The impact of breathing guidance and prospective gating during thoracic 4DCT imaging: an XCAT study utilizing lung cancer patient motion

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Abstract
Two interventions to overcome the deleterious impact irregular breathing has on thoracic-abdominal 4D computed tomography (4DCT) are (1) facilitating regular breathing using audiovisual biofeedback (AVB), and (2) prospective respiratory gating of the 4DCT scan based on the real-time respiratory motion. The purpose of this study was to compare the impact of AVB and gating on 4DCT imaging using the 4D eXtended cardiac torso (XCAT) phantom driven by patient breathing patterns.

We obtained simultaneous measurements of chest and abdominal walls, thoracic diaphragm, and tumor motion from 6 lung cancer patients under two breathing conditions: (1) AVB, and (2) free breathing. The XCAT phantom was used to simulate 4DCT acquisitions in cine and respiratory gated modes. 4DCT image quality was quantified by artefact detection (NCC\textsubscript{diff}), mean square error (MSE), and Dice similarity coefficient of lung and tumor volumes (DSC\textsubscript{lung}, DSC\textsubscript{tumor}). 4DCT acquisition times and imaging dose were recorded.

In cine mode, AVB improved NCC\textsubscript{diff}, MSE, DSC\textsubscript{lung}, and DSC\textsubscript{tumor} by 20\% ($p = 0.008$), 23\% ($p < 0.001$), 0.5\% ($p < 0.001$), and 4.0\% ($p < 0.003$), respectively. In respiratory gated mode, AVB improved NCC\textsubscript{diff}, MSE, and DSC\textsubscript{lung} by 29\% ($p < 0.001$), 34\% ($p < 0.001$), 0.4\% ($p < 0.001$),
respectively. AVB increased the cine acquisitions by 15 s and reduced respiratory gated acquisitions by 31 s. AVB increased imaging dose in cine mode by 10%.

This was the first study to quantify the impact of breathing guidance and respiratory gating on 4DCT imaging. With the exception of DSC_tumor in respiratory gated mode, AVB significantly improved 4DCT image analysis metrics in both cine and respiratory gated modes over free breathing. The results demonstrate that AVB and respiratory-gating can be beneficial interventions to improve 4DCT for cancer radiation therapy, with the biggest gains achieved when these interventions are used simultaneously.

Keywords: 4DCT, thoracic imaging, breathing guidance, respiratory gating

(Some figures may appear in colour only in the online journal)

1. Introduction

4D computed tomography (4DCT) is an imaging modality frequently utilized to incorporate breathing motion in the treatment planning stage of radiotherapy (Ford et al. 2003, Vedam et al. 2003, Keall 2004, Pan et al. 2004). However, image artefacts have been reported in up to 90% of 4DCT images (Yamamoto et al. 2008), compromising the accuracy of tumor delineation (Persson et al. 2010). These artifacts have been linked to irregular breathing (Mutaf et al. 2007, Clements et al. 2013, Zhang et al. 2013). An additional problem is inconsistent inter-fraction breathing motion, where the tumor motion observed during 4DCT treatment planning is not consistent with the motion observed during treatment delivery (Ge et al. 2012), resulting in an increase in the irradiated healthy tissue (Schmidt et al. 2013). The radiation treatment volume itself is often expanded to account for these additional errors (Roman et al. 2012), increasing the radiation dose to the healthy surrounding tissue, thus further increasing the risk of post-treatment radiation toxicities (Rancati et al. 2003, Matsuo et al. 2012, Wang et al. 2013, Scotti et al. 2014).

To reduce the errors associated with irregular breathing motion, the patient breathing guidance system, audiovisual biofeedback (AVB) has been utilized to facilitate regular and consistent respiratory-motion (George et al. 2006, Venkat et al. 2008, Masselli et al. 2009, Kim et al. 2012, Pollock et al. 2015a, 2015b) to improve image quality (Yang et al. 2012, Cossmann 2012), imaging and treatment time (Jhooti et al. 2011, Park et al. 2011, Cossmann 2012), and treatment accuracy (Chen et al. 2007). However, the assessment of patient breathing guidance on 4DCT image quality has yet to be quantified. A study by Cossmann (2012) noted that the more consistent breathing motion as provided by breathing guidance improved the quality of 4DCT images (Cossmann 2012), but this improvement was not quantified. Another study by Lu et al. (2014) investigated the impact of breathing guidance on the match between ITV_{MIP} (internal target volume generated by contouring in the maximum intensity projection scan) and ITV_{10} (ITV generated by combining the gross tumor volumes contoured over the 10 phases of a 4DCT) (Lu et al. 2014); however, no analysis of image quality was performed.

A second method to reduce irregular breathing motion artefacts is prospective gating, which limits the 4DCT ‘beam-on’ time to regular breathing, defined in terms of real-time displacement, velocity and/or phase criteria. A number of experimental and simulation studies have suggested a potential improvement to 4DCT image quality using real-time prospective gating, at some cost to acquisition time (Keall et al. 2007, Langner and Keall 2010, Bernatowicz et al.)
Bernatowicz et al (2015) simulated prospective gated 4DCT acquisition for 8 patients, using the realistic 4D eXtended cardiac-torso (XCAT) deformable digital human phantom (Segars et al 2010, Bond et al 2012) synchronized to measured tumor motion patterns (Mishra et al 2012). They found prospective respiratory gated 4DCT reduced the mean square error (MSE) difference between reconstructed and ground truth thoracic 4DCT images as much as 46% on average, but with an average acquisition time 84% longer than cine mode. Computer-controlled prospective gated 4DCT has yet to be implemented clinically, in part because the anticipated increase in acquisition time may be considered a disadvantage in busy hospital environments. Meanwhile the XCAT has been utilized in a number of simulation studies to quantify the impact of breathing motion on image quality (Cai et al 2011, Rong et al 2012, Bernatowicz et al 2015) and on treatment delivery (Ecclestone et al 2013, Koybasi et al 2014).

The goal of this study is to perform the first comparisons of AVB and prospective gating technologies in view of their impacts on 4DCT image analysis metrics and acquisition time. This is also the first study to investigate the impact of breathing guidance on 4DCT image analysis metrics directly. As in the Bernatowicz study, this work employs the 4D XCAT but with an added emphasis on realistic patient motion. This is achieved by incorporating not only tumor motion, but also simultaneous measurements of chest wall, abdominal wall, and thoracic diaphragm motion. This data is derived from a study by Lee et al (2016) who performed magnetic resonance imaging (MRI) on lung cancer patients whilst they breathed both with and without the aid of AVB (Lee et al 2016). The Lee et al (2016) study extracted lung tumor and thoracic diaphragm motion information from the 2D MR images as well as monitoring external breathing motion from the real-time position management (RPM) system and the Siemens physiological measurement unit (PMU) chest belt.

By programming the 4D XCAT with separate internal and external breathing motion patterns, we aim to perform realistic comparisons of 4DCT imaging across two breathing conditions (AVB and free breathing) and two acquisition modes (cine mode and prospective respiratory gating). We hypothesize that the more regular breathing motion as provided by AVB will result in improved 4DCT image analysis metrics over free breathing, and that the largest improvement in image analysis metrics will come from the use of both AVB and respiratory gating interventions. Other metrics, such as acquisition time, could be more dependent on couch-stay time than motion regularity, particularly in cine mode.

2. Method and materials

To simulate 4DCT imaging as realistically as possible, the XCAT digital phantom was programmed with both the internal and external motion information in addition to lung tumor size and position information obtained in the Lee et al (2016) MRI study (Lee et al 2016).

2.1. Breathing motion data

Breathing guidance utilized by the 10 lung cancer patients in the Lee et al (2016) study was the AVB system, as developed by Venkat et al (2008). Lee et al (2016) analyzed the lung tumor motion regularity of these 10 lung cancer patients and found that AVB significantly improved the regularity of lung tumor motion period and displacement by 73% and 34%, respectively (Lee et al 2016).

10 non-small cell lung cancer (NSCLC) patients underwent two MR imaging sessions, the second session occurring 3–6 weeks after the first. Each session involved imaging the patient under two breathing conditions: (1) with AVB, and (2) free breathing. Sagittal MR
images yielded 2D lung tumor motion (superior–inferior (SI) and anterior–posterior (AP)). Tumor motion was extracted from the centroid of the segmented tumor, tumor segmentation was performed by a region-growing algorithm (Lee et al 2016). External breathing motion of chest motion and abdominal motion was also monitored during MR imaging. Chest motion was monitored by the Siemens PMU belt, and abdominal motion was monitored by the Varian RPM system. Figure 1 illustrates the motion utilized to program the motion of the XCAT phantom.

XCAT programmable motion inputs include chest AP motion, thoracic diaphragm SI motion, tumor AP, SI and left–right (LR) motion. Other XCAT inputs include tumor position within the lung and tumor volume. External motion utilized was the chest displacement information from PMU belt. PMU belt motion was used to program the XCAT chest motion, while diaphragm SI motion, and tumor SI and AP motion was used to program the XCAT internal motion. XCAT tumor LR motion was disabled as it could not be obtained from the sagittal MR images. RPM phase information was used for 4DCT binning. It should be noted that chest motion from the PMU belt was originally normalized and without units. To obtain absolute chest displacement, the PMU motion data was rescaled to have one quarter of the AP motion range of the corresponding RPM signal. This is in accordance with findings presented by Kaneko and Horie (2012).

The inclusion criteria for this study was that free breathing tumor motion be greater than 0.5 cm as stated in the management of respiratory motion in radiation oncology report of AAPM Task Group 76 (Keall 2006). This inclusion criteria made 6 patients across 10 MRI sessions eligible for simulation in this study.
Table 1 details the patient characteristics included in this study, the mean age of patients was 66 years (range: 54–79) with 3 male and 3 female.

### Table 1. Patient tumor motion information, peak-to-peak amplitude is given in brackets.

| Patient | Session number | Tumor volume (cm³) | Free breathing (peak-to-peak amplitude) (cm) | AVB (peak-to-peak amplitude) (cm) |
|---------|----------------|--------------------|---------------------------------------------|----------------------------------|
| 1       | 1              | 21                 | 0.8 (0.7)                                   | 0.7 (0.5)                        |
|         | 2              | 15                 | 0.7 (0.5)                                   | 0.9 (0.4)                        |
| 2       | 1              | 19                 | 0.6 (0.2)                                   | 0.7 (0.3)                        |
|         | 2              | 7                  | 0.8 (0.3)                                   | 0.6 (0.4)                        |
| 3       | 1              | 29                 | 0.6 (0.2)                                   | 0.5 (0.2)                        |
| 4       | 1              | 19                 | 1.9 (1.0)                                   | 2.1 (1.6)                        |
|         | 2              | 20                 | 2.2 (1.4)                                   | 2.9 (2.0)                        |
| 5       | 1              | 73                 | 0.7 (0.2)                                   | 0.6 (0.3)                        |
|         | 2              | 58                 | 0.9 (0.2)                                   | 0.3 (0.2)                        |
| 6       | 2              | 46                 | 0.5 (0.2)                                   | 0.4 (0.2)                        |
| Average (range) |     | 55 (7–73)         | 1.0 (0.5) (0.5–2.2 (0.2–1.4))              | 1.0 (0.6) (0.3–2.9 (0.2–2.0)) |

2.2. Simulation of 4DCT acquisition using XCAT

Our method for simulating 4DCT acquisitions proceeds similar to the retrospective method used by Bernatowicz et al (2015). Briefly, for each simulation the first 60 s of RPM displacement/phase data are analyzed to determine the average breathing period $T_{\text{Avg}}$, as well as the mean ($D_{\text{Mean}}$) and std. dev. ($D_{\text{SD}}$) of displacement in each of 10 phase bins. The subsequent RPM data is then analyzed to derive a schedule of couch shifts and kilovoltage (kV) image acquisitions, used to extract axial slices from the 4D XCAT programmed with the measured patient motion. Figure 2 details the workflow of this study.

In these simulations, the cine mode uses a constant kV imaging frequency corresponding to a gantry rotation time of 0.3 s, and a constant couch-shift frequency corresponding to a cine duration of $T_{\text{Avg}} + 1$ s for each of 30 couch positions. The CT slice acquisition time was determined by multiplying a typical 0.5 s gantry rotation time by a factor of approximately 220/360 (accounting for the angular span required for a single complete reconstruction) resulting in a 0.3 s acquisition time for each CT slice. Cine mode represents the conventional reconstruction 4DCT method for many scanners (Yamamoto et al 2008, Langner and Keall 2010). The respiratory gated mode is similar to the cine mode, except that kV acquisition is triggered only when the real-time respiratory motion falls within a phase-specific displacement gating window $D_{\text{Mean}} \pm D_{\text{SD}}$. The respiratory gated mode disallows duplicate kV acquisitions at the same couch position/phase bin and allows early couch shifts once all 10 phase bins are acquired. The gated mode allows a maximum couch stay of 2500 s at any one couch position, but this limit was never exceeded in any of the simulations. For each kV imaging timepoint, we generate an instantaneous 3D XCAT volume, and extract 4 axial slices (spaced 2.5 mm apart) corresponding to the given couch position. The simulation method does not include a forward/backprojection step (i.e. the simulated CT slices are not reconstructed from a simulated sinogram, rather they are extracted directly from the XCAT volume). This is appropriate as our focus is on motion-induced anatomic discontinuities, rather than image blur.
For the case of perfect 4D sampling (i.e. no duplicate or missing phase/couch combinations), each simulation will nominally produce 1200 axial slices that are binned into 10 respiratory phase bins. We also generate a set of ‘Ground truth’ 4D phase images, which give the average of all instantaneous XCAT volumes generated for each phase bin. These motion-blurred images represent the ‘average’ anatomic geometry during beam-on time. We note that while our simulation of the respiratory gated acquisition was performed retrospectively, the kV triggering is nevertheless based on measured, real-time RPM phase/displacement data as would be the case for a clinical implementation of this gating method.

2.3. Image analysis metrics

Image quality was quantified by (1) an automated method of assessing the presence of image artefacts (Cui et al 2012), (2) MSE intensity difference between the simulated 4DCT and ground images (Bernatowicz et al 2015), and (3) the dice similarity coefficient (DSC) between simulated 4DCT and ground truth images (Bernatowicz et al 2015).

Respiratory related 4DCT image artefacts were assessed utilizing a method developed by Cui et al (2012). Specifically, for each 4DCT phase image we calculate the normalized cross correlation (NCC) of pixel values between each pair of adjacent axial slices:

\[
\text{NCC}(i, z) = \frac{\sum_{x,y} I(i, z)I(1, z + 1)}{\sqrt{\sum_{x,y} I(i, z)^2} \times \sqrt{\sum_{x,y} I(1, z + 1)^2}}
\]

In equation (1), \(i\) specifies the phase bin, \(z\) specifies the axial slice and \(x, y\) refer to the pixel location in the transverse plane. An NCC value closer to 1 indicates better agreement in pixel values between adjacent slices, conversely a value closer to 0 indicates poor agreement. Unlike the DSC metric, the NCC values are calculated in the absence of any tumor intensification. We then obtain an artefact rating, NCCdiff which accounts for the sum of differences in NCC values at couch transition points across each reconstructed 4DCT phase image.
Where $n_{\text{bound}}$ represents the slice index for the transition between the $n$th and $(n + 1)$th couch position. Here, a value of $\text{NCC}_{\text{diff}}$ closer to 0 indicates smaller differences in the NCC values between adjacent axial slice pairs across the image, and hence fewer anatomic discontinuities.

We note that $\text{NCC}_{\text{diff}}$ should not be interpreted as an absolute artefact ‘count’ as it may also capture information about non-artefactual anatomic discontinuities. For example, a slice pair straddling the diaphragm edge will likely exhibit a poorer NCC value than for slice pairs where both slices are just above or just below the edge. Since all 4DCT reconstructions have the same geometry at exhale (aside from the tumor), and thus similar contributions to $\text{NCC}_{\text{diff}}$ from non-artefact discontinuities, we interpret $\text{NCC}_{\text{diff}}$ as an artefact ‘rating’ or ‘quality factor’.

DSC between simulated and ground truth images was assessed in terms of lung volume ($\text{DSC}_{\text{lung}}$) and lung tumor volume ($\text{DSC}_{\text{tumor}}$). To more easily evaluate the tumor volume, the tumor volume was intensified by a factor of 10, as per the method described by Bernatowicz et al (2015). The intensity values of tumor voxels was multiplied by a factor of 10 to aid in segmentation; this modification of the tumor intensities was performed only for the $\text{DSC}_{\text{tumor}}$ analysis so does not affect the NCC or MSE values.

These image analysis metrics were compared across the two breathing conditions (AVB and free breathing) for the two 4DCT acquisition modes (cine and respiratory gated) using the Student’s $t$-test. 4DCT imaging dose and acquisition times were also recorded across the two breathing conditions and two reconstruction methods. It should be noted that the image dose estimate is based on the number of acquired slices; results presented here will be in number of slices as a surrogate for imaging dose.

### 2.4. Correlation between image analysis metrics and respiratory motion

The correlation between the image analysis metrics and lung tumor motion regularity in addition to acquisition time and lung tumor motion regularity was assessed using the Pearson’s correlation coefficient ($R$), and a $p$-value for testing the hypothesis of no correlation. Pearson’s correlation coefficient has been utilized as the correlation test in previous internal–external respiratory motion studies (Ionascu et al 2007, Steel et al 2014). Respiratory motion regularity was quantified by the root mean square error (RMSE) in displacement (Venkat et al 2008) of the respiratory signal of chest motion during beam-on time only. A lower value of RMSE is indicative of more regular motion. We investigated the potential dependence of imaging time on displacement RMSE for both cine and respiratory gated acquisition modes. For the respiratory-gated mode it seems intuitive that highly irregular breathing could affect the scan time. For cine mode the connection between displacement RMSE and scan time is more subtle; since in our study the cine mode uses a ‘patient specific’ cine duration set at one breathing period ($T_{\text{Avg}}$) + 1 s, it follows that irregularities in the breathing period (or alternately, displacement) could affect the cine mode scan times as well.

### 3. Results

#### 3.1. Reconstructed 4DCT Images of XCAT Phantom

Figure 3 illustrates the original MRI and 4DCTs for Patient 4, whose resultant $\text{NCC}_{\text{diff}}$ value in cine mode was the median.
3.2. 4DCT Image Analysis Metrics

NCC$_{\text{diff}}$, MSE, DSC$_{\text{lung}}$, and DSC$_{\text{tumor}}$ values were generated for each 4DCT respiratory bin, as such, 10 metric values were generated for each simulated 4DCT. The results for these metrics are shown in figure 4; average values and their statistical significance are shown in table 2.

Merging the data from the AVB and free breathing conditions, cine mode yielded mean NCC$_{\text{diff}}$, MSE, DSC$_{\text{lung}}$, and DSC$_{\text{tumor}}$ values of 0.099, $9.4 \times 10^{-7}$, 0.980, and 0.889 respectively. Respiratory gating improved the NCC$_{\text{diff}}$, MSE, DSC$_{\text{lung}}$, and DSC$_{\text{tumor}}$ values by 36% ($p < 0.001$), 42% ($p < 0.001$), 0.7% ($p < 0.001$), and 2.3% ($p = 0.01$), over cine mode respectively. With the exception of DSC$_{\text{tumor}}$, the largest improvements were obtained when utilizing both AVB and respiratory gating together, which improved NCC$_{\text{diff}}$, MSE, DSC$_{\text{lung}}$, and DSC$_{\text{tumor}}$ values by 52% ($p < 0.001$), 59% ($p < 0.001$), 1.2% ($p < 0.001$), and 3.5% ($p = 0.01$), respectively, compared to cine mode 4DCT under free breathing. For the DSC values, this translates to an additional 38 cm$^3$ of correctly imaged lung volume and an additional 0.9 cm$^3$ of correctly imaged tumor volume. While we cannot guarantee that the volumes encompassed by these respective contours are imaged correctly, from a treatment planning perspective the impact of modified contours on the dose-volume calculations may still be significant. A surprising result here is that the use of AVB and respiratory gating yielded inferior (though non-significant) DSC$_{\text{tumor}}$ values compared to AVB with cine mode in addition to free breathing with respiratory gating.

3.3. Image dose and acquisition time

Figure 5 shows the mean ± standard deviation 4DCT acquisition times and imaging dose across cine mode and respiratory gated mode for AVB and free breathing patients. Number of slices acquired is given as a surrogate for imaging dose.

The ground truth images in figure 3 also demonstrate some blurring, particularly around the thoracic diaphragm. This blurring arises because the ground truth was constructed from a range of anatomic positions during beam-on time.

Figure 3. Left to right: Original MR image (tumor outlined in blue), simulated inhale phase images for cine ground truth 4DCT, cine mode 4DCT and respiratory gated (Resp. Gated) ground truth 4DCT, and Resp. Gated 4DCT in the sagittal (top) and coronal (bottom) planes for Patient 4. *Coronal MR images acquired at different times to sagittal MR images, only data from sagittal MR images was used to program XCAT motion. Coronal MR image is shown here to demonstrate anatomic comparison to reconstructed 4DCT coronal images.
Merging the data from the AVB and free breathing conditions, cine mode yielded a mean acquisition time of 227 ± 23 s, 31% faster than respiratory gated mode which had an acquisition time of 328 ± 89 s. Interestingly, the impact of AVB on acquisition times was opposite between the two acquisition modes. In cine mode, AVB increased the average imaging time by 15 s compared to free breathing ($p = 0.02$); whereas in respiratory gated mode, AVB reduced the average imaging time by 31 s compared to free breathing ($p = 0.41$). In cine mode, AVB increased the estimated average imaging dose by 10% compared to free breathing ($p = 0.05$); whereas the respiratory gated mode always acquired 1200 slices by construction as this represents the ideal 4D sampling for this simulation (10 phase bins with 120 slices each). It should be noted that the number of slices in respiratory gated mode was 1200 by construction, as 1200 slices represents the ideal dose for this simulation.

### 3.4. Correlation between image analysis metrics and respiratory motion

Table 3 compares values of the displacement RMSE during beam-on time for different breathing conditions and acquisition modes.
For each combination of breathing condition and acquisition mode, the RMSE values are different owing to the different acquisition timing.

Figure 6 shows the variation of the image analysis metrics (NCC\textsubscript{diff}, MSE, DSC\textsubscript{lung}, and DSC\textsubscript{tumor}) and acquisition time as a function of the RMSE values, separated according to breathing condition and acquisition mode. For any given acquisition mode, AVB produced a smaller range of RMSE values compared to free breathing. For each panel of figure 6, table 4 shows the Pearson’s correlation coefficient irrespective of breathing condition.

4. Discussion

This was the first study to quantify the impact of AVB breathing guidance on 4DCT image analysis metrics. As shown in tables 2 and 3, with the exception of DSC\textsubscript{tumor} in respiratory gated mode, AVB significantly improved 4DCT image analysis metrics across both acquisition modes.
The impact to DSC values, while mostly significant, were small (<1%); whereas the magnitude of the impact of AVB to NCCdiff and MSE was considerably larger. Compared to conventional free breathing 4DCT in cine mode, the addition of both AVB and respiratory gated mode improved DSClung, NCCdiff, and MSE by 1.2% (\(p<0.001\)), 52% (\(p<0.001\)), and 59% (\(p<0.001\)), respectively. As illustrated by figure 4, respiratory gated mode yielded better 4DCT image analysis metrics over cine mode, which is consistent with the findings of previous investigations (Langner and Keall 2010, Bernatowicz et al 2015). Bernatowicz et al (2015) reported slight, but significant, improvements in lung errors of 0.4% due to respiratory gated mode compared to cine mode (Bernatowicz et al 2015); comparable to the 0.7% improvement of respiratory gated mode over cine mode demonstrated here.

As shown in table 4, motion regularity (RMSE) during beam-on time significantly correlated with DSClung, NCCdiff, and MSE in cine and respiratory gated acquisition modes, in addition to significantly correlating with acquisition time in respiratory gated mode. It is important to note that other factors beyond RMSE in displacement will impact image analysis metrics and acquisition time. For instance, the average period increased from 4.3 s under free breathing to 4.8 s using AVB. Thus the use of AVB lead to increased cine duration time (\(T_{\text{Avg}} + 1\) s) explaining why AVB produced longer cine acquisition times and increased imaging dose compared to free breathing in figure 5. It should be noted that will not be the case for clinical 4DCT.
protocols using a fixed cine-duration time (as opposed to the patient specific cine duration of $T_{\text{Avg}} + 1$ s). In respiratory gated mode, AVB reduced acquisition times as a result of improved motion regularity, which has been shown to improve gating efficiency in previous studies (George et al 2006, Linthout et al 2009, Lee et al 2014). Also, each simulation will nominally

![Graph](image-url)
produce 1200 axial slices that are binned into 10 respiratory phase bins and respiratory gating is optimized to produce exactly 1200 axial slices, which is why the mean ± standard deviation number of slices for respiratory gating are 1200 ± 0 for both AVB and free breathing, as shown in figure 5.

Furthermore, while DSC\textsubscript{tumor} was the only image analysis metric not to significantly correlate with motion regularity, it was found that DSC\textsubscript{tumor} did significantly correlate with the tumor motion range values (given in table 1) for both cine mode ($r = -0.79$, $p < 0.001$) and respiratory gated mode ($r = -0.86$, $p < 0.001$). Given that the average peak-to-peak amplitude of free breathing was 0.5 cm and 0.6 cm for AVB, this may explain why an improvement was not observed for AVB in respiratory gated mode. Further to this, 4DCT gating and binning is based on the signal of an external surrogate and not the motion of the tumor itself.

This study builds upon previous investigations which assessed the impact of breathing guidance interventions on medical image quality. Yang et al (2012) found that AVB reduced motion blurring and improved Dice coefficient of the tumor in PET images of a thoracic phantom (Yang et al., 2012). Jhooti et al (2011) and Lee et al (2014) observed a reduction in MRI scan time from the use of breathing guidance with only the Lee et al (2014) study noting an improvement in image quality. Importantly, table 4 indicates that respiratory motion regularity (RMSE in displacement) during beam-on time may be a useful metric for predicting quantitative aspects of 4DCT image analysis metrics. It would be interesting to test how well RMSE correlates with other clinically relevant measures of 4DCT image quality (e.g. absolute artefact counts).

A limitation of this study, as evident from figure 3, is that the anatomy of the XCAT digital phantom did not exactly match that of the original MR images. Differences in tumor shape, organ shapes, and organ volumes between the XCAT and MRI scans may be observed. Despite these differences, the XCAT represents a population averaged anatomy, based on visible human data from the National Library of Medicine (Segars et al, 2010, National Library of Medicine), so these results should be relevant to a large percentage of the adult (male) population receiving 4DCT scans. An additional limitation is that our 4DCT simulations assumed x-ray collimation of $4 \times 2.5$ mm at the detectors, whereas newer scanners might have $8 \times$, $16 \times$, or more which would decrease the number of couch transition regions where breathing-induced image discontinuities might occur. In other words, our simulations may overestimate the impact of AVB or respiratory gating for wide field of view 4DCT scanners. This study

| Table 4. Pearson’s correlation coefficient values ($r$) and their $p$-values for the correlations between respiratory motion regularity (RMSE) and image analysis metrics irrespective of breathing condition. |
|-----------------|------------|------------|
|                  | $r$ value  | $p$-value  |
| Cine             |            |            |
| NCC\textsubscript{diff} | 0.89       | <0.001     |
| MSE              | 0.91       | <0.001     |
| DSC\textsubscript{lung} | -0.92     | <0.001     |
| DSC\textsubscript{tumor} | -0.23     | 0.32       |
| Acquisition time | -0.29      | 0.21       |
| Respiratory gated|            |            |
| NCC\textsubscript{diff} | 0.91       | <0.001     |
| MSE              | 0.68       | <0.001     |
| DSC\textsubscript{lung} | -0.91     | <0.001     |
| DSC\textsubscript{tumor} | -0.30     | 0.19       |
| Acquisition time | 0.46       | 0.04       |

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attempted to adapt the XCAT simulations to the MRI acquisition as much as possible by utilizing the several elements of the MRI patient data: tumor motion, diaphragm motion, chest motion, abdominal motion, tumor volume, and tumor position. Despite this, diseased lung can exhibit localised variations in the motion field that are not so easily modelled using XCAT. For tumors in the vicinity of emphysematous or fibrotic regions, the measured motion may appear different compared to the XCAT motion which assumes smoothly varying motion over the lung. Further to this, the MRI data utilized in this study had an acquisition time of approximately 158 s, shorter than the time needed to complete a 4DCT simulation. As such, the motion traces were repeated until the 4DCT image acquisition was complete; the discontinuity between these repeated motion segments is not ideal.

Additionally, a limitation of our RMSE calculation is that we generated a ‘mean’ cycle based on only 10 phase bins, as opposed to a much larger number (e.g. 360) in other studies (Venkat et al 2008, Pollock et al 2015c). This seemed appropriate due to the instantaneous nature of the simulated beam-on events which leads to a sparse amount of displacement data during beam on time, resulting in a larger magnitude of RMSE results compared to previous investigations.

The results presented here support our hypothesis that AVB resulted in improved 4DCT image analysis metrics over free breathing. The respiratory gated mode resulted in improved 4DCT image analysis metrics over cine mode, however, acquisition time was faster in cine mode compared to the respiratory gated mode. This study indicates that respiratory gated mode can benefit from AVB not only in terms of improved image analysis metrics, but also in reduced acquisition times compared to free breathing. AVB and respiratory gated mode represent two emerging techniques to improve the quality of 4DCT images, producing the best image analysis metrics when used simultaneously.

5. Conclusion

This was the first study to compare the impacts of AVB breathing guidance, and prospective respiratory gated acquisition on 4DCT image analysis metrics compared to free breathing cine mode 4DCT. Compared to free breathing, AVB was demonstrated to significantly improve the image analysis metrics of both cine and respiratory gated modes of 4DCT acquisition, and can reduce the amount of time needed to acquire a respiratory gated 4DCT scan. Meanwhile, respiratory-gating consistently yielded better image analysis metrics over cine mode irrespective of the breathing condition. The results presented here demonstrate both AVB and the respiratory gated acquisition mode as potential tools to implement in CT simulation for cancer radiation therapy. Statistically significant improvements in image analysis metrics can be realized for a small increase in time when AVB and respiratory gated mode are utilized simultaneously.

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