Deep-Inspiration Breath-Hold PET/CT of the Thorax

Sadek A. Nehmeh[1], Yusuf E. Erdi[1], Gustavo S.P. Meirelles[2], Olivia Squire[2], Steven M. Larson[2], John L. Humm[1], and Heiko Schöder[2]

[1]*Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, New York; and* [2]*Department of Radiology, Memorial Sloan-Kettering Cancer Center, New York, New York*

The goal of this study was to describe our initial experience with the deep-inspiration breath-hold (DIBH) technique in combined PET/CT of the thorax. This article presents particular emphasis on the technical aspects required for clinical implementation. **Methods:** In the DIBH technique, the patient is verbally coached and brought to a reproducible deep inspiration breath-hold level. The first "Hold" period, which refers to the CT session, is considered as the reference. This is followed by 9- to 20-s independent breath-hold PET acquisitions. The goal is to correct for respiratory motion artifacts and, consequently, improve the tumor quantitation and localization on the PET/CT images and inflate the lungs for possible improvement in the detection of subcentimeter pulmonary nodules. A physicist monitors and records patient breathing during PET/CT acquisition using a motion tracker. Patient breathing traces obtained during acquisition are examined on the fly to assess the reproducibility of the technique. **Results:** Data from 8 patients, encompassing 10 lesions, were analyzed. Visual inspection of fused PET/CT images showed improved spatial matching between the 2 modalities, reduced motion artifacts especially in the diaphragm, and increased the measured standardized uptake value (SUV) attributed to reduced motion blurring, as compared with the standard clinical PET/CT images. **Conclusion:** The practice of DIBH PET/CT is feasible in a clinical setting. With this technique, consistent lung inflation levels are achieved during PET/CT sessions, as judged by both motion tracker and verification of spatial matching between PET and CT images. Breathing-induced motion artifacts are significantly reduced using DIBH compared with free breathing, enabling better target localization and quantitation. The DIBH technique showed an increase in the median SUV by 32.46%, with a range from 4% to 83%, compared with SUVs measured on the clinical images. The median percentage reduction in the PET-to-CT lesions' centroids was 26.6% (range, 3%–50%).

Key Words: deep-inspiration breath-hold; PET/CT; 4-dimensional PET/CT; respiratory gating

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Many imaging protocols have been developed in the recent years to account for respiratory motion artifacts on CT (*1–3*), PET (*3–8*), and combined PET/CT (*3,9*) images. On CT, breathing motion may cause omission of some anatomic levels or repeated scanning of others (*1*), depending on the direction the tumor is moving relative to that of the CT couch. These factors will jeopardize the quality of CT images and, hence, the accuracy in the diagnosis of lesions in the thorax. On PET, respiration may result in blurring of the lesion and, consequently, reducing the corresponding measured standardized uptake value (SUV) (*3–5*). The problem is more challenging in combined PET/CT. In combined PET/CT, CT assists PET in localizing the tumor and is also used to correct for attenuation on the PET images. Therefore, an accurate spatial matching between PET and CT is a prerequisite for accurate diagnosis. However, because of respiration and the difference in the acquisition time required to image the thorax between PET (6–9 min) and CT (~15 s), spatial misalignment between the 2 image sets is not uncommon. This can significantly compromise the interpretation of PET images, resulting in mislocalization of the lesion (*10*) and inaccurate quantitation of the SUV (*5,11*).

Four-dimensional (4D) PET/CT protocols have been developed to account for respiratory motion artifacts in combined PET/CT and, thus, improve the spatial matching between the 2 modalities (*5,9*). The drawback of this protocol is the long acquisition and postprocessing time (*5*). Besides, compared with standard clinical acquisition, a higher dose is delivered to the patient during the 4D CT procedure, whereas the acquisition time per bin is reduced to one third during 4D PET, relative to the standard clinical acquisition time, to account for the multiple gated PET bins. This results in 10 min to acquire one 4D PET field of view (FOV) (*4,5*). The actual acquisition time may become much longer because of breathing irregularities (*4,5*). The main advantage of 4D PET/CT is in the field of radiotherapy, where information about the extents and trajectory of lesion motion is critical for a more precise dose delivery. However, in diagnostic imaging practice, imaging the lesion at one single breathing phase should be sufficient for

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For correspondence or reprints contact: Sadek A. Nehmeh, PhD, Medical Physics Department, 1275 York Ave., Memorial Sloan-Kettering Cancer Center, New York, NY 10021.

E-mail: nehmehs@mskcc.org

accurate quantitation and localization. Previous studies showed the possibility of acquiring PET/CT data at any phase within the respiratory cycle (*5*). Yet, it is favorable to acquire data with fully inflated lungs—that is, at end inspiration. This may improve detectability of subcentimeter pulmonary nodules on CT (*12*) as well as reduce background activity concentration on PET, thus increasing the target-to-background ratio. This technique was widely investigated in CT for radiotherapy planning to improve target immobilization and reduce the radiation dose to normal heart and lung in the treatment of lung and breast cancers (*13–15*).

In this article, we report on the methodology to acquire breath-hold PET/CT data at end inspiration (EI) to correct for respiratory motion artifacts. Because data are acquired at one single breathing phase (EI), it becomes feasible to acquire data for a period of time comparable with that practiced in the standard clinical protocol—that is, 3 min per FOV—thus maintaining a comparable signal-to-noise ratio. We refer to this technique as deep-inspiration breath-hold (DIBH) PET/CT.

MATERIALS AND METHODS

Patient Data and Preparation

Eight cancer patients (age range, 46–73 y old) were included in an institutional review board–approved study. Each of the patients was injected intravenously with 444–555 MBq of ^{18}F-FDG and then underwent an uptake phase in a recumbent position for approximately 1 h. A PET/CT session according to the standard clinical protocol followed at our institution was performed. This was followed by a DIBH PET/CT session. No patient training to follow the "Hold" verbal instruction was required. However, before the imaging session, the patient was asked to hold the breath to optimize the frame length during the DIBH PET sessions accordingly. A 20-s hold period was found feasible for all patients included in this study.

PET/CT Scanner

PET and CT data were acquired on a Discovery LS PET (Advance NXi)/CT (LightSpeed 4-slice) scanner (GE HealthCare). The Lightspeed CT has a 50-cm transaxial FOV and can acquire images with slice thickness ranging between 0.63 and 20.0 mm. The tube current is variable between 10 and 440 mA, and the tube voltage is variable between 80 and 140 kVp, in increments of 20 kVp.

The PET Advance NXi scanner is a whole-body scanner with a transaxial FOV of 55 cm and 15.2 cm along the axial direction. The scanner has septa for the 2-dimensional high-resolution imaging acquisition mode. The intrinsic resolution is 4.2-mm full width at half maximum (FWHM).

Data Acquisition

CT data were acquired in helical mode at an 80-mA, 140-kV setting. PET scanning was then performed for the CT corresponding axial length, at a rate of 3 min per FOV.

The PET/CT session was then followed by the DIBH PET/CT study with the patient in the same position. CT data were acquired with the same settings as in the standard clinical protocol. The real-time position management (RPM) (Varian Medical Systems) system was used to monitor the patient's respiratory motion, using the amplitude gating mode. The patient was instructed to breathe deeply ("Breath IN IN IN") and then to hold the breath ("HOLD HOLD HOLD . . . .", for 20 s). One to 2 s were required to stabilize the hold period, after which CT data were acquired for the whole lungs (~16 s on average). PET data for one FOV were then acquired in nine 20-s independent frames (a total of 3 min). In case the patient failed to hold the breath in any of the frames, additional ones may be acquired instead. In each frame, the acquisition, as in the DIBH CT, was delayed for 1–2 s for the hold period to stabilize. After each "Hold" period, the patient was instructed to breathe normally ("Relax"). PET data were acquired for just one FOV. The total DIBH PET session time (including the normal breathing periods) was on average ~6 min. To ensure that PET data are acquired at a breath-hold position spatially matching that on CT, the amplitude threshold (an RPM option used usually to define the amplitude at which a trigger should be delivered) was set at the breath-hold level during the CT study. In all DIBH PET and CT, the RPM was used just to read the amplitude at which the patient is to be instructed to hold the breath. No trigger was delivered from or to the RPM or the PET/CT scanner as in the case of what was reported earlier (*5*).

TABLE 1
Summary of Patient Characteristics and Locations of Lesions

Lesion no.	Sex	Age (y)	Lesion site	Lesion volume (mL)	SUV_{max} clinical	SUV_{max} DIBH	% diff SUV_{max} (lesion)	% diff d centroid*
1	F	58	L lower lobe	1.4	7.95	10.43	31.2	−14.23
2	M	46	Mediastinum	3.2	8.8	12.26	39.32	−8.4
3			R hilum	3	6.6	8.87	34.4	−32.14
4	F	68	L upper lobe	3.2	3.23	3.97	23	−26.78
5	M	73	Left scapula	6.4	10.65	11.6	8.92	−3.03
6			R third rib	1.3	4.8	8.8	83.33	−23.16
7	M	43	R internal mammary node	7.2	11.5	12.4	7.83	−42.03
8	F	57	R first rib	4.7	4.2	4.9	16.67	−49.5
9	M	64	R lower lobe, R upper lobe	7.6	6.74	7.21	6.97	−43.14
10	M	69	L upper lobe	72.8	22.1	23.6	6.79	−16.86

*Percent differences in the distances "d" between the PET and CT centroids, on standard clinical and DIBH images, respectively, are presented. Negative sign reflects reduction in d in DIBH acquisition compared with clinical image.

Lesions' SUV_{max} measured on both clinical and DIBH PET images are reported together with percent difference (% diff).

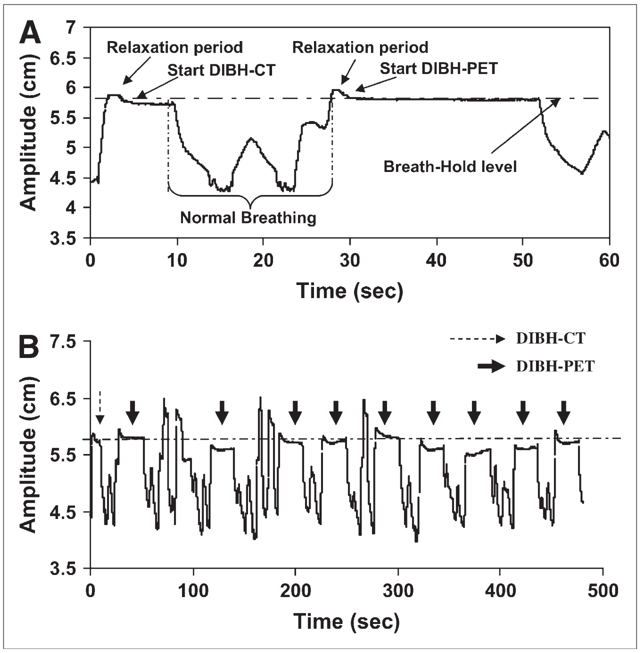

FIGURE 1. (A) RPM breathing signal of 1 patient showing "Hold" periods on CT and the first PET frame are displayed. Dashed line corresponds to inflation level at which patient was instructed to hold the breath. This was defined on the fly on the basis of the lung inflation level read during DIBH CT session. The "Hold" signal exhibited a relaxation period of 1–2 s before it stabilized (arrows). Therefore, it was necessary to wait for 1–2 s before starting the acquisition. (B) Consistency in lung inflation levels throughout DIBH PET/CT sessions is shown.

Analysis

The sinograms corresponding to the DIBH PET 20-s frames were added using the tool provided by the PET/CT manufacturer. The summed dataset corresponded to a 3-min (9 × 20 s) acquisition time, comparable with the standard clinical acquisition time. This was corrected for attenuation using the DIBH CT images and then reconstructed using the ordered-subset expectation maximization algorithm provided by the manufacturer. The same clinical reconstruction parameters were used in the DIBH PET image reconstruction (28 subsets; 2 iterations; postprocessing filter, 6.0-mm FWHM; loop filter, 4.3-mm FWHM). Ten lesions were detected within the DIBH PET FOV. For each lesion, the maximum SUV (SUV_{max}) was measured, on both the clinical and the DIBH PET images. To quantitate the improvement in PET/CT matching in DIBH PET/CT over clinical PET/CT, the CT and PET lesions were contoured by a radiologist, and the coordinates of the corresponding centroids were calculated. The distances "d" between the PET and CT lesions' centroids, in both DIBH (d_{DIBH}) and clinical ($d_{clinical}$) setups, were then calculated. The percent difference between d_{DIBH} and $d_{clinical}$ was reported as a measure of improvement in the PET-to-CT matching. This is defined as:

$$\% diff = \left(\frac{d_{DIBH} - d_{clinical}}{d_{clinical}}\right) \times 100.$$

RESULTS

The patient's sex, age, site of primary disease, CT volumes, and locations of the 10 lesions detected in the DIBH PET FOV are summarized in Table 1. The average CT volume was ~11 mL (range, 1.3–73 mL). The breathing signal of one of the patients is presented in Figure 1. Figure 1A shows the breath-hold period during the DIBH CT session, as well as the hold period for the first DIBH PET session. The hold threshold is also displayed. The lung inflation level was consistent thorough out the DIBH PET/CT study (Fig. 1B). DIBH PET/CT yielded an improved registration between PET and CT images. This is elaborated in the transaxial, coronal, and sagittal views of the fused clinical (Fig. 2A) and DIBH (Fig. 2B) PET/CT images for 1 patient. DIBH also enabled correction for diaphragm

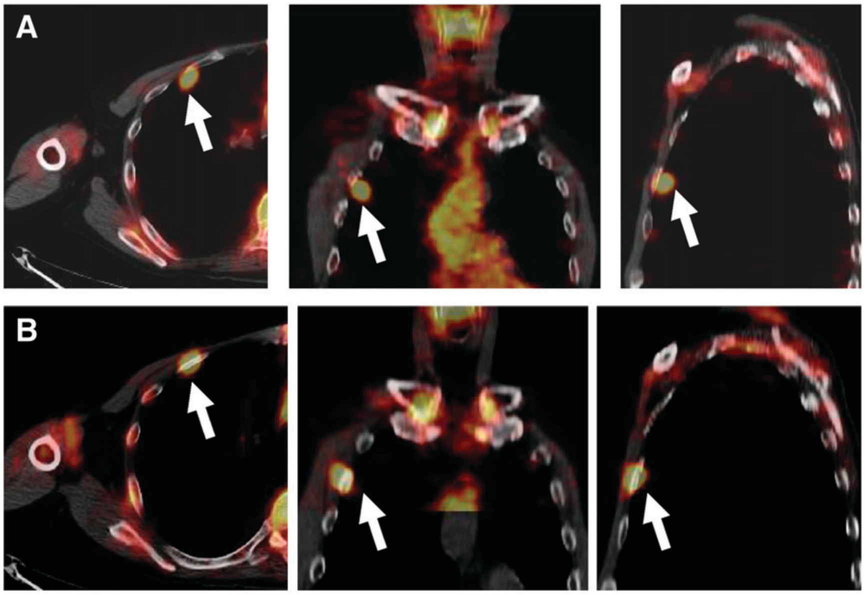

FIGURE 2. Transaxial, coronal, and sagittal views of clinical (A) and DIBH (B) fused PET and CT images are shown. Arrows point to a lesion in rib, based on CT images. PET lesion appears partially in lung on clinical images and just partially matching CT lesion because of respiratory motion. DIBH technique allowed improvement of coregistration between PET and CT and lesion localization.

artifacts due to respiration on the CT images (Figs. 3A and 3B). When using the standard clinical CT images for attenuation correction, these artifacts translate into a region of low activity concentration due to the apparent mixing between lung and diaphragm tissues in that region (Fig. 3C). This artifact was minimized on the DIBH CT attenuation-corrected DIBH PET images (Fig. 3D). The SUV_{max} measurements on both clinical and DIBH PET images as well as the percent difference between the 2 measurements are reported in Table 1. DIBH yielded an increase in median SUV_{max}, compared with clinical measurements, of ~32.6% (range, 4%–83%). On the other hand, the DIBH technique resulted in decreasing the mismatch between PET and CT lesions. This is elaborated in the negative percent differences between d_{DIBH} and d_{clinical}, as shown in Table 1. DIBH PET/CT enabled reducing the distance—thus the mismatch—between PET and CT lesions by a median of 26.6% (range, 3%–50%).

DISCUSSION

In this study, we described the procedure to acquire and clinically implement PET/CT images with the DIBH technique. This method enabled reduced breathing-induced artifacts on PET/CT images of the thorax, which include PET/CT spatial mismatch and target blurring and, consequently, increase the SUV. In 4D PET, data are acquired in several bins, each corresponding to one breathing phase. Because of the limitation on the acquisition time per bin from a clinical practice point of view, a total of 1 min per bin is usually acquired, for a total of 10 bins—that is, a total of 10 min (*2,3*). Because of irregular cycles, the RPM may not trigger the acquisition process on the PET scanner, which will result in prolonging the total time the patient is on the PET table. Comparison with the standard clinical protocol (3 min/bed), the reduction in the acquisition time (1 min/bin) yields a decrease in the signal-to-noise ratio. A

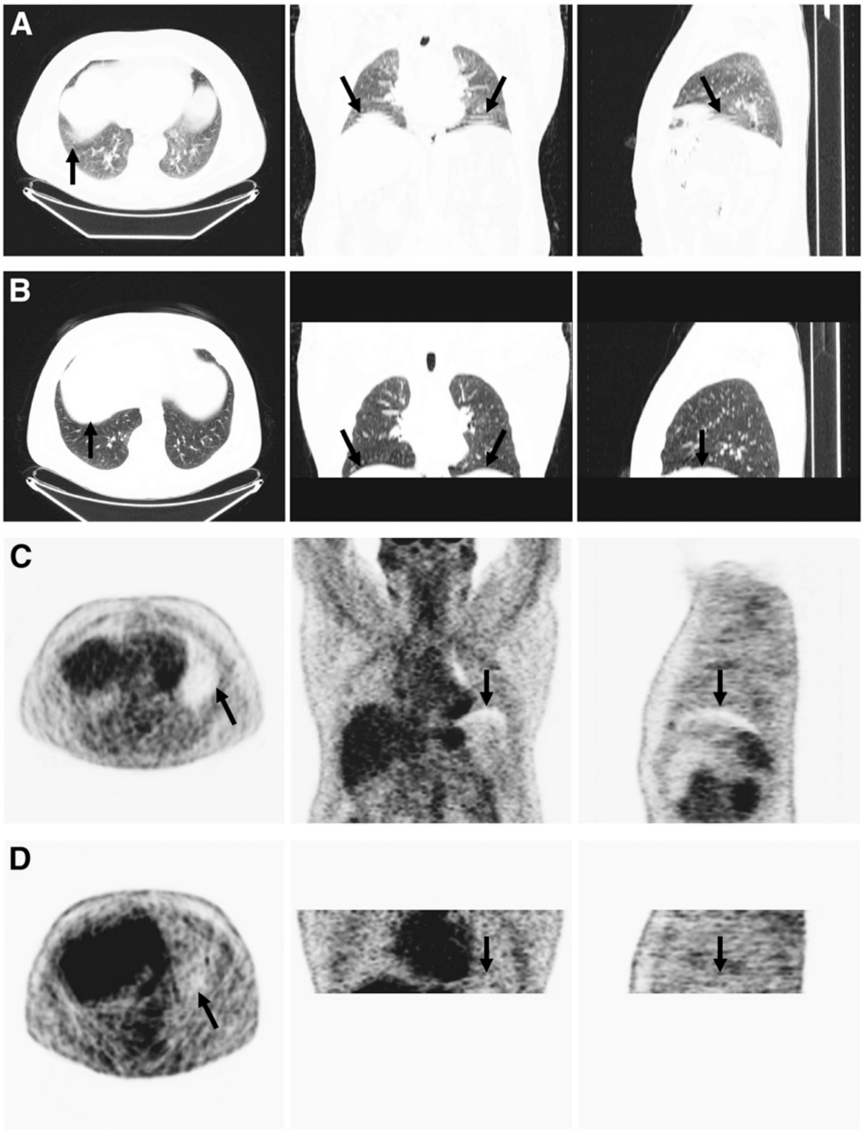

FIGURE 3. DIBH enabled correction for respiratory motion artifacts in diaphragm on CT images (A and B). Because of breathing motion, tissue density in region where the diaphragm moves in and out drops. This yielded a reduced activity concentration in corresponding areas on PET images when CT attenuation correction is performed. This artifact was minimized on DIBH CT attenuation-corrected DIBH PET images.

4D acquisition also requires major training for the patient to follow verbal instructions (breath-in, breath-out) to maintain a regular breathing motion. Unlike radiotherapy, information about the extent of tumor motion is not required for diagnosis, and DIBH PET/CT may have major advantages over 4D PET/CT in this setting. First, no patient training was required. PET data are acquired at one single phase (EI) rather than at all phases. Hence, the patient will have to reproduce the breathing characteristics of just the breath-hold phase rather than for all phases. To ensure reproducibility of the "Hold" period at the same breathing amplitude, the physicist or technologist needs to recognize the patient's breathing pattern and then coach the patient to hold the breath at the same amplitude. The patient should be able to easily follow the instructions and reproduce the breathing amplitude, especially because he or she gets a break period ("Relax") after every "Hold" period. Second, 3 min per bed (equals the standard clinical acquisition time per bed) could be acquired in DIBH, which corresponds to at least 30 min of acquisition time in 4D PET for a total of 10 bins, as in the protocol suggested by Nehmeh et al. (*3–5*). Third, in case of sudden breathing irregularities, the corresponding data may be disregarded from the final DIBH dataset, which is not possible in 4D PET. Finally, the postprocessing time is minimal; DIBH PET and DIBH CT are acquired according to the standard clinical PET/CT protocol. Consequently, no further rebinning of the CT data to spatially match the PET slices is required, as reported by Nehmeh et al. (*3*).

Our results showed an increase in median SUV by 32.46% (range, 4%–83%), compared with SUVs measured on the clinical images. This finding is consistent with earlier reports (*2,3*). DIBH PET/CT also improved the spatial registration between PET and CT images of the thorax. Our results showed an average reduction in the distance between the PET and CT lesions' centroids of ~24% (range, 3%–49%). This resulted in minimizing breathing artifacts especially in the diaphragm. No obvious correlation could be established between the change in the SUV and that in the distance between PET and CT centroids, as a result of DIBH compared with standard clinical acquisition. This is because the change in the SUV should correlate with the tumor size, its motion amplitude, and the accurate matching with CT. In DIBH, data are acquired at just one breathing phase, which does not enable the quantitation of the motion amplitude. This is a major disadvantage over the 4D technique, especially for radiotherapy applications. The reduction in the mismatch between PET and CT should overcome the unwanted effect of spatial misalignment on attenuation correction of PET emission images (*5*) and also help in determining the exact anatomic location of a given lesion.

Here we have shown that the proposed DIBH method is feasible in daily practice; the potential clinical implications will be investigated in future studies.

CONCLUSION

We have described the details to acquire PET/CT data using the DIBH technique to correct for respiration-induced artifacts on the PET/CT images. Lesions in the thorax usually move due to respiration. DIBH PET/CT enabled reducing breathing motion artifacts especially in the diaphragm, increasing the SUV, and improving the coregistration between PET and CT images. Consequently, this resulted in a better localization of the lesion and a more accurate attenuation correction. DIBH is an easy technique to clinically implement and practice, which requires minimal acquisition and processing time and effort. This procedure may improve the accuracy of PET/CT diagnosis for lung lesions.

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