

## REVIEW

# The clinical significance and management of lesion motion due to respiration during PET/CT scanning

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### Abstract

Lesion movement during positron emission tomography (PET) scan acquisition due to normal respiration is a common source of artefact. A PET scan is acquired in multiple couch positions of between 2 and 5 min duration with the patient breathing freely. A PET-avid lesion will become blurred if affected by respiratory motion, an effect similar to that created when a person moves in a photograph. This motion also frequently causes misregistration between the PET and computed tomography (CT) scan acquired for attenuation correction and anatomical correlation on hybrid scanners. The compounding effects of blurring and misregistration in whole-body PET/CT imaging make accurate characterization of PET-avid disease in areas of high respiratory motion challenging. There is also increasing interest in using PET quantitatively to assess disease response in both clinical reporting and trials. However, at this stage, no response criteria take the effect of respiratory motion into account when calculating the standardized uptake value on a PET scan. A number of different approaches have been described in the literature to address the issue of respiratory motion in PET/CT scanning. This review details the clinical significance of lesion movement due to respiration and discusses various imaging techniques that have been investigated to manage the effects of respiratory motion in PET/CT scanning.

**Keywords:** *Respiratory-gated PET; 4D PET/CT; lesion motion; clinical significance.*

### Introduction

Over the past decade, positron emission tomography (PET)/computed tomography (CT) scanning has become an invaluable tool in the evaluation of many oncologic processes. The imaging modality of PET uses positron emitting isotopes attached to specific tracers to image metabolic pathways or other biological processes. As PET scanning often interrogates specific biochemical processes involved in substrate utilization, it is sometimes referred to as metabolic imaging but it can also image a range of molecular targets and physiologic processes and therefore is more accurately a form of molecular imaging. The most common tracer used is fluorine-18 fluorodeoxyglucose (FDG), which evaluates the body's utilization of

glucose. Up-regulation of the insulin-independent glucose transporters GLUT-1 and GLUT-3, as well as the initial rate-limiting enzyme of glycolysis, hexokinase, drive the increased glycolytic metabolism, termed the Warburg phenomenon, which is characteristic of most cancer cells<sup>[1]</sup>. As changes in cell metabolism precede any change in tumour morphology, PET scanning may detect disease before anatomical changes can be visualized<sup>[2]</sup>. Due to limited spatial resolution and the resulting partial volume effects and apparent spillover of very intense activity into surrounding tissues, molecular imaging is less accurate with regard to tumour size than anatomical imaging modalities such as magnetic resonance imaging or CT. In addition, it provides only vicarious anatomical information through the pattern of

glucose use in tissues and organs. In order to overcome these limitations, all modern PET scanners now have a CT scanner attached to the same gantry so that a CT scan can be acquired in the same session. This is termed hybrid imaging. It allows accurate fusion of the powerful metabolic information of a PET scan to the fine anatomical detail of a CT scan. The CT component of the study is also used to provide correction for the attenuation of photons arising from the PET tracer as they pass through the body to the detector, an essential process to provide quantitative PET information.

Because both the PET and CT components of a PET/CT are acquired at almost the same time and in the same geometry, it is expected that images resulting from both modalities will be perfectly aligned. However, this is seldom the case. An inevitable, but not the only, cause of misalignment of the metabolic and anatomical information is normal patient respiration. This is a common source of artefact and can have a profound impact on the ability of a PET scan to detect disease, accurately localize it or provide accurate quantitation of tracer uptake. This is of particular relevance when planning target volumes for radiation therapy. A PET scan is acquired in steps of between 2 and 5 min duration with the patient breathing freely. A PET-avid lesion will become blurred if affected by respiratory motion, an effect similar to that created when a person moves while a photograph is taken with a slow shutter speed in low-light conditions.

Because the CT scan is acquired sufficiently quickly by most modern scanners to freeze this motion for the anatomical component of the study in a random but fixed position of the breathing cycle, misregistration between the PET and co-acquired CT scan can also occur. The compounding effects of blurring and misregistration in whole-body PET/CT imaging make accurate characterization of PET-avid disease in areas of high respiratory motion challenging.

There is also an increasing interest in using PET quantitatively to assess disease response in both clinical practice and trials by evaluating tracer uptake before, during and after treatment using a measure known as the standardized uptake value or SUV. The SUV is a semi-quantitative index of tracer uptake normalized by weight and injected activity and is measured by the PET scanner. Currently, PET response criteria such as the EORTC guidelines do not consider the effect of respiratory motion when calculating the SUV<sup>[3]</sup>. However, both respiratory blurring of activity within a lesion and assignment of inappropriate attenuation correction due to misregistration of the CT and PET data compromise the accuracy and precision of this measure.

There have been a number of different approaches described in the literature to address the issue of respiratory motion in PET/CT scanning<sup>[4–9]</sup>. In a recent article, Nehmeh and Erdi reviewed a number of different respiratory motion protocols that have been investigated and presented their results concentrating on improvement in

image quality and quantitation<sup>[4]</sup>. They showed in their review that a wide range of strategies can be used to compensate for the effects of respiratory motion, each having advantages and disadvantages. The present review concentrates on the clinical significance of lesion movement due to respiration, using examples to illustrate particular clinical scenarios. The most practical current imaging techniques and approaches to manage the effects of respiratory motion in PET/CT scanning and to optimize the resulting images are discussed.

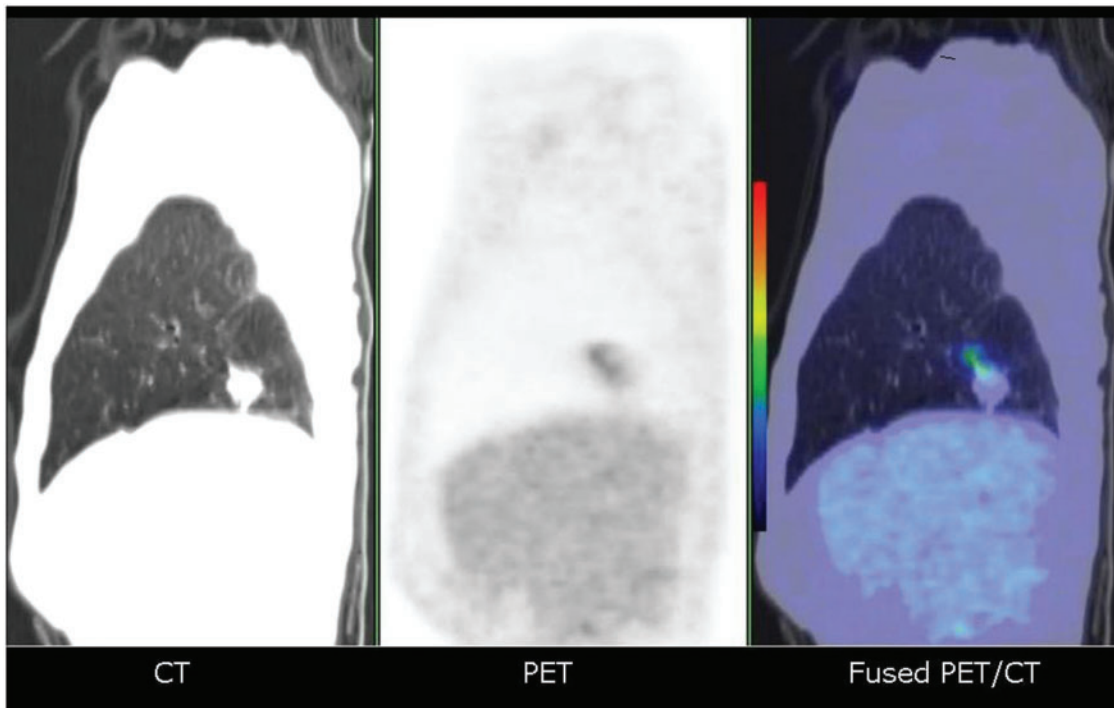
## Clinical significance of lesion motion due to respiration

The areas most affected by respiratory motion are the lower lungs, liver and upper abdomen. The effect of this motion on a whole-body PET scan is to make a PET-avid lesion appear larger but fainter, particularly at its boundaries, which exhibit blurred outlines rather than defined margins. Respiratory motion tends to artificially reduce the SUV<sup>[4–8,10]</sup>. The artefact has the potential to affect the correct diagnosis of diseases, provide inappropriate planning of target volumes for radiotherapy, impair staging of disease before surgery, and may lead to incorrect quantitation in therapeutic monitoring.

## Diagnosis of malignancy

The most common parameter used to characterize a lesion is the SUV<sub>max</sub>, which is the pixel within a region of interest drawn around a tumour that has the highest SUV. Several studies have advocated the use of SUV<sub>max</sub> thresholds for the differentiation of benign and malignant lung nodules. For example, an SUV<sub>max</sub> of less than 2.5 is often used to differentiate benign and malignant lesions in the lung<sup>[11,12]</sup>. An example of a respiratory artefact is shown in Fig. 1. Accurate measurement of the true SUV in a lesion such as this is not possible. A number of studies have shown consistently higher SUV<sub>max</sub> values on a scan corrected for motion compared with a standard whole-body acquisition<sup>[4–8,10,11,13,14]</sup>. In one case, reported in the study by Lupi et al.<sup>[4]</sup>, the SUV on the gated scan was 360% higher than on the ungated scan. However, the clinical significance of this is not clear in practice. Although the lesion in Fig. 1 shows a large amount of blurring and misregistration, an experienced physician would still be able to make an accurate diagnosis of malignancy by using the appearance of the lesion on CT as well as knowledge about the effect of motion in this area of the lung when making a diagnosis. Given the complexity of the decision-making process required, this would make any computer automation or support difficult.

The distance that a lesion moves during respiration determines how severely the PET scan is affected by this artefact<sup>[14]</sup>. The greater the motion, the fainter a PET lesion becomes overall and therefore the more



**Figure 1** Sagittal section of the right lower lobe showing CT (left panel), PET (middle panel), and fused PET/CT (right panel). The PET scan shows significant blurring and misregistration of a malignant lung lesion on the PET scan. The demonstration that the majority of the metabolic abnormality has been attenuated as though arising within normal lung and is elongated in the cranio-caudal dimension compared with the CT lesion indicates substantial respiratory movement of this lesion close to the diaphragm. Accordingly, the combination of radiologic appearances and the assumption that true metabolic activity is significantly underestimated should lead an experienced clinician to strongly suspect a malignant basis for this lesion.

difficult it becomes to detect the lesion. When the effect of motion is combined with a small-sized lesion, which is also subject to a partial volume effect, then a lesion with uptake of a metabolic tracer can become falsely negative (Fig. 2). It is in this situation that strategies for the management of motion need to be in place.

The extent of respiratory motion varies from patient to patient. Diaphragmatic motion was measured in a series of 20 patients who had respiratory-gated (4D) CT scans for radiotherapy planning at the Peter MacCallum PET centre (unpublished data). The median amount of cranio-caudal motion in the right hemi-diaphragm was 21 mm (range 8–56 mm) and the left hemi-diaphragm was 13 mm (range 0–25 mm). The wide range of measured movement indicates that the amount of motion from patient to patient is difficult to predict. Fig. 3 shows an example of a patient with a severely impaired respiratory excursion in the left lung leading to compensation by the right lung producing a large amount of motion. Any lesion in the right lung would likely become falsely negative but the left lung would be unaffected.

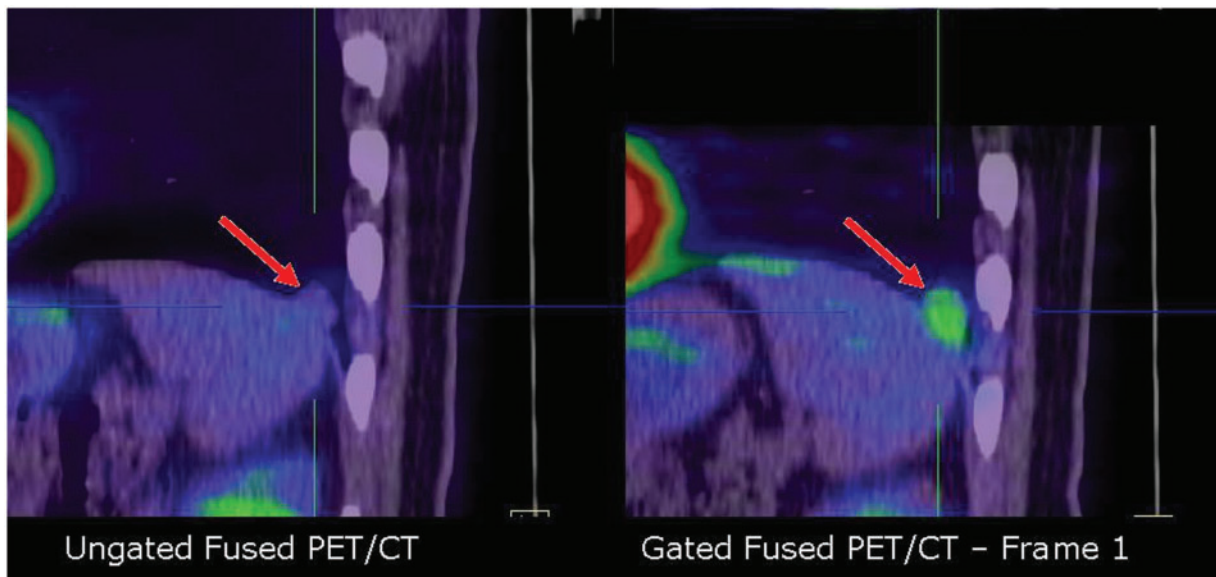
Gated or 4D scanning is a scanning technique that enables imaging of the full range of respiratory motion. A 4D PET or CT scan is performed by acquiring enough data over an area of interest to provide information on the full range of respiratory motion. In both imaging

modalities, a monitoring device records the subject's respiratory trace during the respective acquisitions. The breathing trace is then used to place data in their respective bins based on its position in the respiratory cycle. For example, data acquired when the subject is in full inspiration is placed in the 0% bin. All the data acquired between this point and the next full inspiration is divided evenly between a predetermined number of bins based on a percentage of the respiratory cycle. Then by reviewing all the bins as a cine, it is possible to observe a lesion through the full range of respiratory motion.

## Radiotherapy planning

By using the metabolic information of the PET scan, it is easier to accurately determine and therefore often minimize the target volume in the presence of atelectasis or lung collapse<sup>[15]</sup>. With the ability of modern radiotherapy practice to deliver highly conformal distributions of dose, the accurate delineation of tumour margins is of the highest importance. The use of PET in the radiotherapy planning process, particularly in lung cancer, is now a well-established practice<sup>[16,17]</sup>.

When using a PET/CT scan to plan radiotherapy target volumes, there is an assumption that the blurring effect



**Figure 2** Sagittal section of the right lower lobe showing no FDG uptake on the PET scan without respiratory gating (ungated) (left panel) and positive uptake on the best bin1 of the gated PET scan (right panel) indicated by the red arrow. The lesion was found to be malignant on subsequent surgical pathology.

on a free-breathing PET scan will account for motion of the tumour due to respiration<sup>[16]</sup>. In a target volume based on the blurred area on the PET scan, movement of the tumour due to respiration is accounted for within the target volume (Fig. 4). However, this assumption may not be valid in some situations. Fig. 5 shows a lung tumour in the right lower lobe. The top row shows the whole-body PET/CT scan and there is little evidence of blurring that would indicate respiratory motion. If this scan alone was used to plan a target volume, it is unlikely to include the faint blurring extending into the liver. The second and third rows show the end-expiration and end-inspiration images of a respiratory-gated PET. These 2 frames clearly show respiratory motion that was measured to be as high as 15 mm. As the CT scan was not gated, inappropriate attenuation correction was applied to the inspiration phase of the gated PET scan leading to inappropriate estimation of true counts within the lesion seen in the third row. If the target volume only included the activity seen on the whole-body PET then the lesion would move in and out of the treated area as the patient breathes during treatment.

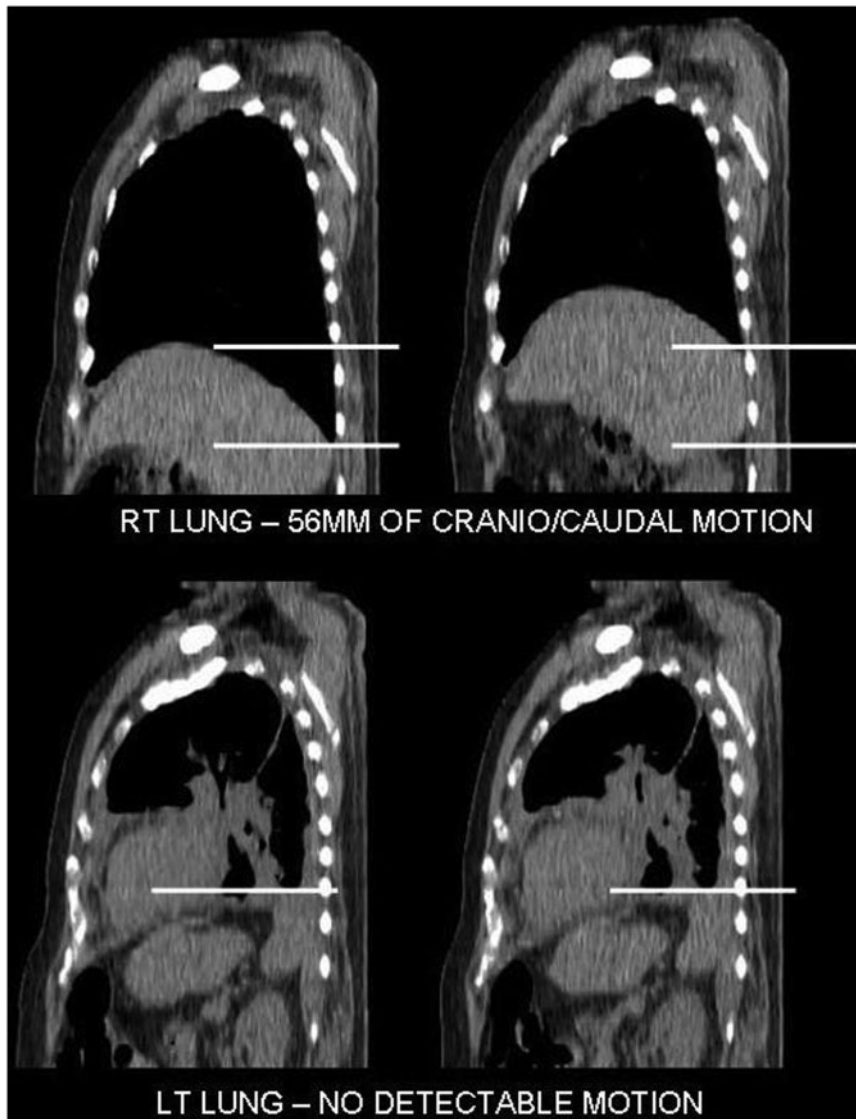
This was shown in a recent paper by Aristophanous et al.<sup>[18]</sup> who analysed the clinical utility of 4D FDG/PET/CT in radiation treatment planning. In this study, they compared the target volumes defined using an ungated PET and an aggregated volume of a 4D PET. They found that the latter was larger than the volume defined on the 3D PET. They concluded that a 4D PET may better define the full physiologic extent of moving tumours compared with 3D PET. Figs. 4 and 5 provide good examples to illustrate that motion

management for PET/CT must consider both imaging modalities and their interaction.

Fig. 6 shows the effects that different breathing patterns can have on the distribution of activity in an ungated PET scan. A Perspex phantom with 4 reservoirs of various sizes (5 mm, 10 mm, 15 mm and 20 mm) was filled with a solution containing fluorine-18. Using a moving phantom (Modus Medical Quasar, London, ON, Canada) the Perspex insert was driven forward and back 40 mm in one direction to simulate respiratory motion. The image in the top row shows the effect on the distribution of activity when the phantom was driven in a sinusoidal pattern. The bottom row simulates the distribution of activity as if there was a pause at the end of the expiration phase, which is not an uncommon breathing pattern. The bottom row shows a dark area with a faint tail of activity compared with top row, which shows an evenly distributed area of uptake. The phantom used had no background activity and relatively uniform attenuation, unlike what would be found in the diaphragmatic region where, for example, the liver has significant FDG uptake and markedly different attenuation characteristics than the adjacent aerated lung. If a lesion in or on top of the liver moved with this pattern of movement, the faint tail may not be visible as it would fade into the background. This simple experiment shows that the distribution of activity seen on ungated PET may also be affected by a patient's respiratory pattern.

These examples illustrate the need to compensate for lesion motion if a PET/CT scan is to be used in radiotherapy planning particularly in areas of high motion such as the lower lobes of the lungs. It is becoming





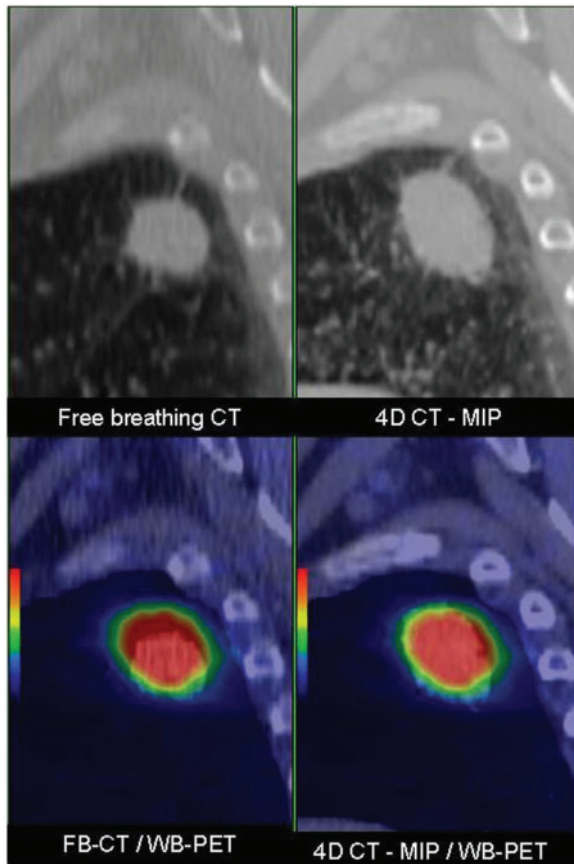
**Figure 3** Sagittal section of the end-inspiration (left) and end-expiration (right) phases of a 4D CT scan.

common practice to use a 4D CT scan in the planning of lung cancer patients<sup>[19–21]</sup>. However, this means that the potential benefits of the FDG-PET in delineating the tumour may be lost. An example is a tumour that is situated on top of the liver. A 4D CT maximum intensity projection (MIP) reconstruction is often used to define target volumes for treatment with radiotherapy. A soft tissue lesion positioned on the dome of the liver would merge with the liver on a 4D CT MIP reconstruction due to respiratory motion. An example of this is shown in Fig. 7. The inferior margin target volume would be difficult to distinguish from the liver as the Hounsfield units of the liver and a soft tissue tumour would be similar. A 4D PET with its high tumour uptake compared with the liver would be ideal for defining the tumour margin. Respiratory-gated protocols are now being investigated to address this clinical situation and these are outlined later in this article.

### Surgical planning

FDG-PET scanning is often used before surgery to determine if there is any spread of disease that would require more extensive surgery or alternative therapies. It is possible that, due to respiratory motion, small lesions particularly in the liver with its high background activity could remain undetected. If any additional metastases remain undetected due to respiratory blurring, it is likely the patient would have a less favourable outcome.

Another potentially important indication for gated scanning is to assess the tethering of a tumour to the chest wall. A tumour that is moving freely within the chest cavity is unlikely to have invaded the chest wall. However, a tumour that is tethered to the chest wall due to invasion is unlikely to show any motion on a gated scan. The extent of resection required for a lung tumour is highly dependent on whether tumour has invaded the



**Figure 4** This figure shows the blurring effect of respiration on ungated whole-body PET imaging. The top left shows the appearance of a lung lesion on a free-breathing CT and the top right shows the lesions when the scan is reconstructed and a MIP reconstruction from a 4D CT. The 4D CT MIP reconstruction is generated by using the maximum pixel values across all 4D CT frames. The bottom left shows the ungated whole-body PET fused with the free-breathing CT and the PET lesion appears larger than the CT lesions. However, when the ungated whole-body PET is fused with the MIP reconstruction, there is much better agreement in the lesion size.

chest wall<sup>[22]</sup>. It is feasible that before surgery, a gated PET/CT scan could be performed in order to give an indication of chest wall invasion. This would enable surgeons to better prepare for surgery, particularly in patients with borderline lung function in whom compromise of chest wall integrity may lead to significant morbidity.

### Therapeutic monitoring

There is increasing interest in the use of PET to measure the effect of treatment in standard clinical practice and clinical trials<sup>[23,24]</sup>. Early response assessment could lead

to better patient management and significantly shorten the time for clinical trials to provide relevant results. This will save money and allow implementation of different therapeutic strategies earlier in the clinic. In FDG-PET, the SUV is a semi-quantitative measure of a tumour's utilization of glucose. Accurate measurement of SUV using PET is dependent on isolating all variables that have an affect on the uptake of the tracer by malignant cells. These include blood sugar level, tracer dose, uptake time, as well as the technical performance of the scanner. Only when all these variables are controlled can the SUV be accurately measured. In clinical trials using PET to assess response to treatment, strict protocols are adhered to in order to ensure any change in SUV can be attributed to the efficacy of a treatment and not any technical factor. However, to date, no response criteria have explicitly taken into account the effect that respiratory motion can have on SUV in particular as motion patterns can change due to the therapeutic intervention.

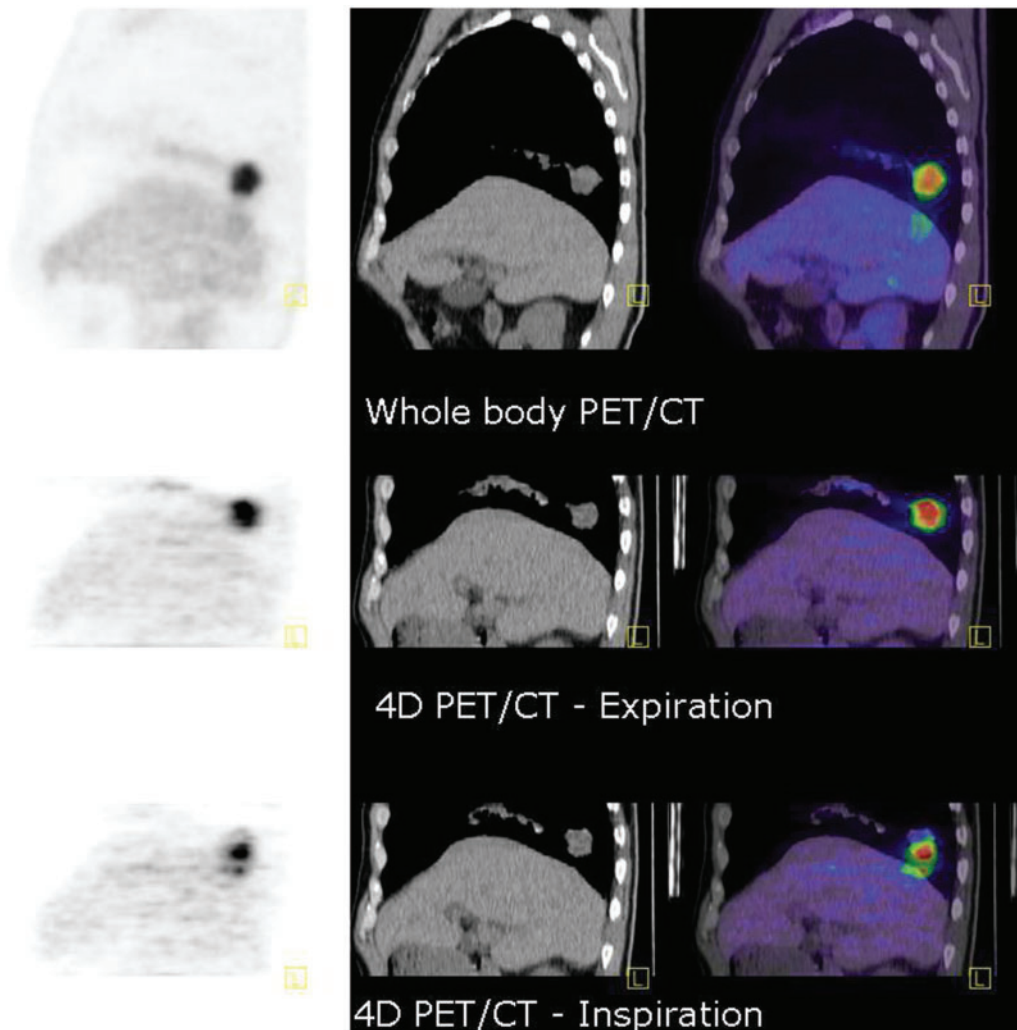
### Strategies to compensate for respiratory motion in PET/CT scanning

There are a number of methods that can be used to compensate for lesion motion due to respiration on a PET/CT scan. The most recent advance is the ability to perform respiratory-gated PET and CT scanning using various respiratory monitoring systems. The various approaches described in the literature to account for respiratory motion include:

- (1) Non-attenuation corrected PET (NAC-PET)
- (2) Deep inspiration breath-hold PET (DIBH-PET)
- (3) Respiratory-gated PET and free-breathing CT (4D PET/FBCT)
- (4) Respiratory-gated PET and breath-hold CT (4D PET/BHCT)
- (5) Respiratory-gated PET and respiratory-gated CT (4D PET/CT)

#### *NAC-PET*

As outlined above, one of the factors that increases the impact of respiratory motion is misregistration leading to inappropriate application of attenuation correction. A simple way to reduce this impact is to look at the PET image without application of attenuation correction. This is a common option used in clinical practice as it does not require any additional camera time or the complex hardware and software options needed to perform respiratory gating (see example in Fig. 8). A study by Reinhardt<sup>[25]</sup> found that out of 174 pulmonary metastases detected on FDG-PET, 6 (4%) were seen on NAC-PET and not on attenuation corrected (AC)-PET. They found that although 41.4% of the 174 lesions were better visualized on the NAC-PET, there was no significant difference in the overall lesion detection between AC- and



**Figure 5** Sagittal section of the right lower lobe on the whole-body PET/CT (top row), expiration PET/CT (middle row), and inspiration PET/CT (bottom row).

NAC-PET. The 6 lesions detected on only NAC-PET were all relatively small lesions (5–11 mm) and would be expected to be more affected by respiratory motion. A limitation of the NAC-PET scan is that it cannot provide any SUV information and therefore is not a suitable option when attempting to quantify metabolic activity. This technique does not correct any blurring or misregistration caused by respiration and therefore may not provide a reporting physician with confidence about a lesion's intensity or its location. The use of NAC-PET reconstruction should only be used if a more sophisticated method for correcting a motion artefact is not available.

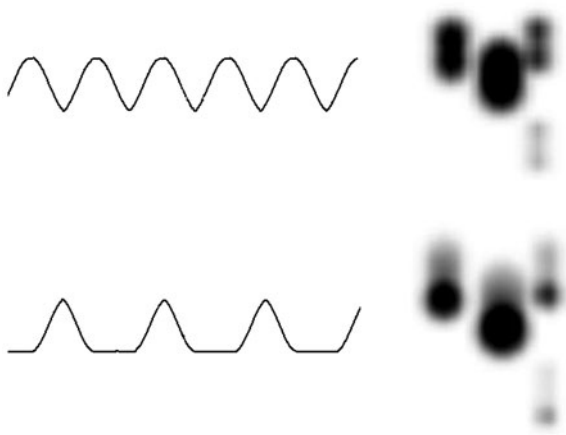
#### *DIBH-PET*

A standard PET scan is acquired in steps of around 2–5 min depending on the camera. As it is not possible for a patient to hold their breath for this long, the DIBH

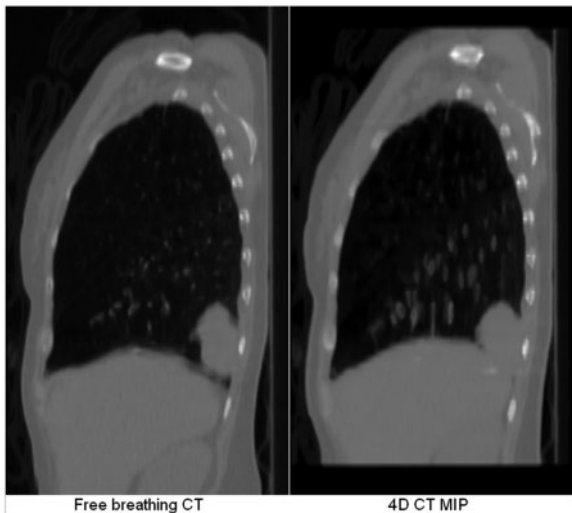
protocol was developed to remove the effect that respiration has on a PET image as well as address the problem of noise on a gated PET scan. The technique of DIBH-PET is an attempt to match the breathing position on both the CT and the PET scan. This method is adapted from the radiotherapy technique to provide a reproducible tumour position for treatment<sup>[26,27]</sup>. The protocol first described by Nehmeh<sup>[28]</sup> involves first coaching a patient to inhale to a point that is reproducible and hold their breath at this position for as long as possible. The breathing position is monitored using one of the commercially available respiratory monitoring devices.

A CT scan is first acquired in this breath-hold position for attenuation correction and anatomical correlation. A PET scan is then acquired over multiple breath-holding phases in the same respiratory position. The patient continues holding their breath until the total acquisition time equals a standard bed step of around 3 min. According to Nehmeh, this normally takes 9 breath holds. In their





**Figure 6** The effect of different respiration patterns on the distribution of activity ungated PET scans in a phantom with no background on 4 different sized objects (5 mm, 10 mm, 15 mm and 20 mm).



**Figure 7** Lower lobe lung lesion on free-breathing CT shows separation between the lesion and liver. However, the lesion on the 4D CT MIP merges the liver making the inferior margin of the tumour difficult to define.

study among a cohort of 8 patients encompassing 10 lesions, they found that the  $SUV_{max}$  was on average 32.6% higher (range 4–83%) compared with standard whole-body PET/CT and reduced the mismatch by an average of 26.6% (range 3–50%).

This method has the advantage of eliminating blurring artefacts caused by motion and greatly decreasing the possibility of a mismatch between the CT and PET scan. Also, the image quality is higher than for a single bin from a respiratory-gated PET as the acquisition time is 3 min compared with typically 1 min for a single bin

from a gated PET, providing better count statistics. The drawback is that some patients may find holding their breath multiple times for up to 3 minutes challenging and therefore patient selection and coaching is important. It also prolongs the scan time. However, while this is an effective protocol to provide a snapshot of the lungs, it does not provide any information about the direction or amount of lesion motion.

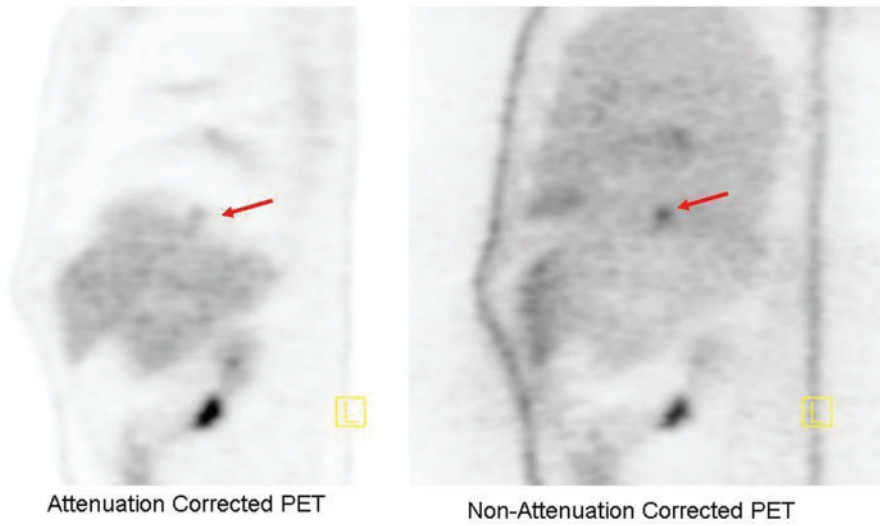
#### 4D PET/FBCT

An alternative to DIBH-PET is to perform a respiratory-gated or 4D-PET scan corrected with a free-breathing CT scan. This method (used in Figs. 2 and 9) involves a list-mode PET acquisition of an area of interest while recording a patient's breathing trace using a respiratory monitoring system. List mode is a technique where all counts are recorded sequentially with time stamps allowing reformatting within precise time intervals. The list-mode data then can be retrospectively reconstructed into multiple phases of the respiratory cycle, or bins, using the respiratory trace. This additional gated scan can be acquired immediately after the whole-body scan and the whole-body CT can be used for attenuation correction of the gated PET scan. As the whole-body CT scan is taken while the patient is free breathing, the position of the lungs in the respiratory cycle is random. This means that only those frames of the gated scan where the metabolic image is aligned with the CT will be appropriately corrected for attenuation. Often this will be a single bin unless a significant interval of the respiratory cycle is spent in a given position, such as expiration. This method requires the operator to manually evaluate the coregistration between the various PET bins and the CT using normal structures such as the liver dome. This comparison between the PET and CT can be performed on most modern PET display platforms. Finding the best bin can be challenging and, in the case of an abnormal respiratory excursion on the CT, there could be no PET bin that matches the CT.

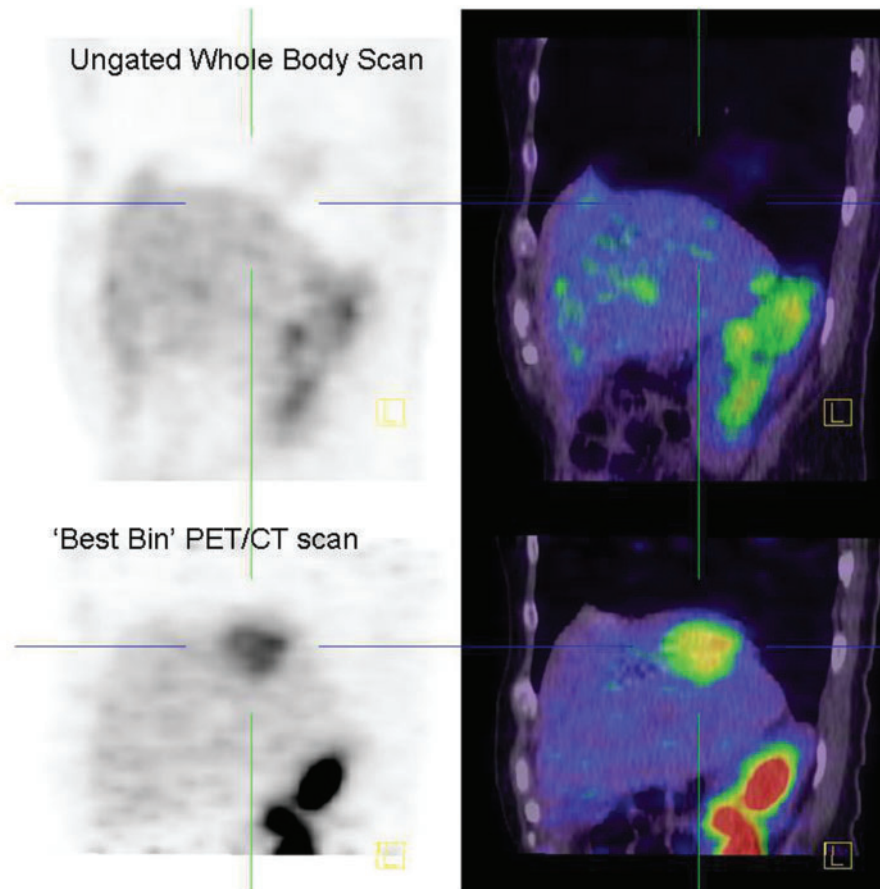
This was described as the best bin method by Lupi et al.<sup>[4]</sup> in their paper investigating the effect that respiratory-gated PET scanning has on the metabolic activity detected in lung lesions. They found that the gated scan produced variable but consistently higher SUVs on the gated best bin scan compared with the ungated whole-body scan (mean increase +77.2%, SD  $\pm$ 4.6). The variability in the difference in SUV could be explained by the variable amounts of motion that lung lesions can display.

This method has the advantage of requiring no additional CT radiation dose and is relatively easy for a patient to comply with as no special breathing instruction are required. However, as only the best bin is accurately corrected for attenuation, most of the data acquired is not used and the images are inherently noisier than the DIBH method. Also, additional equipment such as a respiratory monitoring system and more advanced





**Figure 8** Lesions on the dome of the liver better visualized on PET without attenuation correction (non-attenuation corrected) compared with attenuation corrected PET.



**Figure 9** Sagittal section of liver showing little evidence of FDG-avid disease on the ungated PET scan and a large liver tumour on the best bin of the gated PET scan.



**Figure 10** Varian RPM gating system (top left), Phillips Bellows (top right) and Anzil belt and pressure sensor (bottom).

display software is required to perform a 4D PET scan. These facilities are not available in all institutions.

#### *4D PET/BHCT*

Identifying the best bin can often be difficult as a free-breathing CT is taken at a random phase of the respiratory cycle. This is particularly true in areas of high respiratory motion such as around the diaphragm. One strategy to address this problem is to combine a 4D PET scan with a BHCT). Fin et al.<sup>[29]</sup> described this approach by combining a 4D PET with a shallow end-expiration BHCT. One can apply this BHCT to the end-expiration phase of the 4D PET for attenuation correction and anatomical localization.

The advantage of this method is that as the CT scan is no longer in a random phase in the respiratory cycle the reporting physician can have confidence that the end expiration phase of the 4D PET is the best bin and misregistration should be minimized. The disadvantage of this method is the additional radiation exposure from the additional CT and the best bin will exhibit increased noise compared with the DIBH method. It is also difficult to ensure that the breath-hold is actually coinciding with a phase of the breathing cycle as patients tend to take a deeper breath prior to holding their breath.

#### *4D PET/CT*

The scanning protocol that provides the most information about respiratory motion in terms of direction and

amplitude as well as accurate quantitation is 4D PET/CT. With this approach, a gated CT scan is acquired over the area of interest followed by a gated PET. There are 2 main methods for the acquisition of a gated CT scan. The first involves acquiring a helical CT scan with a very small pitch (0.1) while recording the respiratory trace. The second involves performing an axial cine CT scan in sections with each section scanned for slightly longer than the patient's respiratory period. In both cases, the over scanning ensures that each part of the patient's anatomy is seen by a sufficient number of projections in each phase of the breathing cycle. The CT data can then be retrospectively reconstructed into the number of bins equal to the gated PET scan. When the PET scan is processed, each PET bin can be corrected for attenuation with the corresponding CT bin. Previously, this required a large amount of processing time and iterative multiple processes. Earlier strategies have therefore also used the average scan as a composite of the 4D CT dataset for attenuation correction<sup>[30]</sup>. There are now commercially available products in the newest generation of scanners that have automated this process, making it much easier to apply in routine clinical practice.

The greatest advantage of this approach is that every PET bin will be appropriately corrected for attenuation, and thus each bin will accurately represent the distribution of tracer in the patient. If a gated PET scan is corrected for attenuation with a free-breathing CT scan, there is going to be a large amount of fluctuation in the

$SUV_{max}$  across the reconstructed bins. This observation has also been made by Erdi et al.<sup>[31]</sup>. In their study of 8 lesions in 5 patients there was up to a 30% fluctuation in SUV between end inspiration and end expiration. The method of correcting a gated PET with a gated CT also provides information about the amplitude and direction of motion that can be used in a radiotherapy planning algorithm. The main drawback of this technique is the significant radiation dose conferred to the patient as a result of the gated 4D CT scan. Depending on the exposure factors used, the dose can be up to 10 times that received from a standard diagnostic CT scan of the thorax. In the context of an oncology patient planned for therapeutic irradiation of the region in question, this additional dose can be justified if the additional information is shown to have an impact on the planning of target volumes for radiotherapy and on patient management overall. To date, no study has described the clinical impact or any changes in patient management due to an additional 4D PET/CT scan on either diagnosis or radiotherapy planning.

### Additional requirements to implement motion management for PET/CT

Key components of a motion management system are appropriate imaging hardware and software. This includes a multislice CT scanner and list-mode acquisition for the PET system. Most of these components are available in modern equipment but may need to be enabled by the manufacturer.

In order to perform respiratory-gated scanning on a PET/CT scanner, a system for tracking a patient's breathing must be used. There are at least 3 commercially available respiratory tracking systems used by the 3 main PET/CT vendors. These are:

- (6) The Varian real-time position management (RPM) system
- (7) The Anzai respiratory gating system
- (8) The Phillips Bellows respiratory gating system

The Varian RPM system uses a box with 2 or 6 reflecting dots that is placed above a patient's diaphragm. An infrared camera attached to the end of the scanning table then feeds a video signal of the reflecting box to a PC that runs the Varian RPM software to track the motion of the

box. This system is in common use on both the GE and Phillips PET/CT systems.

The Anzai respiratory gating system uses a belt that is attached to a patient's abdomen with a pressure sensor embedded in the belt. As the patient breathes in, pressure is applied to the sensor and a signal is sent to a PC laptop. This system is used on the Siemens PET/CT scanners but is also functional on GE scanners.

The Phillips Bellows respiratory tracking system uses a belt that fastens around a patient's abdomen similar to the Anzai system. However, instead of a pressure sensor, a bellows device stretches and relaxes as the patient breathes in and out. This stretching of the bellows can then be plotted as a respiratory trace and fed into a camera for use in gated scanning.

These 3 tracking systems use uniquely different methods for recording a patient breathing during a PET/CT scan. Otani et al.<sup>[32]</sup> compared the differences in the timing tags of the Varian and Anzai systems. They attached both the Varian and Anzai systems to each lung cancer patient, acquired a single 4D CT scan, then reconstructed the scan retrospectively using the 2 different traces. They found that the position of the timing tags on different systems were not the same leading to differences in the tumour centroid position and shape in some cases. Based on these findings, this group recommended that the same monitoring systems be used across all modalities within an institution. This is particularly relevant when 4D PET/CT leads to gating of motion adaptive radiotherapy.

### Conclusion

The clinical significance of respiratory motion of a PET/CT scan depends on a number of factors. The motion management scanning protocol used to address any respiratory motion artefact depends on the question that is asked. For example, if the only requirement is for the detection of a lesion, then simply reviewing the non-attenuation corrected PET may be sufficient. This approach will, however, be insufficient in those cases where there is a large amount of respiratory motion. The alternative is to use a respiratory-gated scanning method. In those scenarios where radiation dose must be minimized, such as the diagnosis of a solitary pulmonary nodule of unknown histology, either a DIBH or 4D PET scan may be able to

**Table 1** Summary of the various requirements of motion management protocols for PET and PET/CT image acquisition

	NAC-PET	DIBH-PET	4D PET/FBCT	4D PET/BHCT	4D PET/CT
Additional time on PET/CT scanner	×	✓	✓	✓	✓
Additional equipment	×	✓	✓	✓	✓
Additional radiation	×	×	×	✓	✓✓
Indication: improved quantitation	×	✓	✓	✓	✓✓
Indication: lesion detection	✓	✓	✓	✓	✓
Indication: RT Planning	×	×	×	×	✓

resolve blurring and misregistration artefacts. This may reduce the chance of a false-negative due to respiratory motion. The decision on whether to use DIBH or 4D PET is a trade-off between increased noise on the 4D PET or decreased patient compliance for the DIBH scan. In areas of high respiratory motion, such as around the diaphragm, finding the best bin using the 4D PET only methods can be challenging. In order to increase the confidence in selecting the best bin, a low-dose, mid-expiration breath-hold CT is a good alternative. The gold standard protocol for obtaining the most information about respiratory motion is to gate both the PET and the CT. However, appropriate dose reduction strategies need to be considered. Due to the relatively high additional CT radiation dose, the use of 4D CT must be justified in terms of management impact.

An area where 4D PET/CT is likely to have a high impact is in radiotherapy planning. Until a gold standard for correction of the effects of motion has been determined to be reliable, 4D PET/CT is likely to be the most valuable tool to accurately define target volumes.

In therapeutic monitoring trials using PET to measure response, the accurate quantitation of metabolic activity in lesions affected by motion will be difficult to achieve. This is of particular concern in serial PET/CT scans performed for assessing tumour response to treatment. While more accurate measurement of SUV in areas of high motion has been described using various 4D protocols, it is not clear which one is best.

In conclusion, there are several approaches to managing the effects of respiration on a PET/CT scan. Each of the protocols described have their advantages and disadvantages. The optimal protocol needs to be tailored to suit each individual patient in order to optimize patient outcome. It is likely that in the future respiratory-gated scanning for proven clinical indications will become as routine as cardiac-gated scanning is in myocardial perfusion scanning.

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