}} = 180^\circ$), and septal ($\theta_{\text{center}} = 270^\circ$) walls with defect span ($\Delta\theta$) = 60° , and defect size (Δ_z) = 3 cm.

radius-of-rotation: 25 cm) were obtained covering 180° around each NCAT phantom, from 45° right anterior-oblique (RAO) to 45° left posterior-oblique (LPO), simulating a dual-head cardiac SPECT acquisition. The $256 \times 256 \times 60$ projection data were resized to $128 \times 128 \times 60$ with a pixel size of 0.467 cm and scaled to ~ 7 million total counts to match the count level of a typical Tc-99m sestamibi cardiac SPECT study. The acquisition time was 20 s per projection. Each projection pair, simultaneously obtained from the two SPECT heads, was generated by summing 20 emission frames from 20 NCAT phantoms separated by ~ 1 s time intervals. In this way, the first 30 projections were obtained using the 300 NCAT phantoms. The rest of the 30 projections were obtained in the same way by reusing the 300 NCAT phantoms. The projection data were then incorporated with Poisson noise fluctuations. A total of 10 noise realizations per phantom were created as shown in Fig. 4.

2.F. Patient data

In total, 10 stress MPI SPECT list-mode acquisitions with EKG triggers acquired on a Philips BrightView SPECT/CT system with temporally synchronized VTS tracking of the motion of markers on the patient's chest and abdomen³⁰ were selected for use in this study. The selection was made on the basis of the magnitude of the heart RM between 1.2 and 2.5 cm in the SI direction as determined by the methods presented by J. Dey, et al.¹² Note that the recorded EKG triggers were not employed during image reconstructions. The two heads of the SPECT system were oriented at 90° relative to each other and acquired 60 projection angles in total (30 from each head) over a 180° arc spanning RAO to LPO about the patients. The system-generated CT-based attenuation maps were used for attenuation correction. The list-mode SPECT data were binned into 100 ms projections of 128×128 with a pixel size of 4.67 mm. The amplitude of the RM signals from the chest and abdomen markers corresponding to this 100 ms interval was stored for usage in combining them into seven amplitude-binned SPECT projections sets as detailed in the next section.

FIG. 4. Block diagram illustrates the experimental design of the simulation study. The simulations were performed for the three different respiratory patterns. Each respiratory pattern was simulated for a healthy heart (Normal) and a heart with perfusion abnormality (Perfusion Defect) separately in the mid-anterior, lateral, inferior, and septal regions of the left ventricle.

2.G. RM correction, reconstruction, and polar map analysis

RM correction was performed using the algorithm described by J. Dey et al.¹² The first step in this process was to group the projections into the amplitude-binned projection sets as a function of the respiratory surrogate signal. For the simulation studies, 300 simulated projections grouped as detailed in section 2.E were binned in this way. Four different surrogate signals were investigated for amplitude binning with the phantom studies: (a) external chest marker; (b) external abdomen marker; (c) BW model signal derived from using both chest and abdomen markers; and (d) MRI heart navigator which provides “true” signal. The performance of the signals from the external markers and the BW model were compared against the true signal, as it was the signal used in creating the phantom sets. For the clinical studies, the following two surrogate signals were considered: (a) the external abdomen marker and (b) the BW model. Note that the chest signal acquired was employed in BW model but not in performing amplitude-binning RM correction due to its low magnitude, susceptibility to body motion, and being found to have a lower correlation with the navigator measured heart motion than the abdomen signal in the majority of a combined group of 19 volunteers previously reported.²¹ There is no “truth” to compare against with patient data. The maximum and minimum amplitudes were determined and these ranges were divided into nine equal length interval bins for the simulated studies and seven equal length interval bins for the clinical studies. For each projection angle, projections whose respiratory amplitude fell in the same interval were summed to produce the amplitude-binned projection for that angle. The summed projection in the middle respiratory bin was considered as the reference state, and the projections in the remaining bins were considered as motion states. These amplitude-binned projection sets were then reconstructed. The six degree-of-freedom (6-DOF) respiratory motion estimates for rigid-body motion were obtained by registering the motion states to the reference state. These motion estimates were then incorporated in the Ordered Subset Expectation Maximization (OSEM) algorithm³⁵ with attenuation correction, resolution recovery, and motion compensation. The motion estimated from the amplitude-binned studies was that of the heart, which we assumed in its self to be rigid body. When we corrected this motion in the second pass through reconstruction, we corrected for the estimated motion of the heart, which is the structure of interest in MPI. Given the non-rigid nature of motion of other structures in the slices, their motion would not be correctly compensated. Thus, these structures would have some residual or perhaps even augment respiratory motion blurring. Reconstruction was by five iterations of OSEM followed by a 3D Gaussian filter with an SD of 1 cm.³⁶ For the phantom and clinical OSEM reconstructions, 15 subsets (4 angles per subset) were used. For simulations, attenuation correction was performed using the attenuation map with motion averaged over 300 NCAT phantoms for each of the three respiratory patterns. For the clinical

studies, a 60 s cone-beam CT acquisition was employed during patient breathing intended to obtain RM blurred attenuation maps matching that of SPECT images.³⁷ The average attenuation map estimated from cone-beam CT during free breathing provides a better match to the RM than the attenuation map estimated from the cone-beam CT acquired during the breath-hold.³⁷

In addition to the RM corrected reconstructions, both simulated and clinical projections were also reconstructed without motion correction using the OSEM algorithm. This formed the uncorrected reconstruction dataset, which were used in comparing the RM corrected reconstructions.

Reconstruction results for each dataset were reformatted into short- and long-axes slices and polar map images were generated from the short-axis slices. A normal polar map for quantification was generated for simulations using the reconstructions corresponding to the middle bins from the three respiratory patterns. Smoothing on the polar maps before final presentation and quantitative analysis was performed using a 3×3 moving average filter.

2.H. Data analysis

2.H.1. Phantom data

Normal phantoms: The reconstruction results of the normal phantoms between different respiratory surrogate signals were assessed based on the correlation of the RM estimates with that of the navigator measured motion of the heart and the uniformity of the polar maps. Using the registration algorithm described by Dey J, et al.,¹² motion estimates were computed and averaged over 10 noise realizations for the simulated SPECT projections. A Pearson product-moment linear correlation coefficient (r) was computed as a nonparametric measure of the strength of association of the respiratory motion estimates between the test respiratory signals and the true signal (“truth”). Scatter plots were also used to illustrate the correlation of the test respiratory signals with the true heart motion. In addition, box plots were used for each respiratory signal to examine and compare the extent of heart motion (residual blur) present in each respiratory amplitude bin.

Polar maps of reconstructions of noiseless phantom acquisitions were used to assess the uniformity in the absence of noise. The uniformity of the polar maps was calculated using the uptake values by sampling in 2° steps from the short-axis slices during the polar map generation process. The uniformity is the measure of variation in counts over all short-axis slices from apex to base.³ It was calculated according to Eq. (3)

$$\text{Uniformity}_{\text{Apex-Base}} = 100 \times \left(\frac{\sum_{i=1}^n \{(\text{MAX}_{\text{Slice}} - \text{MIN}_{\text{Slice}}) / (\text{MAX}_{\text{Slice}} + \text{MIN}_{\text{Slice}})\}_i}{n} \right) \quad (3)$$

where n is the total number of short-axis slices, and $\text{MAX}_{\text{Slice}}$ is the maximum and $\text{MIN}_{\text{Slice}}$ is the minimum

number of counts in the n^{th} slice. Theoretically, perfectly uniform short-axis slices would result in a uniformity value of zero. The uniformity values were analyzed using ANOVA and Bonferroni post-hoc analysis to examine the effect of hysteresis and RM correction methods.

Perfusion defect phantoms: To measure the severity of perfusion defects in polar maps, the intensity of the counts in the defect was calculated using a pre-defined region-of-interest (ROI). The ROI was defined interactively by hand using the polar map corresponding to the true signal. Absolute differences between the polar maps reconstructed using the true signal and the test signals (abdomen, chest, and BW) were normalized by the true signal as calculated in Eq. (4). The differences were divided by the polar map of the true signal on pixel-by-pixel basis within the ROI to calculate the errors in intensity and reported as percentages.

$$\%Error_{Intensity} = 100 \times \frac{(|ROI\ Intensity_{Ideal} - ROI\ Intensity_{Test}| / ROI\ Intensity_{Ideal})}{(4)}$$

where $ROI\ Intensity_{Ideal}$ and $ROI\ Intensity_{Test}$ are the summed intensity values within the defined ROI corresponding to the polar maps of the true and the test signals, respectively.

To measure the extent of perfusion defects, blackout polar maps were generated.^{38–40} A blackout pixel in this study is defined as having an intensity value 2.5 standard deviations below the mean of a normal database.³⁸ Percent error for defect area was computed as shown in Eq. (5).

$$\%Error_{Area} = 100 \times \frac{(|Area_{Ideal} - Area_{Test}| / Area_{Ideal})}{(5)}$$

where $Area_{Ideal}$ and $Area_{Test}$ are the areas of the blackout pixels corresponding to the polar maps reconstructed using the true and the test signals, respectively.

The percent errors for both the defect intensity and area were computed as averages over the 10 noise realizations. A paired student's t-test with Bonferroni correction was applied at 95% confidence interval to assess the results between the respiratory signals. A P value of less than 0.05 was considered as statistically significant. The above analysis was also performed on the polar maps obtained from reconstructions without motion correction, to provide a measure of the impact on uncorrected RM on defect severity and extent.

2.H.2. Patient data

The effect of respiratory hysteresis and its correction in clinical studies was assessed visually based on the short and vertical long-axes emission slices, the corresponding polar maps, and quantitatively by comparing the following three parameters for each patient study. The first was the extent of heart motion in the axial direction. This was calculated by measuring the difference of the motions estimated in the end

states by the amplitude-based RM correction algorithm. A paired t -test was used to evaluate the RM estimated by the abdomen and the BW signals. The second was the global differences between the polar maps from the RM uncorrected and each of the two corrected reconstructions, and between the polar maps obtained using the abdomen marker and the BW model signals. The third was regional changes in the polar maps of the uncorrected and corrected reconstructions. These were quantified and compared by calculating the (anterior + Inferior)/(lateral + septal) wall ratios.³⁷

3. RESULTS

3.A. Respiratory motion estimates from simulated NCAT phantoms

Figure 5 shows the motion estimates for the respiratory signals used in motion correction of normal phantoms for the 10 noise realizations of the three different hysteretic patterns (abdomen, chest, and BW), plus the true heart motion (true). The Pearson product-moment linear correlation coefficients (r) for each of the respiratory surrogate signals versus the true are also shown in Fig. 5. In each case, a strong correlation is observed for the BW model either being or sharing the status of being the highest. Despite the indication of a strong correlation, note the deviation between the estimated motions for the surrogate and true signal values, especially with hysteresis.

Figure 6 shows the positional variation of the estimated SI motions through a series of box plots for a more detailed analysis of the surrogate respiratory signals for each simulated 1 s temporal bin as used to correct the respiratory motion. The vertical variation in this figure shows the extent of positional variation of the heart present in the nine respiratory amplitude bins for each of the signals used in binning the three RM patterns. Notice for the true case, there is a clean separation in the estimated SI motion between the respiration amplitude bins for all three extents of respiration, and only a modest extent of positional variation for a given bin. This separation degrades some and the range in variation increases even for the monotonic RM pattern for the three non-true signals. For the case of mild hysteresis, these degrade further, with usage of the chest and BW surrogate signals showing less degradation than the abdomen signal. A very large overlap is observed in the case of strong hysteresis when the abdomen surrogate signal is used in estimation of the superior-inferior motion of the heart, and again the chest and BW surrogate signals show less degradation in the separation. Thus, the use of the surrogate signals as opposed to the true signal cause degradation in positional estimation of the heart, and this degradation increases as the extent of hysteresis increases.

3.B. Comparison of polar maps for simulated NCAT phantom data

Figure 7 presents the polar maps of the normal phantoms together with respective uniformity values (mean $\pm$ standard deviation) for the three hysteretic patterns. The uniformity of

FIG. 5. Plots of respiratory motion as estimated by registration to the reference bin (bin #5) for (a) monotonic, (b) mild hysteretic and (c) strong hysteretic respiratory patterns obtained from the reconstructed NCAT slices of amplitude-binned projections using the surrogate respiratory signals from the abdomen, chest, and the BW model versus the heart navigator (true). Shown are the mean and standard deviation for the 10 noise realizations. Also, shown are the correlation coefficients (r) of the estimates of the respiratory surrogate signals with the true. [Color figure can be viewed at wileyonlinelibrary.com]

FIG. 6. Three rows of box plots for estimated respiratory motion versus respiratory bin number for the monotonic (a), mild, (b) and strong, (c) hysteretic respiratory patterns. From left to right, the motion was estimated using the MRI-navigator-derived true respiratory signal for heart motion with respiration, the VTS-derived abdomen signal, the VTS-derived chest signal, and the Bouc-Wen-derived signal. On each box, the central mark is the median, the edges of the box are the 25th and 75th percentiles, the whiskers are the most extreme data points, and the '+' symbol are the outliers. [Color figure can be viewed at wileyonlinelibrary.com]

the polar maps is influenced by both the extent of motion and the performance of the motion correction method. Significant artifacts in the inferior and for the strong hysteretic pattern the

anterior walls can be seen in the uncorrected polar maps. The use of motion correction in every case decreased the extent of non-uniformity compared to no correction. The ANOVA

FIG. 7. Rows (a), (b), and (c) consist of polar maps for monotonic, mild, and strong hysteretic respiratory patterns from the normal heart phantom reconstructions. Polar maps derived from the uncorrected and respiratory motion corrected reconstructions using the abdomen (Abd), chest, and the Bouc–Wen model (BW), and the heart navigator (True) signals are shown. Uniformity values for the corresponding polar maps are given as mean $\pm$ standard deviation. Note that the apical cooling is expected in the NCAT phantom due to thinning of the wall in this location. Thus, a perfectly uniform polar map is not to be expected and the results for usage of the true signal should be taken as the truth to compare against. [Color figure can be viewed at wileyonlinelibrary.com]

results indicate that there was a statistically significant interaction between the effect of hysteresis and the RM correction methods ($F = 14.76$, $P < 0.001$). Post-hoc analysis showed that methods with RM correction resulted in significantly more uniform values than without ($P < 0.001$), but there were no statistically significant differences in the uniformity values between the RM correction methods. The polar maps presented in Figs. 7(a) and 7(b) corresponding to the monotonic and mild hysteretic patterns show very good uniformity post-correction by each of the signals. The polar maps shown in Fig. 7(c) correspond to the strong hysteretic pattern with the largest extent of motion illustrating the effect of large RM in combination with hysteresis. The presence of large residual motion (1–1.5 cm) in the middle respiratory bins of the abdomen signal [as shown in Fig. 6(c) box plots] causes the intensities in the polar map to be more uniform and is noticed in the corresponding polar map as a loss of apical cooling.

Shown in Fig. 8 are the polar maps and blackout polar maps for one noise realization for each of the three respiratory patterns and all four defect locations. RM correction using any of the surrogate respiratory signals results in polar maps that are visually similar to the true case and the uncorrected case shows obvious RM artifacts.

Figure 9 summarizes the quantitative results accompanied with student's t-test statistical analysis of the perfusion defect studies in terms of intensity (severity) and area (extent). Indicated also are the statistical significance of differences between the uncorrected and corrected sets for each of the three respiratory patterns and the four defect locations. With

the exception of defect D (septal wall) in mild hysteretic pattern, the errors with the correction methods for all respiratory patterns and defect locations were significantly lower than in the uncorrected. Although the errors for intensity and areas corresponding to the chest and the BW signals were smaller compared to the abdomen signal, no statistical significance was found between them for all defect locations in the monotonic and mild hysteretic respiratory patterns. For the strong hysteretic pattern, the errors resulting from using the chest and the BW signals in RM correction were smaller compared to that of the abdomen signal. Statistically significant differences in errors of defect intensity and area between the abdomen and the BW signals were found in defect locations B, C, and D; and C and D, respectively. This suggests that the effect of respiratory hysteresis is more pronounced with large amplitude respiration and use of hysteresis corrected respiratory signal decreases the error in estimating the heart motion resulting in possibly better defect representation.

3.C. Patient data

Using the respiratory signal from chest and abdomen markers, the extent of hysteresis was determined as previously reported.²¹ As indicated in Fig. 10(a), 4 out of the 10 patients exhibited mild hysteretic patterns while the rest exhibited monotonic patterns. Figure 10(a) shows the extent of heart motion in the SI direction as estimated when the abdomen and BW model signals were used to amplitude bin the 100 ms frames. No significant difference ($P = 0.73$) in

FIG. 8. Examples of one noise realization each for polar maps and blackout polar maps of the perfusion defect NCAT phantoms for each of the three respiratory patterns (monotonic, mild hysteresis, and strong hysteresis) and the four defect locations (a), (b), (c), and (d). Polar maps of uncorrected and corrected reconstructions for the abdomen (Abd), chest, Bouc–Wen model (BW), and heart navigator (True) used in motion correction algorithm are shown. [Color figure can be viewed at wileyonlinelibrary.com]

the extent of heart motion when using the two signals was observed. However, anecdotally as shown in Fig. 10(a), one of the hysteresis cases (patient 9) showed a large increase in the magnitude of the estimated RM with the BW over the abdomen signals. Figure 10(b) presents the regional uptake changes as a ratio of (anterior + inferior)/(lateral + septal) walls. The uncorrected polar maps generally had a reduced ratio compared to the corrected polar maps due to the presence of RM. The ratios for the corrected polar maps using the abdomen and BW were generally closer to 1.0 and resulted in similar values for the two signals.

Figure 11 displays the short-axis slices and polar maps for two selected clinical cases. As can be seen in Fig. 10(a), Patient 8 was not considered hysteretic and usage of the abdomen signal in binning the list-mode data for reconstruction resulted in a larger magnitude of RM than when the BW signal was employed. On the other hand, Patient 9 was determined to have hysteretic RM, and the magnitude of this motion was much larger when BW signal was used in

binning. The effect of RM correction can be clearly seen for both patients by the reduction in the artifactual inferior and anterior wall decreases in apparent localization due to RM, as compared to the uncorrected. Minor differences suggestive of a better correction in the quality of the reconstructed slices when employing the BW surrogate signal compared to correction employing solely the abdominal marker data can be noted visibly in the figure for both patients. Examples of these changes are as follows: the clearer definition of the inferior-septal wall and the smaller size of the anterior wall decreased area with BW as opposed to abdomen signal for binning in Patient 8 of Fig. 11. Similar small differences can be noted in these walls for Patient 9.

4. DISCUSSION

Three extents of hysteresis were simulated in the NCAT phantom studies based on measurements made of heart and diaphragm motion with MRI studies of free-breathing

FIG. 9. Histograms showing the average and standard deviation (error bar) of 10 noise realizations each for defect intensity and defect area (expressed as percent errors) in the uncorrected and corrected reconstructions using the respiratory signals from the abdomen, chest, and the Bouc–Wen model for the anterior (a), lateral (b), inferior (c), and septal (d) defect locations. Results are shown for the monotonic, mild, and strong hysteretic respiratory patterns. The calculated errors which are significantly different with $*P < 0.05$, $**P < 0.01$, or $***P < 0.001$ by Paired Student's t -test with Bonferroni correction are indicated. [Color figure can be viewed at wileyonlinelibrary.com]

FIG. 10. (a) The magnitudes of the extent of heart motion estimated in the SI direction using the abdomen (Abd) and Bouc-Wen (BW) signals. In (b) are shown the ratios of the counts in the anterior and inferior to lateral and septal walls of the polar maps for the uncorrected, corrected using the abdomen surrogate signal, and corrected using the BW surrogate signal. Since the anterior and inferior walls are blurred more by respiratory motion than the lateral and septal walls, one would expect in the absence of true perfusion defects, this ratio of wall counts is to be restored closer to 1.0 with respiratory motion correction. Note: The asterisk (*) indicates the studies with hysteretic patterns.

volunteers. Associated abdomen and chest marker motion was simultaneously collected by VTS measurements for usage as external surrogate signals for correcting internal heart motion. The box plots of Fig. 6 showed that the estimated axial motion of the heart from these simulated studies binned using the true signal (MRI navigator determined heart location) was clearly separated between the respiration amplitude bins for all three extents of hysteresis and showed only a modest extent of positional variation within the bins. For the three surrogate signals (abdomen, chest, and BW model), the separation between the bins was degraded and the residual motion increased within the bins as the extent of hysteresis increased. This verified the impact of hysteresis in heart motion on the accuracy of external estimation of this motion with surrogate signals. The degradation in motion estimation was less for the BW model than usage of the abdomen signal indicating a potential for better correction of RM with its usage as opposed to the abdomen signal typically employed clinically.

In looking at the polar maps of Figs. 7 and 8, an obvious change in the appearance was seen with correction for respiratory motion compared to no correction, but no apparent differences were seen when comparing the polar maps corrected using the different signals for the monotonic pattern of respiratory motion, including the true signal. The same was true for the mild hysteretic pattern in these figures. For the strong hysteretic pattern, a substantial difference with correction was noted. However, again little visual difference was seen between the polar maps corrected using the different signals except for apical region of the polar maps showing evidence of more smoothing with usage of the abdominal signal as opposed to the others, including the true. Thus, visually, we were not able to determine a benefit of usage of the BW model for our NCAT phantom studies except for a loss in

FIG. 11. Three short-axis slices (top three rows) and polar maps (bottom row) of Tc-99m sestamibi stress scans for two patients without and with RM correction using the abdomen and the Bouc-Wen signals. Patients 8 and 9 exhibited monotonic and mild hysteretic patterns, respectively. [Color figure can be viewed at wileyonlinelibrary.com]

visualization of apical thinning in the presence of strong hysteresis.

Quantitatively in terms of the % error in the defect intensity, differences were determined with usage of the three surrogate signals in correction as shown in Fig. 9. For the mild hysteretic pattern, there is a non-statistically significant indication of a lower % error with usage of the BW model and chest signals as opposed to the abdomen signal. With the strong hysteretic pattern, three of the four defect locations showed a statistically significant lower % error in defect intensity for the BW model (and one for the chest) surrogate versus the abdomen signal. Also, two of the four defect locations show a statistically significant smaller % error in defect area for the BW model versus abdomen signal for this pattern. These differences are likely due to the residual RM as observed in the middle respiratory bins of the abdomen signal (box plots of Fig. 6), which causes image blurring and loss of contrast resulting in inaccurate representation of perfusion defects despite the RM correction. Thus, these quantitative results indicate a benefit of usage of the BW model in terms of it being better able to portray perfusion defects in the presence of strongly hysteretic motion.

The signal from the chest marker performed very well in comparison to the signals from the abdomen and the BW model in all the three respiratory patterns shown in Fig. 9. However, in the larger group of MRI studies⁶ from which the three studies presented herein were drawn, this was not always the case. Furthermore, the magnitude of chest signal is low and thus more susceptible to contamination when being estimated in the presence of body motion. Therefore, relying on either the abdomen or chest marker surrogate signals could result in decreased accuracy in heart motion estimation.

In clinical studies, the RM correction performed using the signal obtained through the BW model was compared to the correction using the abdomen signal. The abdomen signal was used as the reference respiratory signal for patient data since it is the surrogate signal widely used in clinical setting.^{8–11} Therefore, the comparative analysis of the patient data was performed for the reconstructions corrected using the abdomen and the BW respiratory signals. Our evaluations were based on both the visual observations of the reconstructed images, and quantitative assessments of the polar maps. Based on the selection of patient studies with substantial RM, the patient cases showed large differences between uncorrected and corrected reconstructions. In the short-axis slices and polar maps of Fig. 11, there were modest differences between the two patient studies presented which hinted at a possible improvement in uniformity with usage of the BW model surrogate signal; however, the differences were small and the truth is unknown in these studies.

Using dimensionality reduction via Laplacian Eigenmaps with post-processing steps to normalize between projections, a recent publication⁴¹ has demonstrated the possibility of obtaining a data-driven signal directly from SPECT projections. The signal estimated by this method showed excellent correlation with a standard external method of obtaining a surrogate signal for respiratory motion. If this methodology

is capable of measuring the signal solely from the heart itself, it may provide a direct way to determine hysteretic cardiac motion. However, as currently implemented, it appears that the methodology is sensitive to the motion of activity beyond just the heart region. Thus, in the presence of significant extra-cardiac activity which moves differently than the heart during respiration,^{5,6} this methodology may not be able to accurately capture the hysteretic motion of the heart.

5. CONCLUSION

Through realistic simulations of Tc-99m sestamibi MPI SPECT data, we have studied the effects of respiratory hysteresis and its correction using the BW model. By comparing the estimated axial motion of the heart from simulated studies binned using the true signal to that estimated using the three surrogate signals, we determined a definite impact of hysteresis on the accuracy of heart motion estimation. We also observed that the BW model signal was less impacted than when the abdominal signal was employed. Differences in the polar maps estimated from our NCAT phantom simulations between any of the signals (truth and three surrogate signals) were seen only for the strongly hysteretic respiratory pattern when comparing the abdomen to correction using the other three signals. In clinical studies, only a modest difference was seen in slices and polar maps with application of the abdomen and BW model signals when binning the list-mode data for reconstruction. Thus, we have only limited evidence to suggest the BW model actually improves the reconstructions compared to usage of the abdomen signal although it was observed to provide better accuracy in motion estimation in the simulated studies. Thus, there appears to be the possibility for improved accuracy in reconstruction in the presence of hysteretic RM with the BW model; however, a much larger set of patient studies is needed to determine if such a benefit exists, and if it does exist it is likely to make a significant difference in only a small percentage of studies.

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CONFLICT OF INTEREST

The authors declare that they do not have any conflict of interest.

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