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Respiratory-Gated PET/CT versus Delayed Images for the Quantitative Evaluation of Lower Pulmonary and Hepatic Lesions

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Abstract

Purpose—Respiratory motion degrades FDG PET images of the lower chest and upper abdomen as the blur introduced by breathing motion increases the apparent size of the moving tumor lesions and decreases their apparent uptake, reducing the sensitivity of PET in detection of small-lesions. We assessed the role of delayed and respiratory gated PET acquisition on the quantitative evaluation of lung and liver lesions.

Methods—A retrospective analysis of 64 lesions was performed. After initial non-gated whole body PET/CT, respiratory gating was performed with 15 min in list mode. Non-gated delayed images were obtained by summing all list mode data. SUVmax adjusted for lean body mass (SULmax) was measured in the initial whole body scan, the delayed non-gated scans, and the individual gated bins for each lesion. The axial z-position of SULmax for each lesion in five respiratory-gated bins was determined. The mean SUL of the non-pathological liver parenchyma was also recorded for each patient.

Results—Tumor Lesion SULmax increased by an average of 34% in the delayed non-gated scan as compared to the whole body initial scan and further by an additional 17.2% in respiratory-gated images. The maximum lesion displacement was 6.2 $\pm$ 5.0 mm.

Conclusion—Delayed imaging alone substantially increases the magnitude of the SUL of liver and lung lesions as compared to standard whole body images and may allow for a more accurate definition of the lesion's volume and localization and improve tracer quantitation in malignant lesions in the lungs or upper abdomen. While respiratory gating provides more optimal imaging with greatest increase in SULmax, the benefit is small and delayed imaging appears sufficient in most cases.

Keywords

quantitative PET/CT; respiratory gating; SUV; metabolic activity; FDG

INTRODUCTION

^{18}F -FDG positron emission tomography (PET) has become one of the most useful imaging modalities for cancer diagnosis, staging and assessment of treatment because of its high sensitivity and good specificity (1-5). However, respiratory motion reduces the accuracy of PET as the blur introduced by the breathing motion increases the apparent size of the moving tumor lesions and decreases their apparent uptake on PET images. This motion reduces the sensitivity of PET for detection of small lesions (6-8). This problem is more pronounced near the diaphragm where the amplitude of the respiratory motion is greatest. This may constitute a significant problem and can result in small lesions evading detection.

Unlike CT scans, which are acquired over seconds and a breath-hold is possible, the PET data is acquired over a period of minutes per bed position, and a breath-hold is usually not possible during PET data acquisition in a PET/CT study. Respiratory motion leads to the additional problem of discrepancy between the CT and the PET data, which may result in image artifacts and incorrect quantitation due to inaccurate attenuation correction.

Another complication is that of partial volume effect. As PET systems have limited resolution, smaller objects appear to have a lower concentration of activity than larger objects with the same amount of activity. This effect is also present at the boundaries of various organs. With motion, this effect is increased as the boundary moves across many voxel positions. For these reasons, respiratory motion is a significant problem for both qualitative and quantitative analysis of PET studies.

To address this problem, many different approaches have been proposed in the literature (9-15). These include gated PET (or 4D-PET), respiratory-correlated dynamic PET, deep-inspiration breath-hold PET, motion-corrected PET reconstruction, optimal gating reconstruction, and retrospective data-driven respiratory gating. The gated PET methods look promising. An increase in the standard uptake value (SUV), or SUL (SUV based on lean body mass) of lesions, has been demonstrated using respiratory gating in both on phantom studies and on a small group of patients (9, 16).

Respiratory gating is one of the methods used to reduce the effects of breathing motion and to track the motion of a tumor lesion. In this approach, the PET data are sorted into different gates with respect to the respiratory status. The principal idea is that each respiratory gate will capture only a subset of the total motion and will thus have a reduced number of motion artifacts. On the other hand, the gates contain only a part of the total number of events detected with the scanner, which leads to images that suffer from increased noise (7, 17-19).

The purpose of this study is to evaluate the detectability of pulmonary and hepatic lesions using respiratory-gated PET/CT in a larger sample of patients by assessing the change in lesion SUL between conventional whole body scans, delayed scans, and respiratory-gated acquisitions.

MATERIALS AND METHODS

Institutional review board approval was obtained for this Health Insurance Portability and Accountability Act-compliant retrospective review of PET/CT images and patient records. Informed consent requirements were waived. We retrospectively analyzed the respiratory-gated scans from 49 patients performed at our PET/CT center between 2007 and 2010.

PET/CT protocol

All patients fasted for at least 4 hours before FDG injection. Patients were then taken to the scanner approximately 60 minutes from injection. Patients were scanned either on a GE Discovery ST or a GE Discovery LS PET/CT scanner (GE Healthcare, Waukesha, WI). Studies on the first system were performed in 3D acquisition mode with 4.15 minutes per bed position. The images were reconstructed using OSEM (ordered subset expectation maximization) algorithms, with 128×128 matrix, 21 subsets, 2 iterations, 3mm post reconstruction gaussian filter, standard Z filter, 4.7 mm pixel, and 3.27 mm slice thickness. The 2-dimensional implementation on the Discovery LS used 2 iterations, 28 subsets, a 5.5-mm post reconstruction gaussian filter, and 3.9 mm pixels. All PET data were reconstructed with and without CT-based attenuation correction. Non-contrast CT scan was used for attenuation correction of PET images and for morphologic co-registration. CT parameters include 16-detector row with 50cm axial dynamic field of view (DFOV), weight-based amperage (20–200 automated mA), 120–140 kVp, 3.75mm reconstructed slice thickness, pitch of 0.984, 0.5sec gantry rotation speed, and 512 × 512 matrix.

After the initial non-gated whole body (WB) conventional scan, respiratory-gated PET was performed with 15-min list mode using Real-Time Position Management Respiratory Gating System (RPM, *Varian Medical Systems, Palo Alto, CA*). One bed position containing the equivocal lesion(s) was used for the gated study. The RPM system tracks the motion of reflective markers mounted on a plastic block fastened to the patient's abdomen. The motion of the marker block is monitored by an infrared video camera mounted on the end of the scanner bed and interfaced to the computer. The respiratory cycle was divided into five equal time-based intervals. The list mode PET data are then rebinned and reconstructed according to these respiratory time segments. A CT scan for the same bed position was obtained during shallow tidal-wave breathing.

The decision whether to perform a respiratory-gated acquisition rested on the nuclear medicine attending physician. This decision was prompted by the appearance of an equivocal lung or hepatic lesion on the initial WB scan. This usually meant a lesion seen on CT with minimal FDG uptake on PET. In some cases, respiratory gating was ordered if the location of a lesion was uncertain, such as near liver-lung interface.

Liver and lesion SUL measurements

The conventional and the respiratory-gated scans were imported into a GE Advantage Workstation. The average SUL of the non-pathological liver parenchyma was measured with a spherical region of interest (ROI) with a 3.0 cm diameter in the posterior right lobe in both the initial whole body scan and the delayed scan according to PERCIST 1.0 criteria

(20). Non-gated delayed images were obtained by summing all list mode data without considering the respiratory triggers. The SULmax value for each lesion in the conventional initial whole body scan, delayed scan, and each gated bin were computed. The z-axis position of SUL max pixel was obtained and recorded for each respiratory-gated PET bin.

Statistical Analysis

The data was analyzed by applying paired t-test using MedCalc for Windows, version 12.3.0 (MedCalc Software, Mariakerke, Belgium). Continuous variables are presented as mean $\pm$ SD. The SULmax values for the tumor lesions in the initial conventional whole body scan and the delayed non-gated scan were compared. A similar test was done comparing the lesion SULmax values between the gated bin with the highest SUL for each lesion and the whole body scan, and again between the gated bin with the highest SUL and the delayed non-gated scan. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

There were a total of 49 patients, 27 males and 22 females. The mean age was 63.2 ± 13.0 years, ranging from 23 to 90 years. The mean uptake time for the initial conventional whole body scan was 62.5 ± 13.8 minutes. The mean time from FDG injection to the start of the respiratory-gated image acquisition was 143.1 ± 36.9 minutes. A total of 64 lesions were examined, 40 pulmonary and 24 hepatic lesions were examined. The average size of all lesions considered was 9.5 ± 3.2 mm. The size of hepatic lesions was 10.2 ± 2.8 mm, and that of pulmonary lesions was 9.2 ± 3.4 mm.

The mean liver SUL on the initial conventional whole body scan was 1.53 ± 0.23 . The mean liver SUL was 1.45 ± 0.22 on the delayed scan. The percentage decrease in mean liver SUL was -7.13 ± 7.62 %.

The mean lesion SULmax on the initial conventional whole body scan was 4.1 ± 2.6 (range: 0.8 – 12.5). This increased to 5.5 ± 3.5 on the delayed non-gated scan (range: 0.8 – 15.6). The mean lesion SULmax further increased to a maximum 6.3 ± 3.7 (range: 1.2 – 16.4) on the respiratory-gated images.

The mean percentage increase in lesion SULmax in the delayed non-gated scan as compared to the initial whole body scan was 34.0 ± 29.6 % ($p < 0.0001$) using a paired t-test. The mean percentage increase in lesion SULmax in the respiratory-gated bin with the highest SUL as compared to the delayed non-gated scan was 17.2 ± 18.6 ($p < 0.0001$).

Finally, the mean percentage increase in lesion SULmax in the respiratory-gated bin with the highest SULmax as compared to the initial whole body scan was 55.6 ± 38.6 ($p < 0.0001$). Maximal lesion displacement in the axial direction during respiratory gating was 6.2 ± 5.0 mm. This is summarized in Table 1.

Fig 1 is a plot illustrating the increase in lesion SULmax between conventional whole body scans and delayed non-gated scans, with a further increase in the respiratory-gated bin with the highest SUL for all lesions.

We found a comparable, but on average a non-statistically significant larger change, in hepatic versus pulmonary lesions in terms of apparent metabolic activity. There was however larger displacement along the axial direction for lung as compared to hepatic lesions, but with no statistically significant difference. The mean percentage increase in lesion SULmax in the delayed non-gated scan as compared to the initial whole body scan was 37.9 ± 36.0 % for liver lesions, as compared to 31.8 ± 27.6 % for pulmonary lesions. The mean percentage increase in lesion SUL max in the respiratory-gated bin with the highest SULmax as compared to the delayed non-gated scan was 19.2 ± 22.8 for liver lesions, as compared to 15.3 ± 15.7 % for lung lesions. The mean percentage increase in lesion SULmax in the respiratory-gated images as compared to the initial whole body scan was 60.7 ± 43.1 for liver lesions, as compared to 51.4 ± 36.5 % for lung lesions. Maximal lesion displacement in the axial direction during respiratory gating was 6.0 ± 5.8 mm for liver lesions, as compared to 6.5 ± 4.7 % for pulmonary lesions.

Fig 2 is an example of a study with a small focus of FDG uptake fusing to a lung nodule in the right lower lobe hardly detectable on the conventional whole body PET/CT scan, where it had an SUL of 1.2. In the respiratory-gated images, this nodule had SULmax values of 2.8, 2.1, 2.5, 2.5, and 2.8 on the five equal time-based bins, translating in an increase of 133 % from the whole body scan value to the bin with the highest SUL. The maximal displacement of the lesion was 6.5 mm in the axial direction. SULmax in delayed non-gated images was 2.4, representing an increase of 100% over initial WB scan

Fig 3 is another case with a small focus of FDG uptake fusing to a left hepatic lobe lesion with a SULmax of 5.1 on the conventional whole body PET/CT scan. In respiratory-gated images, this focus had SULmax values of 6.4, 7.1, 7.7, 7.0, and 6.3 on the five equal time-based bins, an increase of 51 % from the whole body scan value to the bin with highest SUL. The maximal displacement of the lesion was 4.4 mm in the axial direction. SULmax in delayed non-gated images was 6.4, an increase of 25.5 % over initial WB scan

DISCUSSION

Our results show that in most cases delayed imaging alone substantially increases liver and lung lesions SUL as compared to standard whole body images. The mean increase in the SULmax value was 34%. Gating further increases measured SULmax by an average of 17% as compared to delayed scans. Similar results have been reported in the literature with a smaller sample of patients. Nehmeh et al reported results from four patients using a 4D PET/CT protocol that showed increases in lesion SUV of up to 16%. In that study, the CT scan used for attenuation correction was also gated using a step-and-shoot protocol (9, 21).

Respiratory gating increased the measured maximum SUV by 22.4% and the average SUV by 13.3% in a study by Werner et al. that included eighteen patients with known pulmonary nodules (16). More recently, Garcia Vicente et al. reported a SUVmax percentage difference mean between conventional and respiratory gated scans of 83.3% (22). These authors evaluated forty-two pulmonary lesions in twenty-eight patients.

The increase in SULmax between delayed and gated scans may be partially due to increase in noise on gated images. To test this, we measured SULmax of the liver in ten scans. This went from an average of 2.07 on initial whole body scan, to 1.92 on delayed non-gated scan, reflecting a decrease in liver metabolic activity with time. SUL max for the liver then increased to a mean of 2.32 on gated images, about 20 % relative increase, reflecting an increase in noise in the gated images. It is difficult to determine precisely the exact contribution to the increase in SUL values due to noise as compared to the increase due to reduction in motion blurring and the decrease in effective lesion volume.

As compared to a conventional whole body scan, gating increased the SULmax value of the lesion by an average of 56 % (table 1). As a consequence, delayed gated imaging may improve the detectability and the quantitation of specific activity of the tracer in cancer lesions. This is especially important when the initial staging and post therapy follow-up scans are compared. The true metabolic activity in tumor lesions needs to be determined to adequately assess the efficacy of the treatment.

This study utilizes gated PET but not gated CT. Conceptually; there could be benefit from gated CT with phase matched attenuation correction. This could be especially true for malignant lung lesions, whose density is usually greater than that of surrounding normal lung parenchyma. An attenuation correction with a phase-matched CT should in principle lead to a higher SUV and SUL values. This may provide an additional benefit over a delayed non-gated image.

Respiratory gating should be reserved for truly equivocal cases when the detection and true FDG activity of a lesion in the lower thorax or the liver is likely to influence the clinical management of the patient. This includes cases when the presence of a metabolically active lesion changes the staging of the tumor and influences the decision about whether the patient should be taken to the operating room for surgical resection versus opting for other systemic therapeutic options. A clinical example would be a primary right lung malignancy with an equivocal lesion in the right lung base on ungated PET that could represent metastatic disease in the liver dome.

The logistics and time constraints of routine clinical practice do not usually favor applying respiratory gating on every patient with a lung or hepatic lesion. This technique requires a respiratory signal tracking device, and additional software and technical expertise to be performed correctly. This is not usually available in the average, community-based clinical practice. Setup time can be awkward and is not conducive to routine implementation. Delayed imaging in most cases should be sufficient.

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Fig 1.

Change in tumor lesion SULmax between initial whole body, delayed non-gated, and best bin gated scans. Tumor Lesion SULmax increased by an average of 34% in the the delayed non-gated scan as compared to the whole body initial scan and further by an additional 17.2% in respiratory-gated images

Fig 2.

(a) A small focus of FDG uptake fusing to a lung nodule in the right lower lobe is hardly detectable on the conventional whole body PET/CT scan (SULmax of 1.2) due to smearing from respiratory motion. (b) This lesion is better appreciated in the delayed non-gated scan (SULmax 2.4)(c) In the respiratory-gated images, this lesion has SULmax values of 2.8, 2.1, 2.5, 2.5, and 2.8, on the five equal-time based bins.

Fig 3.

(a) A small focus of FDG uptake fusing to a left hepatic lobe lesion with a SULmax 5.1 on the conventional whole body PET/CT scan. (b) In the delayed non-gated scan, this lesion had an SULmax of 6.4. (c) In the respiratory-gated images, this had SULmax values of 6.4, 7.1, 7.7, 7.0, and 6.3 on the five equal-time based bins.

Table 1

Summary of mean percentage change in tumor lesion SULmax, mean liver SUL, and lesion displacement.
WB: whole body

% SULmax increase (delayed compared to WB)	34.0 ± 29.6	p < 0.0001
% SULmax increase (highest gated bin compared to delayed)	17.2 ± 18.6	p < 0.0001
% SULmax increase (highest gated bin compared to WB)	55.6 ± 38.6	p < 0.0001
% change in mean liver SUL (delayed compared to WB)	-6.3 ± 7.8	p < 0.001
Maximum lesion displacement in gated images	6.2 ± 5.0 mm	