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^{18}F-Labeled NaF PET-CT in Detection of Bone Metastases in Patients With Preoperative Lung Cancer

Liangjun Rao, Zhen Zong, Zhifeng Chen, Xiaoyan Wang, Xinchong Shi, Chang Yi, and Xiangsong Zhang

Abstract: We compared the diagnostic accuracy of ^{18}F-labeled sodium fluoride (^{18}F-NaF) PET-CT with 99m-technetium methylene diphosphonate (^{99m}Tc-MDP) single photon emission computed tomography (SPECT) to detect bone metastases (BMs) in patients with preoperative lung cancer.

Patients with lung cancer (n = 181) were examined with ^{18}F-NaF PET-CT, and another 167 patients with lung cancer were examined with ^{99m}Tc-MDP SPECT. ^{18}F-NaF PET-CT and ^{99m}Tc-MDP SPECT were evaluated by 2 experienced readers. Lesions were graded on a scale of 0 (degenerative lesion) to 4 (definite BM), and equivocal lesions were determined as indifferent (grade 3).

Based on patient-based analysis, there were only 4 equivocal patients in ^{18}F-NaF PET-CT detection. However, in ^{99m}Tc-MDP SPECT detection, there were 19 equivocal patients, which indicated a significant difference in terms of occurrence ratio ($\chi^2 = 9.005$, $P = 0.03$). Sensitivity and specificity of PET-CT was significantly better than that of SPECT when equivocal reading was categorized as malignant or benign ($P < 0.05$). Based on lesions-based analysis, SPECT produced 26 equivocal lesions of 333 lesions, but PET-CT produced only 5 equivocal lesions of 991 lesions. PET-CT was significantly better than SPECT in the aspect of producing equivocal patients ($\chi^2 = 58.141$, $P < 0.001$). Sensitivity and specificity of PET-CT was significantly better than that of SPECT when equivocal reading was categorized as malignant or benign ($P < 0.05$).

^{18}F-NaF PET-CT is a highly sensitive and specific modality for the detection of BM in patients with preoperative lung cancer. It is better than conventional ^{99m}Tc-MDP SPECT in detecting BM in patients with preoperative lung cancer.

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Abbreviations: ^{18}F-NaF = ^{18}F-labeled sodium fluoride, ^{99m}Tc-MDP = 99m-technetium methylene diphosphonate, BM = bone metastasis, BS = bone scintigraphy, CT = computer tomography, FOV = field of view, NSCLC = nonsmall cell lung cancer, PET = positron emission tomography, SCLC = small cell lung cancer, SPECT = single photon emission computed tomography.

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From the Department of Nuclear Medicine (LR, ZC, XW, XS, CY, XZ); Department of Radiology, the First Affiliated Hospital (LR); and Department of General Surgery, Sun Yat-sen Memorial Hospital (ZZ), Sun Yat-sen University, Guangzhou, China.
Correspondence: Xiangsong Zhang, Department of Nuclear Medicine, the First Affiliated Hospital, Sun Yat-Sen University, No. 58, Zhongshan Er Road, Guangzhou 510080, China (e-mail: zhangraos@163.com).
LR, ZZ, and ZC are co-first authors and contributed equally to this work.
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INTRODUCTION

Lung cancer is the leading cause of cancer-related death in the world, and the bone is one of the most common metastatic sites. Bone metastasis (BM) occurs in approximately 30% to 36% of lung cancer patients.[1–3] Nonsmall cell lung cancer (NSCLC) without distant metastases is potentially curable. Hence, accurate staging of the bone is crucial in all patients with lung cancer for the selection of appropriate therapy. Compared with conventional planar bone scintigraphy (BS) and single photon emission computed tomography (SPECT), it has been proven that positron emission tomography (PET) using ^{18}F-labeled sodium fluoride (^{18}F-NaF) can detect BM more accurately in breast, prostate, thyroid, and lung cancers.[4,5]

Recently, with the widespread use of integrated PET-computer tomography (CT) system, the poor spatial resolution of PET has been substantially compensated by integrated PET-CT with coregistration of anatomical imaging with CT and functional imaging with PET. It is useful to detect local tumor invasion, better differentiation of mediastinal lymph node metastases, and improved assessment of distant tumor metastases including BM. However, compared with conventional 99m-technetium methylene diphosphonate (^{99m}Tc-MDP) SPECT, which is commonly used to rule out BM, the validity of ^{18}F-NaF PET-CT for the detection of BM is still unknown. Therefore, this study was designed to compare the diagnostic accuracy of ^{18}F-NaF PET-CT with ^{99m}Tc-MDP SPECT in the detection of BM in patients with preoperative lung cancer.

MATERIALS AND METHODS

Patients

Our study consisted of 181 patients (2010.7–2011.3) who performed ^{18}F-NaF PET-CT detection and other 167 patients (2010.1–2010.7) who performed ^{99m}Tc-MDP SPECT detection. Patients were included when lung cancer was diagnosed by bronchoscopy and CT. The final diagnosis of lung cancer was obtained based on histopathological findings. The 181 patients (128 men, 53 women; age range, 29–88 years; mean age, 59.8 years) included small cell lung cancer (SCLC, n = 12) and NSCLC (n = 169). The 167 patients (123 men, 44 women; age range, 24–90 years; mean age 58.8 years) included SCLC (n = 8) and NSCLC (n = 159). Exclusion criteria included a history of extrapulmonary cancer, known metastatic bone diseases, pregnancy, or <18 years of age. The study was approved by the hospital ethics committee, and each participant provided written informed consent.

^{99m}Tc-MDP SPECT Detection

BS was performed in 2 dual-head gamma cameras (TOSHIBA GCA-7200A/DI). For data acquisition, the nuclear

medicine computer system was used (GMS-5500/DI, Toshiba, Japan). The dual-head gamma cameras were used with low energy high resolution collimators. The dual-head gamma cameras axial fields of view (FOV) were 400 mm. The whole body BS acquisition was performed 3 hours after an intravenous administration of 740 to 925 MBq ^{99m}Tc-MDP. The anterior and posterior planar BS of the whole body was acquired in our study. When an equivocal lesion was detected in spine or/and ribs on the planar whole-body scan, the additional SPECT regional tomography examination was acquired for the equivocal lesion. In SPECT imaging, a dual-head camera (scan speed between 15 and 20 cm/min, and the acquisition matrix with 256×1024) was used. The scanning time of the planar whole-body scan was approximate between 25 to 35 minutes and the time for the combination of additional SPECT regional tomography was approximate between 120 and 150 minutes. The bone scanning procedure was performed in accordance with procedure guidelines published by the Society of Nuclear Medicine.[6]

^{18}F-NaF PET-CT Detection

PET-CT examination was performed in 3-dimensional (3D) acquisition mode using a Gemini GXL 16 scanner (Philips, Netherlands). For PET, this scanner selected an axial FOV of 560 mm for whole-body scan. At half-maximum (FWHM) at center of the FOV, trans-axial spatial resolution was 4 mm full-width. The acquisition time was 2 min/bed position in 3D mode. PET was performed 60 minutes after an intravenous administration of 185 MBq ^{18}F-NaF approximately. Low-dose CT acquisition was performed before PET scan from the base of the skull to the knee with 120 kV, the upper limit was 100 mA (automated tube current) and transverse 2 and 5 mm section thickness. Using the line of response RAMLA algorithm reconstructed the PET images. CT data were used for attenuation correction.

Definition of Metastatic Bone Disease

PET-CT and SPECT were compared on the basis of patient-by-patient analysis and lesion-by-lesion analysis, and the images were interpreted independently and blindly. The interpretation of SPECT was made as a consensus result of 2 experienced nuclear medicine physicians who were aware of the clinical history and the interpretation of the PET-CT as a consensus result of an experienced radiologist and an experienced nuclear medicine physician. Interpretation of SPECT was performed according to the criteria described by Krasnow et al.[7]

Each lesion with increased uptake of ^{99m}Tc-MDP or ^{18}F-NaF was recorded and categorized as malignant (score 4), most likely malignant (score 3), equivocal (score 2), most likely benign (score 1), or benign (score 0). Abnormally increased uptake lesions were considered to indicate benignancy when they appeared as hot extravertebral osteophytes or the scintigraphic lesions uptake equal to or lower than that in the anterior iliac spine or scintigraphic lesions were involved both sides of the joint. The lesions in rib were considered to indicate malignancy when the lesions presented as elongated uptake, considered to indicate benignancy when scintigraphic lesions involved several adjacent ribs vertically, otherwise as equivocal lesions. The lesions in vertebral were considered to indicate malignancy, when scintigraphic lesions were invasive the vertebral pedicle and the posterior aspect vertebral body or when scintigraphic lesions were invasive the vertebra extensively.[8–10] The criteria for corresponding CT images of PET-CT were the following: lesions were considered to indicate benignancy when bone fractures, degenerative changes, and other benign bone lesions with angular or distinct margin such as bone cysts, compression fracture, or osteophyte. Lesions were considered to indicate malignancy if the lesions were associated with characteristic metastases on corresponding CT, such as lytic lesions with soft-tissue mass, sharply delineated osteoblastic lesion, mixed, or bone marrow changes with asymmetric increased density. If neither malignant nor benign were detected on corresponding CT with increased uptake lesions in PET, the lesions were considered as equivocal.

The final decision terms of the true status of lesions was made after considering all available clinical information, including a follow-up period of at least 6 months. When available, additional radiological studies (CT, radiographs, and magnetic resonance imaging) and ^{18}F-fluorodeoxyglucose PET-CT performed within 3 months of the bone scan were used to reach the overall decision and follow-up bone scans in some patients. Change in character or size of the lesions on radiological studies indicated malignancy, whereas a lesion was considered benign if there was no change. Lesions that showed an increase in size and/or intensity of ^{99m}Tc-MDP uptake on follow-up bone scan were considered malignant. Those that remained unchanged over 9 months without therapy were considered benign.

Statistics

Comparison of each proportion of lung cancer pathological types was performed using Wilcoxon rank sum test. Student t test was used to compare the age of the 2 groups. The sensitivity and specificity were compared with χ^2 test. All statistical tests were 2-tailed and a P-value <0.05 was considered statistically significant.

RESULTS

Patient-Based Analysis

In SPECT detection, the 167 lung cancer patients consisted of 89 adenocarcinoma patients, 30 squamous carcinoma patients, 8 SCLC patients, and 40 cancer patients with other pathological types (adenosquamous carcinoma, lymphoepithelioma-like carcinoma, large cell carcinoma, mucoepidermoid carcinoma, or sarcomatoid carcinoma). In PET-CT detection, the 181 lung cancer patients included 88 adenocarcinoma patients, 43 squamous carcinoma patients, 12 SCLC patients, and 38 other pathological type cancer patients (adenosquamous carcinoma, lymphoepithelioma-like carcinoma, large cell carcinoma, mucoepidermoid carcinoma, and sarcomatoid carcinoma). Using the Wilcoxon rank sum test, the proportions of lung cancer pathological types did not show statistically significant difference between PET-CT detection and SPECT detection ($Z = -0.390$, $P = 0.697$). We studied the 181 patients in ^{18}F-NaF PET-CT detection (age range, 29–88 years; mean age, 59.8 years) and the 167 patients in ^{99m}Tc-MDP SPECT detection (age range, 24–90 years; mean age 58.8 years). Using the Student t test, the age of 2 groups between ^{18}F-NaF PET-CT detection and ^{99m}Tc-MDP SPECT detection did not show statistically significant difference ($t = 0.832$, $P = 0.406 > 0.05$).

In ^{99m}Tc-MDP SPECT detection, 137/167 patients were correctly diagnosed with SPECT, 56/167 patients had metastatic bone disease based on biopsy and imaging follow-up. SPECT missed 6 patients who were identified with BM based on biopsy and imaging follow-up (Figure 1) and also produced 19 equivocal patients (14 BM patients and 5 benign patients)

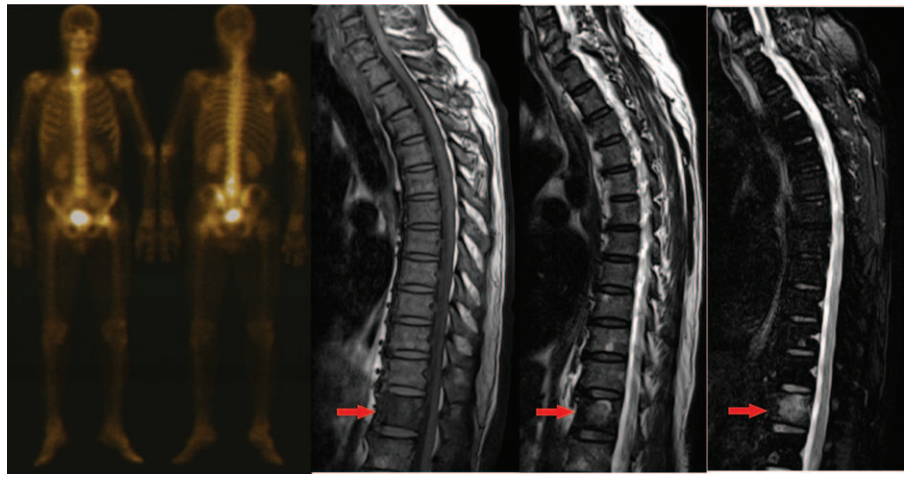

FIGURE 1. A misdiagnosed patient in SPECT who was confirmed to be a bone metastatic patient and finally diagnosed with lung adenocarcinoma at 62 years of age. ^{99m}Tc-MDP SPECT cannot detect the lesion which was detected by MR (MRI detected a bone destruction in the first lumbar vertebra, lower signal in T1WI, high signal in T2WI, and fat-suppression T2WI with significantly high signal). MRI = magnetic resonance imaging, ^{99m}Tc-MDP = 99m-technetium methylene diphosphonate, SPECT = single photon emission computed tomography.

and 5 false-positive patients. In PET-CT detection, 177/181 patients were correctly diagnosed with ^{18}F-NaF PET-CT; 48/181 patients had metastatic bone disease. Only 4 equivocal patients (3 metastases patients [Figure 2] and 1 benign patient) were diagnosed by ^{18}F-NaF. The result of ^{18}F-NaF PET-CT and ^{99m}Tc-MDP SPECT detection are summarized in Table 1. In summary, as a result of ^{99m}Tc-MDP SPECT and ^{18}F-NaF PET-CT detection, the number of equivocal patients was reduced and the clinical management was changed by the ^{18}F-NaF PET-CT based on patient analysis. ^{18}F-NaF PET-CT was significantly better than ^{99m}Tc-MDP SPECT in producing equivocal patients ($\chi^2 = 9.005$, $P = 0.03$). We analyzed the results twice: categorizing the equivocal reading as suggestive of malignancy, and categorizing the equivocal reading as benign. When the equivocal reading was categorized as malignant, ^{18}F-NaF PET-CT misdiagnosed only 1 patient, while 16 patients were misdiagnosed by ^{99m}Tc-MDP SPECT. Using the Chi-square correction method, there was a statistically significant difference ($\chi^2 = 13.356$, $P < 0.001$). When the equivocal reading was categorized as benign, ^{18}F-NaF PET-CT misdiagnosed 3 patients, while ^{99m}Tc-MDP SPECT misdiagnosed 25 patients, which indicated a statistically significant difference ($\chi^2 = 19.046$, $P < 0.001$).

Table 2 summarizes the sensitivity, specificity, accuracy, PPV, and NPV of ^{99m}Tc-MDP SPECT detection and ^{18}F-NaF PET-CT detection. Using the Fisher exact probabilities test and the Chi-square correction method, sensitivity and specificity of PET-CT was significantly better than that of SPECT when equivocal reading was categorized as malignant ($P = 0.029$, $P = 0.005$, respectively). A similar result was seen when equivocal reading was categorized as benign ($P = 0.001$, $P = 0.019$, respectively).

Lesion-Based Analysis

Using ^{99m}Tc-MDP SPECT, 333 bone lesions were detected (Table 3). Of the 260 bone metastatic lesions, ^{99m}Tc-MDP

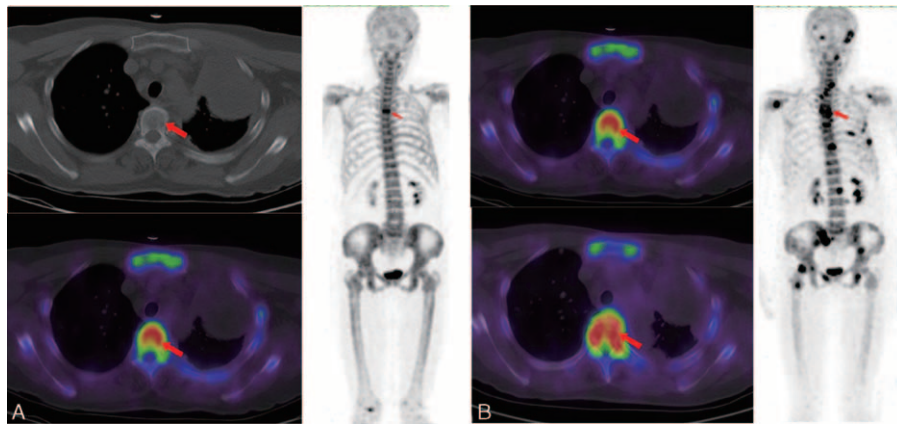

FIGURE 2. An equivocal lesion which was confirmed as metastatic lesion finally in a 56-year-old patient with lung adenocarcinoma. (A) The first ^{18}F-NaF PET-CT detection. (B) Follow-up ^{18}F-NaF PET-CT detection after 2 months. The morphologic and metabolic changes of the lesion were detected compared with the 2 PET-CT detections. More other metastatic lesions are seen in (B). ^{18}F-NaF = ^{18}F-labeled sodium fluoride, PET-CT = positron emission tomography-computer tomography.

TABLE 1. Equivocal Patients and Lesions in ^{18}F-NaF PET-CT and ^{99m}Tc-MDP SPECT for Detection of Bone Metastases

Finding	^{18}F-NaF PET-CT	^{99m}Tc-MDP SPECT
Total	181 (991)	167 (333)
Equivocal	4 (5)	19 (26)

The data in parentheses is equivocal lesion number based on lesion level analysis. ^{18}F-NaF = ^{18}F-labeled sodium fluoride, ^{99m}Tc-MDP = 99m-technetium methylene diphosphonate, PET-CT = positron positron emission tomography-computer tomography, SPECT = single photon emission computed tomography.

SPECT missed 10 lesions (4 at the rib cage, 3 at thoracic spine, 1 at lumbar spine, and 2 at pelvis), which were identified to be BM on the basis of biopsy and imaging follow-up; and also produced 26 equivocal lesions (20 BM lesions and 6 benign lesions) and 8 false-positive lesions (1 at the skull, 5 at rib cage, and 2 at lumbar spine). One lesion was underestimated in the skull by ^{99m}Tc-MDP SPECT. In ^{18}F-NaF PET-CT detection, 991 lesions were assessed (Table 3). Of the 900 metastatic bone lesions, only 5 equivocal lesions (4 BM lesions and 1 benign lesion) were produced. There were no false-positive lesions or false-negative lesions. Table 1 summarizes the results of ^{18}F-NaF PET-CT and ^{99m}Tc-MDP SPECT. ^{18}F-NaF uptake was associated with corresponding morphologic changes on the CT part of the study in 816/900 identified metastases. The only remaining 84 metastases presented with increased ^{18}F-NaF uptake and normal CT findings (Figure 3). One patient about 10/100 osteolytic metastatic bone lesions had no ^{18}F-NaF uptake associated with corresponding osteolytic changes in PET-CT.

In summary, the results of ^{99m}Tc-MDP SPECT and ^{18}F-NaF PET-CT suggested that the number of equivocal lesions was also reduced and the clinical management was changed by the ^{18}F-NaF PET-CT base on lesion analysis. ^{18}F-NaF PET-CT detection was significantly better than ^{99m}Tc-MDP SPECT in producing equivocal lesions ($\chi^2 = 58.141$, $P < 0.001$). We also analyzed the results twice by categorizing the equivocal lesions that were diagnosed as suggestive of malignancy and, again, categorizing the equivocal lesion reading as benign. When the equivocal reading was categorized as malignant, ^{18}F-NaF PET-CT misdiagnosed only 1 lesion while 25 lesions were misdiagnosed by ^{99m}Tc-MDP SPECT. Using the Chi-square correction method, there was statistically significant difference ($\chi^2 = 67.227$, $P < 0.001$). When the equivocal reading was categorized as benign, ^{18}F-NaF PET-CT misdiagnosed 4 lesions, while ^{99m}Tc-MDP SPECT misdiagnosed 39 lesions. There was also statistically significant difference between ^{18}F-NaF PET-CT and ^{99m}Tc-MDP SPECT ($\chi^2 = 97.863$, $P < 0.001$).

Using the Fisher exact probabilities test and the Chi-square correction method, sensitivity and specificity of PET-CT was significantly better than that of SPECT when equivocal lesions reading was categorized as malignant ($P < 0.001$) as well as benign ($P = 0 < 0.05$, $P = 0.001$). There was also statistically significant difference between ^{18}F-NaF PET-CT and ^{99m}Tc-MDP SPECT when equivocal reading was categorized as benign ($P < 0.001$, $P = 0.001$, respectively).

TABLE 3. Location and Final Diagnosis of Bone Lesions With ^{18}F-NaF PET-CT and ^{99m}Tc-MDP SPECT

		Diagnosis		
Body Region	No. of Lesions	Malignant	Equivocal	Benign
Skull	69 (25)	59 (18)	0 (1)	10 (6)
Cervical spine	62 (14)	55 (10)	0 (2)	7 (2)
Rib cage	281 (101)	252 (74)	0 (15)	29 (12)
Thoracic spine	153 (46)	146 (46)	1 (0)	6 (0)
Lumbar spine	120 (49)	107 (26)	3 (3)	10 (20)
Pelvis	215 (55)	210 (47)	1 (5)	4 (3)
Long bones	91 (43)	67 (19)	0 (0)	24 (24)

The data in parentheses is bone lesion number based on ^{99m}Tc-MDP SPECT detection. ^{18}F-NaF = ^{18}F-labeled sodium fluoride, ^{99m}Tc-MDP = 99m-technetium methylene diphosphonate, PET-CT = positron positron emission tomography-computer tomography, SPECT = single photon emission computed tomography.

TABLE 2. Detection of Bone Metastases in Lung Cancer by ^{99m}Tc-MDP SPECT and ^{18}F-NaF PET-CT

	Final Diagnosis										
	Metastases			No Metastases			Interpretation, %				
Modality	M	E	B/N	M	E	B/N	Sensitivity	Specificity	Accuracy	PPV	NPV
Base on patients											
SPECT	36	14	6	5	5	101	89.3 (64.3)	91.0 (95.5)	90.4 (85.0)	83.3 (87.8)	94.4 (84.1)
PET-CT	45	3	0	0	1	132	100 (93.8)	99.2 (100)	99.4 (98.3)	98.0 (100)	100 (97.8)
Base on lesions											
SPECT	229	20	11	8	6	59	95.8 (88.1)	80.8 (89.0)	92.5 (88.3)	94.7 (96.6)	84.3 (67.7)
PET-CT	896	4	0	0	1	90	100 (99.6)	98.9 (100)	99.9 (99.6)	99.9 (100)	100 (95.8)

Analysis considering equivocal results as positive for malignancy. In parentheses, analysis considering equivocal results as negative for malignancy. B/N = benign or normal, E = equivocal, ^{18}F-NaF = ^{18}F-labeled sodium fluoride, M = malignant, ^{99m}Tc-MDP = 99m-technetium methylene diphosphonate, NPV = negative predictive value, PET-CT = positron emission tomography-computer tomography, PPV = positive predictive value, SPECT = single photon emission computed tomography.

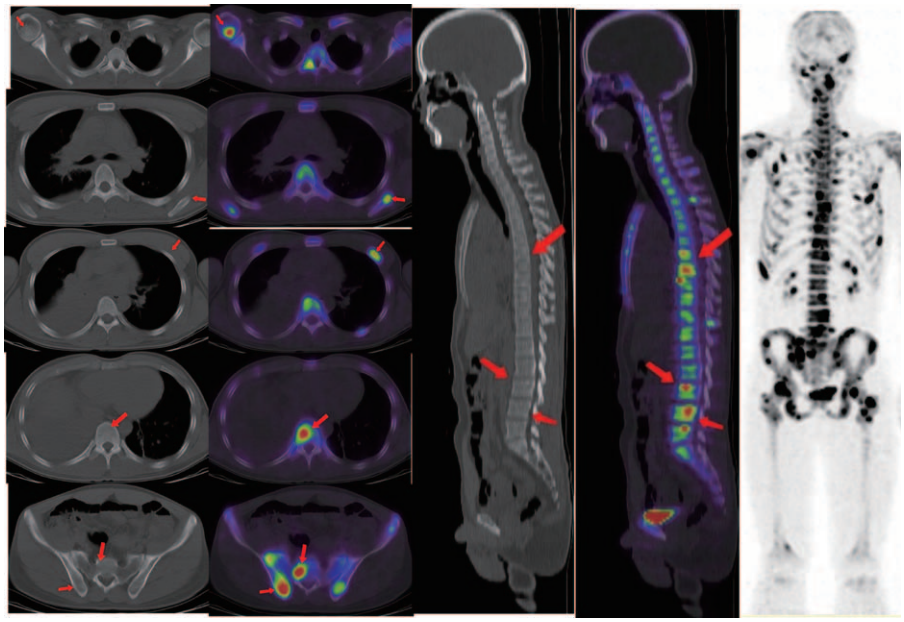

FIGURE 3. The metastatic lesions with abnormal ^{18}F-labeled sodium fluoride (^{18}F-NaF) uptake showed no morphologic changes like osteoblastic or osteolytic changes in a 33-year-old patient with lung adenocarcinoma.

DISCUSSION

Lung cancer is the most common malignant tumor, and the skeleton is a common site of distant metastases in lung cancer. BM occurs in 30% to 36% of lung cancer patients.[1–3] The diagnosis of a patient as having malignant or benign disease on bone scan has profound influence on the management of a lung cancer patient, and the presence of BM indicates shortened patient survival time.[11] Hence, early detection of BM is of high clinical importance in the management of patients with lung cancer and accurate staging for the selection of the appropriate therapy.

Although conventional planar BS is sensitive for detected the advanced bone metastatic lesions, early involvement metastatic lesion may be missed because the planar BS or SPECT relies on the identification of the bone osteoblastic reaction and the blood flow rather than directly detected the tumor itself.[12]

^{18}F-NaF PET has been shown to be superior to conventional planar BS and SPECT in the detection of BM by several studies because it detects the presence of lesion directly by bone mineral metabolism rather than indirectly showing lesion involvement owing to the increased bone mineral turnover especially in lesions with pathologic changes.[13,14] ^{18}F-NaF is an excellent radiopharmaceutical for bone imaging, because fluoride ions is an analog of the hydroxyl group found in the hydroxyapatite bone crystals, which exchange with hydroxyl groups in hydroxyapatite bone crystals to form fluoroapatite. Accompanied by very rapid blood clearance, fluoride ions have the desirable characteristics of rapid and high bone uptake, which results in high bone-to-background ratio in a short time.[15] Fluoride ions are characterized by a 2-fold higher bone uptake than ^{99m}Tc-MDP. High-quality images of the bone can be obtained less than 1 hour after the ^{18}F-NaF intravenous injected. Moreover, ^{18}F-NaF in sclerotic and lytic lesions reflects increased regional blood flow and bone turnover.[14,16] These have allowed the detection of metastatic bone lesion earlier with PET than with BS.[17]

However, ^{18}F-NaF is not tumor specific radiopharmaceutical and, therefore, prone to a high false-positive rate.[18,19] Although PET has been proved to be an effective tool in the management of malignant tumor patients, it provides limited information of the bone lesion morphologic abnormalities. Differentiation between benign lesions and malignant bone lesions is obtained by further validation (CT or magnetic resonance imaging). The remarkable nuclear medicine technological developments in positron imaging devices combined with coregistration CT have resulted in a renewed interest in^{18}F-NaF. Thus, ^{18}F-NaF PET-CT detection can provide precise information regarding both the morphologic and bone mineral metabolism changes occurring in BM, so the specificity of ^{18}F-NaF PET in BM detection can be improved by the use of PET-CT system.[14–16] In our study, 816/900 metastases identified ^{18}F-NaF uptake as associated with corresponding morphologic changes on the CT part of the study. The only remaining 84 metastases cases presented with increased ^{18}F-NaF uptake and normal CT findings (Figure 3). The morphologic characterization of scintigraphic lesions by PET-CT resulted in a lower percentage of equivocal interpretations compared with interpretation of ^{99m}Tc-MDP SPECT, both on patient-based analysis and on lesion-based analysis. The increased clinical accuracy of BM, high-quality images of the bone, greater convenience to referring physicians and patients, and more efficient use of nuclear medicine resources all indicate that the ^{18}F-NaF PET-CT for imaging malignant diseases of the skeleton is very valuable.[13,10]

The use of SPECT imaging alone improves diagnostic accuracy of BM because it enables location, especially in the vertebrate.[9,20] However, it is often insufficient for the precise location and the morphologic abnormalities of bone lesions. In our study, 6 BM patients were missed by SPECT; and also produced 19 equivocal patients and 5 false-positive patients. PET-CT serves as a positron imaging device of correlating anatomical information from CT with functional information from PET, and ^{18}F-NaF is characterized as a 2-fold higher bone uptake than ^{99m}Tc-MDP, hence enabling more accurate localization and characterization of PET lesions by using the CT component. This is of great benefit in

complex structures such as vertebrae (e.g., pedicle or facet joint, respectively) where the localization and morphologic abnormalities of a lesion determines as malignant or benign.[9] Based on the corresponding CT images of PET-CT, lesions were considered to indicate benignancy when bone fractures, degenerative changes, and other benign bone lesions with angular or distinct margin such as bone cysts, fracture, or osteophyte. Lesions were considered to indicate malignancy if the lesions were associated with characteristic metastases on corresponding CT, such as lytic lesions with soft-tissue mass, sharply delineated osteoblastic lesion, mixed, or bone marrow changes with asymmetric increased density. Specificity of the PET-CT is also enhanced from information on the CT characteristics of lesions, which assisted in distinguishing benign lesions from malignant lesions. In our study, only 4 patients and 5 equivocal lesions were produced by ^{18}F-NaF PET-CT. Although ^{18}F-NaF is characterized by a 2-fold higher bone uptake than ^{99m}Tc-MDP, we found that 1 patient in about 10/100 osteolytic metastatic bone lesions had no ^{18}F-NaF uptake associated with corresponding osteolytic changes in PET-CT detection. So, the CT plays an important part in diagnosing these lesions without ^{18}F-NaF uptake.

Compared with ^{99m}Tc-MDP SPECT, ^{18}F-NaF PET-CT showed higher accuracy in detecting BM lesions. The lesion-by-lesion analysis suggests that ^{18}F-NaF PET-CT had not only a much higher rate in detecting bone lesions but also a higher accuracy in differentiating benign lesions from metastasis lesions compared with ^{99m}Tc-MDP SPECT, and there is a significant reduction in the number of equivocal diagnosis and a significant increase in accuracy from ^{99m}Tc-MDP SPECT to ^{18}F-NaF PET-CT, regardless of whether or not patients complained of bone pain. In our study, frequent BM lesions detected by ^{18}F-NaF PET-CT or ^{99m}Tc-MDP SPECT were located in vertebra and rib cage and pelvis, whereas skull was an uncommon location of BM lesion. These results are in agreement with those of other studies.[4,10,13]

Since data collection was performed retrospectively, selection bias may have affected our results. Limitations of this study include the relatively small number of patients, different samples in ^{99m}Tc-MDP SPECT and ^{18}F-NaF PET-CT, and most final diagnosis of lesions were achieved by means of clinical follow-up, including imaging tests. Obtaining histologic proof of all lesions is impractical and unethical when there is no impact in the clinical management. Another limitation is that the number of lesions on the lesion-based analysis should be limited to a certain extent, because rare patients with too much true positive lesions detected by PET-CT may influence the result of this study.

CONCLUSION

This study found that ^{18}F-NaF PET-CT is a highly sensitive as well as specific modality for the detection of BM in patients with lung cancer. It is more specific and more sensitive than SPECT. ^{18}F-NaF PET-CT accurately differentiated malignant lesions from benign lesions and possibly helped to identify potential cause for bone pain in oncologic patients and may beneficially impact the clinical management of patients.

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