

Original Article

Diagnostic role of $^{99}\text{Tc}^{\text{m}}$ -MDP SPECT/CT combined SPECT/MRI Multi modality imaging for early and atypical bone metastases

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Abstract: The bone metastasis appeared early before the bone imaging for most of the above patients. $^{99}\text{Tc}^{\text{m}}$ -MDP ($^{99}\text{Tc}^{\text{m}}$ marked methylene diphosphonate) bone imaging could diagnosis the bone metastasis with highly sensitivity, but with lower specificity. The aim of this study is to explore the diagnostic value of $^{99}\text{Tc}^{\text{m}}$ -MDP SPECT/CT combined SPECT/MRI Multi modality imaging for the early period atypical bone metastases. 15 to 30 mCi $^{99}\text{Tc}^{\text{m}}$ -MDP was intravenously injected to the 34 malignant patients diagnosed as doubtful early bone metastases. SPECT, CT and SPECT/CT images were captured and analyzed consequently. For the patients diagnosed as early period atypical bone metastases by SPECT/CT, combining the SPECT/CT and MRI together as the SPECT/MRI integrated image. The obtained SPECT/MRI image was analyzed and compared with the pathogenic results of patients. The results indicated that 34 early period doubtful metastatic focus, including 34 SPECT positive focus, 17 focus without special changes by using CT method, 11 bone metastases focus by using SPECT/CT method, 23 doubtful bone metastases focus, 8 doubtful bone metastases focus, 14 doubtful bone metastases focus and 2 focus without clear image. Totally, SPECT/CT combined with SPECT/MRI method diagnosed 30 bone metastatic focus and 4 doubtfully metastatic focus. In conclusion, $^{99}\text{Tc}^{\text{m}}$ -MDP SPECT/CT combined SPECT/MRI Multi modality imaging shows a higher diagnostic value for the early period bone metastases, which also enhances the diagnostic accuracy rate.

Keywords: $^{99}\text{Tc}^{\text{m}}$ -MDP, SPECT/CT, SPECT/MRI, integrated image, bone metastases

Introduction

Malignant tumor bone metastasis is the common and multiple diseases China [1]. There are about 2 million new cancer patients, in which almost 1 million are bone metastasis tumor per year [2]. Almost 70% to 85% of lung cancer, breast cancer and prostatic cancer patients with the symptom of bone metastasis, in which more than 70% patients with the bone pain [3, 4]. The bone metastasis appeared early before the bone imaging for most of the above patients. $^{99}\text{Tc}^{\text{m}}$ -MDP ($^{99}\text{Tc}^{\text{m}}$ marked methylene diphosphonate) bone imaging could diagnosis the bone metastasis with highly sensitivity, which could discovered the bone metastasis earlier than the method of X-ray plain film and computed tomography (CT) [5]. However, the specificity of the $^{99}\text{Tc}^{\text{m}}$ -MDP method is not high enough, especially for the early single or atypical focus. The $^{99}\text{Tc}^{\text{m}}$ -MDP method always be

confused with the injury and Small degenerative joint disease. What's most important is that the SPECT/CT resolves this problem successfully, and enhances the diagnostic specificity significantly [6, 7].

It can't discover the morphology changes (destruction of bone) of early period bone metastases by using X-ray or CT scan [8]. The X-ray or CT only observes the normal or doubtfully abnormal bone density changes, but can't confirm the diagnosis. How can we diagnosis or screen this kind of bone metastases in early time? It is our therapeutic or diagnostic goal in the clinical, which could definitively affect the selection of the therapeutic programme, and also influence the prognosis or life quality. In this study, the $^{99}\text{Tc}^{\text{m}}$ -MDP SPECT/CT combined with SPECT/MRI Multi modality imaging was used to diagnosis the early bone metastases, and received higher sensitivity and specificity.

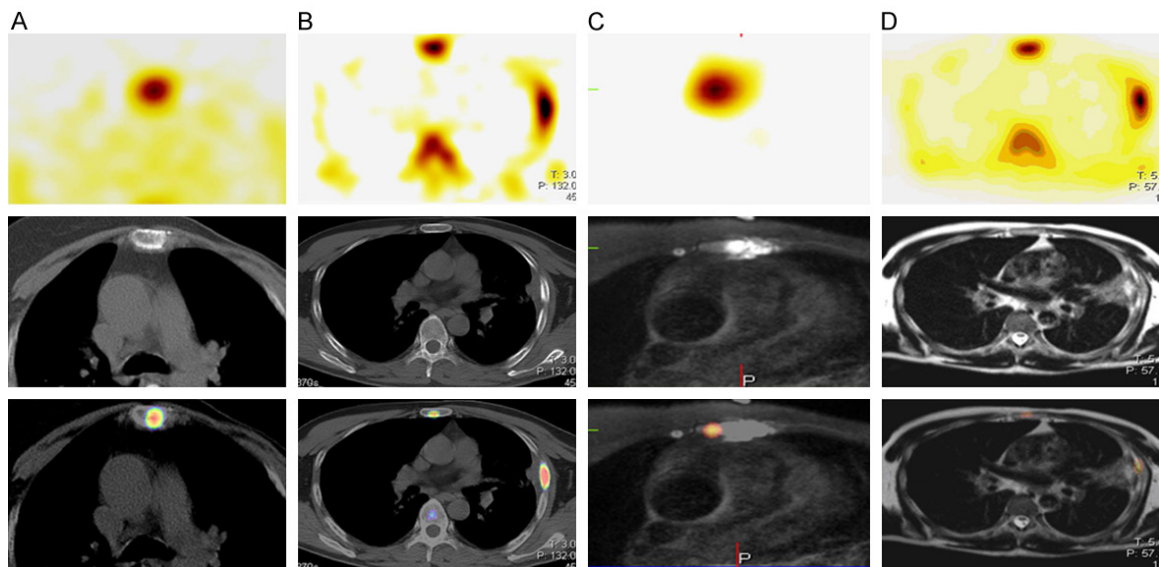


Figure 1. SPECT/CT and SPECT/MRI images in sternum and rib. A. SPECT/CT image in left sternum. B. SPECT/CT image in left rib. C. SPECT/MRI image in left sternum. D. SPECT/MRI image in left rib.

Materials and methods

Patients

Thirty-four patient (mean age, 53 years, range from 30 to 70 years) diagnosed as Malignant tumor from 2008 to 2012 were included in this study, including 13 males and 21 females. In these 34 patients, there are 8 lung cancer patients, 12 breast cancer patients, nasopharyngeal carcinoma 3 patients, cervical carcinoma 5 patients, endometrial carcinoma 2 patients, bladder cancer 1 patient, rectal carcinoma 1 patient and lymphadenoma 2 patients.

This study was approved by the ethics committee of Chongqing Cancer Hospital (No. 2010 [004]), and all patients gave their written consent to participate in this study.

Preparation of patients

Firstly, the radioactivity meter was utilized to detect the dose of $^{99}\text{Tc}^{\text{m}}$ -MDP. According to the above detection, 15 to 30 mCi $^{99}\text{Tc}^{\text{m}}$ -MDP was intravenously injected, and 500 to 1000 ml water was drunk. Three hours post $^{99}\text{Tc}^{\text{m}}$ -MDP administration, SPECT/CT was performed to examine the doubtful bone metastases focus.

Integrated $^{99}\text{Tc}^{\text{m}}$ -MDP SPECT/CT imaging scan

SPECT/CT was performed by using a modern double probe hybrid scanner SIEMENS Symbia

T2 (SIEMENS, Munich, Germany). Non energy dependent Na I probe was used to obtain the rectangular-field view of 38.7 cm×53.3 cm. The SPECT/CT was acquired with the following parameters: 140KeV, window width 15%, image matrix 256 × 1024, scanning speed 15-20 cm/min. For matching of CT slices and SPECT slices, CT was acquired in a shallow breathing position. Directly after CT imaging, the SPECT acquisition protocol was started. Acquisition time was 4.5 min per bed position (5 to 8 bed positions per patient). During imaging, patients were instructed to maintain shallow breathing.

At last, the SPECT/CT integrated imaging was applied by using TruePoint integrated technique (SIEMENS, Munich, Germany), and analyzed by using integrated programme.

Image interpretation

Two experienced nuclear medicine physicians independently interpreted the SPECT scans and two experienced radiologists independently interpreted the CT scans without knowledge of the histological diagnosis, which was not available at the time of interpretation. When the diagnosis was different between observers, the conclusion was discussed to the final diagnosis. The Coronal, Sagittal and Transverse plane of SPECT, CT and SPECT/CT was evaluated, respectively. For the Abnormal concentration of imaging agent, damage of bone or destruction of bone in early period.

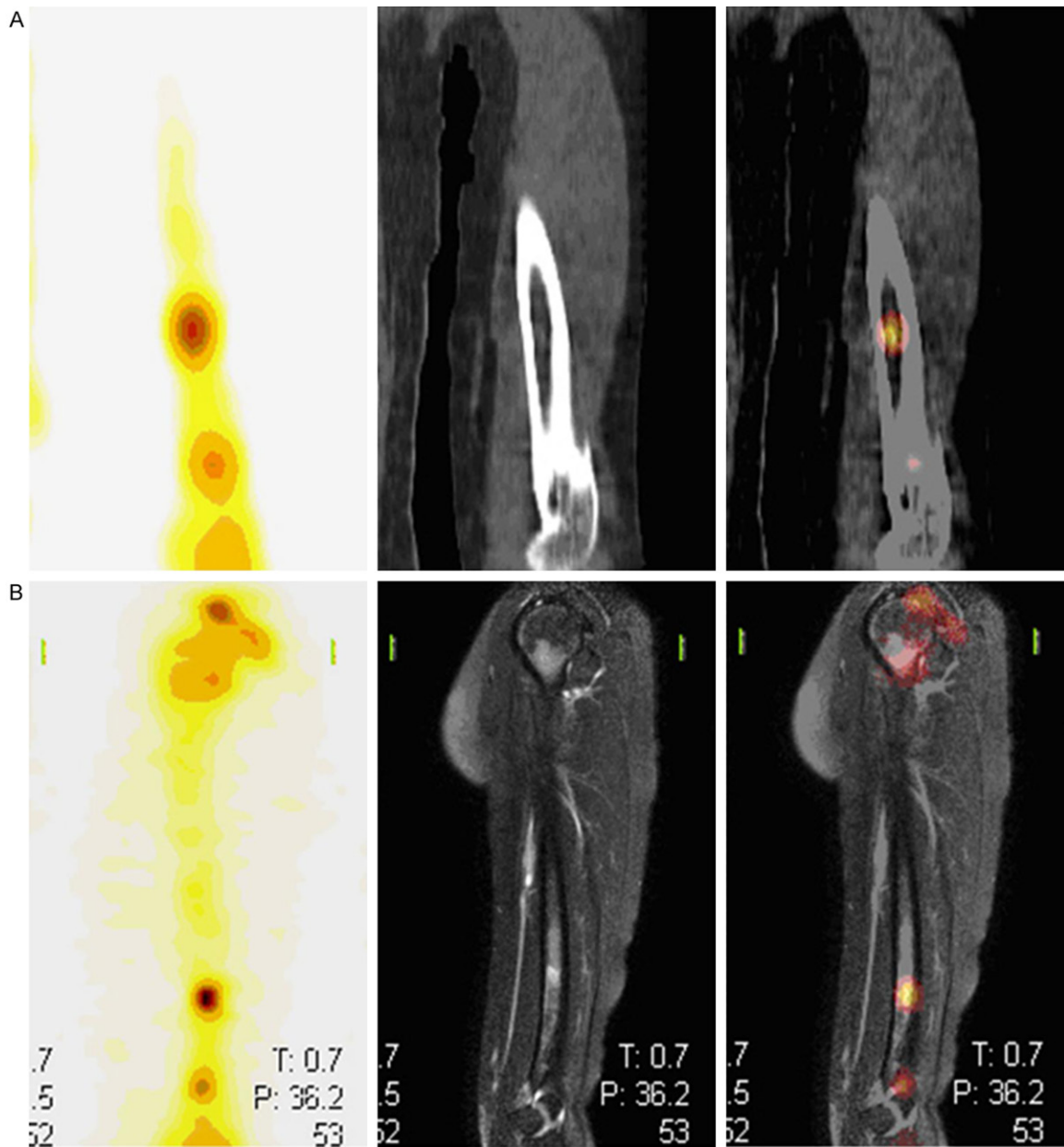


Figure 2. SPECT/CT and SPECT/MRI images in humerus. A. SPECT/CT image in humerus. B. SPECT/MRI image in humerus.

Of CT, SPECT/CT was analyzed. The MRI images in the recent weeks were input the SPECT/CT device, and integrated the SPECT and MRI images. At last, analyzing the SPECT/MRI images to assist the diagnosis focus.

Statistical analysis

Patient-based and lesion-based analysis was performed. The statistical analysis was performed by using the SPSS 10.0 software. Comparison of the detection of early atypical

bone metastases by SPECT/CT combined SPECT/MRI and SPECT/CT or SPECT/MRI was performed using the student's t test with $P < 0.01$ being statistically significant.

Results

Thirty-two patients out of 34 patients with the single focus, and 2 patients with two focus examined by SPECT device. We also analyzed the early period focus, and excluded the obvious bone metastases focus from the research

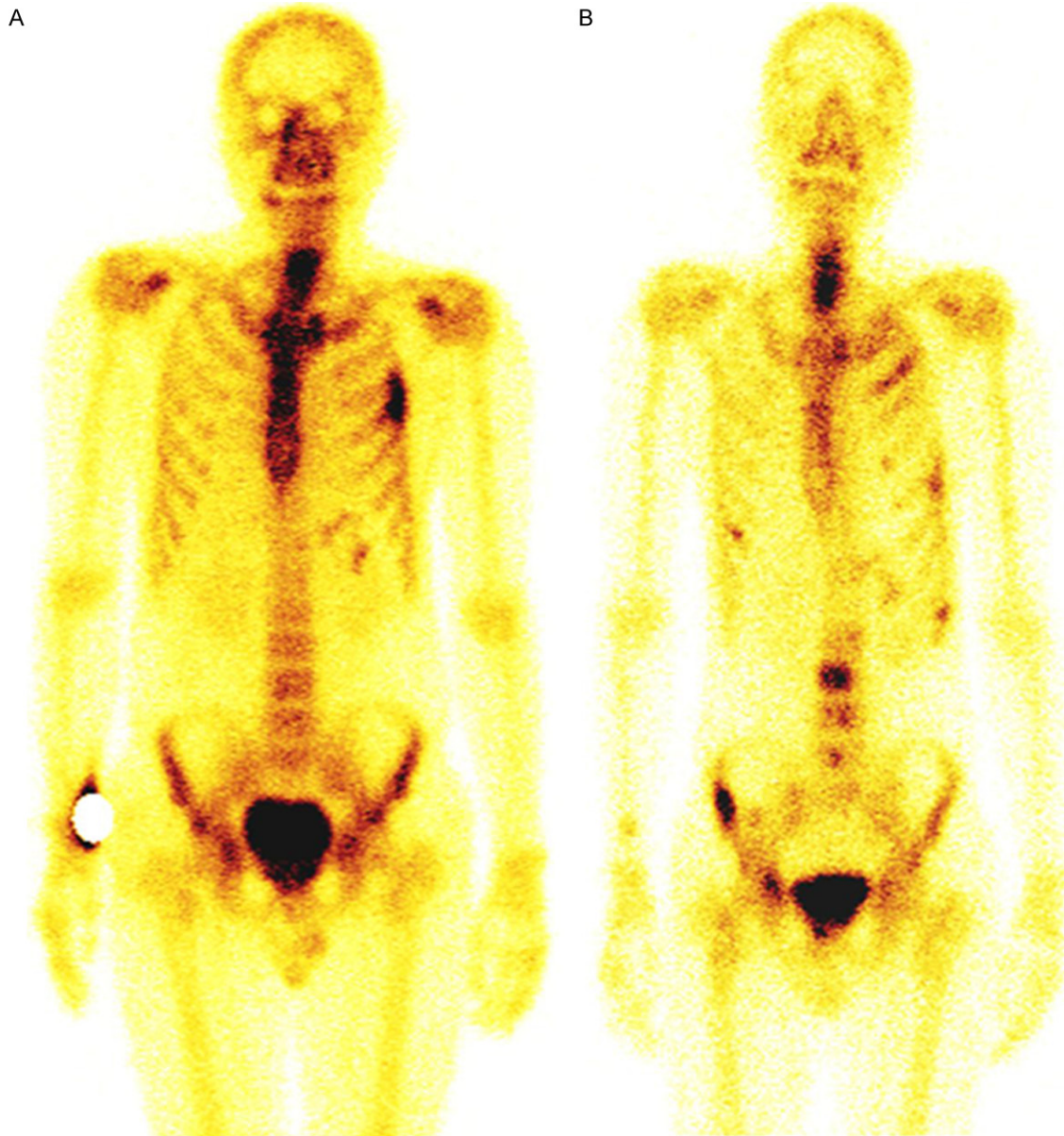


Figure 3. SPECT/CT combined SPECT/MRI images indicate the whole body metastases in a patient. A. Patient diagnosed as the adenocarcinoma afflicted the rib. B. One years post the tumor resection, the adenocarcinoma metastasized to the whole body.

subject. We followed up the patients for two years, and compared diagnostic results and the imaging results.

SPECT/CT and SPECT/MRI images in sternum and rib

All of the 34 patients represented with the characteristics of radioactive concentration in the early period SPECT, which also indicated the slightly increased bone intensity in left sternum (**Figure 1A**) or normal bone intensity in left

rib (**Figure 1B**). Also, 34 doubtfully metastatic focus were discovered by using SPECT method, and 17 Special changed focus were discovered by using CT method (**Figure 1C, 1D**). **Figure 1C** indicated the concentration focus and increased bone intensity in sternum. **Figure 1D** presented with no significant change of the bone intensity in rib, and without any signal changes in adjacent soft tissues. The bone density was slightly increased in CT images, therefore, 17 focus could be recognized as the doubtful metastatic focus. SPECT/CT method

Table 1. Accuracy rate of positive and doubtful focus of SPECT/CT combined SPECT/MRI.

	SPECT/CT	SPECT/MRI	SPECT/CT combined SPECT/MRI
Positive focus	11	8	30
Doubtful focus	23	26	4
Accuracy rate	32.4% (11/34)	23.5% (8/34)	88.2% (30/34)

diagnosed 11 bone metastatic focus, and diagnosed 23 doubtfully metastatic focus (**Figure 1B**, which is diagnosed as doubtful bone metastases).

SPECT/CT and SPECT/MRI images in humerus

Figure 2A indicated the radioactive concentration in left humerus in SPECT images, and bone intensity was increased in CT images. SPECT/CT integrated image could be used to reflect the early bone metastases. SPECT image of SPECT/CT also indicated the radioactive concentration in left humerus, and MRI image showed the increased humerus sclerotin (**Figure 2B**). Combining the SPECT/CT and SPECT/MRI images, the patient was diagnosed as the early bone metastases. However, neither SPECT/CT nor SPECT/MRI could diagnose the bone metastases.

SPECT/CT combined SPECT/MRI images

SPECT/MRI method diagnosed 8 bone metastatic focus, diagnosed 24 doubtful bone metastatic focus, and two without clear image (**Figure 3**). Totally, SPECT/CT combined with SPECT/MRI method diagnosed 30 bone metastatic focus and 4 doubtfully metastatic focus (**Figure 3**). **Figure 3A** indicated the patients diagnosed as the adenocarcinoma afflicted the rib. One year post the tumor resection, the adenocarcinoma metastasized to the whole body (**Figure 3B**).

Accuracy rate of diagnosis of SPECT/CT combined SPECT/MRI

In this study, when compared to the Pathological diagnosis, the accuracy rate of SPECT/CT, SPECT/MRI and SPECT/CT combined SPECT/MRI diagnosis for early period atypical bone metastases is 32.4%, 23.9% and 88.2%, respectively. The accuracy rate of SPECT/CT combined SPECT/MRI is significantly enhanced compared to SPECT/CT or SPECT/MRI (**Table 1**).

Discussion

There are different degrees of imaging agent concentration in all of the 34 patients. In SPECT/CT imaging, CT images represent an atypical change, a part of patients represent a slightly increase or decrease of bone intensity.

Furthermore, a part of patients (11/34) with SPECT/CT could strongly hint bone metastases, and most of patients hint doubtful bone metastases. The focus always represents lower signal of T1 weighted, and represents higher signal of T2 weighted, which is better for the focus indication. However, the images in rib may be affected because of the influence of respiratory movement (2/34 in the present study). For the bone cortex imaging, the SPECT/MRI is worse than SPECT/CT method, some of the small focus adjacent cortex may be mis-diagnosed as benign lesions or missed diagnosed. SPECT/CT method with the better guidelines. SPECT/CT combined SPECT/MRI significantly enhanced the accuracy rate of early period bone metastases, and even achieve 88.2% (30/34).

$^{99}\text{Tc}^{\text{m}}$ -MDP SPECT/CT integrated imaging technique has been the most commonly used modality for the detection of bone metastases because it is highly sensitive for $^{99}\text{Tc}^{\text{m}}$ -MDP, and it is highly specific in detecting lesions. And the $^{99}\text{Tc}^{\text{m}}$ -MDP SPECT/CT bone imaging indicates higher specificity and sensitivity compared to $^{99}\text{Tc}^{\text{m}}$ -MDP conventional imaging [9-11]. The previous studies have also proved that the SPECT/CT method significantly increased the diagnosis of bone destruction compared to conventional method [7, 12, 13]. However, even no diagnostic effects of CT on the early period atypical bone metastases for the patients without obvious bone destruction. Thus, there are also some difficulties for the definite diagnosis of bone metastases.

The former studies have also reported the diagnosis of bone metastases by using SPECT/CT or SPECT/CT combined MRI [7, 14-16]. However, the MRI imaging indicates the length imaging time, and with lower accuracy because affected by the respiratory movement. The advantages of SPECT/CT combined SPECT/MRI for early bone metastases diagnosis depend on the higher sensitivity, higher resolution and

higher screening speed, which could strengthen the observation for small lesion indication and bone cortex.

The present study adopted the integration method, and creatively combined the SPECT/CT and MRI technique, which also combined the merits of both SPECT/CT and MRI methods. In conclusion, ⁹⁹Tc^m-MDP SPECT/CT combined SPECT/MRI Multi modality imaging shows a higher diagnostic value for the early period bone metastases, which also enhances the diagnostic accuracy rate.

Disclosure of conflict of interest

None.

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