Potential of ^{99m}Tc-MIBI for Detecting Bone Marrow Metastases

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In this study, we evaluated the potential of ^{99m}Tc-hexakis-2-methoxyisobutylisonitrile (MIBI) for detecting bone metastases in comparison with a conventional bone tracer. **Methods:** ^{99m}Tc-MIBI and ^{99m}Tc-hydroxymethylene diphosphonate (HMDP) scans were obtained from 99 patients with proven malignant diseases and suspected bone metastases. We compared 373 lesions that showed abnormal uptake on ^{99m}Tc-MIBI scans or ^{99m}Tc-HMDP scans (or both). **Results:** Bone metastases were confirmed in 334 of 373 lesions. Thirty-nine lesions on ^{99m}Tc-HMDP scans had false-positive findings, but only 2 of these lesions had false-positive findings on ^{99m}Tc-MIBI scans. ^{99m}Tc-MIBI and ^{99m}Tc-HMDP scans were equivalent in 168 of 334 lesions (50.3%). ^{99m}Tc-MIBI scans correctly detected more lesions than ^{99m}Tc-HMDP scans: 284 lesions (85.0%) versus 218 lesions (65.3%) ($P < 0.005$), respectively. ^{99m}Tc-MIBI scans showed a markedly higher sensitivity for detecting metastases in the femur and humerus compared with ^{99m}Tc-HMDP scans: 97 of 98 lesions (99.0%) versus 35 of 98 lesions (35.7%) ($P < 0.005$) and 21 of 22 lesions (95.5%) versus 11 of 22 lesions (50.0%) ($P < 0.005$), respectively. ^{99m}Tc-HMDP scans of 17 patients showed no abnormal images. However, ^{99m}Tc-MIBI scans correctly detected bone metastases, and subsequent development of multiple lesions was observed on follow-up ^{99m}Tc-HMDP scans of 15 patients. ^{99m}Tc-MIBI scans were superior to ^{99m}Tc-HMDP scans in the detection of metastases attributed to breast cancer, multiple myeloma, and hepatoma. On the contrary, ^{99m}Tc-MIBI scans were less sensitive than ^{99m}Tc-HMDP scans for detecting bone metastases attributed to prostate cancer in the other skeletal sites except for femur and humerus. **Conclusion:** ^{99m}Tc-MIBI scans have better sensitivity for detecting bone metastases and provide more specific complementary findings than conventional bone scans. ^{99m}Tc-MIBI accumulation attributed to bone marrow metastases may occur at an early stage, before the bone remodeling process in the surrounding bone can be detected on conventional bone scans.

Key Words: bone marrow metastases; bone metastases; ^{99m}Tc-MIBI scan; ^{99m}Tc-HMDP scan

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Bone is one of the most common sites of cancer metastasis. Conventional bone scans are very sensitive in the detection of the altered local metabolism in areas of skeletal remodeling associated with metastatic deposits. However, in particular settings (e.g., myeloma, very aggressive osteolytic lesions, and lesions confined to marrow), bone scans have low sensitivity, and skeletal trauma, degenerative disease, and many other benign active disorders of the bones and joints may produce false-positive readings.

Bone metastases develop from preclinical micrometastases in the bone marrow. Individual tumor cells are believed to reach the skeleton by the bloodstream as single cells by the process of tumor cell shedding and colonize to the bone marrow. Subsequent proliferation results in progressive replacement of the marrow space with tumor, with resultant demineralization and resorption of adjacent trabecular structures. Therefore, treatment strategy requires the detection of bone marrow metastases still in the subclinical stage before skeletal remodeling associated with malignant involvement can be detected on conventional bone scans.

MRI seems to be very sensitive for the detection of bone marrow metastases, especially if it is performed after routine bone scanning, which can be used as a guide to direct MRI. However, the time constraints of MRI limit its routine application for whole-body bone marrow evaluation. In addition, MRI findings are generally nonspecific because the MRI signal depends on the presence and relative proportions of trabecular bone, fat, and water (*1*,*2*).

Recently developed ^{99m}Tc-labeled monoclonal granulocyte antibodies against the nonspecific cross-reacting antigen 95 on the membrane of granulocytes in the blood and on mature granulopoietic cells in the bone marrow permit imaging of hematopoietic bone marrow (*3*,*4*) and may be useful in clinically assessing granulopoiesis or hematopoiesis. However, radioimmunoimaging of hematopoietic bone marrow appears to have a limited value in detecting marrow malignancy because of the restriction to those areas of the skeleton containing hematopoietic marrow and the difficulty in differentiating between the scintigraphically cold appearance caused by malignant involvement and marrow alterations caused by various benign conditions (e.g., focal fatty

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conversion, bone infarction, focal necrosis, Paget's disease, and vertebral marrow degeneration).

^{99m}Tc-Hexakis-2-methoxyisobutylisonitrile (MIBI), which was originally developed as a myocardial perfusion tracer (*5*), is now an established agent for tumor imaging (*6–12*). An animal experimental study has shown that approximately 80% of ^{99m}Tc-MIBI activity in normal bone is found in the red bone marrow (*13*). In a biodistribution study using normal rats, we found that the uptake ratio of bone marrow to bone is significantly lower for conventional bone tracers but is significantly higher for ^{99m}Tc-MIBI, which is promising for detecting marrow malignancy (*14*). Our previous studies on patients with various bone marrow malignancies clearly showed that ^{99m}Tc-MIBI accumulation in the femoral marrow correlated well with the clinical findings of bone marrow malignancy and that ^{99m}Tc-MIBI femoral marrow imaging also was potentially useful for detecting minimal residual disease in acute leukemia (*15,16*).

This study was performed to compare ^{99m}Tc-MIBI scans with conventional bone scans for detection of bone metastases.

MATERIALS AND METHODS

Patients

Ninety-nine patients (39 females, 60 males; age range, 18–91 y; mean age, 60 y) with malignant disease and suspected bone metastases were studied after obtaining informed consent. The patients had lung cancer ($n = 22$), breast cancer ($n = 13$), prostate cancer ($n = 11$), colon cancer ($n = 6$), renal cancer ($n = 6$), hepatoma ($n = 5$), multiple myeloma ($n = 5$), bladder cancer ($n = 4$), gastric cancer ($n = 3$), malignant lymphoma ($n = 2$), thyroid cancer ($n = 2$), esophageal cancer ($n = 2$), pancreatic cancer ($n = 2$), uterine cancer ($n = 2$), osteosarcoma ($n = 2$), and miscellaneous cancers ($n = 12$).

Imaging

^{99m}Tc-Hydroxymethylene diphosphonate (HMDP) scanning was performed first; ^{99m}Tc-MIBI scanning was performed within 2 wk of obtaining the ^{99m}Tc-HMDP scans. ^{99m}Tc-HMDP images were obtained 3–4 h after injection of ^{99m}Tc-HMDP (555 MBq [15 mCi]). Whole-body anterior and posterior images were obtained in a 256 × 256 matrix using a low-energy, high-resolution collimator. Multiple spot images of the skeleton were also obtained for each 4 min. Acquisition of the ^{99m}Tc-MIBI images was begun 1 min after bolus injection of ^{99m}Tc-MIBI (740 MBq [20 mCi]). First, a ^{99m}Tc-MIBI image of the lumbar spine and pelvis was obtained for 5 min in a 128 × 128 matrix using a low-energy, high-resolution collimator. Each spot image of the skeleton was then obtained.

Image Interpretation

^{99m}Tc-HMDP images were evaluated for the presence of focal areas of abnormally increased or decreased skeletal uptake compared with adjacent or contralateral structures. ^{99m}Tc-MIBI activity in skeletal sites was classified into 3 patterns: no detectable activity, homogeneously mild activity, and clearly visualized focal activity (Fig. 1). In a previous study, no clearly visualized focal activity was observed in the femur of the 141 control patients or in the humerus, sternum, and spine of the 124 control patients with presumed normal bone and bone marrow (*15*). We observed homogeneously mild activity in the femur of 16 patients (11.3%), the humerus of 2 patients (1.6%), the sternum of 90 patients (72.6%), and the spine of 111 patients (89.5%). Representative normal ^{99m}Tc-MIBI skeletal images are shown in Figure 2. No detectable activity of ^{99m}Tc-MIBI was evident in the femur of 125 patients (88.7%), the humerus of 122 patients (98.4%), the sternum of 34 patients (27.4%), and the spine of 13 patients (10.5%). Focal ^{99m}Tc-MIBI activity was found in 44 of 45 patients (98%) with proven marrow malignancy.

Therefore, clearly visualized focal activity of ^{99m}Tc-MIBI was interpreted as abnormal in this study. Bone metastases were confirmed by at least 1 other method: plain radiography (32 patients), CT (23 patients), MRI (35 patients), bone marrow cytology (15 patients), or evidence of progressive bone lesions on follow-up ^{99m}Tc-HMDP bone scans (51 patients). Bone metastases could not be classified into lytic, sclerotic, or mixed lesions because plain radiographs or CT scans were not obtained on all patients at approximately the same time as the ^{99m}Tc-HMDP and ^{99m}Tc-MIBI scans were obtained.

A χ^2 test with or without the Yates correction was used to compare proportions.

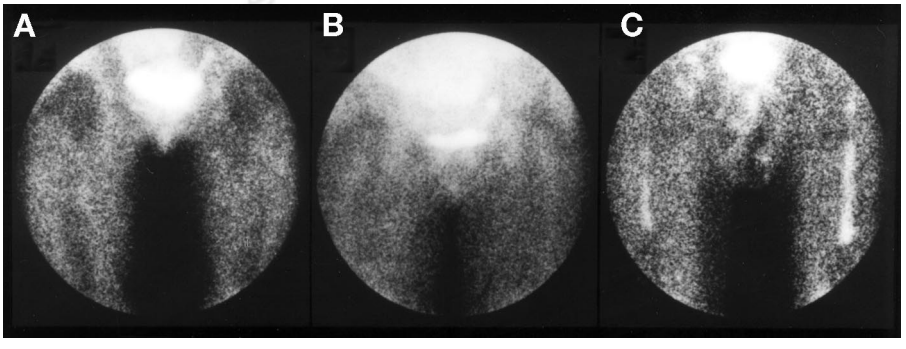

FIGURE 1. Classification of ^{99m}Tc-MIBI activity patterns. (A) No detectable activity in patient with breast cancer was confirmed by lack of abnormal MRI findings. (B) Homogeneous mild activity in patient with lung cancer was confirmed by lack of abnormal MRI findings. (C) Clearly visualized focal activity in patient with malignant lymphoma (non-Hodgkin's) was confirmed by abnormal MRI findings and bone marrow cytology from puncture sites on each anterior iliac crest. Clearly visualized activity of ^{99m}Tc-MIBI was interpreted as abnormal.

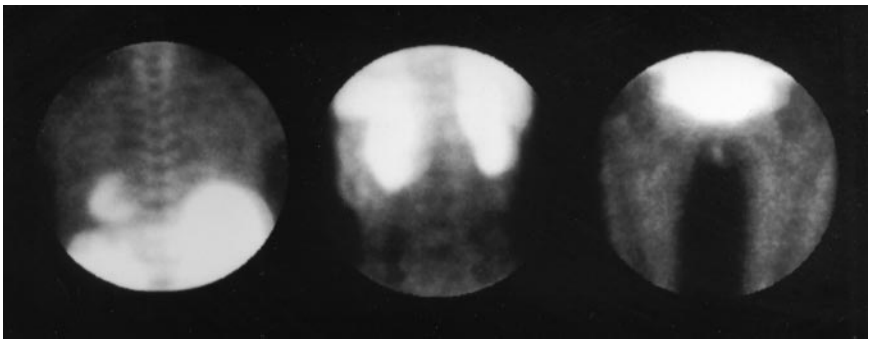

FIGURE 2. Normal ^{99m}Tc-MIBI skeletal images of woman with hypertension with no evidence of cancer. Homogeneous mild activity was found in thoracic spine, ribs, and lumbar spine; no detectable activity was evident in femur.

RESULTS

Conventional ^{99m}Tc-HMDP bone scans showed abnormal skeletal uptake in 257 lesions of 99 patients. ^{99m}Tc-MIBI scans showed abnormal skeletal uptake in 286 lesions. We compared 373 lesions that showed abnormal uptake on ^{99m}Tc-MIBI scans or ^{99m}Tc-HMDP scans (or both). Bone metastases were confirmed in 334 of 373 lesions by plain radiography ($n = 35$), CT ($n = 45$), MRI ($n = 98$), marrow cytology ($n = 22$), or evidence of progressive bone lesions on follow-up ^{99m}Tc-HMDP scans ($n = 134$). False-positive findings were confirmed by plain radiography, CT, or MRI and were found in 39 lesions on ^{99m}Tc-HMDP scans: osteoarthritis ($n = 20$), trauma ($n = 9$), osteoporosis ($n = 6$), spondylosis ($n = 2$), cyst ($n = 1$), and aseptic necrosis ($n = 1$). Only 2 of these lesions (cyst, aseptic necrosis) had false-positive findings on ^{99m}Tc-MIBI scans, and the other 37 lesions showed no abnormal ^{99m}Tc-MIBI activity.

True-positive findings on ^{99m}Tc-MIBI scans and ^{99m}Tc-HMDP scans were confirmed by plain radiography ($n = 30$ and 35, respectively), CT ($n = 35$ and 45, respectively), MRI ($n = 90$ and 66, respectively), marrow cytology ($n = 22$ and 0, respectively), or evidence of progressive bone lesions on follow-up ^{99m}Tc-HMDP scans ($n = 107$ and 72, respectively). ^{99m}Tc-HMDP and ^{99m}Tc-MIBI scans were equivalent in 168 of 334 lesions (50.3%) in which bone metastases were confirmed (Table 1). ^{99m}Tc-MIBI scans correctly detected more lesions than ^{99m}Tc-HMDP scans: 284 lesions (85.0%) versus 218 lesions (65.3%) ($P < 0.005$), respectively. ^{99m}Tc-MIBI scans showed a markedly higher sensitivity for detecting metastases, especially in the femur and humerus, compared with ^{99m}Tc-HMDP scans: 97 of 98 lesions (99.0%) versus 35 of 98 lesions (35.7%) ($P < 0.005$) and 21 of 22 lesions (95.5%) versus 11 of 22 lesions (50.0%) ($P < 0.005$), respectively. Although ^{99m}Tc-HMDP scans detected more lesions in the ribs, thoracic spine, lumbar spine, and pelvis compared with ^{99m}Tc-MIBI scans and ^{99m}Tc-MIBI scans detected more lesions in the sternum compared with ^{99m}Tc-HMDP scans, no significant differences between ^{99m}Tc-HMDP and ^{99m}Tc-MIBI scans in the detectability of these lesions were found.

No abnormal images on ^{99m}Tc-HMDP scans were found in 17 patients (breast cancer [$n = 4$], multiple myeloma [$n = 2$], osteosarcoma [$n = 2$], lung cancer [$n = 2$], hepatoma [$n = 2$], prostate cancer [$n = 1$], gastric cancer [$n = 1$], colon cancer [$n = 1$], uterine cancer [$n = 1$], and synovial sarcoma [$n = 1$]). However, ^{99m}Tc-MIBI scans correctly detected bone metastases in these patients (31 regions in the femur, 8 regions in the ribs, 7 regions in the

TABLE 1
Comparison of Detectability of Bone Metastases Between ^{99m}Tc-HMDP and ^{99m}Tc-MIBI Scans in Relation to Skeletal Sites

Site	No. of metastases	^{99m}Tc-HMDP(+), ^{99m}Tc-MIBI(−)	^{99m}Tc-HMDP(−), ^{99m}Tc-MIBI(+)	^{99m}Tc-HMDP(+), ^{99m}Tc-MIBI(+)	^{99m}Tc-HMDP(+)*	^{99m}Tc-MIBI(+)*	^{99m}Tc-HMDP vs. ^{99m}Tc-MIBI
Rib	57	15	12	30	45 (78.9)	42 (73.7)	NS
Thoracic spine	33	8	6	19	27 (81.8)	25 (75.8)	NS
Lumbar spine	23	9	4	10	19 (82.6)	14 (60.9)	NS
Sternum	18	0	4	14	14 (77.8)	18 (100)	NS
Pelvis	62	12	11	39	51 (82.3)	50 (80.6)	NS
Humerus	22	1	11	10	11 (50.0)	21 (95.5)	$P < 0.005$
Femur	98	1	63	34	35 (35.7)	97 (99.0)	$P < 0.005$
Other	21	4	5	12	16 (76.2)	17 (81.0)	NS
Total	334	50	116	168	218 (65.3)	284 (85.0)	$P < 0.005$

*Value in parentheses is percentage.
^{99m}Tc-HMDP(+) = ^{99m}Tc-HMDP positive; ^{99m}Tc-HMDP(−) = ^{99m}Tc-HMDP negative; ^{99m}Tc-MIBI(+) = ^{99m}Tc-MIBI positive; ^{99m}Tc-MIBI(−) = ^{99m}Tc-MIBI negative; NS = not significant.

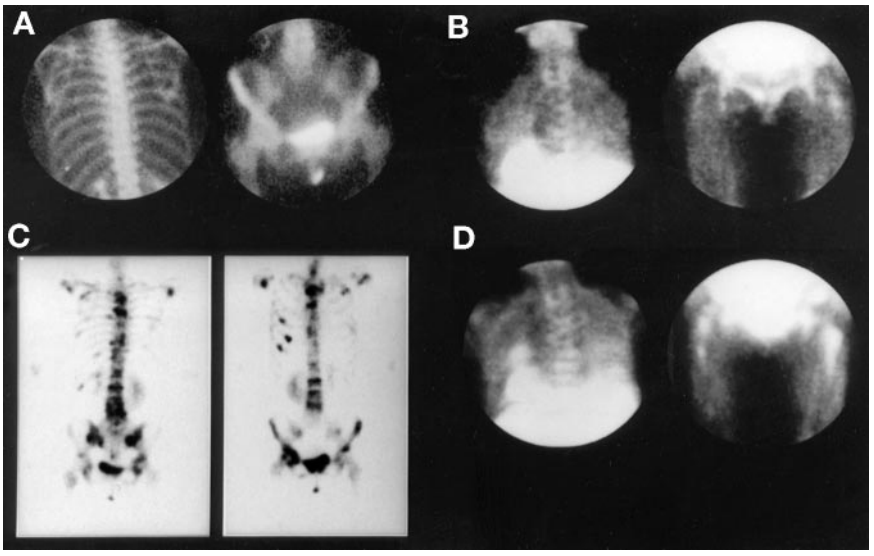

FIGURE 3. Patient with breast cancer. (A) Initial ^{99m}Tc-HMDP scans show no bone metastases. (B) ^{99m}Tc-MIBI scans show multiple lesions in thoracic spine, bilateral proximal femur, and right pubic bone. Findings were confirmed 1 mo later by MRI. (C) Multiple intense accumulations of ^{99m}Tc-HMDP appeared 4 mo later on whole-body scans. (D) Further ^{99m}Tc-MIBI scans (second set) show increased accumulations in thoracic spine, bilateral proximal femur, and left lung metastatic lesion. ^{99m}Tc-HMDP accumulations in more extensive sites, including bilateral proximal femur, appeared 2 mo after obtaining second set of ^{99m}Tc-HMDP scans.

humerus, 7 regions in the pelvis, 4 regions in the thoracic spine, 3 regions in the sternum, and 2 regions in the lumbar spine), which were confirmed by at least 1 other method: plain radiography (2 patients), CT (3 patients), MRI (10 patients), bone marrow cytology (6 patients), or subsequent development of multiple lesions on follow-up ^{99m}Tc-HMDP scans (15 patients). Representative cases are shown in Figures 3–5.

In 5 patients (prostate cancer [$n = 2$], lung cancer [$n = 2$], and renal cancer [$n = 1$]), ^{99m}Tc-MIBI scans showed no abnormal images. However, ^{99m}Tc-HMDP scans correctly detected bone metastases in these patients (4 regions in the thoracic spine; 2 regions each in the lumbar spine, ribs, and pelvis; and 1 region each in the femur and cervical spine). A representative case is shown in Figure 6.

^{99m}Tc-MIBI scans were superior to ^{99m}Tc-HMDP scans in the detection of metastases in all skeletal sites due to breast cancer, multiple myeloma, and hepatoma: 59 of 69 lesions (85.5%) versus 42 of 69 lesions (60.9%) ($P < 0.005$), 30 of 30 lesions (100%) versus 17 of 30 lesions (56.7%) ($P < 0.005$), and 21 of 21 lesions (100%) versus 10 of 21 lesions (47.6%) ($P < 0.005$), respectively (Table 2). In these malignant diseases, we observed more metastatic lesions with ^{99m}Tc-MIBI scans not only in the femur and humerus but also in the other skeletal sites (Tables 3 and 4).

No significant differences were found between ^{99m}Tc-MIBI and ^{99m}Tc-HMDP scans in the detection of metastases in all skeletal sites due to lung cancer, prostate cancer, and the other malignant diseases. We also observed more metastases in the femur and humerus with ^{99m}Tc-MIBI scans in

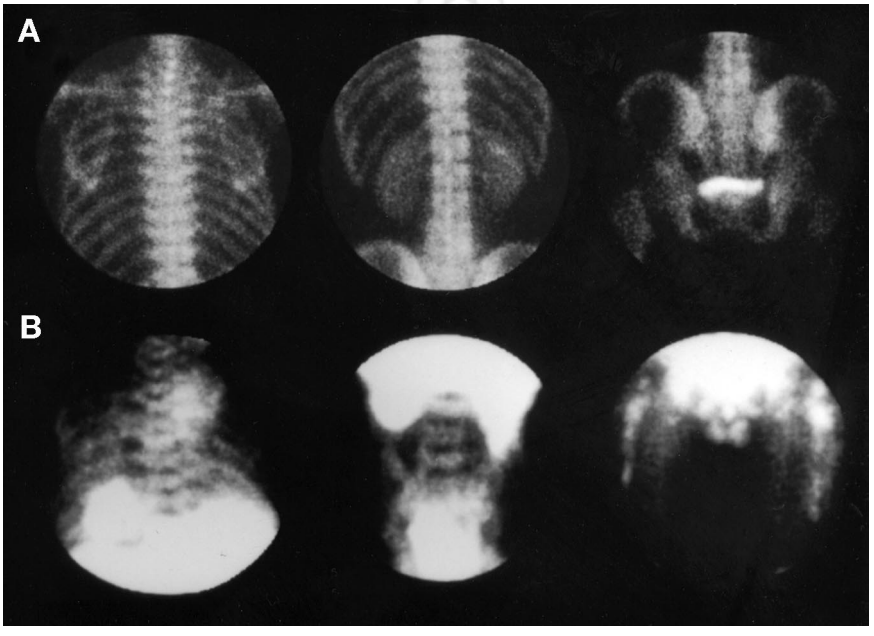

FIGURE 4. Patient with lung cancer. (A) ^{99m}Tc-HMDP scans show no definite bone metastases, although anterior pelvis image could not be obtained. (B) ^{99m}Tc-MIBI scans show increased uptake in multiple regions of ribs, in thoracic and lumbar spine, and in right lung tumor and also show irregular-shaped uptake in bilateral proximal femur in anterior pelvis image. MRI showed multiple metastases in thoracic spine, and bone marrow cytology from puncture sites on sternum showed many lung cancer cells.

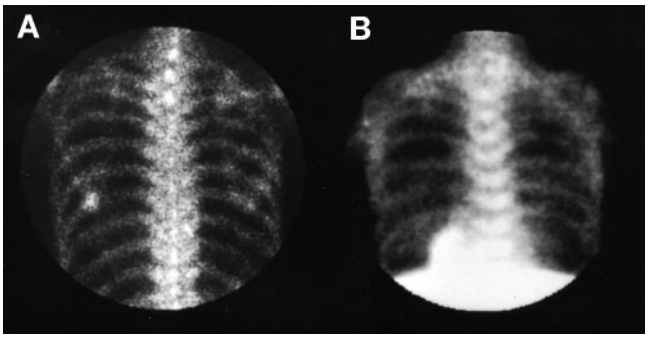

FIGURE 5. Patient with colon cancer. (A) ^{99m}Tc-HMDP scans show no metastases in thoracic spine. (B) Corresponding ^{99m}Tc-MIBI scans reveal diffuse intense uptake in thoracic spine. Bone marrow cytology from puncture sites on each anterior iliac crest indicated positive findings.

these malignancies, especially significantly more metastases in lung cancer: 27 of 29 lesions (93.1%) versus 20 of 29 lesions (69.0%) ($P < 0.05$), respectively. However, ^{99m}Tc-MIBI scans were less sensitive than ^{99m}Tc-HMDP scans for detecting bone metastases due to prostate cancer in the other skeletal sites except for the femur and humerus: 26 of 27 (96.3%) versus 18 of 27 (66.7%) ($P < 0.025$), respectively.

DISCUSSION

This study shows that ^{99m}Tc-MIBI scans can detect bone metastases with better sensitivity than conventional ^{99m}Tc-HMDP bone scans. In addition, ^{99m}Tc-MIBI detects few abnormalities in lesions with skeletal trauma, degenerative disease, and many other benign active disorders of the bones and joints. ^{99m}Tc-MIBI scans showed significantly higher sensitivity for detecting metastases, especially in the femur and humerus, than ^{99m}Tc-HMDP scans. In 17 patients, ^{99m}Tc-HMDP scans did not detect any metastatic lesions, but ^{99m}Tc-MIBI scans correctly detected bone metastases, and subsequent development of multiple lesions was observed on follow-up ^{99m}Tc-HMDP scans of 15 patients.

We have shown in previous animal studies that uptake of ^{99m}Tc-MIBI in the bone marrow is significantly higher than that of a conventional bone tracer and that MIBI is promising for the detection of bone marrow malignancy (*14*). In our recent study of patients with various bone marrow malignancies, the clearly visualized focal accumulation of ^{99m}Tc-MIBI in femoral marrow correlated well with the clinical findings of bone marrow malignancy (*15*), and ^{99m}Tc-MIBI imaging of femoral marrow was considered to be useful for detecting minimal residual disease in acute leukemia (*16*).

Therefore, our results suggest that abnormal ^{99m}Tc-MIBI accumulation related to bone marrow metastases may occur at an early stage before the bone remodeling process through osteoclastic and osteoblastic activity in the surrounding bone can be detected on conventional bone scans, and tumor cells located in the bone marrow may be confined to this site for some time. To definitively establish the usefulness of ^{99m}Tc-MIBI scans for detecting bone marrow metastases, a prospective follow-up study with conventional bone scans and ^{99m}Tc-MIBI scans is required; we are now performing this study on patients with breast cancer.

^{99m}Tc-HMDP scans detected more lesions in the ribs, thoracic spine, lumbar spine, and pelvis than ^{99m}Tc-MIBI scans, although the differences were not significant. The prominent uptake of ^{99m}Tc-MIBI in the heart and liver and the low signal-to-background ratio in the intrathoracic area may cause difficulties in evaluating abnormal activity of ^{99m}Tc-MIBI in the thoracic spine and ribs. It also may be difficult to evaluate abnormal activity of ^{99m}Tc-MIBI in the

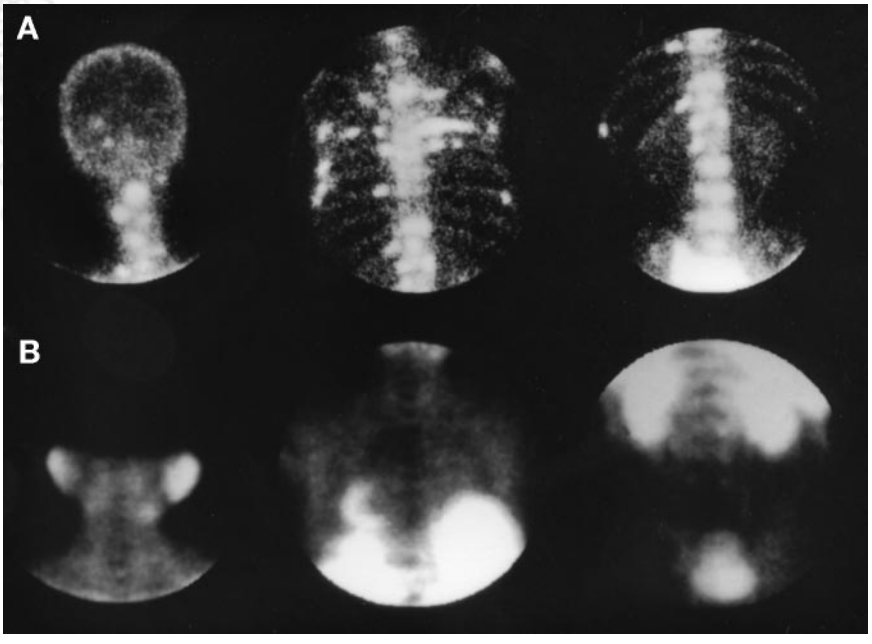

FIGURE 6. Patient with prostate cancer. (A) ^{99m}Tc-HMDP scans show multiple intense accumulations in cervical spine, thoracic spine, lumbar spine, skull, and ribs. (B) In contrast, ^{99m}Tc-MIBI scans do not show any abnormalities.

TABLE 2
Comparison of Detectability of Bone Metastases Between ^{99m}Tc-HMDP and ^{99m}Tc-MIBI Scans in Relation to Underlying Primary Malignancy

Primary malignancy	No. of metastases	^{99m}Tc-HMDP(+), ^{99m}Tc-MIBI(−)	^{99m}Tc-HMDP(−), ^{99m}Tc-MIBI(+)	^{99m}Tc-HMDP(+), ^{99m}Tc-MIBI(+)	^{99m}Tc-HMDP(+)*	^{99m}Tc-MIBI(+)*	^{99m}Tc-HMDP vs. ^{99m}Tc-MIBI
Breast cancer	69	10	27	32	42 (60.9)	59 (85.5)	$P < 0.005$
Lung cancer	68	17	20	31	48 (70.6)	51 (75.0)	NS
Prostate cancer	38	9	4	25	34 (89.5)	29 (76.3)	NS
Myeloma	30	0	13	17	17 (56.7)	30 (100)	$P < 0.005$
Hepatoma	21	0	11	10	10 (47.6)	21 (100)	$P < 0.005$
Gastric cancer	21	4	3	14	18 (85.7)	17 (81.0)	NS
Bladder cancer	17	0	2	15	15 (88.2)	17 (100)	NS
Renal cancer	11	4	4	3	7 (63.6)	7 (63.6)	NS
Colon cancer	11	2	3	6	8 (72.7)	9 (81.8)	NS

*Value in parentheses is percentage.
^{99m}Tc-HMDP(+) = ^{99m}Tc-HMDP positive; ^{99m}Tc-HMDP(−) = ^{99m}Tc-HMDP negative; ^{99m}Tc-MIBI(+) = ^{99m}Tc-MIBI positive; ^{99m}Tc-MIBI(−) = ^{99m}Tc-MIBI negative; NS = not significant.

TABLE 3
Comparison of Detectability of Bone Metastases Between ^{99m}Tc-HMDP and ^{99m}Tc-MIBI Scans in Regions of Femur and Humerus

Primary malignancy	No. of metastases	^{99m}Tc-HMDP(+), ^{99m}Tc-MIBI(−)	^{99m}Tc-HMDP(−), ^{99m}Tc-MIBI(+)	^{99m}Tc-HMDP(+), ^{99m}Tc-MIBI(+)	^{99m}Tc-HMDP(+)*	^{99m}Tc-MIBI(+)*	^{99m}Tc-HMDP vs. ^{99m}Tc-MIBI
Breast cancer	21	0	14	7	7 (33.3)	21 (100)	$P < 0.005$
Lung cancer	29	2	9	18	20 (69.0)	27 (93.1)	$P < 0.05$
Prostate cancer	11	0	3	8	8 (72.7)	11 (100)	NS
Myeloma	11	0	5	6	6 (54.5)	11 (100)	$P < 0.05$
Hepatoma	12	0	10	2	2 (16.7)	12 (100)	$P < 0.005$
Gastric cancer	4	0	3	1	1 (25.0)	4 (100)	NS
Bladder cancer	2	0	0	2	2 (100)	2 (100)	NS
Renal cancer	5	0	4	1	1 (20.0)	5 (100)	NS
Colon cancer	3	0	3	0	0	3 (100)	NS

*Value in parentheses is percentage.
^{99m}Tc-HMDP(+) = ^{99m}Tc-HMDP positive; ^{99m}Tc-HMDP(−) = ^{99m}Tc-HMDP negative; ^{99m}Tc-MIBI(+) = ^{99m}Tc-MIBI positive; ^{99m}Tc-MIBI(−) = ^{99m}Tc-MIBI negative; NS = not significant.

TABLE 4
Comparison of Detectability of Bone Metastases Between ^{99m}Tc-HMDP and ^{99m}Tc-MIBI Scans in Regions Other Than Femur and Humerus

Primary malignancy	No. of metastases	^{99m}Tc-HMDP(+), ^{99m}Tc-MIBI(−)	^{99m}Tc-HMDP(−), ^{99m}Tc-MIBI(+)	^{99m}Tc-HMDP(+), ^{99m}Tc-MIBI(+)	^{99m}Tc-HMDP(+)*	^{99m}Tc-MIBI(+)*	^{99m}Tc-HMDP vs. ^{99m}Tc-MIBI
Breast cancer	48	10	13	25	35 (72.9)	38 (79.2)	NS
Lung cancer	39	13	9	17	30 (76.9)	26 (66.7)	NS
Prostate cancer	27	9	1	17	26 (96.3)	18 (66.7)	$P < 0.025$
Myeloma	19	0	7	12	12 (63.2)	19 (100)	$P < 0.025$
Hepatoma	9	0	1	8	8 (88.9)	9 (100)	NS
Gastric cancer	17	4	0	13	17 (100)	13 (76.5)	NS
Bladder cancer	15	0	2	13	13 (86.7)	15 (100)	NS
Renal cancer	6	4	0	2	6 (100)	2 (33.3)	NS
Colon cancer	8	2	0	6	8 (100)	6 (75.0)	NS

*Value in parentheses is percentage.
^{99m}Tc-HMDP(+) = ^{99m}Tc-HMDP positive; ^{99m}Tc-HMDP(−) = ^{99m}Tc-HMDP negative; ^{99m}Tc-MIBI(+) = ^{99m}Tc-MIBI positive; ^{99m}Tc-MIBI(−) = ^{99m}Tc-MIBI negative; NS = not significant.

lumbar spine and pelvis because ^{99m}Tc-MIBI activity in the gastrointestinal area and kidney may obscure the underlying abnormality. In contrast, detecting abnormal activity of ^{99m}Tc-MIBI in the femur and humerus is easier than evaluating abnormality in the spine, ribs, and sternum, which retain much cellular marrow and show homogeneous mild activity of ^{99m}Tc-MIBI, because femoral marrow and humeral marrow are largely fatty in adults. In an earlier study, mild activity of ^{99m}Tc-MIBI in the femur and humerus was observed in only 16 (11.3%) of 141 control patients and in 2 (1.6%) of 124 control patients with presumed normal bone and bone marrow, but mild activity of ^{99m}Tc-MIBI in the spine was observed most frequently in 111 (89.5%) of 124 control patients (*15*).

^{99m}Tc-MIBI scans were superior to ^{99m}Tc-HMDP scans in the detection of bone metastases due to breast cancer, multiple myeloma, and hepatoma, which are known to show predominantly osteolytic metastases. Also, in lung cancer, which is likely to show osteolytic metastases, ^{99m}Tc-MIBI scans revealed slightly more bone metastases in all skeletal sites and significantly more metastases in the femur and humerus than ^{99m}Tc-HMDP scans. However, in prostate cancer, which is known to show predominantly osteosclerotic metastases, ^{99m}Tc-HMDP scans revealed markedly more bone metastases in the other sites, except for the femur and humerus, than MIBI scans.

^{18}F-FDG PET evaluation of bone metastases in breast cancer showed a higher sensitivity for the detection of lytic bone lesions than conventional bone scans, but it was less sensitive for sclerotic metastases (*17*). This lack of sensitivity in the detection of osteosclerotic metastases has also been reported in patients with prostate cancer (*18*). Sclerotic metastases are relatively acellular and, as such, lower volumes of viable tumor tissue within individual lesions may influence the degree of uptake of ^{99m}Tc-MIBI. Furthermore, a bone marrow biopsy study in bone metastases showed that marrow fibrosis is more pronounced in sclerotic metastases than in lytic metastases (*19*).

Because of retrospective confirmation, we could not classify bone metastases into lytic, sclerotic, or mixed lesions. This study indicates that uptake of ^{99m}Tc-MIBI may be promoted in osteolytic metastases with maintained higher mitochondrial and plasma membrane potentials secondary to increased metabolic activity and may be reduced in sclerotic metastases.

Bone metastases cause considerable morbidity and mortality in osteotropic malignancies. The treatment of bone metastases with conventional chemotherapy has been disappointing. Recent published data show a decreased incidence of new bone metastases in patients with primary breast cancer and marrow tumor cells treated with adjuvant bisphosphonates (*20*). On the basis of these findings, it would be advantageous to introduce a prophylactic therapy for patients at risk for development of bone metastases as early as possible to prevent the development and progression of bone destruction. ^{99m}Tc-MIBI imaging may have potential value for the strategy of prophylactic therapy with bisphosphonates for bone metastases.

CONCLUSION

This study suggests that ^{99m}Tc-MIBI scans have better sensitivity for detecting bone metastases, provide more specific complementary findings than conventional bone scans, and may be a useful method for evaluating bone marrow metastasis. Therefore, ^{99m}Tc-MIBI has potential value in the planning of prophylactic therapy with bisphosphonates for bone metastases.

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