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Clinical Significance of Pulmonary Nodules Missed on Non-Breath-Hold PET/CT

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Abstract

Objective: In clinical practice, PET images are acquired during shallow breathing and CT images of the PET/CT during shallow breathing or at near end-expiration. We determined the clinical significance of pulmonary nodules that were missed on PET/CT acquired during non-breath-hold (NBH) imaging in patients with proven non-thoracic solid malignancies.

Methods: 200 consecutive cancer patients who underwent both PET/CT and diagnostic breath-hold (BH) chest CT within 30 days, and who had a follow-up with BH CT at least 2 years after these baseline studies, were evaluated. NBH CT of the PET/CT was analyzed first, followed by the baseline BH CT. Missed nodules were defined as nodules not detected on NBH PET/CT, but detected on BH CT. Missed nodules were then evaluated on BH CT performed at least 2 years later. A second radiologist was used to evaluate inter observer variability for a subset of 50 patients.

Results: 343 nodules were identified in 121 patients. 166 nodules from 86 patients were classified as missed nodules. Seven of these 166 nodules were excluded due to interval surgery or development of consolidation. When a change in size was counted only if it was ≥2 mm, only 11 of the 159 nodules (6.9%) grew, 113 nodules (71.1%) did not change, and the remaining 35 nodules (22.0%) were not present at follow-up. Malignancy was deemed the most likely diagnosis in only 6 of the original 159 missed nodules.

Conclusion: Although the incidence of pulmonary nodules missed on NBH PET/CT was high, most of these nodules did not show any growth on follow-up and few were proven to be metastatic. Current clinical practice of PET/CT, with acquisition during shallow breathing or at near end expiration is sufficient; performing additional deep inspiration BH CT does not appear warranted.

Keywords: PET/CT; Pulmonary nodules; Lung; FDG-PET; MDCT

Introduction

PET/CT is a widely used imaging modality in oncology. In clinical practice, PET images are acquired during shallow breathing due to the length of scan time, which is in the order of minutes per bed position. The CT component of PET/CT studies is acquired during free breathing or near end-expiration, in order to optimize co-registration with the PET images. Prior studies have shown maximal inspiration or expiration during CT acquisition to be poor for image co-registration in PET/CT of the chest [1,2]. Conversely, diagnostic chest CT images are obtained in maximal inspiration to avoid areas of atelectasis. Therefore, non-breath-hold (NBH) acquisition may limit the detection of pulmonary nodules in PET/CT studies due to respiratory motion artifacts or areas of atelectasis on the CT images. In particular, small pulmonary nodules (≤ 1 cm) are often missed or obscured in NBH acquisitions. Depending on their histology, small nodules may also remain undetectable on FDG PET [3,4]. The incidence of malignancy in small pulmonary nodules in patients with an established diagnosis of cancer is in the range of 10% to 58% and is highly dependent on whether follow-up CT or surgery was used for verification [5-8]. Prior studies have shown a high incidence of missed small pulmonary nodules during NBH PET/CT and have advised additional diagnostic breath-hold (BH) CT for detection of possible small pulmonary metastases missed on standard clinical PET/CT [9,10]. However, small nodules seen on dedicated chest CT are often indeterminate or benign even in patients with established cancer diagnosis [11]. Moreover, the clinical significance of pulmonary nodules seen only on BH CT (but not on standard PET/CT) remains unclear. We conducted the current study to address this question specifically in patients with an established diagnosis of non-thoracic solid primary malignancies.

Materials and Methods

Patient population

Institutional Review Board (IRB) approval was obtained under IRB waiver protocol for retrospective data collection and analysis under waiver number WA0291-10. Accordingly, informed consent was not required. A retrospective database was generated from the institution radiology information system (RIS) database for patients who underwent both PET/CT and diagnostic BH chest CT within 30 days of each other, and who had a follow-up BH CT at least 2 years after the initial PET/CT and BH chest CT. The PET/CT study was indicated for staging and restaging of solid tumor malignancies. Lung cancer patients and any patients who had interval lung surgery were excluded. Patients who had diffuse consolidation on any of the scans (which

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would obscure nodule assessment) or who had obvious pulmonary metastases were also excluded. The first 200 consecutive patients in the database meeting criteria from December 1, 2003 to October 30, 2008 were evaluated.

Image acquisition

All scans were performed using standard clinical PET/CT scanners (either Discovery LS, ST, or STE (all GE Healthcare, Waukesha, WI) or Biograph LSO-16 (Siemens Medical Solutions, Malvern, PA). Patients were asked to fast for 6 hours before the PET/CT scan. Blood glucose was measured on patient arrival in the nuclear medicine clinic; upon confirming a value of < 200 mg/dL (our institutional cut-off), 12 to 15 mCi of fluorine-18 labelled FDG was injected intravenously. Patients also drank diluted oral contrast medium (megluminediatrizoate, Gastrografin, Bristol-Myers Squibb; 2.5% solution, 1000 mL). Patients were asked to void after a 60- to 90-minute uptake period and were then positioned on the scanner table. Following scout view and low-dose CT (5 mm slice thickness, 120 to 140 kV, 80 mA) used for attenuation correction and anatomic localization, PET emission images were obtained for 3 minutes per bed position from the skull base to the upper thigh, with the arms above the head. CT images were reviewed on a workstation integrated with a PACS (Centricity AW Suite version 2, GE Healthcare) that allowed multiplanar reformatting of images.

Maximum inspiration breath-hold axial CT chest was performed with 16 row multidetector computed tomography (MDCT) scanners (GE Lightspeed 16). Scans were acquired from the supraclavicular region to the adrenal glands (2.5 mm slice thickness, 140 kVp, 80 mAs).

Image and patient analysis

A board certified radiologist first analyzed the NBH CT of the PET/CT, and then the BH CT that had been performed up to 30 days before or after the PET/CT. This radiologist was unaware of the patient's history, clinical outcome, or any interventions. Size and location for each nodule were recorded. Only solid nodules without calcification were recorded. Ground glass opacities were not included. Missed nodules were defined as nodules not detected on NBH CT, but detected on BH CT. Missed nodules were followed on the subsequent BH CT performed at least 2 years later. A second radiologist was used to evaluate interobserver variability in a subset of 50 patients, performing the identical image analysis in every fourth patient in the database. After image analysis was complete, clinical information about whether the patient received systemic chemotherapy during the 2 year interval between scans was collected.

Statistical analysis

All analyses were performed using SAS software version 9.2 (SAS Institute, Cary, NC). Descriptive statistics were calculated for patient characteristics and summary statistics were produced for nodules measured by BH CT but missed by NBH PET/CT. The binomial proportion of agreement was calculated for nodules that were measured by both baseline BH and NBH PET/CT. The Rao-Scott chi-square test evaluated the distribution of nodule size change by chemotherapy status, adjusting for correlation between multiple nodules from a single patient. The distribution of agreement between readers was calculated separately for the baseline BH CT, baseline NBH PET/CT, and follow-up BH CT by examining the frequency of lesions that were measured by one reader but missed by the other, lesions with measures that differed by ≤1 mm by the two readers (considered agreement), lesions that differed by >1 mm by the two readers (considered disagreement), and lesions that were measured as 0 by both readers (considered agreement that there were no nodules) (Figures 1 and 2).

Results

Patient characteristics

After excluding patients with no nodules at baseline NBH CT and BH CT, the data consisted of 343 nodules in 121 patients. Table

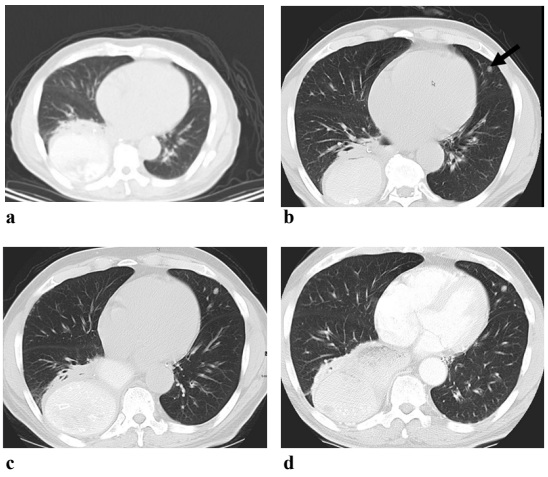

Figure 1: a. A 0.6 cm pulmonary nodule on NBH CT (from PET/CT) in the left upper lobe which was missed by the radiologist. **b.** The radiologist identified the missed micronodule in the left upper lobe on BH CT chest (performed within 30 days of the NBH CT). **c.** Follow-up BH CT chest performed two years later shows mild increased in size of the left upper lobe nodule which measured 0.8 cm. **d.** Further follow-up BH CT chest performed 5 years later (from original NBH CT) showed the left upper lobe nodule to be stable and benign by imaging follow-up.

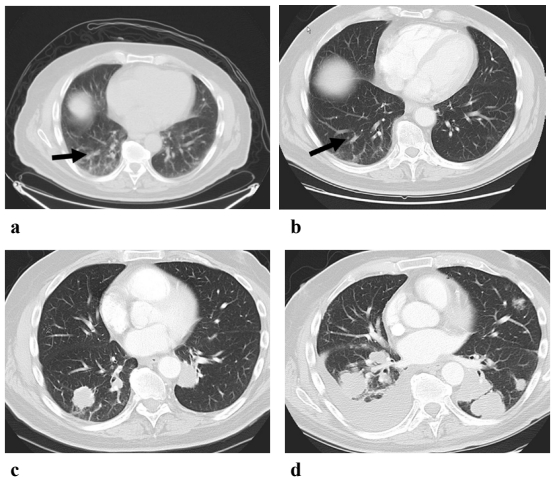

Figure 2: a. A 0.3 cm pulmonary nodule was missed on the NBH CT (from PET/CT) in the right lower lobe secondary to poor inflation at the lung bases (arrow). **b.** The radiologist identified the missed micronodule (arrow) in the right lower lobe on BH CT chest (performed within 30 days of the NBH CT). **c.** Follow-up BH CT chest performed two years later shows increased size of the missed nodule (20 mm). There is also a left lower lobe nodule present. **d.** Further follow-up BH CT chest performed 3 years later (from original NBH CT) shows further increased in size the right lower lobe nodule and numerous pulmonary nodules had grown in the interval. This patient also had liver metastases.

1 shows a summary of patient characteristics in the study. Patient disease status and indication for imaging at baseline was as follows: staging without established metastases (n=22), staging with established metastases (n=19), follow-up with no metastases (n=40) and follow-up with established metastases (n=40). The majority of patients with nodules in the baseline scan had colon, breast or esophageal cancer.

Frequency and distribution of nodules

One hundred sixty-six of the 343 nodules (48%) were only noted on the BH CT, affecting 86 patients. In 36 of these 86 patients, all of the nodules present at baseline were missed on the NBH CT scan. Six of the 166 missed nodules measured 1 mm, while the other 160 nodules were > 1 mm (range: 1-9 mm, median 3 mm). The frequency of missed nodules was higher in the lower lobes than in the upper lobes or middle lobe (Table 2). Regarding the 177 nodules detected by both BH and NBH CT at baseline, the size measurements for 95% (95% CI: 92%, 99%) agreed within 1 mm.

Outcome and significance of missed nodules

Follow-up data was obtained only for the 166 nodules that were missed by NBH PET/CT scan at baseline. Seven of these 166 nodules were excluded because of lung surgery in the interim or development of consolidation, making the initial missed nodule not assessable. The remaining 159 nodules were analyzed for change in size during the 2 year follow-up; change in size was only counted if it exceeded 2 mm. There was no change in size from baseline to follow-up for 113 nodules (71.1%), and another 35 nodules (22.0%) were no longer present at follow-up. The remaining 11 nodules (6.9%) from 10 patients grew in size on follow-up (Table 3). Their size ranged from 1 to 9 mm (median: 3 mm) at baseline, and from 5 to 23 mm (median: 7 mm) at follow-up. Average interval growth was 6.4 mm.

We further evaluated the subsequent fate, likely etiology and potential clinical significance of nodules with interval growth using additional clinical and imaging follow-up of 2-5 years. Table 4 shows that 7 of the 11 nodules (affecting 6 patients) with interval growth between baseline and 2 year follow-up continued to grow and were thus most likely metastatic Of note, all of these 6 patients had extra thoracic metastatic disease, so that the presence of additional metastases to lungs would likely not have altered their clinical management. The primary malignancy was breast or colon cancer.

Of the 159 nodules with 2 year follow-up, 98 (61.6%) were subjected to interval chemotherapy, which was indicated because of known metastatic disease elsewhere, or was given as part of induction chemotherapy or definitive chemoradiotherapy regimens. There was no clear relationship between changes in size of missed nodules and administration of chemotherapy in the interim (p=0.69; Table 5).

Interobserver agreement

Data regarding interobserver agreement (detection and size) for 80 nodules in 31 patients, who had at least one nodule identified in either of the scans, are shown in Table 6. The two readers agreed regarding presence or absence of nodules for 66 of the 80 nodules (83%) for baseline BH CT, for 68/80 nodules (85%) on the follow-up BH CT, and for 67/80 nodules (85%) in the baseline NBH CT of the PET/CT. We then further defined agreement as difference in measured size ≤ 1 mm, and disagreement as size difference ≥ 2 mm between measurements obtained by the two radiologists. In this analysis, the two readers agreed on 78.8% of nodules on the baseline BH CT, on 66.3% of nodules on the follow-up BH CT, and 55.0% of nodules on the baseline NBH PET/CT.

Median age No. of female patients No. Of male patients	61 (48-72) 67 (55.4%) 54 (44.6%)
Diagnosis	Number of patients
colon	40 (33.1%)
Breast	29 (24.0%)
Esophagus	15 (12.4%)
Stomach	11 (9.1%)
Connective and soft tissue	10 (8.3%)
Prostate	9 (7.4%)
Head and Neck	5 (4.1%)
Melanoma	2 (1.7%)

Table 1: Summary of patient Characteristics N=121.

Location	Frequency	Percent
LLL	43	25.9
LUL	29	17.5
RLL	42	25.3
RML	27	16.3
RUL	25	
	Total= 166	

LLL= left lower lobe, LUL= left upper lobe, RLL= Right lower lobe, RML= Right Middle Lobe, RUL= Right upper lobe

Table 2: Location distribution of nodules missed by NBH CT.

	Frequency	Percent	Standard Error of Percent	95% Confidence limits for percent
No change	113	71.1	4.17	62.7, 79.4
Grew	11	6.9	2.19	2.6, 11.3
Disappeared	35	22.0	3.74	14.6, 29.4

Table 3: Distribution of lesion size change as measured on folloe-up BH CT missed nodules on initial NBH CT.

Discussion

The NBH CT of PET imaging is mainly used for the attenuation correction of PET emission images and for localization of PET abnormalities. It is obtained during shallow breathing or near end expiration. This CT in the PET/CT also employs lower mA settings than those used in a dedicated chest CT. This combination of factors has led to concerns that many small lung nodules might be missed with this technique. Our study demonstrates that indeed nearly 50% of small pulmonary nodules ≤ 10 mm can be missed on the NBH CT of the PET/CT scans. Importantly, however, only a small fraction of these missed nodules showed growth over the subsequent 2 years. Moreover, while pulmonary metastasis was the most likely etiology in 6 of the 121 patients with missed nodules at baseline (5%), all of these patients had established metastatic disease outside the chest, further limiting the potential impact on patient management and outcome.

Diagnostic CT of the thorax with single breath-hold inspiration acquisition increases the detection of small pulmonary nodules. Of note, the majority of pulmonary nodules with a diameter ≤ 10 mm are benign and without clinical significance [12]. Reported rates of detection of pulmonary nodules less than 1 cm on helical CT range from 10 – 40% [5,12,13]. Nodules that resolve, decrease in size, or show no growth during a 2-year period, are considered benign. On the other hand, in patients with established cancer diagnosis, 10-58% of nodules were reported to be malignant, depending on whether imaging follow-up or surgery with histopathology was used for verification [5-7,12]. Fleischner Society guidelines recommend CT follow-up at 3-6 months,

Patient	Initial Size	Follow-up size	Chemo therapy	Primary Cancer	Further follow-up studies and metastatic disease status
1	3	7	yes	prostate	3yrs follow-up showed waxing and waning nodules. Metastatic disease to bone and lymph nodes
2	6	8	yes	esophagus	3yrs follow-up showed stable nodules. Patient was disease free
3	2	7	yes	Breast	3yrs follow-up showed progressive increased size of nodules. Metastatic disease to bone and chest wall.
4	4	7	No	Colon	5yrs follow-up showed increased size of nodules. Metastatic disease to liver and peritoneum.
4	5	23	No	Colon	
5	9	15	No	Breast	4yrs follow-up showed stable nodules. Biopsy of nodules grew MAIC.
6	4	6	yes	colon	3yrs follow-up showed increased size of nodules. Metastatic disease to liver, lymph nodes and peritoneum.
7	3	20	yes	colon	3yrs follow-up showed increased size and number of nodules. Metastatic disease to liver
8	1	5	No	Breast	2yrs follow-up showed increased size of nodules. Metastatic disease to liver, bone and lymph nodes.
9	2	7	yes	colon	2yrs follow-up showed progressive increased size of nodules. Metastatic disease to liver and bone
10	2	6	yes	esophagus	4yrs follow-up showed waxing and waning nodules. Metastatic disease to liver

Table 4: Nodule missed by NBH CT which grew.

	Interval Chemotherapy	N (nodules)	Percent
No change N=111	No yes	46 67	40.7 59.3
Grew N=1	No yes	4 7	36.7 63.6
Disappeared N=35	No yes	11 24	31.4 68.6
		Total= 159	

Table 5: Distribution of nodule size change on follow-up by chemotherapy status of missed nodules on baseline NBH CT.

	Baseline BH CT		Follow-up BH CT		Baseline NBH PET/CT	
Missed by one reader	14	17.5	12	15.0	13	16.3
Agreed	63	78.8	53	66.3	44	55.0
Disagreed*	3	3.8	4	5.0	0	0.0
Agreed no nodules**	0	0.0	11	13.8	23	28.8

*Disagreement of size occurred only when size difference greater than 1mm was read
**Agreement between readers on studies which contained no pulmonary nodules

Table 6: Distribution of agreement between first and second reader among scan that had two readers.

9-12 months and 12 months for nodules 6-8 mm in high-risk patients [14]. For nodules ≤ 4 mm, follow-up CT at 12 months is recommended.

In our study, the incidence of missed pulmonary nodules ≤ 1 cm on NBH CT was 166 (47% of all nodules) and affected 86 patients (43% of the entire patient population studied). The majority of missed nodules were located in the lower lobes (26% left lower lobe, 25% right lower lobe), probably due to insufficient inflation of lung bases during the NBH CT of the PET/CT. Allen-Auerbach [9] reported a similar 48% incidence of nodules missed on NBH CT, affecting 34% of their patient population. The average number of missed nodules per patient is also comparable (1.9 [166/86] in the present study versus 2.6 [125/48] in their study). Another study reported that 45 of 117 (38%) small pulmonary nodules were only detected when an additional low-dose deep inspiratory chest CT was included as a part of a PET/CT protocol [10]. The mean size of these nodules was 3.8 mm. Twenty-nine of their patients (80.6%) had at least one of their nodules only seen on the low dose inspiratory chest CT. These and other reports have prompted concerns and led to recommendations that deep inspiration BH CT of the chest be added routinely to current PET/CT protocols. Here we show that the vast majority of missed nodules ≤ 1 cm are clinically insignificant: with at least 2 year follow-up, 71% of missed nodules showed no change in size (thereby reasonably excluding malignancy as etiology), and another 22% disappeared. Only 7 of 11 nodules with measurable growth within 2 years from baseline were ultimately deemed to be metastatic, and all 6 of the affected patients had extra thoracic metastases. It is thus unlikely that earlier detection of (additional) pulmonary metastases would have altered their clinical management. Overall, the additional cost and radiation burden associated with unnecessary deep inspiration BH CT does not appear justified.

Our study was conducted in a group of patients with new or previously established diagnosis of cancer. Therefore, a large percentage (61.6%) of patients received treatment in the 2 year time frame between baseline and follow-up CT scans. Thus, one might argue that the relative stability or resolution of the majority of pulmonary nodules was secondary to treatment effect. However, our analysis showed no clear relationship between the fate of nodules (stable, increase, or resolution) and therapy, suggesting that our conclusions apply equally to patients with or without chemotherapy in the 2 year interim from baseline scan. Of note, there was no patient in whom small nodules only seen on BH CT were the only relevant finding. It is therefore

unlikely that detection of new or additional nodules on BH CT would have affected patient management. In fact, no prior study has proven that additional pulmonary nodules detected on deep inspiration BH CT are relevant and critical for management in a cancer population. Current recommendations to supplement standard PET/CT with an additional BH CT are thus based on conjecture (detecting more small nodules is inherently beneficial) rather than on evidence.

We evaluated consecutive patients without any preselection (e.g., based on primary disease site or pre-test likelihood for lung metastases). However, the lungs are a well-established site of metastatic disease in the vast majority of patients in this study. We do not believe that the results would differ significantly in more selected patients (e.g. locally advanced breast cancer), because small nodules missed on PET/CT but seen on the separate BH CT would have to meet 3 criteria to be considered clinically relevant: (a) nodule is metastatic, (b) missed metastatic nodule is the only site of metastatic disease, and (c) nodule can be clearly characterized as metastasis on the deep inspiration BH CT scan. This is an unlikely scenario: larger nodules are rarely missed on PET/CT and on the other hand small nodules are usually not well characterized on imaging and may not be amenable to biopsy either, possibly necessitating further CT scans for follow-up. Only one board certified radiologist was used in our image analysis and images were not read in consensus with another physician. However, our reader did generate data (in terms of incidence of missed pulmonary nodules) similar to that reported in the literature. Our second reader only reviewed a subset of 50 patients. Of note, the primary objective of this study was not to evaluate interobserver variability. Instead, the second reader was recruited for internal quality control and to establish a baseline interobserver value for our study. Interobserver agreement amongst radiologists for the detection of pulmonary nodules on low dose CT has been reported as fair to poor with kappa values of 0.120 – 0.458 [15] and on full diagnostic BH CT with kappa values of 0.67 – 0.81 [16]. In our study, the two readers agreed regarding presence of absence of nodules in 83% for the baseline BH CT, in 85% for follow-up BH CT, and in 85% for baseline NBH low dose CT of the PET/CT.

Conclusion

Although the incidence of missed pulmonary ≤ 1 cm on non breath-hold CT during standard clinical PET/CT is high, the great majority of these nodules remain clinically insignificant on long-term follow-up in an oncologic patient population. Current clinical practice of PET/CT, with CT acquisition during shallow breathing or at near end expiration, is therefore sufficient; performing additional deep inspiration BH CT solely for the purpose of detecting small pulmonary nodules does not appear warranted.

References

1. Goerres GW, Burger C, Kamel E, Seifert B, Kaim AH, et al. (2003) Respiration-induced attenuation artifact at PET/CT: technical considerations. Radiology 226: 906-910.
2. Goerres GW, Kamel E, Heidelberg TN, Schwitter MR, Burger C, et al. (2002) PET-CT image co-registration in the thorax: influence of respiration. Eur J Nucl Med Mol Imaging 29: 351-360.
3. Imdahl A, Jenkner S, Brink I, Nitzsche E, Stoelben E, et al. (2001) Validation of FDG positron emission tomography for differentiation of unknown pulmonary lesions. Eur J Cardiothorac Surg 20: 324-329.
4. Nomori H, Watanabe K, Ohtsuka T, Naruke T, Suemasu K, et al. (2004) Evaluation of F-18 fluorodeoxyglucose (FDG) PET scanning for pulmonary nodules less than 3 cm in diameter, with special reference to the CT images. Lung Cancer 45: 19-27.
5. Keogan MT, Tung KT, Kaplan DK, Goldstraw PJ, Hansell DM (1993) The significance of pulmonary nodules detected on CT staging for lung cancer. Clin Radiol 48: 94-96.
6. Munden RF, Pugatch RD, Liptay MJ, Sugarbaker DJ, Le LU (1997) Small pulmonary lesions detected at CT: clinical importance. Radiology 202: 105-110.
7. Ginsberg MS, Griff SK, Go BD, Yoo HH, Schwartz LH, et al. (1999) Pulmonary nodules resected at video-assisted thoracoscopic surgery: etiology in 426 patients. Radiology 213: 277-282.
8. O JH, Yoo IeR, Kim SH, Sohn HS, Chung SK (2007) Clinical significance of small pulmonary nodules with little or no 18F-FDG uptake on PET/CT images of patients with nonthoracic malignancies. J Nucl Med 48: 15-21.
9. Allen-Auerbach M, Yeom K, Park J, Phelps M, Czernin J (2006) Standard PET/CT of the chest during shallow breathing is inadequate for comprehensive staging of lung cancer. J Nucl Med 47: 298-301.
10. Juergens KU, Weckesser M, Stegger L, Franzius C, Beetz M, et al. (2006) Tumor staging using whole-body high-resolution 16-channel PET-CT: does additional low-dose chest CT in inspiration improve the detection of solitary pulmonary nodules? Eur Radiol 16: 1131-1137.
11. Baek SJ, Kim SH, Kwak JM, Cho JS, Shin JW, et al. (2012) Indeterminate pulmonary nodules in rectal cancer: a recommendation for follow-up guidelines. J Surg Oncol 106: 481-485.
12. Benjamin MS, Drucker EA, McLoud TC, Shepard JA (2003) Small pulmonary nodules: detection at chest CT and outcome. Radiology 226: 489-493.
13. Henschke CI, McCauley DI, Yankelevitz DF, Naidich DP, McGuinness G, et al. (2001) Early lung cancer action project: a summary of the findings on baseline screening. Oncologist 6: 147-152.
14. MacMahon H, Austin JH, Gamsu G, Herold CJ, Jett JR, et al. (2005) Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. Radiology 237: 395-400.
15. Leader JK, Warfel TE, Fuhrman CR, Golla SK, Weissfeld JL, et al. (2005) Pulmonary nodule detection with low-dose CT of the lung: agreement among radiologists. AJR Am J Roentgenol 185: 973-978.
16. Wormanns D, Diederich S, Lentschig MG, Winter F, Heindel W (2000) Spiral CT of pulmonary nodules: interobserver variation in assessment of lesion size. Eur Radiol 10: 710-713.