

Evaluation of Oncologic Patients with Suspected Lesions on Planar Bone Scintigraphy Using SPECT/CT

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Abstract

Aim: This study aimed to evaluate the diagnostic accuracy of Single photon emission computed tomography/Computed tomography (SPECT/CT) to clinical management in oncologic patients with indeterminate lesions on planar bone scintigraphy. **Methods:** A total of 1170 oncologic patients who underwent planar bone scintigraphy between March 2010 and September 2012 were retrospectively reviewed. Benign and malignant lesions could be differentiated on planar bone scintigraphy in 670 patients, whereas the remaining 500 patients with indeterminate findings were included in the study. The final diagnosis was established by clinical follow-up, diagnostic computed tomography, magnetic resonance imaging, Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography, biopsy, or a combination of these reference standard methods. **Results:** Of the 500 patients included in the study, 261 were male and 239 were female, with a mean age of 59.5 ± 14.3 years. Based on SPECT/CT findings, 306 patients (61.2%) were classified as benign, 129 (25.8%) as malignant, and 65 (13.0%) as indeterminate. Of the 306 patients classified as benign on SPECT/CT, 4 (0.8%) were subsequently confirmed to have bone metastases, whereas 4 (0.8%) of the 129 patients classified as malignant were ultimately diagnosed as benign. Of the 65 patients with indeterminate SPECT/CT findings, 21 (4.2%) were confirmed to have malignant lesions, whereas 44 (8.8%) were found to have benign lesions. The sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy of SPECT/CT were 97.3%, 86.3%, 75.3%, 98.7%, and 89.6%, respectively ($p < 0.001$). **Conclusion:** SPECT/CT improves diagnostic accuracy in oncologic patients with indeterminate findings on planar bone scintigraphy and provides significant clinical value in the evaluation of skeletal lesions, particularly by markedly increasing specificity.

Keywords: Bone scintigraphy, SPECT/CT, bone metastasis, hybrid imaging

1. Introduction

Accurate staging is an important component of effective cancer management, particularly for improving patient outcomes and survival.¹

Skeletal metastases are common in several malignancies and significantly influence prognosis and therapeutic decisions. Therefore, accurate detection and localization of

bone involvement are crucial in oncologic imaging. Whole-body bone scintigraphy is widely used for the evaluation of bone metastases owing to its high sensitivity in detecting early metabolic changes in bone. It can identify increased osteoblastic activity before structural changes become evident on conventional radiography. However, its main limitation is relatively low specificity and limited anatomical localization, as it primarily provides functional information.²⁻⁶

Single photon emission computed tomography/Computed tomography (SPECT/CT) provides more precise lesion localization and improves diagnostic confidence. Compared with planar bone scintigraphy, it has been shown to enhance diagnostic accuracy and provide additional clinically relevant information, particularly in cases with equivocal findings.⁷⁻¹⁴

The aim of this study was to investigate the diagnostic accuracy and additional contribution of SPECT/CT in oncologic patients who underwent bone scan, but for whom a final diagnosis could not initially be determined.

2. Materials and Methods

2.1. Patients

Ethical approval was obtained from the Ethics Committee of Ankara Numune Training and Research Hospital (Meeting Date: September 5, 2012; Decision No. 2012-438). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. In this single center retrospective study, 1170 oncologic patients who were directed to the Nuclear Medicine Department for assessment of bone metastasis and who underwent both bone scintigraphy and SPECT/CT between March 2010 and September 2012 were analyzed. In 670 of these patients, a benign/malignant distinction was achieved using whole-body bone scintigraphy. The remaining 500 patients, in whom no definitive differentiation could be made on whole body imaging, were later evaluated with SPECT/CT. Final diagnoses were established using clinical follow-up, diagnostic CT, magnetic resonance imaging (MRI), Fluorine-18 Fluorodeoxyglucose Positron emission tomography/Computed tomography (PET/CT), biopsy, or a combination of these methods. Patient follow-up was completed in March 2013.

2.2. Image Acquisition

Whole-body bone scan was performed 2-4 hours after intravenous injection of 15-20 mCi (555-740 MBq) Technetium-99m (Tc-99m) methylene diphosphonate. Imaging was acquired using dual- and single-head gamma cameras equipped with low-energy high-resolution parallel-hole collimators, including Infinia/Hawkeye 4 (GE Healthcare, USA) and DVH-S (Mediso, Hungary). Whole-body images were obtained with a matrix of 256 x 1024 at a scan speed of 14 cm/min.

SPECT/CT imaging was performed using an Infinia dual-head gamma camera combined with a 4-slice CT scanner Infinia/Hawkeye 4 (GE Healthcare, USA). CT acquisition parameters were 140 keV and 2.5 mA, with a slice thickness of 4.6 mm. CT images were obtained in multiple slices using a 512x512 matrix over approximately 4 minutes.

2.3. Image Evaluation and Data Analysis

Planar bone scintigraphy and SPECT/CT images were retrospectively assessed by two experienced nuclear medicine physicians at different times and independently of each other. Initially, planar bone scintigraphy images were assessed, followed by interpretation of SPECT/CT fusion images. Based on planar scintigraphy findings, patients were categorized into three groups: benign, malignant, and suspicious. On planar bone scintigraphy, lesions showing uptake equal to or less than that of the anterior iliac crest or around joints such as the knees, wrists, and elbows were considered benign when compatible with degenerative changes. Typical benign patterns also included clustered focal uptake in ribs

suggestive of traumatic fractures, mild uptake at anterior rib ends due to trauma, and increased uptake in joint regions consistent with osteoarthritic or degenerative changes. Findings considered malignant included randomly distributed multiple intense focal or diffuse uptake throughout the skeleton, linear intense rib uptake, diffuse uptake involving a vertebral body or pedicle, intense uptake in bones other than joints with no joint involvement, and uptake greater than that of the anterior iliac crest. Suspicious findings included solitary focal uptake, uptake extending into adjacent joints, costovertebral uptake indistinguishable from facet joint involvement, vertebral uptake with unclear relationship to intervertebral disc space, irregular or heterogeneous uptake patterns, and photopenic areas.

SPECT/CT fusion images were also classified as benign, malignant, or suspicious. Evaluation was based on fused axial, sagittal, and coronal CT and SPECT images. Lesions were considered benign when increased tracer uptake corresponded to CT findings such as degenerative osteophytes, facet joint involvement, vacuum phenomenon, subchondral cysts, disc space narrowing, Schmorl's nodes, subchondral sclerosis, compression fractures, fracture healing/callus formation, or well-defined, focal, mild sclerosis. Findings were considered malignant when CT demonstrated bone destruction, expansion, cortical disruption, irregular, well-defined marked sclerosis, disruption of the periosteal integrity, osteolytic lesions with or without soft tissue mass, purely lytic lesions without sclerosis, or osteoblastic lesions causing asymmetric bone marrow density increase. Cases that could not be clearly classified as benign or malignant were categorized as suspicious.

2.4. Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean $\pm$ standard deviation for continuous variables and as frequency and percentage for categorical variables. The association between SPECT/CT findings and final diagnosis (metastatic vs. non-metastatic) was evaluated using Pearson's chi-square test. Diagnostic performance of SPECT/CT was assessed by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. A p-value of < 0.05 was considered statistically significant.

3. Results

Of the 1170 patients, 660 were female (56.4%) and 510 were male (43.6%), with a mean age of 58.9 ± 13.8 years (range: 9–94 years). In 670 patients, a benign/malignant distinction was achieved using planar bone scintigraphy. The remaining 500 patients, in whom no definitive differentiation could be made, were included in this study. Among these 500 patients, 261 were male (52.2%) and 239 were female (47.8%), with a mean age of 59.5 ± 14.3 years (range: 14–94 years) (Table 1).

Table 1. Demographic characteristics of patients with and without a definitive benign/malignant distinction on planar bone scintigraphy

Variables	Benign/Malignant differentiation achieved	Benign/Malignant differentiation not achieved	Total
Number of patients	670	500	1170
Age (years)	58.4 ± 13.3	59.5 ± 14.3	58.9 ± 13.8
Age range (years)	9-87	14-94	9-94
Sex			
Male	249 (37.2%)	261 (52.2%)	510 (43.6%)
Female	421 (62.8%)	239 (47.8%)	660 (56.4%)

The most common primary malignancies were breast cancer in 146 patients (29.2%), prostate cancer in 109 patients (21.8%), and lung cancer in 30 patients (6.0%), while the remaining patients were classified under other malignancies (Table 2).

Table 2. Primary Tumor Types and Frequencies in 500 Patients with Indeterminate Benign-Malignant Findings on Planar Bone Scintigraphy

Diagnosis	Number of patients	Frequency (%)
Breast cancer	146	29.20
Prostate cancer	109	21.80
Lung cancer	30	6.00
Colon cancer	22	4.40
Bladder cancer	21	4.20
Gastric cancer	21	4.20
Renal cell carcinoma	14	2.80
Hepatocellular carcinoma	12	2.40
Malignant melanoma	7	1.40
Nasopharyngeal cancer	6	1.20
Other cancers*	31	6.20
Total	500	100.00

*Other cancers: esophageal cancer, brain tumor, endometrial cancer, soft tissue sarcoma, gallbladder cancer, leukemia, tongue base cancer, cervical cancer, duodenal cancer, histiocytosis, gastrointestinal stromal tumor, polycythemia vera, parathyroid carcinoma, adrenal tumor, hypopharyngeal cancer, ameloblastoma, laryngeal cancer, lymphoma, ovarian cancer, testicular tumor, neuroendocrine tumor, pancreatic cancer.

After planar bone scintigraphy, these 500 patients underwent further evaluation with SPECT/CT. Assessment was performed on a patient basis rather than lesion count, considering the presence or absence of metastasis. Based on SPECT/CT findings, 306 patients (61.20%) were classified as benign, showing findings such as osteophytes, degenerative changes, fractures, and compression fractures. A total of 129 patients (25.80%) were classified as malignant, demonstrating findings such as bone destruction, expansion, cortical disruption, irregular, well-defined sclerosis, and disruption of the periosteal integrity. The remaining 65 patients (13.00%) were categorized as indeterminate.

Lesion distribution was as follows: vertebra in 199 patients (39.8%), costosternal region in 118 patients (23.6%), pelvis in 99 patients (19.8%), lower extremities in 45 patients (9.0%), upper extremities in 22 patients (4.4%), and cranium in 17 patients (3.4%). Benign lesions identified by SPECT/CT were most frequently located in the vertebrae and costosternal region. Malignant lesions were most commonly observed in the pelvis, followed by the vertebrae and costosternal region. Indeterminate lesions were most frequently detected in the vertebrae, pelvis, and costosternal region (Table 3).

Table 3. Distribution of Benign, Malignant, and Indeterminate Increased Tracer Uptake According to Lesion Location in 500 Patients with Indeterminate Benign-Malignant Findings on Planar Bone Scintigraphy

Lesion Localization	Benign	Malignant	Indeterminate	Total	Localization (%)
Vertebra	140	37	22	199	39.80
Costosternal region	78	30	10	118	23.60
Pelvis	43	39	17	99	19.80
Lower extremities	24	13	8	45	9.00
Upper extremities	14	6	2	22	4.40
Cranium	7	4	6	17	3.40

Lesion Localization	Benign	Malignant	Indeterminate	Total	Localization (%)
Overall Total	306	129	65	500	100.00
Overall Percentage (%)	61.20	25.80	13.00	100.00	—

Final diagnoses were established using clinical follow-up, diagnostic imaging methods, or a combination of these modalities. In total, 261 patients (68.7%) were evaluated with diagnostic CT, 104 patients (27.4%) with MRI, 7 patients (1.8%) with PET/CT, and 8 patients (2.1%) underwent biopsy.

In 173 patients who could not undergo advanced imaging, diagnosis was based on clinical follow-up. Of these, 128 (74.0%) were classified as benign and 45 (26.0%) as malignant.

Overall, metastasis was detected in 150 patients (30%), while 350 patients (70%) had no evidence of metastasis.

When SPECT/CT findings were compared with final diagnoses, 4 of 306 patients (0.8%) classified as benign were found to have metastases, while 4 of 129 patients (0.8%) classified as malignant were ultimately determined to be benign. Among the 65 indeterminate cases, 21 (4.2%) were malignant and 44 (8.8%) were benign according to final diagnosis.

Based on the final diagnosis, the sensitivity, specificity, PPV, NPV, and accuracy of SPECT/CT were 97.3%, 86.3%, 75.3%, 98.7%, and 89.6%, respectively ($p < 0.001$).

4. Discussion

Whole-body bone scintigraphy remains one of the generally applied method for the demonstration of the bone metastasis because of its high sensitivity and whole-body imaging capability.¹⁵⁻¹⁶ Skeletal metastases occur in approximately 30-70% of patients with advanced stage cancers, particularly in breast, prostate, and lung cancers.¹⁷ The accurate detection or exclusion of skeletal metastasis has a direct effect on tumor staging, therapy selection, prognosis, and patient survival. Therefore, distinguishing metastatic lesions from benign skeletal abnormalities is a fundamental objective of oncologic imaging.¹⁸⁻²⁰

Bone scintigraphy detects increased osteoblastic activity and may identify metastatic disease earlier than conventional radiography. However, Tc-99m-labeled diphosphonates accumulate in both malignant and benign conditions, including degenerative disease, fractures, inflammatory changes, and postoperative remodeling. Consequently, although bone scintigraphy demonstrates excellent sensitivity, its specificity remains relatively low. Furthermore, the lack of precise anatomical information and the overlap of adjacent skeletal structures on planar imaging frequently make lesion characterization difficult, especially in the vertebral column, ribs, and pelvis, where degenerative changes are highly prevalent.²¹⁻²⁴

SPECT/CT overcomes many of these limitations by combining functional and anatomical information. This enables precise localization of radiotracer uptake and facilitates differentiation between degenerative, traumatic, and metastatic lesions. The greatest diagnostic benefit has been reported in anatomically complicated regions such as the spine and pelvis, where planar scintigraphy alone often produces equivocal findings.²⁵⁻²⁸

In the present study, SPECT/CT correctly characterized most lesions that were considered indeterminate on bone scan. Furthermore, it substantially improves the specificity of planar bone scintigraphy while maintaining its high sensitivity for detecting skeletal metastases.

Our findings are compatible with previous reports evaluating the diagnostic performance of SPECT/CT. It was demonstrated that hybrid SPECT/CT significantly augmented lesion characterization compared with bone scan and SPECT alone, particularly in the

spine, thorax, and pelvis, increasing specificity from 19% with planar scintigraphy to 81% with SPECT/CT while maintaining excellent sensitivity.^{15,16} Similarly, Zhao et al. reported significantly higher sensitivity and overall diagnostic performance for SPECT/CT compared with SPECT or side-by-side SPECT and CT evaluation.¹⁸ It was also documented that SPECT/CT resolved approximately 92% of equivocal lesions identified on SPECT by accurately localizing radiotracer uptake and differentiating benign degenerative lesions from metastatic disease.²³

Comparable findings have been reported by previous studies which showed that hybrid imaging significantly reduced the number of indeterminate lesions and increased diagnostic confidence.^{19,21,25,29} Collectively, these studies support the growing evidence that SPECT/CT is better than scintigraphy for the evaluation of equivocal bone lesions.

In our study, vertebral lesions represented the largest proportion of equivocal findings, followed by the costosternal region and pelvis. This observation is consistent with previous reports, as these anatomical regions are common sites of both metastatic disease and degenerative skeletal changes.^{15-17,23} Degenerative facet arthropathy, osteophyte formation, compression fractures, and other benign vertebral abnormalities frequently produce increased tracer uptake that cannot be reliably differentiated from metastatic disease on planar scintigraphy alone. The addition of CT enables accurate identification of these structural abnormalities, thereby substantially improving diagnostic specificity.^{15,18,25-26}

Another important clinical advantage of SPECT/CT is the reduction in unnecessary additional imaging. Patients with indeterminate findings on planar scintigraphy often require further evaluation with CT, MRI, or PET/CT, resulting in increased healthcare costs, delayed diagnosis, and greater patient anxiety. This method may establish a definitive diagnosis in many equivocal cases, shorten the diagnostic pathway, facilitate earlier treatment decisions, and improve patient management.^{17,18,25,28}

Although low-dose CT does not replace diagnostic CT or MRI, it provides sufficient anatomical information to characterize most benign skeletal abnormalities and many metastatic lesions. Nevertheless, purely osteolytic lesions or early bone marrow infiltration without structural changes may remain difficult to identify using low-dose CT alone.^{20,22,30} Therefore, additional cross-sectional imaging should still be considered in selected patients when clinical suspicion persists despite negative or equivocal SPECT/CT findings.

One of the strengths of the current research is the large number of patients with equivocal planar bone scintigraphy findings. Compared with previously published series, which generally included between 37 and 125 patients,^{15,18-19,21,23,29} our study evaluated 500 consecutive patients, providing a more comprehensive evaluation of the diagnostic accuracy SPECT/CT in routine clinical practice. Despite methodological differences among published studies, including variations in CT acquisition protocols, scanner technology, patient populations, and reference standards, the overall evidence consistently demonstrates that SPECT/CT significantly increases the specificity of bone scintigraphy without compromising its excellent sensitivity.

This study has limitations. Retrospective design may have introduced selection bias. Histopathological confirmation was not available for all patients, as biopsy of every suspicious lesion was neither technically feasible nor ethically justified. Therefore, final diagnoses were established using a combination of clinical follow-up, biopsy, and serial imaging, which reflects routine clinical practice but does not represent a uniform reference standard.

5. Conclusions

Our results are in agreement with the existing literature and demonstrate that SPECT/CT greatly improves the diagnostic accuracy of bone scan in oncologic patients with indeterminate skeletal lesions. The high sensitivity and markedly improved

specificity observed in this study underscores the using of SPECT/CT as a additional imaging modality for indeterminate lesions on bone scan.

This method substantially reduces equivocal findings on planar bone scintigraphy and improves diagnostic confidence. These findings may facilitate clinical decision-making and reduce the need for additional imaging examinations.

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Ethics committee name, approval date, and approval number: Ethical approval was obtained from the Ethics Committee of Ankara Numune Training and Research Hospital (Meeting Date: September 5, 2012, Decision No. 2012-438).

Clinical trial registration number: This study is a retrospective study.

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