Published in final edited form as:

Int J Radiat Oncol Biol Phys. 2008 January 1; 70(1): 243–252. doi:10.1016/j.ijrobp.2007.09.013.

The effect of a novel amplitude/phase binning algorithm on commercial 4DCT quality

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Abstract

Purpose—Respiratory motion is a significant source of anatomic uncertainty in radiotherapy treatment planning, and may result in errors of portal size and subsequent radiation dose. While 4DCT allows for more accurate analysis of the respiratory cycle, breathing irregularities during data acquisition may cause considerable image distortions. The aim of this study was to examine the impact of respiratory irregularities on 4DCT imaging, and to evaluate a novel image reconstruction algorithm based upon percentile-based tagging of the respiratory cycle.

Materials/Methods—Respiratory correlated helical CT was acquired on 11 consecutive patients. Inspiration and expiration datasets were reconstructed using the default phase based method as well as a novel respiration percentile based method using patient specific metrics to define ranges of the reconstruction. Image output was analyzed in a blinded fashion for both the phase and percentile based reconstructions to determine the prevalence and severity of image artifacts.

Results—The percentile-based algorithm resulted in a significant reduction in artifact severity compared to the phase-based algorithm, although overall artifact prevalence did not differ between the two algorithms. The magnitude of differences in respiratory tag placement between the phase and percentile based algorithms was correlated with the presence of image artifacts.

Conclusions—We conclude that our novel 4DCT reconstruction method may be useful to detect clinically relevant image distortions that may otherwise go unnoticed, and to reduce image distortion associated with some respiratory irregularities. Further work is necessary to assess the clinical impact on areas of possible irregular breathing.

Keywords

4DCT; radiotherapy; respiratory gating; lung motion; breathing motion

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Conflict of Interest Notification: The Washington University authors have ongoing research collaborations with Philips Medical Systems. Additionally, one author is employed by Philips Medical Systems and has a financial interest in this research.

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INTRODUCTION

Respiratory motion is a significant source of anatomic uncertainty in radiotherapy treatment planning for both lung^{1–5} and abdominal⁶ tumors. CT imaging studies used for treatment planning may contain various image artifacts^{7–9}, and improperly estimate both the position and volume of critical structures, leading to errors both in portal size and radiation dose⁷. In IMRT treatment, the interplay of both target and beam motions may influence dose delivery¹⁰. The importance of precise motion estimates in this setting has been demonstrated by several studies of respiratory motion during IMRT^{11–13}. Similar effects may be seen in intensity-modulated charged particle therapy, where variation in internal tissue density further impacts the delivered dose¹⁴. These motion estimates are also of paramount importance during gated treatment¹⁵.

Methods employed to reduce radiotherapy errors due to respiratory motion include breath holding during CT image acquisition^{16–18}, active patient control of breathing^{19, 20}, and modeling of tumor motion based upon external markers of respiration^{1, 2, 21–23}. While respiratory control techniques can reduce treatment planning errors^{16, 17, 24}, many lung cancer patients are unable to precisely manipulate their breathing. Fluoroscopy has been used to assess organ motion^{24–26}, but poor soft tissue resolution, and the lack of 3D data inherent to fluoroscopic imaging limit the precise determination of trajectories^{27, 28}.

4DCT imaging is a new technique that utilizes time-resolved CT images to directly incorporate organ motion into treatment planning, allowing for a more accurate determination of organ and tumor trajectories^{29, 30}. Unfortunately, breathing irregularities during data acquisition can cause considerable image distortion that may not be readily apparent during visual inspection of images. Commercial 4DCT images are currently reconstructed using a phase-based respiratory binning method that may result in numerous image misalignments due to irregularities in respiration amplitude and frequency³¹. While manual phase sorting methods that allow the user to select each 0% phase point have also been proposed, such methods may not allow for correction of irregularities in breathing that occur between the manually selected phase points³². In addition, manual re-tagging of the respiratory curve may be both time consuming and user dependent. Pure amplitude based sorting methods have also been studied, but may not account for changes in trajectory that occur between inspiration and expiration, as shown in fiducial tracking studies³. We propose that pure phase and pure amplitude based models are both inappropriate for 4DCT binning, due to the irregularity of breathing observed in many patients for whom 4DCT imaging is utilized.

At our institution, we have previously developed a patient specific statistical method, based upon respiration amplitude percentiles, to model breathing motion with improved compensation for respiratory irregularities^{33, 34}. The use of percentiles takes into consideration the relative time a patient reached each respiration amplitude, so that breathing data is much less affected by the few extreme breaths (deep inhalation or exhalation) often seen during the entire scanning session. We have previously found that this algorithm more accurately predicts internal air content of the reconstructed images, as well as the respiratory surrogate amplitude as compared with a phase based algorithm using a research image acquisition protocol³⁴. However, this study did not investigate the use of commercially acquired helical data nor did it systematically assess the image quality of each reconstruction.

The purpose of this study is to apply our breathing motion model as a novel 4DCT respiratory binning technique. We propose that our technique may reduce the prevalence and severity of 4DCT image artifacts when compared to the widely used phase-based binning method.

METHODS AND MATERIALS

Respiratory correlated helical CT data was acquired under an IRB protocol for 11 consecutive patients ranging in age from 57–86, with diagnoses of primary lung cancer (10), and bile duct adenocarcinoma (1), using a 16-slice CT scanner (Brilliance, Philips Medical Systems, Cleveland, Ohio) along with a pneumatic bellows belt around the abdomen. The regularity of breathing varied across each of the 11 patients. The helical 4DCT technique has been described previously³⁵. The patients were not coached during image acquisition. While it is well known that coaching improves breathing pattern reproducibility^{36–38}, coaching is not employed at our institution. Since many of these patients do not receive gated radiation therapy, we do not have a method of following their breathing patterns throughout the course of radiation therapy, and we are concerned that respiratory coaching at the time of simulation may introduce a systematic error in radiotherapy planning and delivery. Images were acquired with a slice thickness of 3 mm, a scanner period of 0.44 seconds, and a collimator width of 16×1.5 mm. The collimated 3mm slice thickness was chosen over a 1.5 mm slice thickness to allow for sufficient visualization of lung and abdominal features, while maintaining a reasonably sized 4DCT dataset. The radiation dose delivered to patients in our clinic during a 4DCT scan has previously been measured at 8 cGy³⁹. The scanner pitch ranged from 0.059 to 0.15 to ensure that at least 1 breathing cycle was imaged for each longitudinal position. Inspiration and expiration datasets were reconstructed using the default phase based method as well as our novel amplitude percentile method, using patient specific metrics to define ranges of the reconstruction.

Phase Based Reconstruction

Respiratory tags were placed in a semi-automatic fashion at the local maxima of each respiratory waveform (Figure 1a) to determine the 0% phase point (peak inhalation), using a method that has been previously described⁴⁰. Respiratory correlated CT images were then reconstructed in 10% time increments of the breathing period as per our clinical routine. The CT image set representing 0% phase reconstruction was used for each phase based inspiratory dataset. To select each expiratory dataset, images representing each respiratory phase were manually observed to determine which phase-based image was most correlated with maximal expiration, based upon diaphragm position, according to our routine clinical protocol. For 9 patients, maximal expiration was based upon the 50% phase reconstruction, and for 2 patients, maximal expiration was based upon the 60% phase reconstruction. Figure 1b illustrates the 50% respiratory phase tags for one patient.

Percentile Based Reconstruction

We have developed a 4DCT binning technique based on both the percentile amplitude and direction (inhalation or exhalation) of tidal breathing. Respiratory data from each scanning session was retrospectively processed using MATLAB® data analysis software (The Mathworks, Natick, MA) to determine the frequency that each respiration amplitude was observed for each patient. A histogram displaying the frequency distribution of respiration amplitudes for one patient is shown in Figure 2a. Based on the distribution of amplitudes observed, individualized respiratory percentiles were assigned to each amplitude value for each waveform (Figure 2b). Respiratory tags were then placed on the breathing curve at the 90th and 5th percentiles of tidal volume for each respiratory cycle (Figures 3a, 3b)⁴⁰. To control for hysteresis, tags were always placed prior to the local maxima or minima for each respiratory cycle. If individual inspiratory or expiratory breaths failed to reach the 90th or 5th percentiles of breathing, respectively, then tags for such breaths were placed at end-inspiration or end-expiration. Inspiration and expiration CT image datasets were then reconstructed based upon the percentile tag placements.

Comparison of Tag Placement

The placement of corresponding phase and percentile-based respiratory tag pairs was analyzed using MATLAB® software. To account for variation in respiratory frequency between patients, time differences between corresponding phase/percentile tags were normalized to a percentage of each patient's mean respiratory period. These normalized differences in tag placement were then sorted in descending order across all patients to determine the 15 tag pairs corresponding to the 5 largest, 5 smallest, and 5 nearest-median differences in tag placement between the phase and percentile algorithms for both inspiratory and expiratory binning. Examples of large, medium, and small differences in tag placement are shown in Figure 4. Because our goal was to analyze artifacts in the lungs, tags were only included for this analysis when they corresponded to an image that intersected the lungs.

Comparison of Reconstructed Image Datasets

For each of the 30 phase/percentile tag pairs selected (15 each for inspiration and expiration), CT images for each algorithm were contoured using Pinnacle³ treatment planning software (Philips Medical Systems, Cleveland, Ohio) to illustrate the scanner gantry position corresponding to tag placement (Figure 4). The presence of image artifacts in the coronal plane for each contoured region was then assessed in a randomized, blinded manner by 3 of the coauthors (P.J. Parikh, J.P. Hubenschmidt, D.A. Low), all of whom have extensive clinical and research experience in 4DCT image analysis. Image artifacts were defined to include any definitive distortions of patient anatomy, such as abrupt anatomical shifts between adjacent slices, or inappropriate repetition of identical patient anatomy over several image slices. The specific survey method used is illustrated in Figure 5. For each region, image evaluators scrolled throughout coronal image slices to assess for the presence of any image artifacts between the highlighted axial planes. This restriction of the artifact survey to the highlighted craniocaudal regions ensured that artifacts observed were correlated with specific scanner gantry positions for each investigated respiratory tag. Each gantry position was known to correlate with a specific point on the respiratory tracing. Therefore, each region of interest in the CT images was known to correlate with a specific level of irregular breathing (large, medium, or small), based upon the recorded respiratory tracing. Due to the positions of these respiratory tracing irregularities, they would not always correlate with a complete anatomic structure, such as the whole diaphragm, or the whole bronchus. Therefore, our survey instrument specifically limited the area of interest to image levels that correlated with respiratory irregularities. For example, in Figure 5, irregular breathing occurred during the imaging of the lower half of the diaphragm, but not during the imaging of the upper half of the diaphragm. Therefore, only the lower half of the diaphragm was included in the evaluation of image quality. When artifacts were present on both the phase and percentile reconstructed images, participants additionally assessed on which image, if any, the artifact was more severe.

Statistical Analysis of Artifact Comparison

Statistical analysis was performed using NCSS statistical analysis software (NCSS, Kaysville, UT). The proportion of artifacts observed in images reconstructed using the phase-based and amplitude-based algorithms was compared using the Fisher's exact test for each tag-difference stratification (Table 1). Fisher's exact test was also employed to assess for statistically significant differences in the proportion of artifacts present in images reconstructed for the large, medium, and small tag difference stratifications. When artifacts were present for both the phase and percentile based reconstructions, a one-sample proportion test using the binomial model was used to evaluate the significance of observed differences in severity.

RESULTS

Comparison of Tag Placement

A histogram illustrating the range and frequency of occurrence of differences in tag placements observed for both the inspiratory and expiratory datasets is shown in Figure 6. The median normalized difference in corresponding phase/percentile respiratory curve tag placements for the inspiratory dataset was 4.4% of the mean respiratory period (range 0 – 57%). The median normalized difference in corresponding phase/percentile respiratory curve tag placements for the expiratory dataset was 6.5% of the mean respiratory period (range 0–70%). The normalized differences in tag placement were significantly larger for the expiratory dataset compared to the inspiratory dataset ($p<.002$). Stratified properties of the tag pairs in the large, medium, and small difference groupings used for the blinded analysis are shown in Table 1.

Artifact Prevalence as a Function of Tag Difference Magnitude

Results of the blinded image analysis are shown in Table 2. Artifacts were noted in 28/60, 19/60, and 11/60 images corresponding to large, medium, and small differences in tag placement. Differences in artifact prevalence as a function of tag group stratification (large/medium/small) were statistically significant for the large compared to the small tag difference groups ($p<0.002$), but not for the large-medium ($p<0.14$) or medium-small ($p<0.14$) comparisons. Several sample images from the blinded analysis are shown in Figures 7–10. The images shown in Figures 7 and 8 illustrate a large difference in tag placement, while those shown in Figures 9 and 10 illustrate medium and small differences in tag placement. Percentile based reconstructions appear on the left, while phase based reconstructions are shown on the right.

Artifact Prevalence as a Function of Tagging Algorithm

For both the inspiratory and expiratory data sets, there was no statistically significant difference in the prevalence of artifacts between the phase and percentile-based tagging methods for the large, medium, or small tag difference stratifications (Table 2).

Artifact Severity as a Function of Tagging Algorithm

In 19/30 cases where image artifacts were present on both the phase and percentile-based reconstructions, the artifacts were noted to be more severe on the phase-based algorithm in 12 cases, equivalent in 6 cases, and more severe on the percentile-based algorithm in 1 case. This difference in artifact severity count between the two algorithms was statistically significant ($p<0.006$). Examples of various differences in artifact severity are shown in Figures 7–10. In Figure 7, greater artifact severity was noted for the phase based (right) image, due to artifact obstruction of the right mainstem bronchus. In Figure 8, a greater artifact discontinuity of the left mainstem bronchus was noted for the phase based (right) image. In Figure 9, discontinuities in the pulmonary vasculature were noted for the phase based (right) image. Figure 10 illustrates a control example for a patient with regular breathing, where there were only small differences in tag placement between the percentile and phase based algorithms, and no image quality differences were noted.

DISCUSSION

Our analysis was a comparison of reconstructed images from the same patient using one respiratory binning algorithm compared to another, rather than a comparison of image quality between different patients. Though we used a helical CT acquisition method, our analysis is not intended to specifically address the strengths and benefits of helical compared to axial 4D

CT image acquisition. We have previously studied both amplitude and phase based 4dct image quality in a qualitative manner utilizing axial image acquisition with similar results³⁴.

We have attempted to minimize bias in our image analysis, through a blinded review of 4dct images by trained experts. However, we recognize that any qualitative image review may be subject to the bias of the reviewers. While a more quantitative analysis would be desirable, such a method is not yet feasible, since there is no 'gold standard' reference image. Even if we had performed breath hold ct scanning at end inspiration and end expiration, it is not clear that the measured image positions would correlate with those in a dynamically breathing patient. Quantitative phantom studies would be predicated on the input function given to the phantom. Phantoms driven using a sinusoidal function would have no errors when using phase based reconstruction, while those driven using an amplitude based function would have no errors with an amplitude based binning system. The method used of blinded image analysis represents a best attempt at scientifically evaluating clinical images by trained experts who routinely utilize 4dct imaging for treatment planning.

The image analysis technique used in our study represents a departure from that used in prior evaluations of image quality, but one that we propose is more appropriate for the analysis of artifacts due to breathing irregularities. Prior analyses of reconstruction artifacts have used a single anatomical structure for analysis, most commonly the diaphragm. While this is an appropriate method for the analysis of regular breathing, it is inadequate for the study of irregular breathing, because scanner gantry position coincides with the level of the diaphragm for only a small subset of the total image acquisition time. By limiting analysis to the diaphragm image levels only, data is lost corresponding to clinically significant breathing irregularities that may occur while image data is acquired at other anatomic levels. In our study, the examination of z-levels throughout the entire lung that were correlated with irregular breathing provided for a more robust analysis than examination of the diaphragm alone.

Clinical applications of 4DCT imaging are based upon the assumption that each binned image set uniformly represents a single, reproducible point in the breathing cycle. Analysis of our data reveals that this assumption is frequently not valid for phase based reconstructions. Figure 11 illustrates the respiratory amplitude percentiles contributing to each CT slice using both phase and percentile tagging algorithms, for the same patient whose sample images are shown in Figure 7. Determination of this data is based upon a previously described cardiac Philips reconstruction algorithm⁴¹ that is similar to the algorithm presently used for pulmonary 4DCT reconstruction. Of note, for the 0% phase and 90th percentile amplitude reconstructions, respiration percentiles that actually contributed to each image slice ranged from 77.2–99.9 and from 78.3–89.4, respectively. Binned 4DCT image sets for both phase and percentile tagging algorithms are therefore not representative of a uniform respiration amplitude throughout the image, although improved uniformity was noted for the percentile-based algorithm. This flatter curve may explain the statistically significant reduction in severity of artifacts observed with the percentile-based tagging method, since there were fewer discontinuities in respiratory percentile contributing to adjacent axial slices (Figure 11). Of note, the artifact shown in the right mainstem bronchus in Figure 7 correlates directly with the large discontinuity in respiratory amplitude at slice 70, in Figure 11. In this example case, the greater uniformity of amplitude based tagging correlated with a reduction in artifact severity (Figure 7), as gauged by blinded image analysis. Aside from contributions to artifacts, a uniform z-level/respiration percentile profile is desirable to improve the specificity of 4DCT binning for each point in the respiratory cycle.

In our analysis, differences between the phase and amplitude tag placements were significantly larger for the expiratory compared to the inspiratory dataset. This likely resulted from deviations in the expiratory phase-based tag placements from the desired end-expiratory points

on the respiratory curve. Due to irregularities in breathing rate, a single phase tag (i.e. 50% for expiration), is unable to consistently tag the local minima of the respiratory curve, and may therefore result in substantial deviation from the desired uniform, expiratory tag placement. This inconsistency inherent to phase based tagging of irregular breathing resulted in the larger tagging differences noted for the expiratory compared to the inspiratory dataset.

An additional contributing factor to artifact appearance and location is the redundancy of information obtained during image acquisition. Due to the low-pitch scanning required for helical 4DCT, image slices are frequently reconstructed with data from several respiratory cycles. This phenomenon of redundancy in the acquisition data also explains why some artifacts were observed in the small tag difference groups, since the respiratory tags in these groups may have been adjacent to other respiratory tags that were associated with a more irregular pattern of breathing. In respiratory correlated CT, the changes in signal amplitude are greater than that found in cardiac correlated ct, which may be why more artifacts are found in respiratory correlated ct compared to cardiac correlated ct when using phase based algorithms. This further complicates the quality assurance process of review of these images.

The statistically significant difference in the prevalence of artifacts between the large and small tag difference groups suggests that the magnitude of difference in tag placement between our percentile and the default phase-based algorithms may be useful in identifying artifact locations based upon the respiratory tracing. Tagging discrepancies between the two algorithms may therefore indicate the need for re-scanning of patients, in particular when the involved region of the image is critical for treatment planning. Incorporation of this automated respiratory analysis into 4DCT scanning software has the potential to improve the quality and efficiency of 4DCT imaging.

Further work is necessary to evaluate the clinical impact of irregular breathing during 4dct image acquisition. Breathing irregularities may be ignored, for example, if they occur during image acquisition of slices that are not needed for radiotherapy treatment planning. However, there is no guarantee that irregularities will only occur during parts of the ct scan that are not relevant for a patient's treatment planning. Moreover, further study is needed to determine the extent to which the clinical impact of these image artifacts is predicate to the delivery technique of the radiation therapy.

CONCLUSIONS

Percentile based tagging of the respiratory curve for 4DCT imaging reduces the severity of image artifacts. Comparison of percentile and phase based respiratory tag placements may also be useful to alert the clinical user to the presence of image artifacts, since a greater artifact prevalence was observed for large differences in tag placement. Percentile based tagging results in more uniform amplitude contributions to each binned image set, and constitutes an improved measure of each patients 'normal' respiratory cycle due to compensation for large irregular breaths. Our algorithm provides a rational and validated method to improve 4DCT image quality and treatment planning.

Acknowledgments

This research was first presented at the 2006 ASTRO annual meeting.

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Figure 1. Phase-based respiratory tagging at the 0% (a) and 50% (b) phases for one representative 4DCT patient.

Figure 2.

- (a) Histogram displaying the frequencies of each respiration amplitude occurrence during image acquisition for the patient in (1). Respiration amplitude was sampled every .04 seconds.
- (b) Illustration of the relationship between respiration amplitude and percentile for the same patient.

Figure 3. Percentile-based respiratory tagging at the 90th (a) and 5th (b) percentiles for a representative 4DCT patient.

Figure 4.

Shown from left to right are examples of large (57%), medium (4.8%), and small (0%) differences in inspiratory tag placement between the percentile (triangle) and phase (inverted-triangle) tagging algorithms. Each tick mark on the axis represents 50% of the mean respiratory period for each patient.

Between the shaded planes:

- Is an artifact present in image A?
Yes No
- Is an artifact present in image B?
Yes No
- On which, if either image, is the artifact more severe?
A B Neither

Figure 5.

Illustration of image contours for one tag-pair of interest for both the percentile (left) and phase (right) based algorithms. A substantial diaphragm artifact is present in the image on the right. The survey instrument used for the image comparison is also shown (below).

Figure 6.

Histogram illustrating the range and frequency of occurrence of differences in tag placement between the phase and percentile algorithms for both the (a) inspiratory and (b) expiratory datasets.

Figure 7.

Sample image from the blinded analysis, showing both percentile (left) and phase (right) based reconstructions for a large difference in tag placement. Greater artifact severity was noted for the phase-based (right) image, due to artifact obstruction of the right mainstem bronchus.

Figure 8. Sample image from the blinded analysis, showing both percentile (left) and phase (right) based reconstructions for a large difference in tag placement. Greater artifact severity was noted for the phase-based (right) image, due to greater discontinuity of the left mainstem bronchus.

Figure 9. Sample image from the blinded analysis, showing both percentile (left) and phase (right) based reconstructions for a medium difference in tag placement. Greater artifact severity was noted for the phase-based (right) image, due to discontinuities in the pulmonary vasculature.

Figure 10.

Sample image from the blinded analysis, showing both percentile (left) and phase (right) based reconstruction for a small difference in tag placement. The image serves as a control example for a patient with regular breathing, and no image quality differences were noted between the two reconstruction algorithms.

Figure 11.

Respiration percentiles contributing to the reconstruction of each image slice for a 72 slice image set using (a) 0% phase based binning and (b) 90th percentile based binning for one representative patient. Greater uniformity is seen with the percentile based algorithm.

Table 1

Normalized tag pair differences (± 1 standard deviation) used for the blinded image analysis of large, medium, and small differences in tag placement for inspiratory (insp) and expiratory (exp) images. Differences were normalized to a percentage of each patient's mean respiratory period.

Tag Difference Magnitude	Mean Normalized Tag Difference
Large (Insp)	29% $\pm$ 20%
Medium (Insp)	4.77% $\pm$ 0.2%
Small (Insp)	0% $\pm$ 0%
Large (Exp)	38% $\pm$ 20%
Medium (Exp)	6.559% $\pm$ 0.05%
Small (Exp)	0.18% $\pm$ 0.2%

Table 2

Results of the blinded image analysis.

Tag Comparison Group	Proportion of phase based images with artifact	Proportion of percentile based images with artifact	p
Large (Insp)	10/15	5/15	0.14
Medium (Insp)	4/15	6/15	0.7
Small (Insp)	3/15	4/15	1
Large (Exp)	6/15	7/15	1
Medium (Exp)	4/15	5/15	1
Small (Exp)	3/15	1/15	0.6
Sum	30/90	28/90	0.87