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Original Article

A Comparison of Bone Scan Using between F-18 NaF PET/CT and Tc-99m MDP

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Abstract

Objective: To study bone scintigraphy using between F-18 NaF PET/CT and Tc-99m MDP scan for detecting bone metastases.

Material and Methods: Thirteen patients (5 males, mean age 55.4 years, range 34-74 years) who were suspected bone metastases with single or two equivocal lesions on Tc-99m MDP bone scan were recruited between October 2010 and October 2012. All these patients underwent F-18 NaF PET/CT scan within one week after Tc-99m MDP bone scan. The sensitivity, specificity and accuracy of Tc-99m MDP bone scan and F-18 NaF PET/CT in differentiating metastatic bone lesion from benign lesion by patient-based and lesion-based analyses were studied.

Results: F-18 NaF PET/CT could identify all seven patients with malignant bone metastases that Tc-99m MDP bone scan was interpreted as malignancy in only three patients (42.9%) and equivocal in the rest of these patients. For lesion-based analysis of the overall 75 lesions, the sensitivity, specificity and accuracy of Tc-99m MDP bone scan were 48%, 83.3% and 70.7% and F-18 NaF PET/CT were 100% for all parameters. Besides the ability of F-18 NaF PET/CT to accurately identify malignancy from benign lesion, unenhanced CT portion of PET/CT can show extra-osseous findings that may change patient management.

Conclusion: F-18 NaF PET/CT provides an excellent bone image quality and higher accuracy than Tc-99m MDP bone scan. Then F-18 NaF PET/CT is a good choice for evaluating bone metastases.

Keywords: Bone scan, F-18 NaF PET/CT, Tc-99m MDP, bone metastases.

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Introduction

Bone metastases are the most common malignant bone tumor and occur in 30%-70% of all cancer patients(1). In 1971, Subramanian and McAfee developed Tc-99m MDP for bone imaging and this technique has been the method of choice for routine skeletal surveys(2,3). Although F-18 NaF (511 keV; half-life, 110 minutes) was introduced as a radiopharmaceutical for bone imaging by Blau et al in 1962, the image quality of a gamma camera was poor because it performed best at lower energy levels(4,5). In the early 1990s, Phelp et al used F-18 NaF as a model for the development of whole body PET because of the favorable skeletal kinetics of F-18 NaF(6).

For the past few years, there was a problem with Tc-99m shortage that affected nuclear medicine services around the world. Reimbursement for F-18 NaF was approved by Centers for Medicare and Medicaid Services and many nuclear medicine centers in the USA started to use this radiopharmaceutical for routine PET bone scan.

The aim of this study was to prospectively compare the detection of bone metastases by Tc-99m MDP planar bone scan and F-18 NaF PET/CT in patients with a known primary tumor.

Materials and Methods

Subjects

Descriptive prospective study was performed at Division of Nuclear Medicine, Faculty of Medicine Siriraj Hospital between October 2010 and October 2012. Thirteen patients (5 male and 8 female: mean age 55.4±10.6 years; range 34-74 years) were referred for evaluation of suspected (11 patients) or progression (2 patients) of bone metastases in the course of the disease. The patients had various oncologic diseases including cancer of the breast (n = 6) and one patient in each of the following cancers of thyroid, prostate, ovary, colon, pyriform sinus, kidney and nasopharynx. The study was approved by the Siriraj Ethics Committee for Human Experiment and a written informed consent was obtained from each subject.

Planar whole body bone images were performed 3 hours after intravenous injection of 20 mCi Tc-99m MDP using a dual-head gamma camera (Infinia Hawk Eye: GE Healthcare). F-18 NaF PET/CT study was studied within 1 week after Tc-99m MDP bone scan. Imaging was performed 60 minutes after intravenous injection of 10 mCi F-18 NaF using a Discovery PET/CT system (GE Healthcare). Low-dose CT acquisition was performed first with 140 kV, 80 mA, 0.8 seconds per CT rotation, a pitch of 6 and a table speed of 22.5 mm/second. A PET emission scan was performed immediately after acquisition of the CT without changing patient's positioning. Five to 7 bed positions were performed with an acquisition time of 3 minutes per bed from skull to midthigh. PET images were reconstructed using an ordered-subsets expectation maximization algorithm. CT data were used for attenuation correction. Studies were interpreted on a Xeleris workstation.

Image interpretation

Whole body bone scan and F-18 NaF PET/CT were interpreted blindly and separately. Interpretation of PET/CT was done as a consensus reading of a nuclear medicine physician and a radiologist. Each area of abnormal increased uptake of Tc-99m MDP or F-18 NaF was categorized as normal, benign, equivocal or malignant. Lesions on bone scan were classified as benign when they appeared as hot osteophytes or located around joints. Vertebral lesions were categorized as malignant when they involved the posterior aspect of the vertebral body and pedicle or involved the vertebra extensively[7]. Rib lesions were considered malignant when they appeared as elongated uptake. When they involved vertically several ribs, they were categorized as benign. CT data of PET/CT were used to categorize as benign when they appeared at the corresponding areas as degenerative changes, fractures or benign bone lesions. The osteoblastic metastases were classified as malignancy. Lesions not classified as benign or malignant were categorized as equivocal. Lesions on F-18 NaF PET/CT that were not visible on bone scan were classified as normal on bone scan. Patients were monitored for 6 months and the final diagnosis was concluded from their medical records.

Statistical analysis

Both patient-based and lesion-based analyses were performed. The sensitivity, specificity, accuracy, positive predictive value and negative predictive value with 95% confidence intervals were analyzed for the diagnosis of bone metastases from benign lesion.

Results

Patient-based analysis

From 13 patients, seven patients (53.8%) had bone metastases according to definite F-18 NaF PET/CT findings and follow-up imaging. A lesion with abnormal increased uptake on F-18 NaF PET scan was identified as bony metastasis if CT data of the corresponding area also showed osteoblastic metastasis. Thus F-18 NaF PET/CT could identify all 7 patients with malignant bone metastases. The rest of patients had benign bone lesions which were determined by benign findings at the corresponding location on CT part of F-18 NaF PET/CT. Follow-up for at least 6 months of these patients with benign bone lesions had no clinical or imaging evidence of bone metastasis.

In 7 patients with bone metastases on F-18 NaF PET/CT, Tc-99m MDP bone scan was interpreted as equivocal (n=4; 57.1%) and malignancy (n=3; 42.9%) (Table 1). In 6 patients with benign PET/CT findings, planar bone scan was interpreted

Table 1 Assessment of bone metastases by Tc-99m MDP planar bone scan (BS) and F-18 NaF PET/CT (PET/CT) in 13 patients

	Final diagnosis					
	Bone metastases (n=7)			No bone metastases (n=6)		
Modality	Metastases	Equivocal	Benign	Metastases	Equivocal	Benign
BS	3	4	0	0	3	3
PET/CT	7	0	0	0	0	6

Table 2 Location and diagnosis of 74 lesions seen on F-18 NaF PET/CT

Site of increased F-18 NaF uptake	Number of lesions	Diagnosis	
		Malignant	Benign
Skull	5	1	4
Spine	30	4	25
Thorax	17	10	6
Pelvis	15	9	7
Long bones	8	2	6
Total	75	27 (36%)	48 (64%)

as equivocal (n=3; 50%) and benign lesion. Among 7 patients with equivocal results on planar bone scan, PET/CT accurately identified the presence of bony metastases in 4 patients (57.1%) and excluded bone metastases in 3 patients (42.9%).

Lesion-based analysis

Seventy-five lesions with increased F-18 NaF uptake were studied. Location and final diagnosis of these lesions were shown in Table 2. Twenty-seven lesions (36%) showed osteblastic metastases on the CT part of the PET/CT images. Fourty-eight lesions (64%) showed benign abnormalities on the CT part in the corresponding location with increased F-18 NaF uptake.

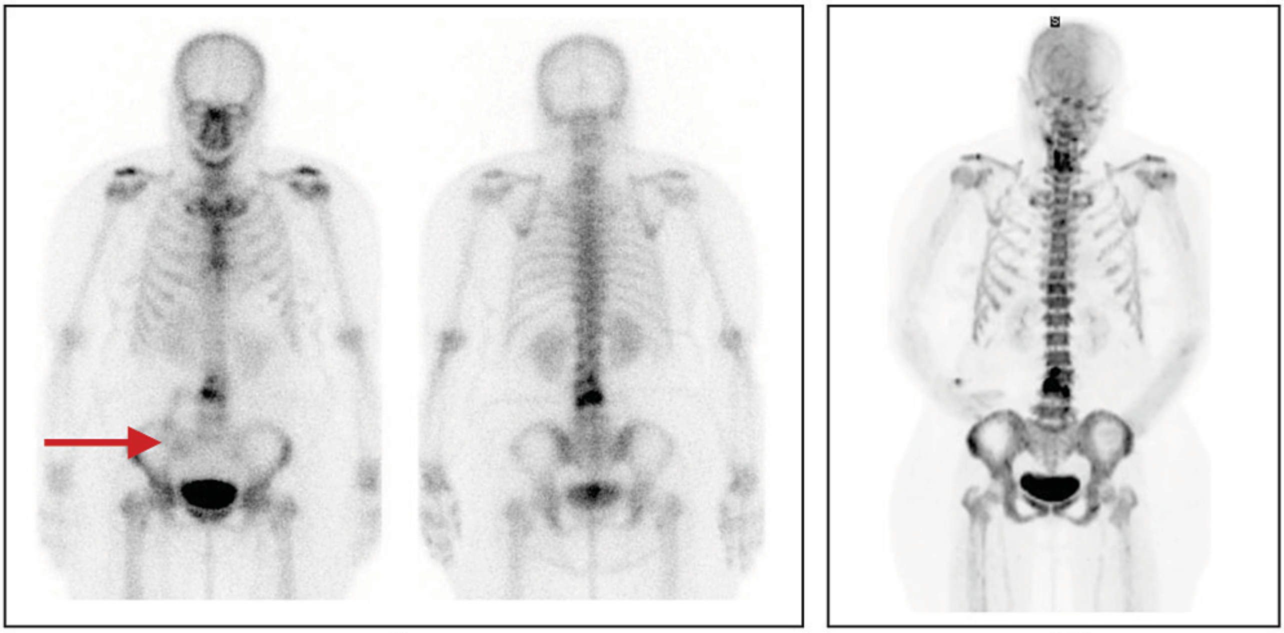
In 27 bone metastatic lesions on PET/CT, bone scan was interpreted as benign/normal (n=14; 51.9%), equivocal (n=8; 29.6%) and malignancy (n=5; 18.5%) (Table 3). In 48 benign bone lesions on PET/CT findings, bone scan was interpreted as benign/normal (n=40; 83.3%), equivocal (n=7; 14.6%) and malignancy (n=1; 2.1%). Among 15 equivocal lesions on bone scan, PET/CT accurately confirmed the presence of bony metastases in 8 lesions (53.3%) and excluded bone metastases in 7 lesions (46.7%). There were 3 equivocal lesions on bone scan that PET/CT demonstrated no abnormality in one lesion (Fig 1) and extra-osseous abnormalities in 2 lesions (Fig 2).

Additional extra-osseous findings on unen-hanced CT images of F-18 NaF PET/CT scan

The unenhanced CT images of F-18 NaF PET/CT scan were analyzed. From 13 patients, 6 patients (46.2%) showed additional extra-osseous findings which four of them were previously known before their participation in this study (Table 4). The other two patients showed clinically significant new extra-osseous findings. In one patient, there was progression of right mastoiditis (patient no. 2) while the other patient (patient no. 4) showed multiple new abnormal lesions as followed: a mass in descending colon with pericolic nodes, a nodule at right peri-renal and right buttock and a mass at left lateral aspect of urinary bladder (Fig 2).

Table 3 Assessment of bone metastases by Tc-99m MDP bone scan (BS) and F-18 NaF PET/CT (PET/CT) (lesion-based)

		Diagnosis		Sensitivity(%)	Speciificity(%)	Accuracy(%)	PPV(%)	NPV(%)
		Malignant	Benign	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
BS	+	13	8	48.1	83.3	70.7	61.9	74.1
	-	14	40	(28.7, 68.1)	(69.8, 92.5)	(59.0, 80.6)	(38.4, 81.9)	(60.4, 85.0)
PET/CT	+	27	0	100	100	100	100	100
	-	0	48	(87.2, 100)	(92.6, 100)	(95.2, 100)	(87.2, 100)	(92.6, 100)



A) B)

Fig 1 A) Planar bone scan anterior and posterior show equivocal lesion at right iliac bone (arrow) from artifact as compared with normal appearance on F-18 NaF PET (B).

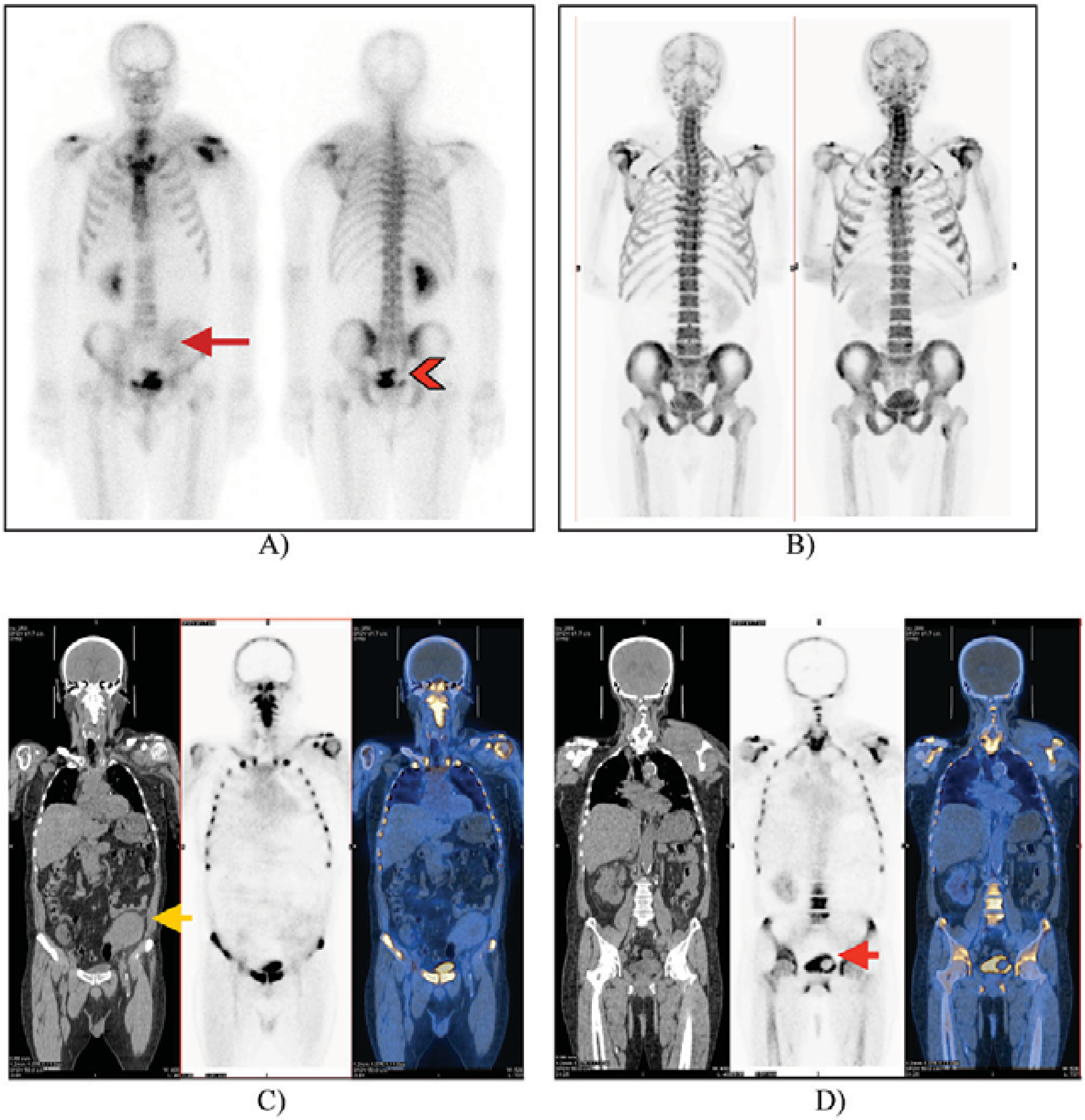


Fig 2 A) Anterior and posterior planar bone scan show two equivocal lesions at left iliac bone (arrow) and scarum (arrow head) B) PET/CT clearly demonstrated false-positive lesions from C) colonic mass in the left lower abdomen superimposed left iliac bone (arrow) and D) recurrent mass in left lateral aspect of urinary bladder (arrow) mimics lesion in sacrum.

Table 4 Additional extra-osseous findings on unenhaced CT of F-18 NaF PET/CT

Patient no.	Age (years)	Sex	Type of cancer	Incidental findings on CT
1	48	M	Cancer of pyriform sinus	- A large mass at right oropharynx - Cervical metastatic lymph nodes - Active chronic lung disease
2	54	M	Naopharyngeal cancer	- Right mastoiditis
3	65	F	Thyroid cancer	- Pulmonary nodule and right paratracheal node
4	57	M	Renal carcinoma	- Pulmonay metastases - Mediastinal and abdominal lymphadenopathy - A mass in descending colon with pericolic nodes - A nodule at right perirenal and right buttock - A mass at left lateral aspect of urinary bladder
5	49	F	Breast cancer	- Atelectasis and pleural thickening post radiation fibrosis with pulmonary metastases
6	49	F	Breast cancer	- Right pleural mass and effusion

Discussion

Tc-99m MDP bone scan is a well-accepted imaging for the detection of bone metastases due to its high sensitivity and cost-effectiveness but its main drawback is lack of specificity[8]. The uptake mechanism of F-18 NaF in the skeleton is dependent on regional blood flow and new bone formation resembles that of Tc-99m MDP but has better pharmacokinetic characteristics including faster blood clearance and twice higher uptake in the bone[9]. At the beginning, imaging of 511-keV annihilation photons produced by the decay of F-18 was not suitable by gamma-camera but the use of PET/CT machine has significantly improved the specificity of F-18 NaF imaging as the CT component can demonstrate morphologic characterization of abnormal uptake and accurately differentiate between benign and metastatic lesion[9,10].

In this study, most of the equivocal lesions on planar bone scan were found in ribs (n = 6). Four patients in this group have their rib lesions as a single bone scan abnormality. This is an especially difficult group which was found around 7% of patients with bone metastases[11]. The probability of a malignant cause for a solitary increased uptake in patients with a known primary cancer varies with the site of the abnormality on bone scan. Tumeh et al reported that solitary rib lesions were rare in cancer patient and were usually due to benign disease[12]. McNeil estimated the frequency of a malignant cancer in a solitary rib lesions vary between 1% and 17%[13]. In our four patients with a single rib abnormality, three patients had rib fracture and only one patient had osteoblastic bony metastasis. The rest of equivocal ribs on bone scan (n = 2) were osteoblastic bony metastases. Other equivocal lesions on bone scan were found in the spines (n = 5), pelvis (n = 3) and skull (n = 1). Two lesions in lumbar spines were degenerative changes as clearly demonstrated on CT part of PET/CT (Fig 3). These two lesions were confirmed on follow-up MRI scan. Bony destruction was clearly identified in other three equivocal spine lesions on CT part of PET/CT (Fig 4). All three equivocal lesions in the pelvis were false-positive which were clearly identified on CT part of PET/CT as shown in Fig 1 and Fig 2. Therefore all equivocal bone scan abnormalities should be correlated with the results of other more specific investigations. In clinical practice, a radiograph of the area showing abnormal uptake should be obtained. If standard radiographs were normal, CT of bone can be used in evaluating the significance of a scan abnormality[14,15]. Thus the use of hybrid PET/CT or SPECT/CT systems can significantly improved the specificity of bone imaging by the combination of cross-sectional functional and anatomic imaging for definite diagnosis.

This study showed that the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of Tc-99m MDP bone scan were 48%, 83.3%, 70.7%, 61.9% and 70.7%, respectively and F-18 NaF PET/CT were 100% for all parameters. The similar result were published by Even-Sapir, et al who reported the sensitivity, specificity, positive predictive value and negative predictive value of Tc-99m MDP bone scan of 70%, 57%, 64%, and 55% and F-18 NaF PET/CT of 100% for all parameters[7]. Besides the ability of F-18 NaF PET/CT to accurately identify malignancy from benign lesion, unenhanced CT portion of PET/CT can show extra-osseous findings that may change patient management.

Many research showed that NaF-18 bone scan with PET/CT has undoubtedly superiority than Tc-

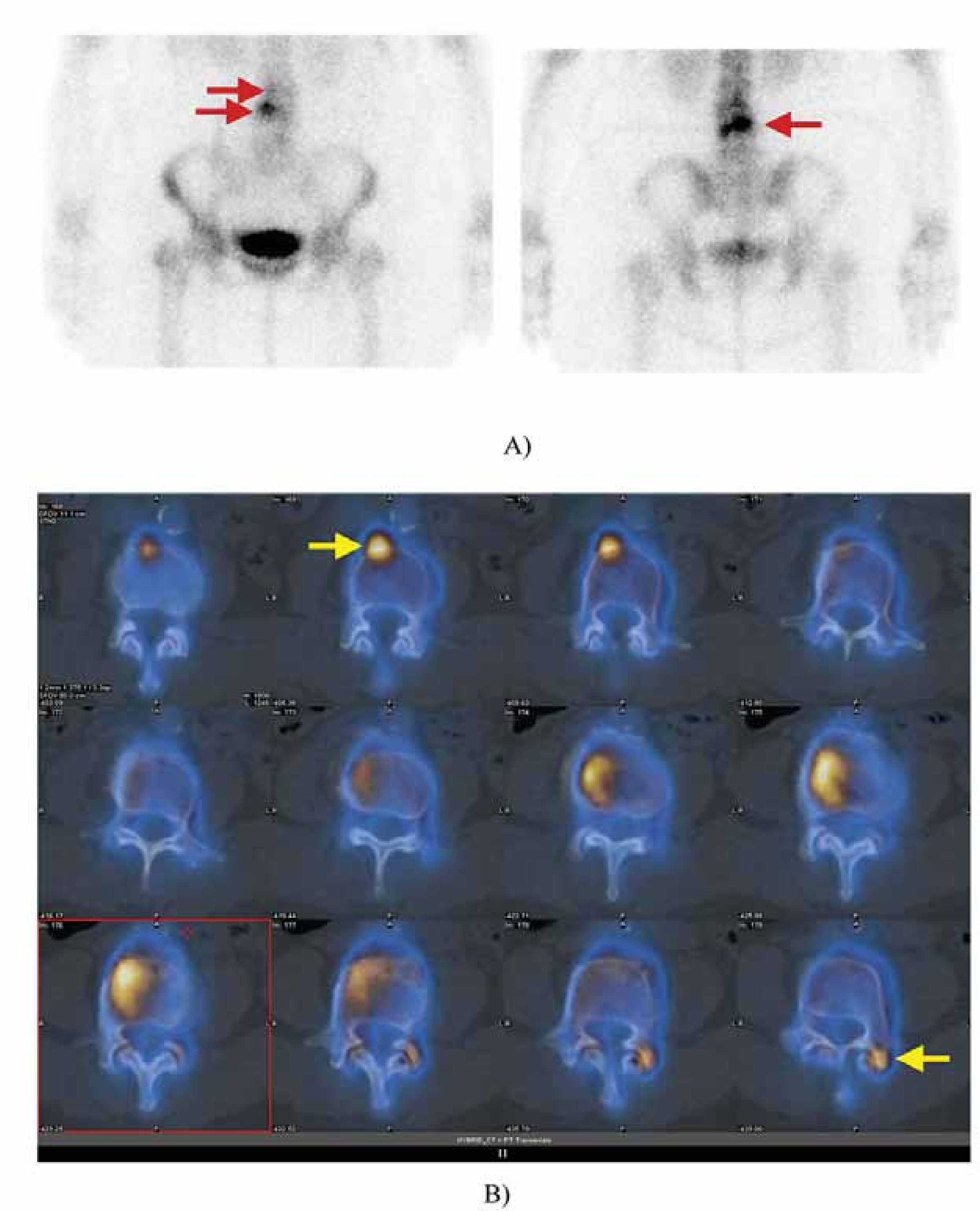
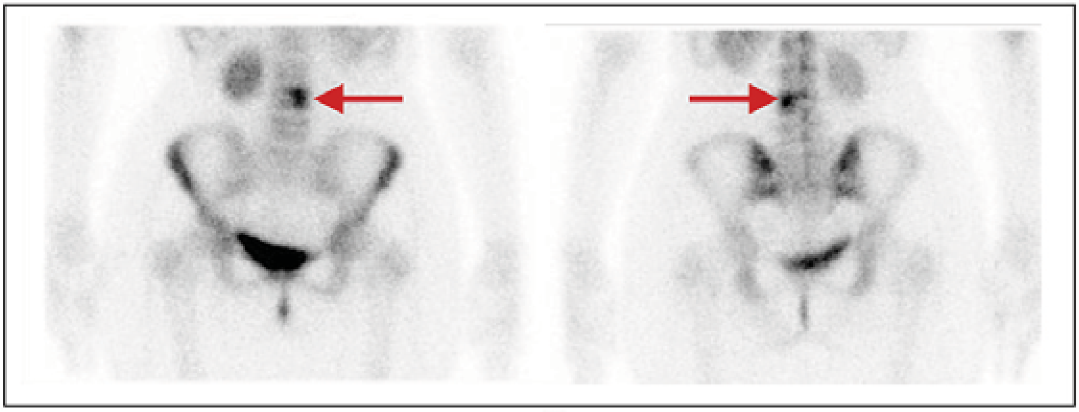
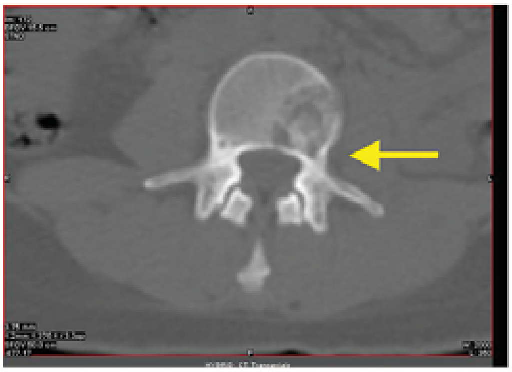


Fig 3 A) Anterior and posterior spot images of Tc-99m bone scan show increased radioactivity uptake at L3 and L4 (arrows) B) Fusion PET/CT image shows degenerative change at L3 and L4 (arrow)



A)



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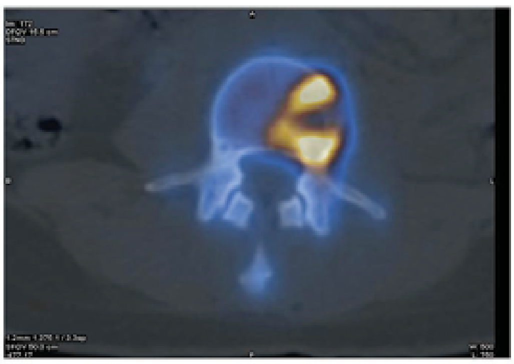

D)

Fig 4 A) Anterior and posterior spot images of Tc-99m bone scan show increased radioactivity uptake at left aspect of L4 (anterior) B) CT part of PET/CT image shows bony destruction (arrow) C) PET shows abnormal metabolism at the corresponding bony destruction (arrow) and D) Fusion PET/CT of bony metastasis.

99m MDP with gamma camera and similarly to this study. At present, PET/CT seems to be under-used in Thailand due to the cost of the study. Bone imaging with NaF-18 PET/CT may be a good option for the patient who can afford the cost but rewarding in terms of higher accuracy in identifying malignancy. This study would like to introduce the new option for bone metastases imaging.

Conclusion

Tc-99m MDP bone scan is good for screening abnormal bone lesions but specificity is poor while F-18 NaF PET/CT is superb in characterization of abnormal bone lesions. Even though the cost of PET/CT is relatively high, higher accuracy in identifying malignancy is rewarded. Then F-18 NaF PET/CT is a good choice for evaluating bone metastases.

Acknowledgements

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