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Extension of the NCAT phantom for the investigation of intra-fraction respiratory motion in IMRT using 4D Monte Carlo

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Abstract

The purpose of this work was to create a computational platform for studying motion in intensity modulated radiotherapy (IMRT). Specifically, the non-uniform rational B-spline (NURB) cardiac and torso (NCAT) phantom was modified for use in a four-dimensional Monte Carlo (4D-MC) simulation system to investigate the effect of respiratory-induced intra-fraction organ motion on IMRT dose distributions as a function of diaphragm motion, lesion size and lung density.

Treatment plans for four clinical scenarios were designed: diaphragm peak-to-peak amplitude of 1 cm and 3 cm, and two lesion sizes—2 cm and 4 cm diameter placed in the lower lobe of the right lung. Lung density was changed for each phase using a conservation of mass calculation. Further, a new heterogeneous lung model was implemented and tested. Each lesion had an internal target volume (ITV) subsequently expanded by 15 mm isotropically to give the planning target volume (PTV). The PTV was prescribed to receive 72 Gy in 40 fractions. The MLC leaf sequence defined by the planning system for each patient was exported and used as input into the MC system. MC simulations using the dose planning method (DPM) code together with deformable image registration based on the NCAT deformation field were used to find a composite dose distribution for each phantom. These composite distributions were subsequently analyzed using information from the dose volume histograms (DVH). Lesion motion amplitude has the largest effect on the dose distribution. Tumor size was found to have a smaller effect and can be mitigated by ensuring the planning constraints are optimized for the tumor size. The use of a dynamic or heterogeneous lung density model over a respiratory cycle does not appear to be an important factor with a 0.6% change in the mean dose received by the ITV, PTV and right lung. The heterogeneous model increases the realism of the NCAT phantom and may provide more accurate simulations in radiation therapy investigations that use the phantom. This work further evaluates the NCAT phantom for use as a tool in radiation therapy research in addition to its extensive use in diagnostic imaging and nuclear medicine research. Our results indicate that the NCAT phantom, combined

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with 4D-MC simulations, is a useful tool in radiation therapy investigations and may allow the study of relative effects in many clinically relevant situations.

1. Introduction

Intensity modulated radiotherapy (IMRT) (Intensity Modulated Radiotherapy Collaborative Working Group 2001) offers the ability to create highly conformal dose distributions. This allows the escalation of radiation dose to the target while simultaneously sparing larger volumes of healthy tissue than is possible using conventional and three-dimensional (3D) conformal radiation therapy. However, the use of IMRT techniques can create steep dose gradients at the edges of the target volumes and so careful consideration must be given to targets that move.

Many studies have investigated the effect of motion in radiotherapy and shown that it can be a large source of error between planned and delivered dose distributions if it is not accounted for (Bortfeld *et al* 2002, Court *et al* 2008, Flampouri *et al* 2006, Ford *et al* 2003, Jiang *et al* 2003, Langen and Jones 2001, Lujan *et al* 2003, Rosu *et al* 2007, Schaefer *et al* 2004, Seco *et al* 2007, 2008, Shimizu *et al* 2001, Yu *et al* 1998). The use of four-dimensional computed tomography (4D-CT) and periodic portal imaging has allowed the nature of the target volume to be seen both over the course of a breathing cycle and throughout a course of radiotherapy, respectively (Keall 2004, Keall *et al* 2004, Liu *et al* 2007, Low *et al* 2003, Maxim *et al* 2007, Pan *et al* 2004, Rietzel *et al* 2005a, 2005b, Rosu *et al* 2006, Vedam *et al* 2003). The use of these techniques has been increasing in recent years and is one attempt at minimizing volumes of healthy tissue irradiated during a course of radiotherapy.

Changes in lung density *during* a respiratory cycle may have an effect on the dose distribution during a fractionated radiotherapy treatment. To date, few studies have considered this effect. This may be because a considerable effort is required to extract density information for the heterogeneous lung tissue over a 4D-CT dataset (Flampouri *et al* 2006). To mitigate some of the above problems encountered with real patients, a mechanical phantom designed to mimic motion and density changes over a breathing cycle was recently tested (Serban *et al* 2008). This approach was shown to have promising applications but with limitations. Densities of the materials in this phantom are fixed, deformable registration techniques employed in the study are aided by nylon wires and Lucite beads, and at a peak-to-peak amplitude piston motion of 2 cm, the lung volume was observed to change by 40%. As noted by the authors, this change exceeded real patient lung expansion for the same amplitude. Another approach used contouring techniques in conjunction with a 3D printer to create a physical model of the lung. However, this method is very labor intensive and does not allow 4D studies to be performed on a single phantom (Xu *et al* 2006).

In place of mechanical phantoms, computational phantoms offer another approach in investigating the effect of motion and dynamic lung density in IMRT treatments. Until recently, computational phantoms provided neither the level of anatomical detail, nor the flexibility of simple mechanical phantoms. However, the most advanced computational phantoms are now based on tomographic images or high-resolution color photographs of

real patient anatomy and are available in sub-millimeter anatomical detail (Caon 2004, Dimbylow 2005, Fill *et al* 2004, Xu *et al* 2000, Zaidi and Xu 2007). In addition, 4D motion, such as motion due to respiration and the beating heart, are now incorporated into many computational phantoms (Garrity *et al* 2003, Segars 2001, Segars *et al* 1999, Zhang *et al* 2008).

Monte Carlo simulations are particularly well suited for motion studies involving the lung due to their accuracy in low density, highly heterogeneous materials (Seco *et al* 2005). Furthermore, Monte Carlo studies have been shown to be an efficient and accurate method of determining dose in 4D motion studies (Keall 2004, Paganetti *et al* 2005, Seco *et al* 2008).

The combination of computational phantoms and MC dose calculation algorithms has already been investigated and shown to be possible. Previous efforts have focused on using the NCAT phantom in a Monte Carlo environment to investigate the effect of irradiating a gross target volume (GTV) via lesion tracking in a 3D conformal treatment (3DCRT). An IMRT plan was also developed for a static anatomy in this study (Riboldi *et al* 2008). Another closely related study used the VIP-Man phantom (Xu *et al* 2000) in a 4D IMRT study to investigate motion effects with a standard conformal treatment plan and 4D gated and image-guided IMRT treatments (Zhang *et al* 2008). However, this study used a constant lung density throughout all respiratory cycles and did not investigate delivery of the IMRT plan in a free-breathing scenario. It also used a 'reverse-transformation' of the motion curves used to deform the anatomy initially to perform the mapping of dose distributions of each phase. While this approach should be sufficient, the study did not provide any quantification of the accuracy of this method.

The present investigation focuses exclusively on using the NCAT phantom in a non-clinical implementation of 4D IMRT treatments of artificial lung lesions. It uses a deforming lung anatomy to model step-and-shoot IMRT delivered in a free breathing scenario. This study is novel first in its use of an existing computational phantom previously used for low-resolution nuclear medicine and recently for pediatric CT dosimetry (Li *et al* 2008). Second, the study is novel in the modifications made to the NCAT phantom to allow

- varying lung density over a respiratory cycle;
- the introduction of a heterogeneous lung anatomy.

Third, the accuracy of the deformation model used in the NCAT phantom was quantified in greater depth than has been shown previously. This work ultimately shows that the NCAT phantom can be used not just for nuclear medicine studies, but is suitable for radiation therapy and dosimetry studies and thus provides an alternative to the VIP-Man and other phantoms used to date in radiation therapy applications.

2. Material and methods

2.1. The NCAT phantom

The Non-uniform rational B-spline (NURBS) cardiac and torso (NCAT) phantom (Segars 2001), figure 1, is an anthropomorphic computational phantom based on the visible human

dataset (Spitzer and Whitlock 1998). The phantom uses non-uniform rational B-spline surfaces to represent 3D human anatomy and also allows the incorporation of 4D cardiac and respiratory motions (Garrity *et al* 2003, Segars 2001, Segars *et al* 1999). The anatomical parameters of the phantom are set using an input file so that the anatomy parameters can be scaled to dimensions and values different to that of the default visible human parameters. One example is the level of desired anatomical detail for the blood vessels and lung airway. The dynamic nature of the phantom is invoked by specifying whether respiratory and/or cardiac motion is to be included. If motion is to be included, the input file also contains settings that control the amplitude, period, number of cardiac or respiratory phases and starting phase of any lung or heart motion. The input file is read into the phantom software which then generates voxelized images of the phantom at a user-defined resolution for each phase of the defined motion. Each voxel represents the linear attenuation coefficients (LAC) of each tissue type.

2.2. NCAT motion vectors

Organ motion and deformations of anatomical structures are defined mathematically in the NCAT phantom. Further, the phantom can output a motion vector for each voxel of the voxelized phantom with the number of vectors being dependent on the user-defined resolution. The voxel displacement map *between* phases can be generated or the displacement maps for each of the phases back to any particular reference phase can be generated. This feature allows deformable image registration relative to any respiratory phase. The fact that NCAT has the ability to output transformation coordinates between any desired phase means there is no need to resort to other methods of deformable image registration which have been shown to have varying degrees of accuracy in the mapping dose distributions for 4D studies (Heath and Seuntjens 2006, Yan *et al* 1999). In our study, the reference respiratory phase was chosen to be full-exhale.

In a real patient, respiratory motion results in the sliding of lung anatomy within the thoracic cavity. The NCAT phantom models inspiration as follows: during inspiration, the ribs rotate upward and outward and the diaphragm contracts downward and in the anterior direction. This opens up empty space in the torso. The program then expands the lungs to fill in the empty space. In other words, over the course of inspiration, lung voxels are added at each phase until full-inhale when the maximum number of lung voxels for the phantom configuration is reached. The opposite occurs during expiration. As such, no sliding of the lung surfaces or anatomy is modeled in the NCAT respiratory model. This also means that the deformation of the lung has no impact on the deformable mapping of the surrounding ribs. Rather, it is the opposite—the movement of the ribs impacts the deformation of the lung anatomy.

By default, the density value of every voxel tagged as lung is a constant over the entire respiratory cycle (Segars 2001). However, this is not a realistic representation of human anatomy. In fact, lung tissue displays a range of densities from close to 0 g cm^{-3} up to over 1 g cm^{-3} but with a mean value of 0.3 g cm^{-3} (Seco *et al* 2008, Serban *et al* 2008). It is also region dependent.

After a deformation, the corners of the tracked voxels are in a new position. Importantly, due to the spline-based phantom deformations the new voxel corner positions are not usually integer translations and in fact, the voxel may no longer even be an equal sided cube. Thus, in order to use this displacement map with a voxelized data set, the mapping values are rounded to the nearest integer. The accuracy of this rounding procedure on the anatomy must be quantified since the deformation is no longer exact. To do so, we compared the anatomy of the full-inhale respiratory phase mapped back to the reference phase to that of the reference phase itself by means of the correlation coefficient (CC):

$$CC = \frac{\sum_x (A(x) - \bar{\mu}_A) \cdot (B^T(x) - \bar{\mu}_B)}{\sqrt{\sum_x (A(x) - \bar{\mu}_A)^2} \cdot \sqrt{\sum_x (B^T(x) - \bar{\mu}_B)^2}}, \quad (1)$$

where μ_A and μ_B are the mean intensity values of the images A and B , respectively. T represents the transformation (Yu 2005). The CC ranges from 0 to 1 where a perfect match between voxels (no difference) is assigned a value of 1, and no correlation having a value of 0. Furthermore, the CC was calculated using only the voxels that belong to the NCAT phantom and not the entire $256 \times 256 \times 256$ grid to avoid bias. It should be noted that the CC does not include information about the accuracy of the deformation.

2.3. NCAT phantom parameters and lung density modification

To create a population of phantoms suitable for our study, two magnitudes of diaphragm motion were set; 1 cm and 3 cm. This gave tumor center-of-mass (COM) peak-to-peak amplitudes of 0.9 and 2.8 cm, respectively. The 0.9 cm tumor motion amplitude value represents the majority of clinically observed tumor amplitudes, while the 2.8 cm case may represent a patient with large tidal volumes which might necessitate the use of gated delivery or tracking techniques. Spherical tumors with diameters of 2 cm and 4 cm were used to cover a large range of tumor sizes. The tumor diameters were selected to provide the range of tumor sizes encountered in the clinic (Langen and Jones 2001, Liu *et al* 2007, Maxim *et al* 2007, Pan *et al* 2004, Rietzel *et al* 2005a, Seppenwoolde *et al* 2002, Stevens *et al* 2001).

By default the NCAT phantom respiratory model reflects a chest breathing patient with a chest surface expansion of approximately 2 cm. The chest surface expansion was changed to 2 mm in order to reflect an abdominal breathing patient which may better represent older patients and/or those undergoing respiratory distress who are not suitable candidates for motion management strategies such as breath hold techniques.

For our study, five equally spaced (in time) breathing phases were used. Five phases of binning has previously been shown to provide sufficient accuracy when calculating a composite dose (Flampouri *et al* 2006). Each phase represents 1 s of the total 5 s duration. The equal spacing and free breathing delivery of radiation mean that no time weighting of the dose distributions is necessary when calculating a composite dose. The equal temporally spaced phases correspond to different lung volumes and hence lung voxel densities.

To model the density change in lung voxels at each respiratory phase, a conservation of mass calculation was used to keep the product of lung density and number of lung voxels constant. It is recognized that this approach does not account for the regional dependence of lung density variation. However, the modification is expected to be a more accurate representation of the lung anatomy over the breathing cycle than the default NCAT and regional dependence and even gross dynamic changes are not accounted for in other 4D capable phantoms that the authors are aware of. Looking at figure 2(A), the phases are phase 1: 0% relative lung volume and reference 0.3 g cm^{-3} lung density; phase 2: mid-inhalation and 50% relative lung volume, phase 3: full inhalation or 100% relative lung volume; phase 4: one-third exhalation or 66% relative lung volume and phase 5: two-thirds exhalation or 33% relative lung volume.

To create the heterogeneous lung model, random sampling from a tissue probability density function approximated from the work of Seco *et al* was used to calculate and set the density of voxels in the lung for each of the five respiratory phases. Based on a modified normal distribution, the mean lung density was set according to the lung density for each phase calculated using the conservation of mass above and a standard deviation of 0.15 g cm^{-3} was used. No values below 0.1 g cm^{-3} were sampled (figure 2(B)). Further, the method is flexible enough that sampling from any desired distribution could be incorporated.

2.4. IMRT treatment plans

The CORVUS (Best nomos, Pittsburgh, PA) treatment planning system was used to generate IMRT plans for each of the phantoms. To import the phantom anatomy into the treatment planning system, the DICOM-RT toolkit (Spezi *et al* 2002) was used to convert the NCAT binary phantom data into the Digital Imaging and Communication in Medicine (DICOM) 3.0 format. Only the full-exhale, mid-inhalation and full-inhale breathing phase anatomy was used to contour the ITV. This is because the tumor traces a well-defined path over the entire respiratory cycle because the NCAT respiration model does not include hysteresis and the tumor is a rigid solid. For each phantom anatomy, a visual inspection of the ITV created using the three phases superimposed over all five tumor positions confirmed that each ITV encompassed the tumor in all respiratory phases. Further, in addition to the tumor being rigid and tracing a well-defined path, it has known boundaries and volume and so the gross tumor volume is equal to the clinical target volume (CTV). Therefore, the ITV can be defined as the union of the CTV in the full-exhale, mid-inspiration and full-inhale images for each phantom in accordance with ICRU Report 62 (ICRU 1999). An electron density correction (relative to water with value 1.0) for the ITV was used to provide a uniform dose throughout the ITV consistent with the approach of Rosu (Rosu *et al* 2007). A 15 mm isotropic expansion was placed on each individual ITV to create the planning target volume (PTV). This is in accordance to our clinical practice and because our tumor is spherical. The prescription dose of 72 Gray (Gy) to the ITV was set to be delivered as 40, 1.8 Gy fractions with the constraint that 95% of the PTV received the full 72 Gy. The treatment plan was initially optimized on the full-exhale image anatomy for the most challenging case—3 cm diaphragm motion and 4 cm diameter lesion. In this case, one set of gantry angles that met these conditions was 0° , 30° , 100° , 250° and 330° (figure 3). These same angles were then used for the remaining phantoms. A summary of the treatment goals

and clinical constraints for each structure are shown in table 1. After each plan optimization, the MLC leaf sequence files for each of the NCAT phantom plans were saved for use in the Monte Carlo simulations on all of the five respiratory phases.

The right and left lungs for the three phases of each phantom were contoured using the General Electric (GE) Advantage Workstation automatic segmentation tools and these contours were subsequently imported into CORVUS. The liver, heart and spinal cord were then manually contoured in CORVUS as additional organs at risk. The spinal cord was defined as the inner margin of the vertebral body. No esophagus was contoured as it is not present in the NCAT phantom's organ set.

2.5. Monte Carlo dose calculations

The general approach for the 4D Monte Carlo system used for this study has been outlined elsewhere (Riboldi *et al* 2008, Seco *et al* 2007, 2008). Briefly, 14 tissue subsets were used for the Monte Carlo dose calculations in accordance to the approach used by Vanderstraeten *et al* (2006). As the density values for each voxel are provided by the NCAT model, no stoichiometric calibration was necessary. The Monte Carlo dose calculation is performed in three steps. First, a model of the Varian 2100C/D treatment head operating at 6 MV was designed within the EGSnrc Monte Carlo code (Kawrakow 2000). The beam is defined by a phase space containing all particles at the level of the flattening filter in the treatment head. Second, particle transport through the MLC and jaws is performed using a method described by Siebers *et al* (2002) and expanded by Seco *et al* (2008). Here, the MLC leaf sequence files for each patient were used. Finally, dose computation is performed by the dose planning method (DPM) Monte Carlo code (Sempau *et al* 2000). DPM offers improved efficiency over EGSnrc in a patient geometry. Both codes were benchmarked against each other and showed agreement within 1% (Riboldi *et al* 2008). The low-energy electron and photon cutoff energies were set to 200 keV and 50 keV, respectively.

For our study a dose rate of 500 MU min⁻¹ was used. At least 100×10^6 histories were simulated for each respiratory phase giving a relative statistical uncertainty in dose values of below 1%.

The final dose distribution for each phantom anatomy is found via the following process. For one gantry angle the dose distributions for each of the five breathing phases are calculated via Monte Carlo. Next, these dose distributions are each mapped back to the reference phase (phase 1: full-exhale) one at a time using the NCAT deformation fields. Then, the total dose distribution for this gantry angle is calculated using a weighted sum of the mapped dose distributions (each distribution has a weighting of 0.2 to reflect the equally spaced time each of the five phases spends in the respiratory cycle). This dose calculation, mapping of the distributions and weighted summation of the five phases, is repeated for all five gantry angles. Finally, the cumulative dose distribution (all phases and all gantry angles) is calculated by adding the dose distributions from each gantry angle. Dose volume histograms for the ITV, PTV and right lung were then created from the composite dose distributions for subsequent analysis.

3. Results

3.1. Conservation of mass dynamic lung density

Figure 2(A) shows the effect of changing the lung density over the respiratory cycle. The minimum densities are 0.2718 g cm^{-3} and 0.2337 g cm^{-3} , or a 9.4% and 22.1% reduction for the 1 cm and 3 cm diaphragm motion, respectively. This is consistent with Rosu *et al* who found that the range of lung densities between inhalation and exhalation was 0.16 g cm^{-3} to 0.35 g cm^{-3} (Rosu *et al* 2007). It is also close to the peak densities shown to exist within GTV contours that extend into the lung in the work of Seco *et al* (2008).

3.2. Image registration assessment

Figure 4 shows the result of mapping the full-inhale data anatomy back to the full-exhale reference phase using the modified NCAT displacement map. We see a good match visually with all bony anatomy landmarks showing agreement to within 2 pixels (3 mm). More quantitatively, a CC of 0.95 for a 1 cm diaphragm motion indicates a good match between intensity levels of the mapped and reference image. The 3 cm diaphragm motion has a lower CC of 0.89 due to larger out of field anatomy effects such as the superior border of the phantom and also greater deformation in the lung anatomy. Ultimately, figure 4 indicates that an accurate deformable image registration is able to be achieved in the volume of interest using the NCAT deformation vectors.

3.3. Dose distribution analysis

The dose volume histograms for the ITV, PTV and right lung for the mean of 30 simulations of the fractionated IMRT plans for all phantoms are shown in figure 5. Curves are normalized so that D50 of the PTV is equal to 72 Gy. D50 is the dose received by 50% of the PTV volume. The normalization was necessary due to the Monte Carlo absolute dose calculations not matching the dose values calculated using the planning system. It is uncertain as to why this occurred but there may be some errors in transferring the planning systems fluence values into the Monte Carlo dose computation engine. For clarity, each line indicates the mean DVH for the 30 simulations of each patient. The most significant feature of figure 5 is the large difference in dose falloff for the 1 cm peak-to-peak diaphragm motion (0.9 cm tumor motion) and 3 cm peak-to-peak diaphragm motion (2.8 cm tumor motion). This is seen by the large shift in position of the hot and cold spots representing over- and under-dosage, respectively, between the two motion magnitudes. Another supporting feature is the widely varying values between the dose representing the 95% and 5% volume coverage for both the ITV and PTV.

An important feature of figure 5 is the consistency of the curves for all lung density situations. This shows that our study indicates that dynamic or heterogeneous lung density is not a significant factor in changing the dose distribution in IMRT treatments when calculated using Monte Carlo simulations. Finally, there appears to be little difference in the dose variation with tumor size but this is likely due to the ITV and PTV being large enough to encompass the increased lesion size. For all structures in all patients, the standard deviation of the mean dose is 0.3 Gy. This indicates that our Monte Carlo system is performing accurately but also, since our system randomly selects a breathing phase to

deliver each segment, the initial phase chosen has little effect on total dose delivered. This is of course expected given that the ITV should encompass the lesion in all respiratory phases. It is also evidence that the interplay effect is of little importance over the course of a fractionated IMRT treatment, which is consistent with findings of previous studies (Bortfeld *et al* 2002).

The effect of lesion size appears to be negligible most likely due to the ITV and PTV being large enough to accommodate the increased lesion size and still meeting the planning constraints. Finally, table 2 shows that for phantoms with a dynamic lung density, there is a small increase in the mean dose for the ITV and right lung which was not obvious from figure 5. As pointed out by Rosu *et al* this increase could possibly be a consequence of the reduced attenuation of the primary beam in lung tissue (Rosu *et al* 2007).

4. Discussion

This study has developed and applied a novel implementation of a computational phantom to study questions relevant to IMRT treatments. We have shown that it is possible to modify the lung densities of the NCAT computational phantom to provide a more realistic anatomy and validated the model using a 4D Monte Carlo simulation framework. Extension of this work could be applied to find class solutions based on various anatomical and physiologically relevant parameters (e.g. tumor size, shape, motion magnitude). This could be useful in aiding the study of managing organ motion during treatment delivery; currently one of the most challenging aspects of modern radiation therapy.

Some advantages of using computational phantoms include reducing the time necessary for gaining institutional review board approval and the need to search through patient databases to find appropriate subjects for inclusion into a study.

The relative changes observed in this study are consistent with previous findings indicating that the phantom can provide important information on the effect of changes in patient anatomy or set up. One example is the observation that motion of the target acts to broaden the penumbra (Bortfeld *et al* 2002, Chui *et al* 2003, Jiang *et al* 2003).

The respiration model on this phantom appears to provide realistic anatomy deformations and tumor trajectories even without accounting for tissue sliding. By modifying the lung density we more realistically reflect density changes over a breathing cycle. As stated earlier, our method of varying the density does not account for regional dependences observed in real patients, such as density differences between the apex of the lung or region around the diaphragm for example. However, we feel the modifications deliver a significant improvement to the NCAT phantom and offer something that other present generation computational phantoms lack. The phantom is still not perfect and further work could be done to improve its realistic description of the human body. For example, the esophagus is not present in the NCAT phantom organ set. Ideally, such an important dose limiting structure in lung radiotherapy would be available. Additionally, the trachea was not contoured since its primary and secondary branches are relatively far from the volume of

irradiation. The next generation NCAT phantom, the extended cardiac–torso or XCAT phantom, is currently being developed to include a more detailed anatomy.

When using the NCAT deformation vectors for image registration in a voxelized dataset, it must be remembered that the values do not represent required integer voxel shifts by default. We have shown that by rounding the computed deformation field to reflect the whole voxel shifts necessary for deformable image registration in voxelized dataset provides an acceptable degree of accuracy. As a caveat, special care must be taken when selecting the desired phantom volume to study to ensure that any targets or organs of interest are not close to the edge of the volume. This is because motion may result in these structures moving outside of the volume and thus affect the accuracy of any composite dose calculations.

We did not include cardiac motion since our lesion was far enough away from the heart and this was much smaller than the respiratory induced motion. Furthermore, it would have been the same for all patients and since this is a relative study the inclusion of the effect was not a priority. However, this feature is implemented in the NCAT phantom and could prove useful in cases where the lesion is desired to be placed close to the heart wall.

Our work shows an example of how the NCAT tool can be used to answer clinically relevant questions. Despite the obvious fact that we need patient specific dose images for treatment planning it can be extremely useful for relative studies. There were some limitations and approximations in our study.

Tumor size has been shown to not be a significant factor as the differences in mean dose to the ITV as a function of tumor size are all less than 1.5%. This is due to our treatment plans satisfying the planning constraints for all tumor sizes in all patient plans. Further, the default spherical tumor shape may affect the ability to make clinically relevant conclusions. However, since these tumor parameters are specified via a binary file, it would not be a difficult task to specify any desired size or shaped lesion before incorporating it into the phantom anatomy.

Lung density variations do not appear to impact the dose able to be delivered with IMRT. Since the dose calculations were performed with Monte Carlo techniques, which are adept at accounting for heterogeneous materials, the effect of using heterogeneous lung voxel values versus constant ones implies that for cumulative dose calculations the effect is small, so long as the dose calculation method is accurate for both situations. However, the NCAT lung anatomy is not truly homogeneous as the respiratory tree is included in our default model. For a truly homogenous lung anatomy, all details in the lung could be removed and all of the region corresponding to lung may be set to a fixed density of 0.3 g cm^{-3} .

The observed increase in dose to the ITV as a function of diaphragm motion is most likely caused by our normalization to D50 of the PTV. By specifying that the point of normalization is relative to the PTV, any under dosage to the PTV (i.e. a PTV dose of less than 72 Gy), will be reflected in an increase to the ITV dose since the normalization factor would be greater than 1 to bring the dose to the PTV back to 72 Gy. Such reductions in PTV dose are a result of the moving anatomy—i.e. the plan is being delivered to an anatomy that does not reflect what was planned on. Any voxels labeled as PTV that move outside of the

field receive a lower dose. Once they are subsequently mapped back into the PTV structure on the full-exhale data set, the lower dose values in these voxels cause an overall reduction in PTV dose. This indicates that due to respiratory motion, one must be careful using an expansion of the PTV as a means of ensuring target coverage in lung IMRT, and then using the PTV as the optimization criteria. This should reduce the chances that the ITV, or more importantly, any healthy tissue within the ITV receives a larger than prescribed dose.

The mean dose to the ITV when lung density is dynamic or heterogeneous differs by a maximum of 0.5% compared to the scenario where the lung voxels are kept constant. This maximum difference is for the scenario of a 3 cm diaphragm motion and 2 cm diameter tumor with dynamic lung density. This indicates that the use of a dynamic or heterogeneous lung density during free breathing application of IMRT therapy for lung tumors does not appear to alter the dose delivered to any clinically relevant level. This differs from Rosu *et al* (2007) in that motion-induced changes to the dose distribution are much smaller than those created by heterogeneities. However, this is due to their homogenous lung being set to a density of 1 g cm^{-3} and not 0.3 g cm^{-3} as was the case in our study. Any observed effects due to density changes in our study would thus be expected to be smaller. Also, in their study the homogenous region was the entire lung versus our case where the lung voxels are treated separately from the blood vessels and bronchial structures present. Further, their study used anterior/posterior opposed beams and 3D conformal therapy for targets in the lung and a time-weighted summation to calculate the composite dose in a free breathing scenario rather than five equally spaced dose distributions.

Overall, the NCAT phantom has been shown to provide insights into how patient motion, tumor size and tissue density changes can affect dose distributions. We studied the effect of target motion on the dose distribution in IMRT of lung tumors using a modified NCAT phantom incorporating the effect of intrafraction lung density variation on the dose distributions. The NCAT phantom may prove to be of further value in the field of radiation therapy, extending its use from diagnostic and nuclear medicine studies it is predominantly used for currently.

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Figure 1.
The NCAT phantom. (A) Anterior view of the phantom and (B) volume rendered image of the anterior aspect of the phantom.

Figure 2. Modification of the NCAT lung voxel values. (A) Gross dynamic changes of the lung voxel density values as a function of respiratory phase causes a homogenous change in all lung voxels at each breathing phase to the right. (B) The probability density function that the lung voxels are randomly sampled from to create the heterogeneous lung model seen to the right.

Figure 3. Treatment planning for the NCAT phantom. (A) ITV delineation for the 3 cm diaphragm motion and 4 cm diameter lesion. (B) Treatment beam orientations selected to optimize IMRT fluence patterns to achieve the treatment goals of table 1.

Figure 4.

Difference images in anatomy between the mid-coronal planes of the mapped image and the reference image. The absence of information along the inferior border of the image reflects the fact that the regions corresponding to the kidneys were outside of the field of view (FOV) in full-inhale and so no anatomy information existed when using the deformation map to warp the anatomy back to our full-exhale reference phase. The color bars on the right represent differences in LAC for each voxel. The correlation coefficient (CC) is calculated using only voxels corresponding to the NCAT phantom anatomy and not the entire $256 \times 256 \times 256$ grid.

Figure 5.

DVH results for all phantom patients. The top of each figure indicated the normalized DVH for the ITV, PTV and right lung, while the absolute difference in volume at each dose level is presented below each set of DVHs. In the legend, the CONST refers to the situation where lung density was set to a constant over all respiratory phases, DYN is where the lung density is changed as a function of respiratory phase and HETERO is the situation where the density values for each lung voxel are sampled from the density probability density function. Consistent values for all lung anatomy situations are seen with only small variations in volume coverage for each dose level.

Table 1

Treatment goals and planning constraints for the population of NCAT phantoms.

Organ	Tissue type	Dose goal or dose limit (Gy)	%vol below goal or % vol above limit	Minimum allowed dose (Gy)	Maximum allowed dose (Gy)
ITV	Basic	72	5	68	74
Tissue	Basic tissue	72	0	0	72
Lung (L)	Basic structure	20	20	0	60
Lung (R)	Basic structure	20	20	0	72
Spinal cord	Critical structure	42	0	42	42
Heart	Basic structure	15	10	10	50
Liver	Basic structure	25	25	0	72

Table 2

Mean and standard deviations of 30 simulations for each phantom anatomy studied. Phantom anatomy is named according to 'DIAP_': diaphragm motion set to be 1 or 3 cm, and 'LES_' indicating the tumor size of 20 or 40 mm. The suffix of '_const' refers to the anatomy where lung voxel density is kept constant over all respiratory phases, while '_dyn' and '_hetero' refer to the cases where density of all lung voxels is changed at each breathing phase or set to be heterogeneous, respectively. All values are in Gy.

Phantom anatomy	ITV		PTV		RLUNG	
	$\bar{D}$	σ_D	$\bar{D}$	σ_D	$\bar{D}$	σ_D
DIAP_1CM_LES_20 MM_const	74.13	0.20	71.60	0.07	18.87	0.01
DIAP_1CM_LES_20 MM_dyn	74.26	0.20	71.60	0.08	18.91	0.01
DIAP_1CM_LES_20 MM_hetero	74.06	0.24	71.61	0.07	18.88	0.01
DIAP_1CM_LES_40 MM_const	73.58	0.15	71.65	0.08	26.04	0.01
DIAP_1CM_LES_40 MM_dyn	73.70	0.13	71.64	0.08	26.07	0.02
DIAP_3CM_LES_20 MM_const	76.93	0.26	68.84	0.13	21.54	0.02
DIAP_3CM_LES_20 MM_dyn	77.37	0.29	69.00	0.16	21.65	0.02
DIAP_3CM_LES_40 MM_const	76.07	0.20	69.05	0.12	29.58	0.05
DIAP_3CM_LES_40 MM_dyn	76.25	0.31	69.06	0.28	29.64	0.12