

## Comparison of Tc-99m Sestamibi and F-18 FDG-PET in the Assessment of Multiple Myeloma

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**Abstract.** *Background:* Tc-99m methoxy-isobutyl-isonitrile (MIBI) has been reported to be a useful tracer in patients with multiple myeloma (MM). Few articles have reported the potential value of fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) in the evaluation of MM. Therefore, the purpose of this study was to compare the diagnostic abilities of the MIBI scan and the FDG-PET scan in the evaluation of MM. *Materials and Methods:* Twelve patients with MM were included. All patients received a radiological skeletal survey, MIBI scan and FDG-PET scan. *Results:* Thirty-four lesions (19 soft tissue lesions and 15 skeletal lesions) plus 5 cases of bone marrow involvement were detected. The conventional skeletal X-ray survey detected 4 soft tissue lesions (21.1%), 12 skeletal lesions (80%), but no bone marrow involvement (0%). The MIBI scan found 4 cases of bone marrow involvement (80%), 13 soft tissue lesions (68.4%) and 12 skeletal lesions (80%). The PET scan detected 5 cases of bone marrow involvement (100%), 17 soft tissue lesions (89.5%) and 14 skeletal lesions (93.3%). *Conclusion:* Both the MIBI and the FDG-PET scans are useful in the evaluation of patients with MM. However, FDG-PET can detect more lesions than the MIBI scan in patients with MM.

Multiple myeloma (MM) accounts for approximately 10% of hematological malignancies (1). MM is characterized by malignant proliferation of clonal plasma cells and excessive formation of monoclonal immunoglobulin. The staging of myeloma patients, especially those with low-burden and focal disease, requires accurate imaging methods. Radiography is the mainstay of diagnostic imaging

evaluation of patients with MM, with X-ray total bone survey searching for osteolytic and/or osteoblastic lesions being the oldest, classic method. Computed tomography (CT) and magnetic resonance imaging (MRI) have been shown to be more sensitive than conventional plain radiographs (2-6). However, whole-body CT and MRI have still not been accepted worldwide.

Several nuclear medicine tests have been used for the detection of MM. Bone scintigraphy with Tc-99m methylene diphosphonate (MDP) is relatively insensitive when compared to conventional radiographs (7, 8). In recent years, a number of reports have been published concerning Tc-99m methoxy-isobutyl-isonitrile (MIBI) as a useful tracer in patients with plasma cell dyscrasias. In comparative studies, the MIBI scan proved to be superior to a skeletal X-ray survey in detecting bone and bone marrow involvement (9-11).

Positron emission tomography (PET) using the glucose analog fluorine-18 fluorodeoxyglucose (FDG) has the unique ability to reveal nodal and extranodal manifestations of lymphoma in a single examination. A high accuracy for FDG-PET in detecting lymphoma infiltration of the bone marrow has been reported (12, 13). However, the published data regarding the accuracy of FDG-PET in detecting MM is limited, with only a few articles reporting the potential value of FDG-PET in the evaluation of MM (14-19).

The purpose of this study was to evaluate the abilities of the MIBI scan and FDG-PET in the evaluation of MM and the results were compared to those from traditional X-ray surveys.

### Materials and Methods

Twelve patients (8 women and 4 men, aged 30 to 74, with a mean of 49 years) with MM were included in this study. Conventional radiographic skeletal surveys of the skull, chest, spine, pelvis, humerus and femur were carried out on all patients. In addition, all patients received both a F-18 FDG-PET scan and Tc-99m MIBI scan. All these tests were performed within one week. Biopsy or additional imaging, such as MRI and CT, was used adjacently to confirm or clarify sites of suspected lesions.

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*Key Words:* FDG-PET, MIBI scan, multiple myeloma, bone marrow involvement, soft tissue lesions, skeletal lesions.

*Tc-99m MIBI scintigraphy and FDG-PET scanning.* Anterior and posterior whole-body scans were obtained using a two-headed gamma camera (Siemens, E.cam) 10 min after intravenous injection of 740 MBq Tc-99m MIBI. A further single photon emission computed tomography (SPECT), focusing on the thoracic level and suspected lesion noted in the whole-body scan, was also performed.

The PET studies were performed using a whole-body PET scanner (Siemens Ecat Exact HR plus, Knoxville, TN, USA). All patients were imaged after fasting for a minimum of 6 h, except for water and medications. Their blood sugar level was checked prior to injection, which in all patients had to be less than 120 mg/dl. FDG was injected intravenously in doses of 370 MBq. Whole-body imaging commenced 60 min after the injection of F-18 FDG. The patients were asked to lie supine on the imaging bed of the PET camera. The image was performed at each level from the head to the upper knee. The images were reconstructed and displayed in 3-D and axial, saggital and coronal reconstructions for interpretation. Traditional skeletal X-ray films were interpreted by one experienced reader. Both the Tc-99m MIBI image and F-18 FDG-PET images were evaluated by two blinded and independent nuclear specialists.

**Results**

Thirty-four lesions (19 soft tissue lesions and 15 skeletal lesions) plus 5 cases of bone marrow involvement were detected. The results are shown in Table I. The conventional skeletal X-ray survey detected 4 soft tissue lesions (21.1%) and 12 skeletal lesions (80%). None of the 5 cases of bone marrow involvement was detected by plain X-rays. In the evaluation of skeletal lesions, the MIBI scan found 12 skeletal lesions (80%) and FDG-PET found 14 skeletal lesions (93.3%) (Figure 1). In the 19 known soft tissue lesions, the MIBI scan detected 13 soft tissue lesions (68.4%) and FDG-PET detected 17 soft tissue lesions (89.5%) (Figure 2). In the evaluation of bone marrow involvement, 4 cases (80%) were detected by MIBI scan and 5 cases (100%) by FDG-PET (Figure 3).

The FDG-PET and MIBI scans were concordant in 11 soft tissue lesions (57.9%), 11 skeletal lesions (73.3%) and 4 cases of bone marrow involvement (80%). The FDG-PET scan detected some lesions that the MIBI scan did not detect (6 soft tissue, 3 skeletal lesions and 1 case of bone marrow involvement), whereas the MIBI scan detected some lesions (1 skeletal and 2 soft tissue lesions) that the FDG-PET scan did not detect. However, the FDG-PET scan generally detected more disease sites than the MIBI scan.

**Discussion**

A radiological skeletal survey is the classic method for the assessment of MM. However, its sensitivity is unsatisfactory for soft tissue lesions and bone marrow involvement. In our study, the traditional skeletal X-ray survey showed an 80%

Table I. *The detection rates of three diagnostic modalities in patients with MM.*

	Lesions Detected		
	Bone marrow	Soft tissue	Bone
Radiological skeletal survey	0 (0%)	4 (21.1%)	12 (80%)
MIBI scan	4 (80%)	13 (68.4%)	12 (80%)
FDG-PET	5 (100%)	17 (89.5%)	14 (93.3%)
Total lesions number	5	19	15

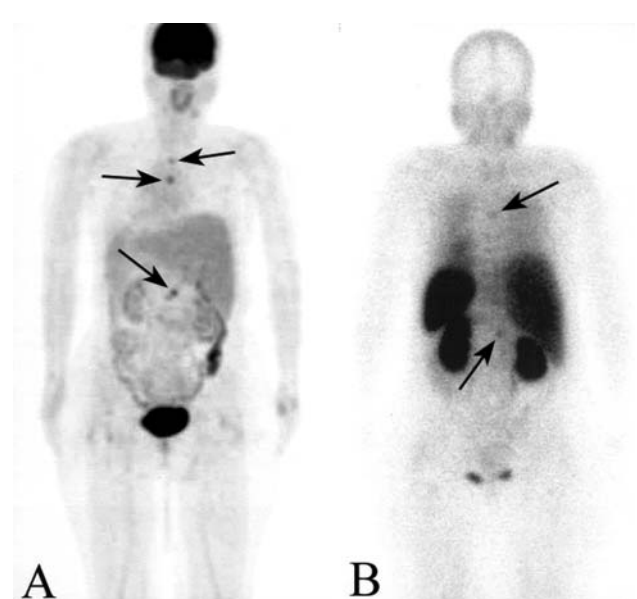


Figure 1. *Skeletal involvement in MM. (A) Posterior projection view of FDG-PET performed 1 hour after intravenous injection of 370 MBq F-18 FDG shows increased FDG uptake in the T4, T6 and L1 spines (arrows). (B) Posterior whole-body image performed 10 minutes after injection of 740 MBq shows mildly increased Tc-99m MIBI in the T6 and L1 spines (arrows). The FDG-avid lesion in the T4 spine was not visualized by MIBI scan.*

detection rate for the skeletal lesions, but only 21.1% for the soft tissue lesions and 0% for bone marrow involvement. Both the MIBI and FDG-PET scans have been proven to be more useful than radiological skeletal surveys in the assessment of patients with MM, especially in the evaluation of soft tissue and bone marrow. Although high-resolution CT and MR have allowed the identification of myeloma sites in patients with negative radiography findings (2-6), both the MIBI scan and FDG-PET have the advantage of whole-body screening.

In the detection of skeletal lesions, all 3 diagnostic modalities showed good detection rates. Both the X-ray

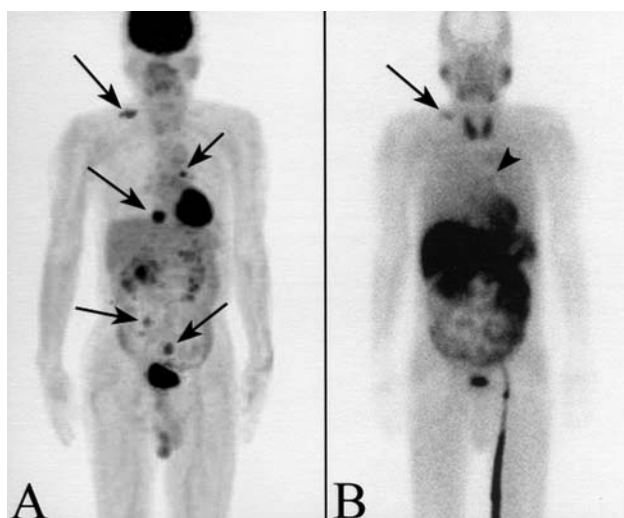


Figure 2. Soft tissue involvement in MM. (A) Anterior projection view of FDG-PET performed 1 hour after intravenous injection of 370 MBq F-18 FDG shows multiple FDG-avid lesions in the right supraclavicular region, middle mediastinum, low mediastinum and the abdomen (arrows). (B) Anterior whole-body image performed 10 minutes after injection of 740 MBq Tc-99m MIBI shows an area of increased Tc-99m MIBI uptake in the right supraclavicular region (arrow). The FDG-avid lesion in the middle mediastinum is barely visible (arrowhead). The lesions in the low mediastinum and the abdomen are difficult to identify because of the interference from intense liver uptake and physiological excretion of Tc-99m MIBI into the bowel.

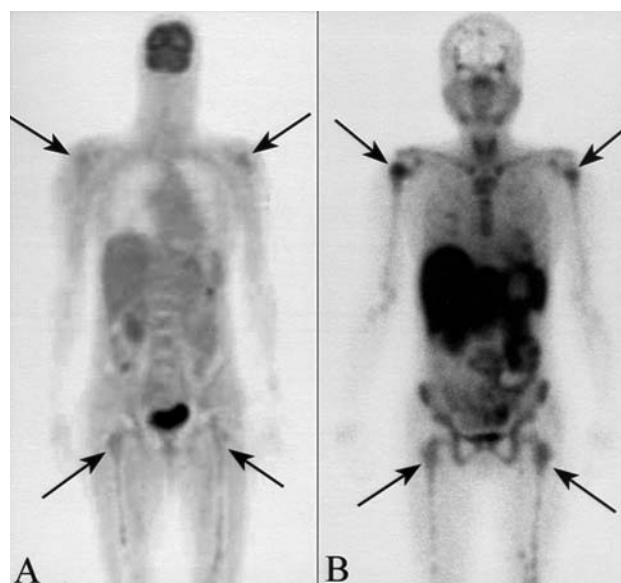


Figure 3. Bone marrow involvement in MM. (A) Coronal section of FDG-PET performed 1 hour after intravenous injection of 370 MBq F-18 FDG shows increased FDG uptake in the bone marrow over bil. femurs and bil. humerus. (B) Anterior whole-body view of MIBI scan also shows significantly increased Tc-99m MIBI in the bil. femurs, bil. humerus, pelvic bone and sternum.

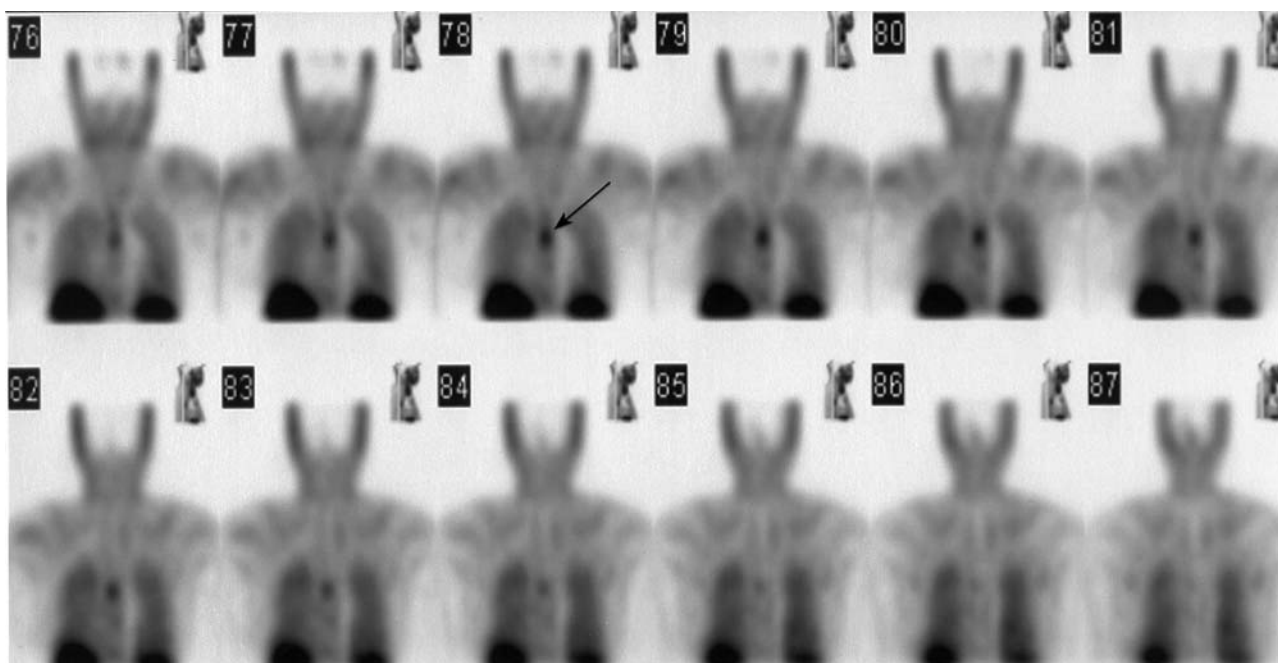


Figure 4. MIBI scan of the same patient as in Figure 1. The coronal sections of the MIBI scan show a lesion in the T6 spine (arrow), which is more clearly seen than in the planar image shown in Figure 1. However, the FDG-avid lesion in the T4 spine was not detected by this scan and the FDG-avid lesion in the L1 spine is beyond the field of this image.

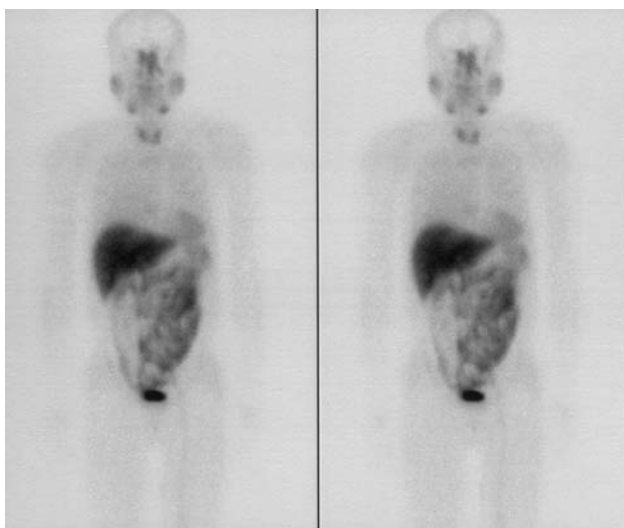


Figure 5. Anterior whole-body image performed 10 minutes after injection of 740 MBq Tc-99m MIBI shows significant bowel activity, which is commonly noted in MIBI scans. The physiological excretion of Tc-99m MIBI into the intestine may make the detection of abdominal lesions difficult.

total bone survey and MIBI scan detected 80% of known skeletal lesions. FDG-PET had a higher detection rate of 93.3%. In the detection of soft tissue lesions, FDG-PET showed a much better detection rate than the MIBI scan (89.5% vs. 68.4%), especially for lesions in the abdomen. We suggest that the following factors might be responsible for the better detection rate of FDG-PET: i) The PET imaging resolution is better than that of SPECT. Moreover, only planar MIBI images were available in some regions since SPECT was not performed for a whole-body survey routinely in the MIBI study (Figure 4). The detection rate for planar images was even worse than that for SPECT; ii) The MIBI scan may show false-negative in cases of multidrug-resistant myeloma associated with p-glycoprotein expression (20, 21). MIBI is excreted by the cells through the p-glycoprotein or multidrug resistance-related protein. This protein is frequently expressed in myeloma cells, especially in cases after treatment (21). Therefore, FDG-PET may be particularly useful in cases of multidrug-resistant myeloma associated with p-glycoprotein expression, which may be reflected by an MIBI scan showing early tracer washout (20); and iii) The detection of abdominal lesions by MIBI may be obscured by intense MIBI activity in the bowel (22) (Figure 5).

In the detection of bone marrow involvement, the MIBI scan has been proven to be clinically useful (9-11, 23). Previous studies showed that the *in vitro* MIBI uptake in bone marrow mononuclear cells from patients with MM is significantly correlated with the percentage of plasma cell infiltration and that the tracer is localized inside malignant

plasma cells (23). In our study, the MIBI scan also showed a good detection rate for bone marrow involvement in patients with MM. As for the FDG-PET scan, Schirrmeyer *et al.* found a high detection rate (91%) for bone marrow involvement in MM (19). In our study, the FDG-PET detection rate was 100% for the 5 patients with bone marrow involvement, which suggests that FDG-PET can play a great role in the evaluation of bone marrow involvement in patients with MM.

Few studies are available comparing detection rates between the MIBI scan and FDG-PET in patients with MM. To date, only one case report and one original paper comparing these detection rates have been published (15, 17). In the original paper, Mileschkin *et al.* found that the MIBI scan generally detected more disease sites than FDG-PET, particularly additional bony sites (17). However, their results were not in accord with ours. In our study, FDG-PET detected more lesions than the MIBI scan. One possible factor, which may have contributed to the discordance, is the difference in PET scanners used in these two studies. Mileschkin *et al.* used a dedicated PET scanner based on sodium iodide detectors, which had a lower spatial resolution than the bismuth germinate (BGO) detectors used in this study.

FDG uptake by tumor reflects the accelerated glycolysis usually occurring in malignant cells. The enhanced glycolytic rate of malignant cells, which is associated with increased activities of rate-controlling enzymes for glycolysis, facilitates tumor detection with FDG-PET. The mechanism of Tc-99m MIBI concentration has been studied in both normal and malignant cells (24, 25). The strong electronegative mitochondrial and plasma membrane potentials are considered relevant factors. Tc-99m MIBI is sequestered in the cytoplasm and mitochondria of cells in response to the electrical potentials generated across the membrane layers (26). Malignant tumors maintain higher mitochondrial and plasma membrane potentials secondary to increased metabolic requirements, which promotes concentration of MIBI within the inner mitochondrial matrix (27).

In conclusion, both the MIBI and FDG-PET scans are useful in the evaluation of patients with MM. However, FDG-PET may detect more lesions than the MIBI scan in patients with MM.

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