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Evaluation of the effect of respiratory and anatomical variables on a Fourier technique for markerless, self-sorted 4D-CBCT

I. Vergalasova¹, J. Cai¹, W. P. Segars², and F. F. Yin¹

I. Vergalasova: iv4@duke.edu

¹Department of Radiation Oncology, Duke University Medical Center, Durham, NC

²Department of Radiology, Carl E. Ravin Advanced Imaging Laboratories, Duke University Medical Center, Durham, NC

Abstract

A novel technique based on Fourier Transform theory has been developed that directly extracts respiratory information from projections without the use of external surrogates. While the feasibility has been demonstrated with three patients, a more extensive validation is necessary. Therefore, the purpose of this work is to investigate the effects of a variety of respiratory and anatomical scenarios on the performance of the technique with the 4D Digital Extended Cardiac Torso phantom. FT-Phase and FT-Magnitude methods were each applied to identify peak-inspiration projections and quantitatively compared to the gold standard of visual identification. Both methods proved to be robust across the studied scenarios with average differences in respiratory phase < 10% and percentage of projections assigned within 10% of the gold standard > 90%, when incorporating minor modifications to region-of-interest selection and/or low-frequency location for select cases of diaphragm amplitude and lung percentage in the field-of-view of the projection. Nevertheless, in the instance where one method initially faltered, the other method prevailed and successfully identified peak-inspiration projections. This is promising because it suggests that the two methods provide complementary information to each other. To ensure appropriate clinical adaptation of markerless, self-sorted 4D-CBCT, perhaps an optimal integration of the two methods can be developed.

1. Introduction

Motion management of thoracic and abdominal carcinomas has been and continues to be a challenge for radiation therapy. The difficulty arises from the variability of respiratory parameters such as amplitude, period, regularity, and baseline that can vary not just across patients, but even within the same patient measured only minutes apart. This is evidenced from the compilation of studies presented by AAPM Task (TG) Group Report 76 (Keall et al., 2006), which accordingly recommends that patient respiration be assessed on an individual basis. To date, there has been a substantial improvement in assessing respiratory motion during the simulation and planning stages of the treatment process, associated with the introduction of four-dimensional CT (4DCT). (Keall et al., 2004, Pan et al., 2004, Rietzel et al., 2005, Rietzel et al., 2004, Underberg et al., 2004, Vedam et al., 2003) 4DCT allows for time-resolved volume images of the anatomy that describe the target's trajectory during the course of respiration.

While 4DCT has largely been translated into the clinical flow to account for target motion during simulation, motion management during the localization stage is still under development. For example, the use of the gantry-mounted kV imager or the MV imager has been proposed for reconstruction of four-dimensional cone-beam CT (4D-CBCT) images, with a similar end result of providing volumetric information of anatomical motion as a function of the patient's respiration. (Dietrich et al., 2006, Kriminski et al., 2005, Sonke et al., 2005, Chang et al., 2006, Li et al., 2006b, Lu et al., 2007, Purdie et al., 2006, Sillanpaa et al., 2005, Kida et al., 2011, Rit et al., 2009) Typically, 4DCT involves retrospective sorting (according to either phase or amplitude) of either the sinogram or already reconstructed axial images, whereas 4D-CBCT involves retrospective sorting of x-ray projections prior to reconstruction.

In its initial stages, 4D-CBCT faced practical difficulties such as severely long scan times and high imaging dose to the patient. Since then, however, there has been a large amount of investigation into the optimization of 4D-CBCT imaging (i.e. to reduce scan time and/or dose), ranging from customizable image acquisition parameters (Maurer et al., 2010, Lu et al., 2007) to various iterative reconstruction algorithms that can deal with under-sampling (Ahmad et al., 2011, Bergner et al., 2010, Bergner et al., 2009, Hartl and Yaniv, 2009, Leng et al., 2008a, Leng et al., 2008b, Li et al., 2007, Li et al., 2006a). In addition, several different groups have focused on directly extracting motion information from projection data and thus eliminating the need for an external surrogate measure of respiration to correlate the image acquisition with the patient's respiration. (Kavanagh et al., 2009, Lewis et al., 2010, Rit et al., 2005, Siochi, 2009, Zijp, 2004) The importance of this stems from the potential introduction of error into the reconstructed 4D volumes due to the demonstrated existence of uncertainty in the relationship between the external marker and the actual motion of the internal anatomy. (Gierga et al., 2005, Hoisak et al., 2004, Koch et al., 2004, Yan et al., 2006)

Although these groups (Kavanagh et al., 2009, Lewis et al., 2010, Rit et al., 2005, Siochi, 2009, Zijp, 2004) have found a variety of solutions to eliminate the need for external surrogates, each is still bounded by a different set of constraints. While some require fiducial markers or extensive image processing procedures and others have not been validated with patient cone-beam data, the most common limitation among these methods is the reliance on the presence of the diaphragm in the field of view of all acquired projections. Therefore, a recent technique was also proposed for the extraction of respiratory phase from cone-beam projection data by Vergalasova et al. (2012). The novelty of this technique lies in its simplicity, efficiency and most importantly that it does not require the diaphragm to be visible in the projection data.

This technique (Vergalasova et al., 2012) involves manipulating the basics of Fourier Transform (FT) theory to facilitate identification of peak-inspiration projections. A detailed explanation of the specific procedure behind the technique can be found in the publication. The feasibility study demonstrated successful achievement of markerless, self-sorted 4D-CBCT reconstruction. However, the study was limited to a small dataset of previously acquired slow-gantry projection data (Lu et al., 2007), consisting of two phantom respiratory cycles and three lung carcinoma patients. Slow-gantry acquired projections are relevant

because the technique relies on detecting intensity differences that occur between consecutive projections, ideally arising only from anatomical motion resulting from respiration. Gantry rotation speeds slower than the current clinical standard CBCT (6°/s) are necessary so that the intensity changes from respiration are not confounded with the large anatomical changes arising from rotation of the x-ray source and the subsequent new path length of the photons through the body.

Therefore, in order to perform a thorough assessment and thus validate the robustness of the technique, a large amount of slow-gantry patient projection data would be required. However, this is currently not feasible due to manufacturer imposed constraints on clinical CBCT image acquisition parameters. Since this type of projection data currently exists in a limited amount, an alternative method is to use the next closest representation – a digital human phantom. (Segars et al., 2008, Segars et al., 2010, Segars and Tsui, 2009) They have developed an innovative tool, known as the 4D Digital Extended Cardiac Torso (XCAT) phantom, based on real segmented human imaging data. The XCAT provides the capability of simulating and customizing realistic representations of human anatomy with respiratory and cardiac motion. The cardiac motion model is based off high-resolution multi-slice cardiac-gated CT data of healthy male and female subjects. The respiratory motion model is also based on an analysis of respiratory-gated CT data of 20 normal subjects. Therefore, this work aims to assess the performance of the markerless technique across a diverse set of simulated respiratory and anatomical variables that may be encountered in the patient population with the 4D XCAT phantom.

2. Methods and Materials

2.1 Summary of the Fourier technique

It is important to have an overall understanding of the technique that is detailed in the publication by Vergalasova et al. (2012) prior to describing the experiments of this study. The Fourier technique consists of two separate methods, one based on the phase information of the FT and the other based on the magnitude information. The phase dictates where in the image a particular frequency component is present, whereas the magnitude dictates how much of that particular frequency component is present. The phase information is relevant because of the shift theorem, which dictates that a geometric shift in Cartesian space directly relates to a phase shift in Fourier space. Since respiratory motion presents itself as geometric shifts between consecutive projections, then it is logical to expect that we can track this motion as phase shifts in Fourier space to extract a respiratory signal.

Additionally, consecutive projections demonstrate intensity changes as a result of respiratory motion associated with the diaphragm moving superiorly/inferiorly and/or the thorax retracting/expanding. This makes the magnitude information of the FT pertinent because of the DC component, or offset, which is essentially the average of all of the intensities contained within that projection and will therefore change as a function of respiration, allowing extraction of a respiratory signal.

Initially, the image processing steps of the procedure is identical for both the FT-Phase and FT-Magnitude techniques. First, a simple region-of-interest (ROI) that encompasses the lung

region (from the apex to the lung down), but maintains the horizontal width (lateral dimension of the patient) of the projection is selected; Next, a logarithm is performed, with the purpose of decreasing the dynamic range and therefore improving the contrast, but note that for the XCAT-generated projections, it is not taken as in the original feasibility study with patient data – step 2 in Figure 1 of Vergalasova et al. (2012) – because projections that were output from the algorithm were already logarithm transformed; Each ROI is then symmetrically padded with zeros above and below to facilitate extraction of the same point in Fourier space in the following steps, independent of the amount of lung present in the projection; The 2D FT is then calculated, along with the phase and magnitude components.

For the FT-Phase technique, the first low-frequency location is selected along the y-axis, i.e. the direction of superior-inferior motion. Low frequency is relevant because the large anatomical motion resulting from inspiration that we are interested in is typically encoded as low-frequency information in Fourier space. The phase value at this location is extracted for every projection and subsequently plotted to constitute the respiratory signal. Peak-inspiration projections are then automatically extracted from this signal, enabling respiratory phase assignment to all projections. The only difference in this half of the procedure for the FT-Magnitude technique is that instead of selecting the first low-frequency location, the DC component is selected as the point-of-interest for the aforementioned reasons. The magnitude value at that point is plotted and again, peak-inspiration projections are automatically identified.

2.2 XCAT phantom

The XCAT phantom uses non-uniform rational b-splines (NURBS) surfaces to construct anatomical objects based on patient data. The advantage of such a hybrid phantom is that it can be as detailed and realistic as a voxelized model, while still being flexible enough to accurately model motion and variations in anatomy. The 4D XCAT used in this study is the latest version of hybrid phantoms developed by Segars et al. (Segars et al., 2008, Segars et al., 2010, Segars and Tsui, 2009) and provides the user with a multitude of capabilities, including the ability to generate both female and male anatomy, as well as the ability to import patient-specific cardiac and respiratory models.

There are two time curves that separately control the respiration: one defines the magnitude of diaphragmatic motion and the other the magnitude of the AP expansion of the chest. These curves can be scaled as necessary or completely replaced with any desired pattern. The diaphragm curve controls the motion of not just the diaphragm, but also organs such as the heart, liver, stomach, spleen, and kidneys which all move together at a scaled down magnitude. The AP curve controls the upward (anterior dimension of patient) and outward (lateral dimension of the patient) rotation of the ribcage to expand the chest. A motion vector field is also set up in order to define the motion of other organs affected by respiration (abdominal organs, blood vessels and surrounding muscle tissue). These vectors are then applied to the control points defining the organs to create deformations of those structures to match the respiratory motion. The ability to change parameters such as diaphragm motion, chest expansion, respiratory cycle duration and respiratory pattern make it possible to create a multitude of respiratory scenarios that may be encountered amongst

patients receiving radiation treatment. Furthermore, spherical lesions (or patient-specific lesions extracted from CT) of specified size, location and density can be added to the XCAT anatomy to follow either the motion of the lungs or any specified motion trajectory.

The XCAT anatomy of the 3D male and female phantom models (with the exception of the heart and brain) are based on high-resolution CT data obtained from the National Library of Medicine (NLM) Visible Human anatomical data. Although the male/female anatomy of the XCAT was derived from the Visible Human data, it was instead scaled down to match the dimensions of a US male/female adult (18–64) in the 50th percentile due to the larger than average size of those two subjects. The percentiles were measured from the PEOPLESIZE program and the default male/female XCAT phantom sizes are defined in detail by Segars et al. (2010).

Segars et al. (2008) also developed an x-ray projection algorithm to complement the XCAT software. This algorithm is able to quickly and accurately calculate CT projections from the surface definition (i.e. NURBS file) of an input XCAT phantom and the specified imaging geometry. Options for image geometry include parallel beam, cone-beam with a flat panel detector, cone-beam with a cylindrical detector and fan-beam with a cylindrical detector. The algorithm also requires the x-ray spectra to be specified with provided choices of 100, 120, and 140 kVp. Additional input parameters that are customizable are detailed in Table 1, which specifies the values used in this study. The output projections are 32-bit, little endian, floating-point binary files of matrix size specified by the input number of rows and channels.

2.3 Respiratory variables

For the following set of simulated respiratory scenarios, all phantoms were generated of the same male anatomy ranging from the neck to pelvic region. A spherical tumor of 2.0 cm in diameter was placed in the same location of each phantom – at the anterior portion of the chest, approximately midway between the apex of the lung and the diaphragm.

2.3.1 Respiratory cycle duration—Simulations were first performed to assess the performance of the Fourier technique across a variety of respiratory cycle (RC) lengths representative of the range of patient respiration. Four phantoms were generated with RCs of 3, 4, 5, and 6 seconds in length by scaling the provided sinusoidal breathing curve generic to the XCAT software. Both magnitudes of diaphragm motion and chest expansion were set at the default levels typical of tidal breathing: 2.0 cm and 0.5 cm, respectively.

2.3.2 Inspiration to expiration ratio—Actual patient respiration is rarely sinusoidal in nature and furthermore is usually divided unevenly between inspiration and expiration, with expiration typically lasting longer than inspiration. (Vergalasova et al., 2011) In order to study the effect this may have on the accuracy of the Fourier technique, the simulated respiratory cycles with inspiration to expiration (I/E) ratios of 0.52, 0.35, 0.26, and 0.21 were used as input for XCAT phantom generation. Each respiratory cycle was 5 seconds long and exhibited the same default magnitudes of chest and diaphragm motion as previously specified.

2.3.3 Diaphragm motion amplitude—Since the magnitude of diaphragmatic motion often determines the amount of motion in the surrounding organs in the chest, five XCAT phantoms were generated with diaphragm motion magnitudes of 0.25, 0.50, 1.0, 1.5, and 2.0 cm. Again, RC length remained at 5 seconds and chest expansion at 0.5 cm.

2.3.4 AP chest wall motion amplitude—The magnitude of AP chest wall motion was also studied as an additional variable that may affect the performance of the technique. Thus, five XCAT phantoms were also generated with varying AP chest wall motions of 0.25, 0.50, 1.0, 1.5 and 2.0 cm. Again, RC length remained at 5 seconds and the diaphragm amplitude at 2.0 cm.

2.3.5 Tumor and organ-derived trajectories—Actual tumor and diaphragm trajectories were studied next. Continuously acquired sagittal cine MRI data of three healthy volunteers (H1, H2, and H3) from a previous study (Cai et al., 2007) (frame rate = 10 fps; FOV=300–360 × 200–240 mm; slice thickness= 7 mm; matrix=128 × 128) enabled tracking of diaphragm motion with an in-house Matlab algorithm. The extracted trajectories are displayed in Figure 1. Because these were healthy volunteers without tumors, a separate tumor motion curve was not imported. Instead, the tumor trajectory was set to follow the general motion of the lungs (as in the previously simulated cases).

For three lung carcinoma patients (C1, C2, and C3), both diaphragm and tumor trajectories were successfully extracted from sagittal MRI slices. These are plotted together, per patient, in Figure 2. The curves imported as the diaphragm motion were either extracted from the patient's diaphragm or pulmonary vessels, whichever was visible due to the selected sagittal position (centered on the tumor). In total, six sets of XCAT phantoms were generated to exhibit these specific trajectories (amplitude and time-wise). Note that a small degree of smoothing (rflowess – locally weighted linear regression smoothing process) was applied to the extracted profiles. However, sharp edges were still present (Figure 2: C2) due to the limiting resolution of the MRI images from which the motion trajectories were extracted.

2.3.6 External surrogate-derived irregularities—Since the diaphragm- and tumor-derived trajectories were limited in sample size, three additional extremely irregular trajectories were extracted from a clinical database of Varian Real-time Position Management (RPM) (Varian Medical Systems, Palo Alto, CA) patient profiles. Thus the profiles displayed in Figure 3 were selected: one exhibiting baseline shift (BS), one exhibiting inconsistent inspiration/expiration peak amplitudes (IPA), and the last exhibiting a combination of the said irregularities (BS & IPA). These were each input as the diaphragm curve of the generated XCAT phantom anatomy.

2.3.7 Image acquisition parameters—Once the XCAT phantoms were generated, the provided CT-projection software was then used to obtain cone-beam projections. The specifications input into the software are listed in Table 1 and were chosen in such a manner to best mimic the conditions (image geometry, detector size, etc.) of projection data typically acquired in the clinic. This remained the same for all simulated respiratory variables. However, note the z-axis translation parameter did vary (between –250 mm and –350 mm) in order to simulate projections with and without the diaphragm in the field of

view, per studied respiratory scenario. Since the diaphragm is typically an easily discernible oscillating structure in the projections, it was important to also simulate the opposite extreme of not having the diaphragm present at all, to assess the impact this may have on the technique's performance.

Image acquisition parameters such as gantry rotation speed (GRS), frame rate (FR), acquisition time (AT) and number of projections acquired (NPA), per respiratory variable are listed in Table 2. These were determined using the framework developed by Maurer *et al* (2010) for optimized 4D imaging. The framework calculates these parameters by relating the patient's respiration to the restrictions imposed upon by the desired 4D reconstruction (i.e. length of phase window and number of phase bins) with a few simple formulas. More details on the framework can be found in their publication. The advantage of using such a framework is evident from Table 2, where 4D-CBCT reconstructions can be achieved without a substantially larger dose, at the expense of a slightly longer scan time. This is how the future clinical implementation of our technique for 4D-CBCT is envisioned.

2.4 Anatomical Variables

The phantoms generated for the different respiratory variables were entirely of the same default anatomy representative of a US 50th percentile male. Therefore, it was important to next investigate the anatomical effects of height, weight, gender, tumor location and amount of lung in the projection FOV on the accuracy of the Fourier technique.

In order to study the effects of these anatomical variables, the following XCAT projection datasets were generated according to respiratory profile C3 of Figure 2. Accordingly, the optimized image acquisition parameters of this profile were: GRS=0.9°/s, FR=2.8 fps, AT=223 sec, and NPA= 621 projections, replicated from row C3 of Table 2. This particular profile was chosen as the template for studying anatomical variations because of its realism, being that it was extracted from MRI images of a lung cancer patient and that it captures different magnitudes of tumor and diaphragm motion with some degree of irregularity in peak-amplitudes between consecutive cycles. The diameter of the tumor always remained at 2.0cm and it was placed midway between the apex of the lung and diaphragm in a majority of the experiments, other than the tumor location studies, of course.

2.4.1 Physical and adipose dimensions—Although the default XCAT phantom was scaled according to the 50th percentile US male, the software is flexible in allowing the user to adjust the dimensions, both in terms of physical size and adipose content. The impact of increasing phantom size (i.e. decreasing image contrast), was studied first. In order to examine this, both male and female anatomical phantoms were first generated with the default 50th percentile measurements (M_{Default} , F_{Default}). (Segars et al., 2010) The male phantom dimensions of long axis, short axis, height, chest (long and short axes) and skin (long and short axes) were scaled to 120% of the default at an interval of 5% ($M_{105\%}$, $M_{110\%}$, $M_{115\%}$, and $M_{120\%}$). The same dimensions of the female phantom were also identically scaled, in addition to the long axis, short axis and height of both breasts ($F_{105\%}$, $F_{110\%}$, $F_{115\%}$, and $F_{120\%}$). A maximum increase of 20% was chosen for both male and

female phantoms because it was unrealistic to further increase the height of each beyond 2113.2 mm (6'11" male) and 1952.4 mm (6'4" female), respectively.

2.4.2 Adipose dimension only—Given that the amount of plausible adipose content has a much wider range, each 120% scaled phantom (male and female) was then further scaled up to 140, 150 and 160% only in the adipose dimensions – long and short axes of the chest and skin ($M_{140\%}$, $M_{150\%}$, and $M_{160\%}$), as well as the breasts for the female phantoms ($F_{140\%}$, $F_{150\%}$, and $F_{160\%}$). The largest phantom from the previous section was chosen as the starting point in order to examine the potential challenges presented for the largest of patients, with the reasoning that if the technique is robust at the extreme, then it should be adequate for smaller patients as well.

2.4.3 Patient body mass index (BMI) templates—Segars et al. (2010) are currently in the process of further developing the XCAT tool by providing a large database of phantoms segmented from CT scans of patients of many different ages, sizes and genders. Therefore, in addition to scaling the default XCAT male and female anatomies, six additional phantoms (three male and three female) were selected for study to serve as a more realistic verification than simply scaling the default phantom size. The datasets were selected according to the scanned patient's body mass index (BMI). BMI is used to measure a person's body fat content relative to height and weight. BMI can be divided into the following categories: a) underweight: BMI < 18.5, b) normal weight: 18.5 ≤ BMI < 24.9, c) overweight: 25 ≤ BMI < 29.9, and d) obese: BMI ≥ 30. A male and female phantom was selected from each of the three main BMI categories (excluding the underweight category) and the specific attributes of each patient are detailed in Table 3 below.

2.4.4 Tumor location—The location of the carcinoma is a critical variable to explore because it essentially determines the amount of motion information that is present in the cone-beam projection data. Five tumor locations (subject to respiratory-induced motion) were selected for study to span the chest and abdomen areas: 1) upper portion or apex of the lung; 2) mid-region of the lung, adjacent to the chest wall; 3) mid-region of the lung, adjacent to the mediastinum; 4) upper region of the liver; and 5) lower region of the liver. Locations below the lungs were studied because the carcinomas found in this anatomical region are also relevant to radiation therapy and may be affected by respiratory-induced motion. For example, carcinomas of the liver, pancreas and kidneys may also be targeted with radiation and thus would be eligible for 4D on-board imaging prior to treatment.

Two sets of projections were generated per tumor location (1–5): one set with the tumor following the trajectory of the chest (with the magnitude of motion dependent on the tumor location in the lungs/abdomen) and the other set with the tumor following the specific input tumor curve (dashed line of C3 profile of Figure 2), labeled as lungs and tumor, respectively.

2.4.5 Lung percentage—While the previous section explores the effect of which part of the chest/abdomen is present in the projection data, a more systematic experiment is necessary to determine if there is a threshold for the amount of lung in the projection necessary for the technique to successfully identify peak-inspiration projections. This was

accomplished by starting with projections that contained 100% of the lung in the image and shifting the central axis of the detector 10.0 cm in both superior and inferior directions, at an interval of 2.0 cm. The percentages of lung that were generated at each of the opposing shifts (i.e. toward the head vs. toward the abdomen) were relatively similar, but it was important to examine both directions because of the varying degrees of anatomical motion present at the extremes of both shifts (i.e. the apex of the lung vs. the abdomen), as displayed with Figure 4. The 10.0 cm shifts generated percentages of lung ranging from 48–89%. These percentages were calculated relative to the central projection with 100% of the lung in the FOV, at $z = 250\text{mm}$ as specified in Table 1. The computation is simply a ratio of the number of pixels within the attenuation range of lung tissue present at the same angle AP projection and time point of respiration.

2.5. Image Noise

In addition to the studied various anatomical characteristics, there are external factors prevalent in on-board x-ray imaging that may affect the performance of the technique. One such important factor, inherent to cone-beam imaging, is the presence of noise in the projections. Noise diminishes image quality by adding a grainy or textured appearance and is concerning because it can degrade the visibility or contrast of objects present in the image.

First, noiseless projection datasets of the XCAT phantom were generated for three selected lung percentages from the previous section: upper 68%, 100%, and lower 45% (Figure 4). This set of data was selected for study because it was deemed to be the most challenging for the Fourier technique, particularly the superiorly shifted lung percentages of 48%. The next step was to introduce a realistic level of noise to the projections, as would be seen in clinical patient projections acquired with a digital on-board imaging detector. A noise model was developed using such projections acquired with a gantry-mounted kV imager and flat panel detector on a Varian TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, CA). The acquisition parameters were 140kVp, 15mA, and 20ms and the imaged object was a wedge-step phantom consisting of a total of 40 different combinations of aluminum and acrylic. (Li et al., 2012)

Across the rows, the same thickness of aluminum was used, but with different thicknesses of acrylic. Conversely, the same thickness of acrylic was used across the columns with varying thicknesses of aluminum. For each of the 40 different combinations of acrylic and aluminum, a rectangular region-of-interest (ROI) of 110 pixels wide by 70 pixels high was used to measure the mean and standard deviation of the intensity values in the ROI. Prior to measuring this and building the noise model, it was important to initially convert the intensity values in the XCAT projections and the step-wedge phantom projection to attenuation coefficients so that they were on the same scale. This was done by first dividing the image by the average intensity value for air and then taking the logarithm.

After the scale was properly converted, the mean vs. standard deviation was plotted per corresponding ROI and a quadratic fit was applied to generate a noise model according to Equation 1 below.

$$y=0.0085x^2-0.0016x+0.0055 \quad (1)$$

Next, noise was randomly added pixel-by-pixel to each noiseless XCAT projection across all five datasets selected for study according to the following: 1) input the pixel value as the mean (or x) into the model; 2) use the output standard deviation (or y) as the standard deviation input into a Gaussian random number generator with a mean of zero; 3) take the random output and add it to the original pixel value in the projection. Each projection was then saved to generate a new projection dataset with noise, to which FT-Phase and FT-Magnitude could be applied for evaluation.

In order to test additional levels of noise, the standard deviation input into the Gaussian random number generator (step 2) was scaled by a multiple of 2, 4 and 8. Sample projections with the different degrees of noise are displayed in Figure 5 below.

2.6 Quantitative Evaluation

Upon identification of peak-inspiration projections, all projections in between consecutive peaks were assigned respiratory phase, defined as the percentage of the respiratory cycle that has passed since peak-inspiration (represented by 0% or 100%). Note that this definition of phase should be adjusted accordingly when different parts of the anatomy move out of phase with each other (i.e. specify organ used to determine peak-inspiration). Linear interpolation of phase was implemented according to the number of projections between consecutively identified peaks. For example, if there are 6 projections between two consecutive peak-inspirations, then respiratory phase is assigned in increments of 100% divided by 6 (16.7%) to each projection between consecutive peaks of 0%.

The same quantitative metrics used to assess the performance of the technique in the initial feasibility study (Vergalasova et al., 2012), were also used here. Note, that phase unwrapping is performed immediately after signal extraction in order to prevent phase jumps in the extracted signal by adding multiples of $\pm 2\pi$ radians when consecutive points have a difference over the tolerance of π radians. This is performed prior to identification of peak-inspiration projections and is thus accounted for ahead of quantitative comparison with equations (1) and (2).

The average difference in assigned respiratory phase (ADRP) between manually selected peaks (gold standard) versus automatically extracted peaks (FT-Phase & FT-Magnitude) was then calculated as:

$$ADRP(\%) = \frac{1}{n} \sum_{i=1}^n |Phase(i_{Manual}) - Phase(i_{FT})| \quad (1)$$

In addition, the percentage of projections assigned from Fourier peak extraction that were within 10% respiratory phase of the projections assigned from manual peak extraction was computed (PP10):

$$PP10(\%) = 100\% * \frac{N_{Projs} \{ |Phase(i_{Manual}) - Phase(i_{FT})| \leq 10\% \}}{Total Projs} \quad (2)$$

Please note that the gold standard in these studies is defined in the same respect as the initial feasibility study (Vergalasova et al., 2012). Projections exhibiting peak-inspiration were visually identified and recorded with excellent certainty because of known input profiles, as well as the ability to easily discern the trajectory of the spherical tumor in the phantom chest cavity.

3. Results and Discussion

3.1 Respiratory variables

Table 4 presents the results for the quantitative assessments of all of the studied respiratory variables, with and without the diaphragm in the field of view, in category blocks. Figure 6 presents selected cases of this same data in histogram format to illustrate how the percent difference in respiratory phase (relative to the gold standard) is distributed among the projection dataset. Note that difference category variables have a different total number of projections per dataset (detailed in the figure caption).

3.1.1 Respiratory cycle duration—The first block of Table 4 represents the results for the effect of respiratory cycle duration on the Fourier technique. It is evident that across the span of respiratory cycles studied, the ADRP is overall less than or equal to 1.0% (well below the 10% phase criterion), both with and without the diaphragm and for both FT-Phase and FT-Magnitude. Furthermore, the PP10 results show that a large majority (97.3% and greater) of the projections across both Fourier methods are assigned phase within 10% of the manual method. This is also illustrated with Figure 6.

3.1.2 Inspiration to expiration ratio—The second block of rows of Table 4 depicts the results obtained for the varying degrees of I/E ratios. Again, the results of both Fourier methods have almost ideal ADRP (0.20% and less) and PP10 (99.5% and above) values across all simulated I/E ratios, both with and without the diaphragm. This is confirmed by Figure 6.

3.1.3 Diaphragm motion amplitude—The diaphragm amplitude category of data is the third block depicted in Table 4 and is the only respiratory variable studied that demonstrated an initial difference in performance between FT-Phase and FT-Magnitude, depending on the visibility of the diaphragm in the projection set. When the diaphragm is absent, both perform equivalently (ADRP=0% and PP10=100%) across all diaphragm amplitudes (also see Figure 6). However, when the diaphragm is visible, a clear threshold of performance for the FT-Magnitude method develops. For the studied amplitudes below 1.5 cm (i.e. 0.25, 0.5, and 1.0 cm), there was an obvious degradation of the FT-Magnitude method that became more severe (greater ADRP and lower PP10) as the diaphragm amplitude decreased, whereas FT-Phase maintained its accuracy in phase assignment (ADRP=0% and PP10=100%), with and without the presence of the diaphragm.

Since the FT-Magnitude technique performed accurately when the diaphragm was not visible in the FOV of the projection data, we investigated the performance of the technique by simply omitting the diaphragm from the selected ROI of the projections with the diaphragm in the imaging FOV. In this case, FT-Magnitude resulted in ideal ADRP and PP10, respectively across all amplitudes of 0.25, 0.5, and 1.0 cm as demonstrated with Table 5.

The performance of the FT-Magnitude technique was initially degraded at amplitudes below 1.5 cm because there was not enough of a change in the average of intensities (i.e. the DC-component value) throughout the projections, due to the diaphragm intensities dominating the average. Thus, small changes in the diaphragm were not able to cause a distinct enough change in the DC-component of each projection, making it difficult to detect the true peaks and valleys. Without the diaphragm present, FT-Magnitude was however successful at detecting peak-inspiration projections, even at small motion amplitudes. This is because there was enough relative change in the average intensity values of the relatively “less intense” lung anatomy. It was therefore intuitive to discern and demonstrate the accuracy of the FT-Magnitude method when omitting the diaphragm from the selected ROI for those projections with smaller diaphragmatic motion. This was an important observation, as it helped us to understand situations where the technique may struggle and thereby adapt to those scenarios with slight modifications, in order to successfully result in accurate markerless 4D-CBCT reconstruction.

3.1.4 AP chest wall motion amplitude—As expected, varying amplitudes of AP chest wall expansion did not affect the robustness of the technique because this motion is orthogonal to the dimension of relevance. Both Fourier magnitude and phase methods perform excellently in determining peak-inspiration phase projections with ADRP 1.5 and PP10 99.2, which is further verified with Figure 6.

3.1.5 Tumor and organ-derived trajectories—Block 5 of Table 4 lists the phase assignment performance of trajectories derived directly from cine MRI data. The first 3 rows are of the three healthy volunteers (H1, H2, and H3) and the next 3 rows are of the lung carcinoma subjects (C1, C2 and C3). From this set of more realistic breathing and tumor trajectories, it is still evident that both Fourier methods perform equivalently for most of the cases, except for C1 being several percentage points off from the rest, but still well within desirable ADRP (less than 10%) and PP10 (above 90%) limits (H1–H3: ADRP 2.2%, PP10 98.1% and C1–C3: ADRP 4.4%, PP10 92.2%) for FT-Phase. This can also be seen in Figure 6 by comparing FT-Phase vs. FT-Magnitude.

3.1.5 External surrogate-derived irregularities—Lastly, the bottom block of data of Table 4 represents the accuracy of the Fourier technique across select irregularities extracted from patient RPM profiles. For each irregularity, both methods of the Fourier technique accurately assigned respiratory phase to the projection dataset, relative to the gold standard. Across both diaphragm scenarios, the maximum ADRP value was 2.3% and the minimum PP10 value was 95.2%.

While the results of Figure 7 support the results displayed in Table 4 and Figure 6 in terms of accurately identifying peak-inspiration projections, it is important to notice that the extracted respiratory signal may only be used with phase-based sorting rather than amplitude-based sorting. This is because the amplitudes of the peaks (relative to each other) do not match that of the imported curve seen in the first row (BS) of Figure 3. Since applying phase-based sorting cannot account for the differences in amplitude within the same phase window, a large variance of motion amplitudes may be grouped into a single phase bin because they are all in fact “peak-inspiration”. This suggests that perhaps for extremely irregular respiratory patterns, the best method for 4D-CBCT reconstruction lies with amplitude-based sorting (for which the technique in its current form is not suited for) rather than phase-based sorting.

3.2 Anatomical variables

Table 6 presents the results for the quantitative assessments of all of the studied anatomical variables in category blocks, in the order that they were presented in the Methods section and as before, Figure 8 presents selected cases of the same data in histogram form as the number of projections versus their percent difference in respiratory (from the gold standard). Note in this case, all variables have a total of 621 projections per set.

3.2.1 Physical and adipose dimensions—Increasing the physical size and adipose dimensions up to 120% of the default XCAT did not have a deleterious effect on neither the FT-Phase nor the FT-Magnitude method as evidenced by the first block of Table 6. All of the listed ADRP values fall well below the 10% phase difference criterion. Similarly, the PP10 results are 90% and above, demonstrating that a large majority of projections were assigned respiratory phase within 10% of how the gold standard technique assigned respiratory phase.

3.2.2 Adipose dimension only—Further increasing only the adipose content of the largest male and female XCATs ($M_{120\%}$ and $F_{120\%}$) from the previous section to 160% also did not have a substantial effect on the results, as shown in the second category block of Table 6. Again, both ADRP and PP10 were well within the constraints of less than 10% and greater than 90%, respectively. This is confirmed by Figure 8.

3.2.3 Patient BMI templates—The selected male and female patient XCAT templates of different BMI categories (described in Table 3) used as templates for the XCAT further validated the robustness of the techniques across a variety of patient sizes, as seen by the third grouping of data in Table 6. Each categorized normal, overweight, and obese XCAT phantom resulted in an ADRP < 10% and PP10 > 90%.

3.2.4 Tumor location—It is evident from the fourth block of Table 6 that both Fourier components maintained their accuracy at identifying peak-inspiration projections across the five studied tumor locations. Furthermore, all locations resulted in nearly equivalent ADRP and PP10 values, for both the specified tumor trajectory and the appropriately scaled motion trajectory of the lungs.

3.2.5 Lung percentage—As expected, the percentage of the lung present in the FOV of the projection data is a crucial factor in determining the success of the Fourier techniques. While both Fourier techniques perform equivalently well across all shifts below the central 100% (lung percentages: lower 45–88%) toward the abdominal region, Table 6 demonstrates that the FT-Phase technique failed at the two utmost upper percentages of 48 and 59% with ADRP=6.5% and 29.5% and PP10=78.7% and 24.8%, respectively. Conversely, the FT-Magnitude technique upheld its accuracy with equivalent performance across all of the superior shifts (lung percentages: 48–89%).

Upon examining the failure of the FT-Phase technique at the upper 48 and 59% lung percentages more closely, it became evident that the FT-Phase component was struggling due to the size of the ROI. Because there was less and less of the lung present in the image FOV, the ROI continued to decrease in size as the detector was shifted superiorly, but the first low frequency location was still chosen in Fourier space. With the decreased ROI size, a lower frequency location (between 0 and 1) would have been more appropriate, but because the data is discretized, it was of course impossible to select a fractional low-frequency location. Therefore, we reexamined the performance of the FT-Phase component for the utmost upper percentages by using the entire projection size and selecting the second low-frequency location instead. Larger low frequency locations are relevant for larger ROI sizes, as previously demonstrated with the studies performed to initially determine the optimal frequency selection in the publication by Vergalasova et al. (2012). The results are demonstrated in Table 7 below and clearly demonstrate that the FT-Phase method can be robust for these lung percentages with slight modifications to the ROI size and low-frequency selection.

3.3. Image Noise

Table 8 describes the results for the three datasets selected from the previous lung percentage section on the accuracy of FT-Phase vs. FT-Magnitude across different levels of noise. Note that for the upper 48% of the lung, the modified ROI size (entire projection) and second low-frequency location (as in Table 7) was used for analysis here. The results demonstrate that the added noise did not substantially alter the performance across all levels of noise and lung percentages for the FT-Magnitude technique. This was also true for a majority of the cases with the FT-Phase techniques, except for at the 4σ and 8σ levels at the upper 48% of the lung. The tabulated values show that FT-Phase starts to break down slightly at the 4σ level, but really fails at the 8σ level. While both of those noise levels would not be clinically acceptable, taking a closer look revealed an extremely noise extracted respiratory signal. After applying some minor smoothing (locally weighted linear regression) to those curves, ADRP was improved to 3.8% and 4.4%, while PP10 was improved to 92.9% and 91.1% for the 4σ and 8σ noise levels, respectively.

4. Conclusions

The XCAT studies implemented in this work provide a comprehensive evaluation of the two Fourier methods. With several minor adjustments to ROI and/or low-frequency selection, both methods demonstrated robustness across all studied respiratory and anatomical scenarios. Prior to making those adjustments, it was interesting to note that in the few

instances where one method was initially found to have a weakness (i.e. diaphragm amplitudes for FT-Magnitude under respiratory variables and lung percentage in the FOV for FT-Phase under anatomical variables), the other method prevailed and was able to accurately assign respiratory phase to the projection dataset. This is very promising in terms of moving forward, as it suggests that the techniques complement each other and perhaps there is an optimal integration of the two that may result in the future safe and practical clinical implementation of a markerless, self-sorted 4D-CBCT technique. While still in the preliminary stages, we envision the implementation of this to be with a user-interactive software that would simultaneously display the extracted respiratory signal according to both techniques and thus would enable both verification of a good signal (in cases that the two matched), while at the same time allowing the user to spot failures if there was a mismatch.

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Figure 1. Plots of the extracted diaphragm trajectories of three healthy volunteers (H1, H2, and H3) input as the diaphragm curve of the associated XCAT generated anatomy. Displacement is in the superior-inferior (SI) direction of motion.

Figure 2. Tumor and organ-derived trajectories of three lung carcinoma patients (C1, C2, and C3) input into the XCAT phantom as tumor and diaphragm curves, respectively. Displacement is in the superior-inferior (SI) direction of motion.

Figure 3.

External surrogate-derived trajectories exhibiting respiratory irregularities of baseline shift (BS), irregular peak amplitudes (IPA), and a combination of the two (BS & IPA) that were input as diaphragm curves into the XCAT. Displacement is in the superior-inferior (SI) direction of motion.

Figure 4.

Demonstration of projections with the extreme 10.0 cm shifts in both inferior ($Z_{150\text{mm}}$, lower 45% of lung) and superior ($Z_{350\text{mm}}$, upper 48% of lung) directions as compared with the central projection with 100% of the lung in the FOV at $Z_{250\text{mm}}$.

Figure 5.
A display of different levels of noise added to the XCAT projections, per scaled standard deviation (σ).

Figure 6.

Histograms of a representative set of respiratory variables displaying the distribution of projections and their percent difference in assigned respiratory phase relative to the gold standard for FT-Phase and FT-Magnitude techniques. Respiratory cycle (RC), inspiration/expiration ratio (I/E), diaphragm amplitude (DA), and anterior-posterior chest expansion amplitude (AP) each have a total of 367 projections, whereas carcinoma patient 1 (C1) had 579 total projections and a combination of baseline shift and irregular peak-inspiration amplitude (BS & IPA) had 469 total.

Figure 7.

Extracted respiratory signal according to both FT-Phase and FT-Magnitude techniques along with marked peak-inspiration projections for the Baseline Shift (BS) only imported curve. The red circles represent the gold standard peak-inspiration projections and the black squares represent the automatically extracted ones per technique.

Figure 8.

Histograms of a representative set of anatomical variables displaying the distribution of projections and their percent difference in assigned respiratory phase relative to the gold standard for FT-Phase and FT-Magnitude techniques. Note that all datasets (physical and adipose dimensions, adipose dimension only, patient BMI templates, tumor location, and lung percentage) had a total of 621 projections.

Table 1

The specific input parameters of the CT-projection algorithm used to generate CBCT projections of XCAT phantoms for respiratory experiments. Note the z-axis translation is either 250 or 300mm, depending on whether the diaphragm is included in the field of view.

CT Projection Algorithm Specifications	Input
Image geometry	Cone-Beam
X-ray spectra	120 kVp
Projection angles	0–200°
X-axis translation	–80 mm
Y-axis translation	0 mm
Z-axis translation	250 or 300 mm
Detector height	400 mm
Detector width	300 mm
Number of rows	512
Number of channels	384
Source-to-patient distance	1000 mm
Patient-to-detector distance	500 mm
Exposure per projection	2 mAs
Half-fan angle	N/A
Detector efficiency	0.8
Variance of electronic noise	0
Poisson noise	yes

Table 2

CBCT acquisition parameters specific to each simulated respiratory variable or its overall category, computed based on an optimal 4D-imaging scheme.

Variable	GRS (°/s)	FR (fps)	AT (s)	NPA
Respiratory Cycle Length	1.1	2.0	183	367
Inspiration/Expiration Ratios	1.1	2.0	183	367
Diaphragm Amplitude	1.1	2.0	183	367
AP Chest Wall Amplitude	1.1	2.0	183	367
Healthy Volunteer 1 (H1)	1.2	3.5	160	556
Healthy Volunteer 2 (H2)	1.0	2.8	201	560
Healthy Volunteer 3 (H3)	0.9	3.0	212	644
Carcinoma Patient 1 (C1)	1.0	2.9	198	579
Carcinoma Patient 2 (C2)	1.2	2.8	165	459
Carcinoma Patient 3 (C3)	0.9	2.8	223	621
Baseline Shift (BS)	1.3	2.9	150	429
Irregular Peak-Inspiration Amplitude (IPA)	1.3	3.2	152	482
Baseline Shift & Irregular Peak-Inspiration Amplitude (BS & IPA)	1.2	2.8	168	469

Table 3

Patient BMI characteristics of templates segmented from CT images and imported as XCAT phantoms.

Gender	Age (yrs)	Height (cm)	Weight (kg)	BMI
Male	63	170	72.1	24.9
Male	47	185	96.8	28.3
Male	38	173	107.1	35.8
Female	27	173	55.6	18.6
Female	37	170	77.1	26.8
Female	63	153	81.3	34.7

Table 4

Results for the quantitative metrics of average difference in respiratory phase (ADRP) and percentage of projections assigned within 10% phase (PP10) of the gold standard across all simulated respiratory variables, with and without the presence of the diaphragm. Results are blocked off by category: respiratory cycle (RC), inspiration/expiration ratio (I/E), diaphragm amplitude (DA), anterior-posterior chest expansion amplitude (AP), healthy volunteers (H1–H3), carcinoma patients (C1–C3), baseline shift (BS), irregular peak-inspiration amplitude (IPA), and a combination of baseline shift and irregular peak-inspiration amplitude (BS & IPA).

Variable	NO DIAPHRAGM					DIAPHRAGM				
	ADRP (%)					PP10 (%)				
	FT-Phase	FT-Mag	FT-Phase	FT-Mag	FT-Phase	FT-Phase	FT-Mag	FT-Phase	FT-Mag	FT-Mag
RC=3s	0.6	0.3	0.3	97.5	99.0	0.6	0.6	97.5	97.5	97.5
RC=4s	0	0	0	100	100	0	0.6	100	98.1	98.1
RC=5s	0	0	0	100	100	0	0.3	100	99.2	99.2
RC=6s	0	0.2	0.2	100	100	0	1.0	100	97.3	97.3
I/E=0.52	0	0.2	0.2	100	99.5	0	0	100	100	100
I/E=0.35	0	0.2	0.2	100	99.5	0	0	100	100	100
I/E=0.26	0	0	0	100	100	0	0	100	100	100
I/E=0.21	0	0	0	100	100	0	0	100	100	100
DA = 0.25 cm	0	0	0	100	100	0	40	100	11.2	11.2
DA = 0.50 cm	0	0	0	100	100	0	34.1	100	26.2	26.2
DA = 1.0 cm	0	0	0	100	100	0	18.2	100	45	45
DA = 1.5 cm	0	0	0	100	100	0	4.2	100	98.1	98.1
DA = 2.0 cm	0	0	0	100	100	0	1.5	100	99.2	99.2
AP = 0.25 cm	0	0	0	100	100	0	0	100	100	100
AP = 0.50 cm	0	0	0	100	100	0	1.5	100	99.2	99.2
AP = 1.0 cm	0	0	0	100	100	0	0	100	100	100
AP = 1.5 cm	0	0	0	100	100	0	0	100	100	100
AP = 2.0 cm	0	0	0	100	100	0	0	100	100	100
H1	1.1	2.0	2.0	100	98.6	0.5	0.7	100	100	100

Variable	NO DIAPHRAGM						DIAPHRAGM					
	ADRP (%)			PP10 (%)			ADRP (%)			PP10 (%)		
	FT-Phase	FT-Mag	FT-Phase	FT-Phase	FT-Mag	FT-Mag	FT-Phase	FT-Phase	FT-Mag	FT-Phase	FT-Mag	FT-Mag
H2	2.2	2.2	2.2	99.8	99.8	99.8	2.0	1.8	1.8	99.8	99.8	99.4
H3	1.2	1.3	1.3	98.1	98.9	98.9	0.7	0.7	0.7	100	100	100
C1	4.4	1.9	1.9	92.2	98.6	98.6	1.9	1.7	1.7	98.8	98.8	99.1
C2	0.8	0.9	0.9	100	100	100	0.7	0.7	0.7	100	100	100
C3	2.8	2.0	2.0	96.8	97.3	97.3	1.2	1.3	1.3	99.5	99.5	99.8
BS	1.2	1.6	1.6	100	100	100	0.9	1.0	1.0	100	100	100
IPA	1.7	3.3	3.3	95.2	100	100	2.3	1.9	1.9	99.8	99.8	100
BS & IPA	0.2	1.1	1.1	100	100	100	0.2	0.5	0.5	100	100	100

Table 5

ADRP and PP10 results for FT-Magnitude when adjusting ROI selection to exclude diaphragm for smaller amplitudes of diaphragmatic motion.

FT-Magnitude		
Diaphragm Amplitude	ADRP (%)	PP10 (%)
0.25 cm	0	100
0.5 cm	0	100
1.0 cm	0	100

Table 6

ADRP and PP10 results across all simulated anatomical variables, blocked off by category: physical and adipose dimensions, adipose dimension only, patient BMI templates, tumor location, and lung percentage.

Variable	ADRP (%)		PP10 (%)	
	FT-Phase	FT-Mag	FT-Phase	FT-Mag
M _{Default}	3.0	2.9	95.3	95.3
M _{105%}	4.9	2.9	91.9	94.0
M _{110%}	2.8	3.1	93.6	95.3
M _{115%}	2.3	2.8	96.3	94.4
M _{120%}	2.3	3.2	94.5	93.6
F _{Default}	1.5	3.2	98.6	94.0
F _{105%}	4.8	4.5	90.0	93.1
F _{110%}	2.6	2.8	93.1	95.3
F _{115%}	2.4	3.4	95.8	93.6
F _{120%}	2.3	3.6	96.3	95.0
M _{Ad-140%}	3.1	1.8	94.7	97.4
M _{Ad-150%}	3.6	2.1	94.4	97.4
M _{Ad-160%}	3.9	1.8	94.9	97.4
F _{Ad-140%}	2.7	3.3	95.3	97.4
F _{Ad-150%}	2.4	3.1	95.3	97.4
F _{Ad-160%}	2.4	1.5	95.3	97.4
M _{BMI=24.9}	4.1	3.6	93.2	91.5
M _{BMI=28.3}	3.0	4.3	93.7	94.7
M _{BMI=35.8}	3.0	3.3	94.4	94.7
F _{BMI=18.6}	3.7	2.5	90.5	95.0
F _{BMI=26.8}	2.7	3.0	94.8	94.4
F _{BMI=34.7}	2.5	2.9	95.3	95.3
1: Lungs	4.1	3.6	91.8	94.7
1: Tumor	4.1	3.6	91.8	94.7
2: Lungs	2.1	2.9	96.0	95.3
2: Tumor	2.1	2.2	96.0	97.3
3: Lungs	2.1	2.2	96.0	97.6
3: Tumor	2.1	2.9	96.0	95.3
4: Lungs	1.6	3.1	97.3	95.7
4: Tumor	3.0	3.1	93.6	95.7
5: Lungs	1.6	3.2	97.3	95.3
5: Tumor	1.6	3.2	97.3	95.3
Upper 48%	29.5	1.9	24.8	97.3

Variable	ADRP (%)		PP10 (%)	
	FT-Phase	FT-Mag	FT-Phase	FT-Mag
Upper 59%	6.5	2.3	78.7	96.3
Upper 68%	3.8	2.5	94.8	95.0
Upper 77%	3.6	3.1	95.7	92.4
Upper 89%	2.2	3.7	95.5	95.3
Center (100%)	1.7	2.4	97.3	95.7
Lower 88%	1.6	2.0	97.6	96.6
Lower 75%	1.6	2.0	97.6	96.6
Lower 63%	1.6	2.0	97.6	96.6
Lower 53%	1.6	2.0	97.6	96.6
Lower 45%	1.6	2.0	97.6	96.6

Table 7

ADRP and PP10 results for the FT-Phase when adjusting ROI size and low-frequency selection at upper lung percentages of 48 and 59% in the projection FOV.

FT-Phase		
Lung Percentage	ADRP (%)	PP10 (%)
Upper 48%	2.0	97.3
Upper 59%	3.9	94.7

Table 8

Results for varying levels of noise applied onto XCAT projections with different percentages of lung in the FOV. The numbers in front of each σ category represent the multiplier applied to the standard deviation input into the Gaussian random number generator.

Image Noise	ADRP (%)		PP10 (%)	
	FT-Phase	FT-Mag	FT-Phase	FT-Mag
Upper 48% (1 σ)	2.5	2.5	96.9	95.3
Central 100% (1 σ)	1.7	2.3	97.3	95.7
Lower 45% (1 σ)	1.8	2.3	97.5	95.7
Upper 48% (2 σ)	3.3	2.8	94.4	96.1
Central 100% (2 σ)	1.9	2.1	96.9	95.7
Lower 45% (2 σ)	1.6	2.4	97.6	95.7
Upper 48% (4 σ)	5.4	5.5	87.8	92.9
Central 100% (4 σ)	1.7	2.9	96.6	96.0
Lower 45% (4 σ)	1.7	2.6	97.6	95.0
Upper 48% (8 σ)	13.9	3.9	58.8	92.3
Central 100% (8 σ)	2.6	3.2	97.1	95.3
Lower 45% (8 σ)	2.0	1.5	97.6	98.4