

# Comparison of Single Photon Emission Computerised Tomography (SPECT) with Planar Wholebody Bone Scan (WBBS) in Diagnosis of Solitary Vertebral Lesion in Non-Skeletal Malignancies in Terms of Diagnostic Accuracy

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## ABSTRACT

**Objective:** To compare single photon emission computed tomography (SPECT) with planar whole body bone scan (WBBS) in diagnosis of solitary vertebral lesion in non-skeletal malignancies in terms of diagnostic accuracy.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** Nuclear Medical Centre, Armed Forces Institute of Pathology, Rawalpindi, July 2014 to June 2016.

**Methodology:** After fulfilling the inclusion and exclusion criteria and taking written informed consent, 74 patients of various extra-skeletal malignancies were enrolled in the study. Patients were injected with 740 MBq of <sup>99m</sup>Tc-methylene diphosphonate (MDP) intravenously. WBBS images were acquired in anterior and posterior projections 3 hours after injection. SPECT images of the desired vertebral region were acquired subsequently along with low dose CT. All the images were read by two experienced nuclear medicine physicians. Lesions were diagnosed as definitely benign, indeterminate/equivocal and definitely malignant separately on WBBS and SPECT. With SPECT/CT as gold standard, sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and accuracy were calculated.

**Results:** For planar WBBS, sensitivity was 91.43%, NPV was 86.96%, specificity was 51.28% and PPV remained 62.75%. For SPECT, sensitivity and NPV were 100%, specificity was 92.31% and PPV remained 92.11%. Accuracy remained 70.27% and 95.95% for planar WBBS and SPECT, respectively.

**Conclusion:** SPECT imaging significantly increases the specificity ( $p < 0.05$ ) of <sup>99m</sup>Tc-MDP skeletal scintiscanning and accurately diagnoses the equivocal lesions as compared to planar images.

**Key Words:** Metastasis, WBBS, SPECT, SPECT/CT, <sup>99m</sup>Tc-MDP.

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## INTRODUCTION

Diagnosis of distant metastasis is a mainstay in the staging of a malignancy as it determines the course of disease.<sup>1</sup> Skeleton is one of the most common sites of distant metastasis.<sup>2</sup> Most common site of skeletal metastasis is vertebral column (39%),<sup>3</sup> with highest predilection for lumbar spine (52%), followed by dorsal (36%) and the cervical spine (12%).<sup>4</sup> However, it is imperative to rule out coexisting benign etiologies like those in disc, facet joints and pars inter articularis and other sports injuries.<sup>5</sup>

Among conventional techniques, plain X-ray can only detect the lesion when there is loss of at least 50% bone substance with an overall sensitivity of around 50%.<sup>1</sup> Presently, WBBS is the investigation of choice for detection of skeletal metastasis, followed by SPECT of indeterminate lesions. Further investigation of equivocal lesions is done with plain X-rays, CT and MRI.<sup>6</sup> CT is highly sensitive for both osteolytic and osteoblastic lesions but not for marrow lesions. Magnetic resonance imaging (MRI) is a high contrast and high resolution technique for localisation of skeletal metastasis including that of bone marrow and their soft tissue extension.<sup>3</sup>

SPECT/CT is a well-established hybrid technique that can characterise skeletal lesions as definitely benign or definitely malignant instead of indeterminate or equivocal.<sup>7</sup> However, it puts increased radiation burden on patient in addition to extra cost and issue of non-availability in our setup. 740 MBq of <sup>99m</sup>Tc-MDP used for

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WBBS or SPECT imaging exposes the patient to 4.2 to 5.2 mSv with an additional dose of 3.8 to 4.2 mSv for the CT component.<sup>8</sup>

The rationale of this study was to ascertain superiority, or otherwise, of SPECT over WBBS imaging in localisation of vertebral metastasis with SPECT/CT as gold standard. Furthermore, objective of the study was to determine diagnostic accuracy of SPECT imaging in comparison with SPECT/CT, and subsequently employing the technique in metastatic workup of equivocal or indeterminate skeletal lesions, thus saving the cost and radiation burden to the patient along with overcoming the issue of non-availability of SPECT/CT.

### METHODOLOGY

This cross-sectional study was carried out at Nuclear Medical Centre, AFIP, Rawalpindi, from July 2014 to June 2016 after approval from Hospital Ethical Committee. Through non-probability consecutive sampling, 74 patients, who fulfilled inclusion and exclusion criteria, were included after written informed consent. Patients of both genders with extra-skeletal malignancy reporting for metastatic workup and having a solitary vertebral lesion on planar WBBS were included in the study. Patients having characteristic multiple hot lesions on WBBS were excluded. Moreover, patients with history of previous chemotherapy or radiation therapy, neo-adjuvant therapy, allergic to bisphosphonates were also excluded from the study.

All patients were given 740 MBq (20 mCi) <sup>99m</sup>Tc-MDP (PINSTECH) intravenously. Patients were advised plenty of liquids and frequent urination post injection. Images were acquired at 3 hours post-injection with

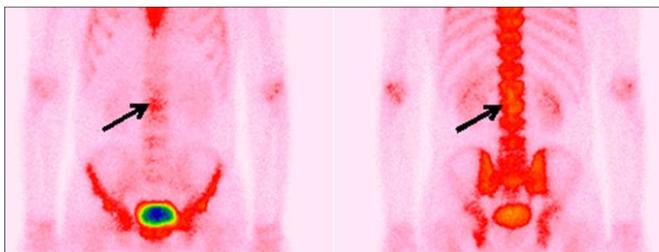
hybrid SPECT/CT Siemens Symbia T6 camera. WBBS images were acquired with energy window of 20% around photopeak of 140keV, using low energy high resolution (LEHR) collimator and 1024 X 256 matrix at a speed of 12cm per minute. It was followed by SPECT with same energy window and collimator with matrix size of 256 x 256. 64 projection images were acquired in circular orbit with 30 sec/image acquisition time. Low dose CT was acquired with 130 Kv, 100mAs, pitch of 1, and a 512x512 matrix. Standard filters were applied and reconstruction was done with filtered back projection.

Images were read by two experienced nuclear medicine physicians (with at least 5 years experience). Lesions were classified as definitely benign, equivocal and definitely malignant on both planar WBBS and SPECT. Diagnosis was confirmed on SPECT/CT. The criteria used for diagnosis of benign/malignant lesion on SPECT/CT are summarised in Table I. For the purpose of calculating sensitivity, specificity, NPV, PPV and accuracy, equivocal lesions were considered as malignant.

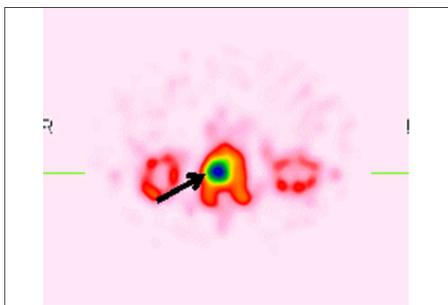
The data was analysed using SPSS version 20. Frequencies and percentages were calculated for qualitative variables like gender, type of tumour and location of metastasis. Mean + SD was calculated for quantitative data like age. In addition, frequencies with percentages were calculated for all categorical variables including sensitivity, specificity, negative predictive value, positive predictive value and accuracy with 2 x 2 contingency tables for WBBS and SPECT separately. Comparison between the two techniques was done using independent t-test, level of significance set at p <0.05.

### RESULTS

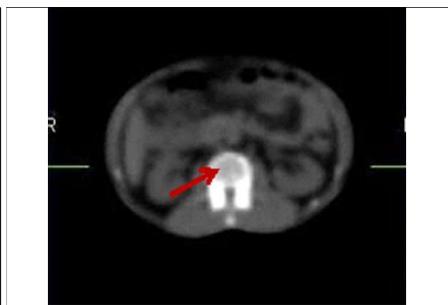
A total of 74 patients were analysed with ages ranging from 31 years to 77 years (58.66 ±10.11 years) with 45.94% (34) females and 54.05% (40) males. Thirty-two (43.2%) patients had carcinoma prostate followed by carcinoma breast in 37.8% (28), lung (9.5%), renal cell (5.4%), medullary thyroid (2.7%) and colorectal (1.4%) carcinomas. Fifty-one (68.9%) patients had lesion identified in lumbar region, 25.7% (19) in thoracic spine, 4.1% (3) in sacrum, and 1.4% (1) had lesions in cervical



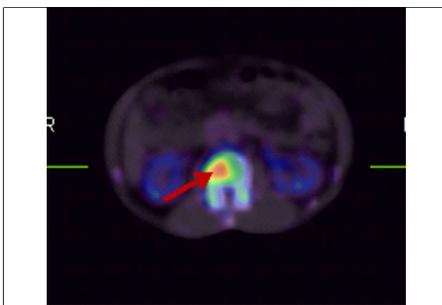
**Figure 1:** Anterior & posterior planar images of lumbar spine showing solitary photon-rich focus (black arrowheads).



**Figure 2:** SPECT at L2 showing photon-rich focus in vertebral body (black arrowhead).



**Figure 3:** CT at L2 showing a lytic lesion (red arrowhead).



**Figure 4:** Fused SPECT/CT showing a metastatic lesion (red arrowhead).

**Table I:** Diagnostic criteria on SPECT/CT.

Benign	Malignant
Facet joint	Body
Costovertebral joint	Pedicle
Transverse	Cold lesion
Spinous process	Lytic lesion
Adjacent vertebra disc	

**Table II:** Comparison of planar WBBS vs. SPECT/CT.

WBBS	SPECT/CT		
	Malignant	Benign	
Malignant	32	19	PPV 62.75%
Benign	3	20	NPV 86.96%
	SEN 91.43%	SPC 51.28%	ACC 70.27%

WBBS: Whole-body bone scan; SPECT: Single photon emission computerised tomography; CT: Computerised tomography; MRI: Magnetic resonance imaging; PET: Photon emission tomography; MDP: Methylene diphosphonate; <sup>99m</sup>Tc: Technetium - 99m.

**Table III:** Comparison of SPECT vs. SPECT/CT.

SPECT	SPECT/CT		
	Malignant	Benign	
Malignant	35	3	PPV 92.11%
Benign	0	36	NPV 100.00%
	SEN 100.00%	SPC 92.31%	ACC 95.95%

WBBS: Whole-body bone scan; SPECT: Single photon emission computerised tomography; CT: Computerised tomography; MRI: Magnetic resonance imaging; PET: Photon emission tomography; MDP: Methylene diphosphonate; <sup>99m</sup>Tc: Technetium - 99m.

spine. On SPECT/CT 66.2% (49) had lesion in vertebral body; out of which, 5 lesions were lytic and 44 were sclerotic. This was followed by facet joint which had lesion in 16.2% (12) patients. Rest of the patients had lesions identified in pedicle (9.5%), disc (5.4%) and transverse and spinous processes (2.8%).

Planar WBBS images showed that lesions were benign in 23 patients, indeterminate in 36, and malignant in 15 patients. SPECT images demonstrated that lesions in 36 patients were benign, 8 were indeterminate, and 30 were malignant. Standard evaluation of SPECT/CT images revealed benign lesions in 39 patients and malignant lesions in 35 patients. The results are summarised in Table II.

Out of 36 indeterminate lesions identified on planar WBBS, 41.66% (15) were diagnosed as benign on SPECT/CT while rest of the 58.33% (21) were malignant. Similarly, out of 8 indeterminate lesions identified on SPECT, 25% (2) were diagnosed as benign on SPECT/CT and 75% (6) as malignant, as shown in Table III. Moreover, 20% (3/15) patients diagnosed as malignant on WBBS were found benign on SPECT/CT while only 3.3% (1/30) evaluated as malignant on SPECT were diagnosed as benign on SPECT/CT. In addition, 8.7% (2/23) lesions declared benign on WBBS

were diagnosed malignant on SPECT/CT while no such case was noted in case of SPECT.

Based on these results, for planar WBBS, sensitivity was 91.43% NPV 86.96%, specificity 51.28% and PPV was 62.75%. For SPECT, sensitivity and NPV were 100%, specificity was 92.31% and PPV remained 92.11%. Accuracy remained 70.27% and 95.95% for planar WBBS and SPECT, respectively (p = 0.04).

## DISCUSSION

Skeletal scintigraphy with <sup>99m</sup>Tc labelled bisphosphonates is a highly sensitive technique for detection of skeletal metastasis that can scan complete skeleton at reasonable cost.<sup>9</sup> However, due to its low specificity, a solitary focal lesion in spine seen on WBBS has 60-70% probability of being metastatic.<sup>10</sup> SPECT adds to the utility of scintigraphy as it improves target to background ratio and the image contrast which improves diagnostic specificity.<sup>11</sup> Incorporation of anatomic imaging like CT further adds to the diagnostic accuracy of SPECT.<sup>12</sup>

Addition of SPECT/CT to WBBS significantly enhances sensitivity and specificity while lowering the proportion of indeterminate diagnosis. However, the most important outcome is the modification in patient management plan by up or down staging of disease by more precisely identifying a metastatic lesion.<sup>13</sup> In addition to characterising indeterminate skeletal lesions by accurately demarcating anatomy of pedicles, vertebral bodies, facet joint and intervertebral discs, SPECT/CT can identify lytic lesions, thus differentiating benign from malignant.<sup>7</sup> Studies have shown that a lesion in pedicle has highest (87.7% to 100%) probability to be malignant followed by vertebral body (36.8 - 57.3%), spinous process (18.7 - 81.3%) and facet joint (0.8 - 21.4%).<sup>14</sup>

Although, PET and MRI have the ability to detect earliest metastatic infiltrations with quantification, yet their utility is limited, due to non-availability and high cost.<sup>15</sup> FDG PET/CT is more sensitive, specific and accurate technique for detection of skeletal metastases than conventional bone scans, especially in vertebral and pelvic lesions.<sup>16</sup> However, PET/MRI supersedes PET/CT with improved conspicuity in bone metastases detection, though overall detection rate remains same for the two.<sup>17</sup>

This study shows the advantage of SPECT over planar WBBS. Sensitivity and NPV remained 100% for SPECT and 91.43% and 86.96%, respectively for WBBS proving both of them to be excellent screening tools. However, SPECT has shown much higher specificity and PPV, 92.31% and 92.11%, respectively, as compared to 51.28% and 62.75%, respectively for WBBS (p = 0.01). Diagnostic accuracy for WBBS and SPECT was 70.27% and 95.95%, respectively (p = 0.04). In this study, for the purpose of calculation, we considered all equivocal cases as positive for malignancy. This enabled a

sensitivity close to 100% but reduced the specificity significantly. SPECT considerably enhances the confidence with which a lesion is reported as definitely benign or malignant instead of indeterminate or equivocal. WBBS diagnosed nearly half (36/74) of the lesions as indeterminate which were reduced to 10.8% (8/74) with SPECT, thus reducing the cost of further investigation.

Comparing WBBS with SPECT/CT, 35.29% (18/51) lesions considered as malignant (indeterminate cases included) on WBBS were evaluated as benign on SPECT/CT. In this regard, 41.66% (15/36) indeterminate lesions and 20.0% (3/15) definitely malignant lesions were diagnosed as benign, thus reducing the specificity of the test. Reasons behind these false diagnoses were intervertebral disc infections spreading to adjacent vertebral bodies, compression fractures, and facet joint pathologies. In addition 8.7% (2/23) patients that were found definitely benign on WBBS came out to be malignant on SPECT/CT due to presence of lytic lesion.

Comparing SPECT with SPECT/CT, only 7.9% (3/38) lesions considered as malignant (indeterminate lesions included) on SPECT were evaluated as benign on SPECT/CT. In this regard, 20.0% (2/8) indeterminate lesions and 3.3% (1/30) definitely malignant lesions were diagnosed as benign. Reasons behind these false diagnoses were intervertebral disc infections. Calculating the impact on management, treatment of more than 27.0% (20/74) patients undergoing only WBBS and less than 5% (3/74) of patients undergoing SPECT was altered by SPECT/CT.

Several studies have compared WBBS, SPECT, and SPECT/CT in equivocal lesions and have shown a substantial improvement in specificity with SPECT/CT. However, no significant local data has been published in this regard. Sedonja *et al.* compared 37 patients without known malignancy with 38 patients of malignancy. SPECT was able to detect 58/64 (90.63%) lesions correctly while planar scintigraphy could only evaluate 42/(65.63%) lesions ( $p=0.01$ ).<sup>18</sup> Another study was done at University Hospital Zurich, where out of 37 patients, planar scintigraphy could only identify 64% lesions correctly while SPECT diagnosed 86% with 100% result on SPECT/CT.<sup>19</sup> Compared to these results, in this study, 52/74 (70.27%) were diagnosed correctly by WBBS and 71/74 (95.95%) patients were correctly diagnosed on SPECT/CT.

Talbot *et al.* showed sensitivity and specificity of 78% and 48%, respectively for WBBS; and 87% and 91%, respectively for SPECT.<sup>20</sup> Compared to this, sensitivity and specificity of WBBS were 91% and 51% while those of SPECT were 100% and 92% in this study.

Review of recent meta-analysis done on comparison of various other diagnostic modalities for skeletal metastasis have revealed spectrum of results with

varying relations between sensitivities, specificities and accuracies of different modalities. Liu *et al.* showed that on per-patient basis, sensitivity of SPECT was comparable with PET; and MRI and was significantly higher than that of WBBS and CT. However, it showed specificity of WBBS that was not significantly different from MRI and CT, but higher than SPECT and even PET. Diagnostic odd ratios (DORs) were better for SPECT than WBBS. However, MRI was the best and CT the lowest.<sup>21</sup>

In another recent meta-analysis, Yang *et al.* found that, on per-patient basis, the pooled sensitivity estimates for scintigraphy (86.0%) was significantly better than CT (72.9%). However, both were significantly lower than PET (89.7%) and MRI (90.6%). On the contrary, the pooled specificity estimates for scintigraphy (81.4%) was significantly lower than CT (94.8%), MRI (95.4%) and PET (96.8%). However, on per-lesion basis, the pooled sensitivity estimates for scintigraphy (75.1%) were not significantly different from CT (77.1%) but both were significantly lower than MRI (90.4%) and PET (86.9%). Similarly, the pooled specificity estimates for scintigraphy (93.6%) was higher than CT (83.2%), but lower than MRI (96.0%) and PET (97.0%).<sup>22</sup>

There were a few imitations in this study. Sample size was considerably small with very few patients having lytic lesions. Since lytic lesions were major cause of false negatives on WBBS, more patients with tumors that produce lytic pathologies could have affected the results. Therefore, it is recommended that patients with such tumors should undergo SPECT or preferably SPECT/CT during their metastatic workup. However, those tumors that produce osteoblastic metastasis can be assessed by WBBS aided with SPECT.

## CONCLUSION

WBBS and SPECT are highly sensitive techniques for detection of skeletal metastasis. However, WBBS with its low specificity becomes unable to differentiate between metastatic and concurrently occurring benign lesion in vertebral column. SPECT, on the other hand, has reasonably high specificity and can be employed as diagnostic tool for vertebral metastasis instead of SPECT/CT, which remains the gold standard.

### ETHICAL APPROVAL:

This cross-sectional study was carried out at Nuclear Medical Centre, AFIP after approval from Hospital Ethical Committee.

### CONFLICT OF INTEREST:

No conflict of interest, financial or otherwise, has been involved in carrying out this research.

### AUTHORS' CONTRIBUTION:

ZSD: Conception and design of study, acquisition of data,

statistical analysis of data, drafting of manuscript, final approval.

UIF: Concept and design of study, statistical analysis of data, drafting and revising the manuscript, final approval.

FH, MR: Data interpretation (interpretation of scans), revision of manuscript, final approval.

AJ, KHM: Acquisition of data, statistical analysis of data, drafting of manuscript (literature review), final approval.

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