

# Is there Still Enough Diagnostic Confidence with Bone Spect Scintigraphy Alone: A Retrospective Evaluation and Extended Review of the Literature

S. Gratz<sup>\*,1,3</sup>, H. Höffken<sup>1</sup>, W. Kaiser<sup>3</sup>, K.J. Klose<sup>2</sup> and T.M. Behr<sup>1</sup>

<sup>1</sup>Department of Nuclear Medicine, <sup>2</sup>Department of Radiology of the Philipps University, Marburg, Germany

<sup>3</sup>Department of Nuclear Medicine, Stuttgart, Germany

**Abstract:** *Aim:* Single photon emission computed tomography (SPECT) dramatically increases the sensitivity of bone scanning for detection of spinal abnormalities. However, the level of specificity obtained by SPECT remains controversial and increased diagnostic confidence can be obtained with new imaging modalities such as fused PET/CT and SPECT/CT. *Patients and Methods:* Between 7/2005 and 7/2007 ninety one patients with different malignant primary tumors were investigated. Following injection of 555 MBq <sup>99m</sup>Tc – MDP planar and SPECT images were performed in all patients. *Results:* Out of a total of 145 spinal lesions was confirmed by radiography, SPECT detected 133 (91%). In contrast, planar scintigraphy detected only 99/145 (68%) lesions. SPECT uptake pattern including the vertebral body and an adjacent pedicle was seen in 9/28 (32%) of metastatic lesions and in 1/2 (50%) cases of spondylitis. SPECT uptake pattern including the pedicle alone was seen in 45/115 (39%) of degenerative alterations. Focal lesions limited to the lateral part of the vertebral body, especially to the pars interarticularis (n=8), facet joints (n=14) and costotransversal joints (n=6), were correctly diagnosed as spondylarthrosis and costotransversalarthrosis in all cases. Furthermore, SPECT uptake pattern of spondylitis was biconcave, whereas metastatic lesions showed focal or linear uptakes. *Conclusion:* SPECT without image fusion still gives sufficient diagnostic confidence for the differentiation of benign and malignant spine lesions. Uptake patterns localized at the facet joints or localized at the pedicles are indicative for benign lesions, whereas continuous uptake patterns of the vertebral body and adjacent pedicle remain suspicious for malignancy.

**Keywords:** Bone scanning, SPECT, image fusion, malignancies of the spine.

## INTRODUCTION

The addition of SPECT to <sup>99m</sup>Tc bone scanning has been reported to improve the diagnostic accuracy of <sup>99m</sup>Tc bone scanning for detecting malignant bone involvement and to allow for a straightforward comparison with other tomography-based techniques such as CT and MRI [1-4].

The number of new imaging modalities, such as PET, PET/CT and more recently SPECT/CT technology for the detection of bone metastases is rapidly growing. Increased <sup>18</sup>F-Fluoride uptake in malignant bone lesions reflects the increase in regional blood flow and bone turnover characterizing these lesions [2, 5, 6]. Taking advantage of both the favourable characteristics of <sup>18</sup>F-Fluoride and the better performance of PET, <sup>18</sup>F-Fluoride PET has been reported to be more sensitive for detection of metastases than <sup>99m</sup>Tc bone scanning [2, 3, 6-9].

However, differentiating between bone metastasis and a benign lesion often remains to be imprecise [1, 10]. The location of lesions on SPECT/CT images provides useful information to help differentiate these two conditions [11]. SPECT imaging alone is reported to be insufficient for the precise localization of bone lesions; hence, correlation with anatomic images such as CT scans or MR images is often necessary to increase the specificity of scintigraphic findings [10].

But still, even with SPECT/CT false-negative results were found in case of metastatic lesions located near the articulation or a metastatic lesion being undetectable on CT images. These false-negative cases were pitfalls in image interpretation of bone lesions. Positive <sup>99m</sup>Tc bone scans that showed findings not detected on CT images might require further MR imaging.

Even though the number of readers trained in fusion imaging and the number of centres with PACS is slowly increasing, to our knowledge the majority of PET/CT or SPECT/CT systems remains not commonly used owing to their increased costs and comparative lack of availability. Moreover, image fusion often has to be performed manually, and the fusion should be confirmed by means of consensus of at least one nuclear medicine physician and one radiologist. This is a time-consuming procedure that might limit the routine use of this technique.

In the present retrospective study, we investigated a.) whether SPECT detects spinal lesions not found by planar <sup>99m</sup>Tc bone scanning, b.) whether uptake pattern correlates with the malignancy of the lesion, and c.) whether SPECT gives sufficient diagnostic confidence for differentiating malignant from benign spinal lesions.

## PATIENTS AND METHODS

### Patients

The present study is a retrospective evaluation of clinical data available concordant with local ethics committee approvals and was performed from 7/2005 - 7/2007. The

\*Address correspondence to this author at the Department of Nuclear Medicine, Philipps University of Marburg, Seelbergstrasse 11, D-70372 Stuttgart, Germany; Tel: 001-49-711-5538241; Fax: 001-49-711-5538246; E-mail: Nuklearmedizin-Gratz@gmx.net

evaluation of patient data was anonymous. Ninety one patients (57 female, 34 male, mean age  $59.38 \pm 26.10$  years) with known malignant tumors and suspected spinal metastases underwent  $^{99m}\text{Tc}$  - MDP bone scintigraphy, including planar scans and SPECT. 29 patients received chemotherapy, but no external radiation therapy involving the region of interest was started prior to scanning. Patients suffered from breast (n=36), prostate (n=14), kidney/bladder (n=10), or colorectal cancer (n=9), bone/Ewing sarcoma (n=9), lung cell (n=7), or ovarian cancer (n=6). Patients were followed clinically for at least two years.

## Methods

**Data acquisition** Planar scans and SPECT were performed 3-4 hr after injection of 555 MBq  $^{99m}\text{Tc}$  - MDP in all patients. A double headed gamma camera (Prism 2000, Picker, Cleveland, Ohio) was used for planar whole body imaging (n=91) and most SPECTs (n=58). SPECT imaging of the spine was initiated wherever the presence of anomalies was suggested by planar scans, CT, MRI, or bone pain in the thoracic (n=29) or lumbar (n=62) region. A parallel hole high resolution, low energy (HR) collimator was used to capture the 140-keV  $^{99m}\text{Tc}$  peak. For whole body scans, a 1024x256 matrix was used with a pre selected acquisition time of 20 min/image. Planar details of the head, chest, abdomen and extremities were acquired in anterior and posterior views with the same gamma camera (Prism 2000, Picker; 256x256 matrix, HR collimator, 15 min/image).

**SPECT and reconstruction.** Data were acquired in step and shoot mode using a double headed gamma camera (Prism 2000, Picker, Cleveland, Ohio) with a 128x128 matrix over 30 minutes, at 60 images ( $3^\circ$  angle steps). Parallel hole high resolution, low energy collimators were used to capture the 140-keV  $^{99m}\text{Tc}$  peak. For SPECT image reconstruction, an iterative algorithm was applied [12].

**Verification.** Complete data sets were available from all patients. 146 radiograms, 60 CTs, 56 MRIs, 13 biopsies, and clinical follow-up periods of 2 years were available for obtaining the final diagnosis, which was then correlated with SPECT findings. Radiographic imaging was performed within 3 weeks of bone scanning to assist in the establishment of a final diagnosis. During this time, the patients' clinical follow-up was performed by internal medicine/oncological or surgical/orthopedic departments.

**Image interpretation** All scans were evaluated online by a group of three nuclear medicine physicians experienced in interpreting SPECT. Physicians did not have access to the results of other clinical investigations at the time they were reading scans. All radiographs and CT scans were reported independently of each other and of the nuclear medicine studies by a board certified radiologist. For comparison with CT scans and radiographs, SPECT lesions were categorized according to size and location: 1.) Uptake extending throughout less than 50% of vertebral body mass, 2.) above 50% of vertebral body mass, 3.) increased uptake in vertebral body and adjacent pedicle (unilateral vs both sides, continuous between the body and the pedicle vs localized, singular vs multiple), 4.) facet joint, 5.) pars interarticularis and 6.) spinous process. SPECT lesions were defined as sites of supranormal activity levels. Furthermore, T/B ratios (T-Target / suspicious bone lesion) (B-Background / normal bone)

were established and were correlated with the final diagnosis of the bone alterations.

## DIAGNOSTIC CRITERIA

During image interpretation, lesions seen on planar and SPECT scans were classified as benign or malignant based on the following criteria:

On planar scans, lesions were considered *malignant* when supra normal activity levels were observed in the vertebral body. When interpreting SPECT, lesions were considered malignant if altered uptake was seen (a) in the central part of the vertebral body alone, (b) both in the vertebral body and the adjacent pedicle, or (c) in the pedicle alone.

To establish a final diagnosis, a lesion detected by bone scintigraphy was classified as *malignant* in the presence of at least one of the following: (a) CT and / or MRI evidence of destruction in the same vertebral region, (b) plain radiography showing a blastic or lytic lesion with progression on follow-up plain radiographs, or (c) biopsy proven metastatic disease at the site of the lesion.

On planar scans, lesions were considered *benign* if the increase in activity level in the vertebral body was low, or if deformations of the lateral part of vertebral bodies were observed in combination with decreased or normal activity levels.

In SPECT, lesions were considered *benign* if alterations were limited to (a) the lateral or ventral part of the vertebral body, (b) to the spinous process or (c) pars interarticularis (indicative for osteophytes), in case of lesions limited to the small facet joints (indicative for spondylarthrosis) or costovertebral joints (indicative for costovertebralarthrosis). To establish a final diagnosis of a *benign* process, lesions seen on scintigraphy were classified as benign if (a) correlative imaging studies showed a benign lesion in the same location, (b) the patient had neither clinical signs of spinal malignancy nor evidence of metastatic disease detected by follow-up bone scintigraphy or radiographic imaging (CT, MRI, conventional radiography) after a minimum of 6 months, and (c) follow-up bone scintigraphy showed improvement or no change of appearance of the lesion and no new lesions.

## STATISTICAL ANALYSIS

The degree of agreement between the three reviewers was measured with the  $\kappa$  statistic.  $\kappa$  values were reported as follows: 0, agreement is a random effect; less than 0.20, poor agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, substantial agreement; and 0.81-1.00, almost perfect agreement [13]. For the calculation of  $\kappa$  values, SAS 8.01 for Windows (SAS Institute, Cary, NC) was used.

## RESULTS

Out of a total of 145 spinal lesions was confirmed by CT and MRI. SPECT detected 133/145 (91%) spinal lesions (65 thoracic and 80 lumbar), whereas planar scans detected only 99/145 (68%) lesions. Smaller lesions (n=12), including small syndesmophytes, low level ligament ossifications, and smaller osteophytes, were missed by planar scintigraphy in

12/12 and by SPECT in 5/12 cases. Vertebral bone metastases (n=28) and cases of vertebral osteomyelitis (n=2) were correctly diagnosed by planar scans in 19/28 and by SPECT 28/28. In two patients with marginally increased leukocytes (WBC), C-reactive Protein (CRP) and erythrocyte sedimentation rate (ESR), spondylitis was a serendipitous finding. As for benign spinal lesions, only 69 (60%) out of 115 known degenerative alterations were detected by planar scans. Activated degenerative lesions limited to facet joints, pars interarticularis, pedicles, or the posterior part of the vertebral body, in particular, were often missed by planar bone scans (16/61) (25%). In contrast, lesions covering more than 50% of the vertebral body area, its lateral part, and lesions limited to the spinous process were detected more often (37/41) (88%) (Table 1).

**Table 1. Planar Scintigraphy and SPECT Compared to the Overall Final Results Found by CT, MRI and Radiography**

Overall Radiographically Verified Lesions	Planar Scintigraphy	SPECT
Metastases (n=28)	19 (67%)	28 (100%)
Osteomyelitis (n=2)	2 (100%)	2 (100%)
Benign bone lesions with		
- lower activity (n=12)	missed	missed
- higher activity (n=103) facet joint, pars interarticularis	69 (60%)	103 (100%)
pedicles, posterior part (61/103)	16 (25%)	61 (100%)
lateral part, spinous proc. (37/41)	37 (88%)	41 (100%)

In 9/28 (32%) (Fig. 1) of metastatic lesions uptake in the vertebral body and the adjacent pedicle was observed. This pattern was seen in 45/115 (39%) degenerative alterations (Figs. 2-4), as well as in 1/2 (50%) cases of vertebral osteomyelitis. Uptake between the vertebral body and the adjacent pedicle was mostly continuous in metastatic (7/9) (77%) and osteomyelitic lesions (1/1). In contrast, focally localized uptake was predominantly observed in degenerative alterations (39/45) (86%). Most metastatic spinal lesions were mixed lytic / osteoblastic metastases. A pattern of increased uptake in the vertebral body and adjacent pedicle in vertebral metastases was demonstrated more frequently by SPECT (> 50% of CT verified metastatic bone infiltrations). The level of uptake was not found to be correlated to whether metastases were lytic or osteoblastic. The semi quantitative evaluation T/B ratio (uptake of bone (Target) as compared to the uptake of the Background (B)) became positive at ratios of 1.3 for planar bone scan and at 1.6 for SPECT. However, a correlation of T/B ratios and the pathological disorder could not be found.

In 15/16 (94%) metastatic lesions with increased uptake limited to the vertebral body, uptake was noted in the central part of the vertebral body. In the remaining lesion, uptake of the frontal vertebral body was increased. In this case, an ulcerated malignant paravertebral lymphoma had caused secondary lytic destruction of the frontal part of the vertebra.

Localization of degenerative lesions varied widely. 45/115 (39%) lesions were located in the vertebral body and in the pedicle, 12 (10%) in the vertebral body only, 12 (8%) in the ventral part, 19 (16%) in the lateral part, and 22 (19%) in the facet joints and/or pars interarticularis. Regarding lesions limited to the vertebral body and pedicles, final results are shown in Table 2.

One of two spinal lesions caused by vertebral osteomyelitis displayed increased uptake in the vertebral body and in the pedicle, whereas in the other, uptake was limited to the vertebral body.

In our group of patients, the sensitivity of detection of spinal lesions differed significantly between planar scans and SPECT, at 60% and 92%, respectively. Spinal metastatic disease was detected with a positive and negative predictive value of 68% and 71% for SPECT, respectively. When SPECT detected lesions with an increased uptake in the vertebral body and adjacent pedicle, the overall specificity for detecting benign lesions was 79%. Sensitivity was increased to 87%

- in case of lesions which were focally limited to the facet joints (n=14) and pars interarticularis (n=8) (All of these were correctly diagnosed as spondylarthrosis), and
- if focally localized uptake between the vertebra and the adjacent pedicle was interpreted as benign (39/45; 86%) whereas continuous uptake was interpreted to be malignant (7/9; 77%).

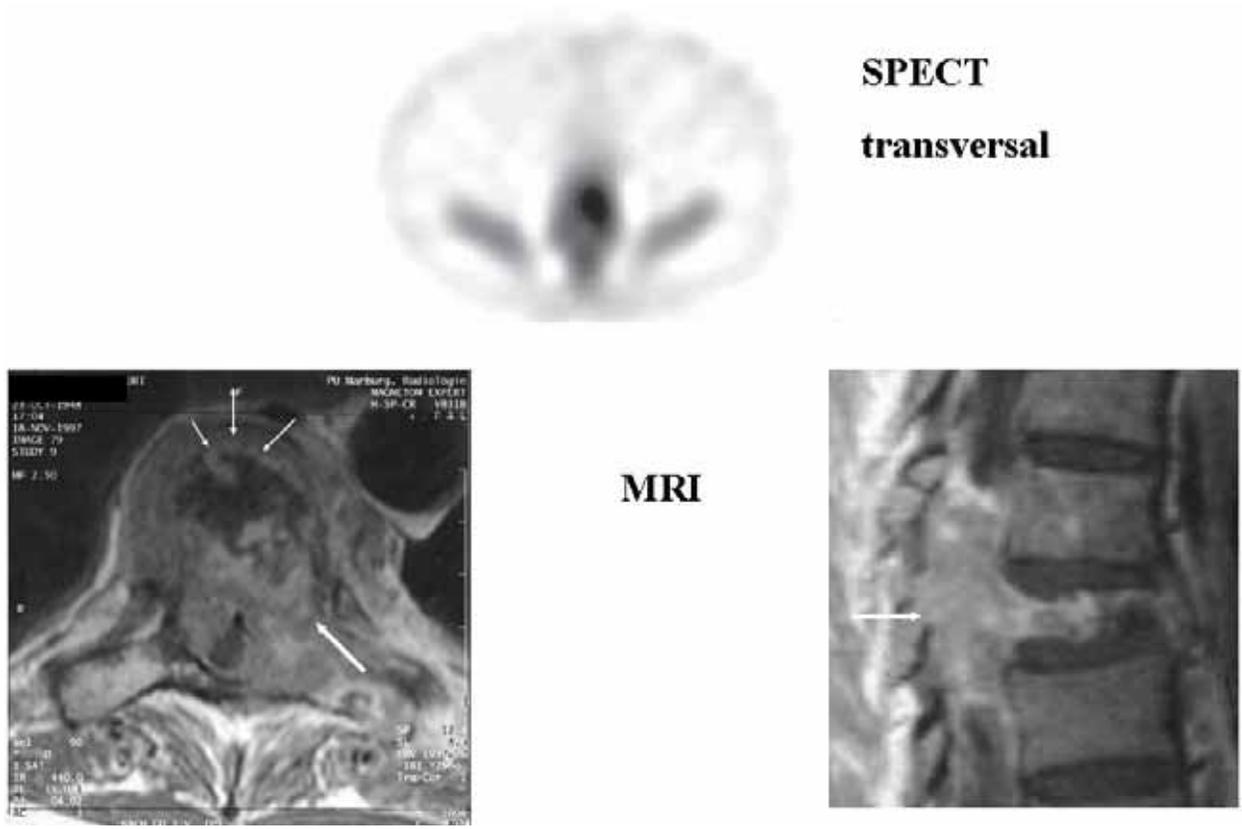
All lesions and the overall final results are listed in Table 3.

## DISCUSSION

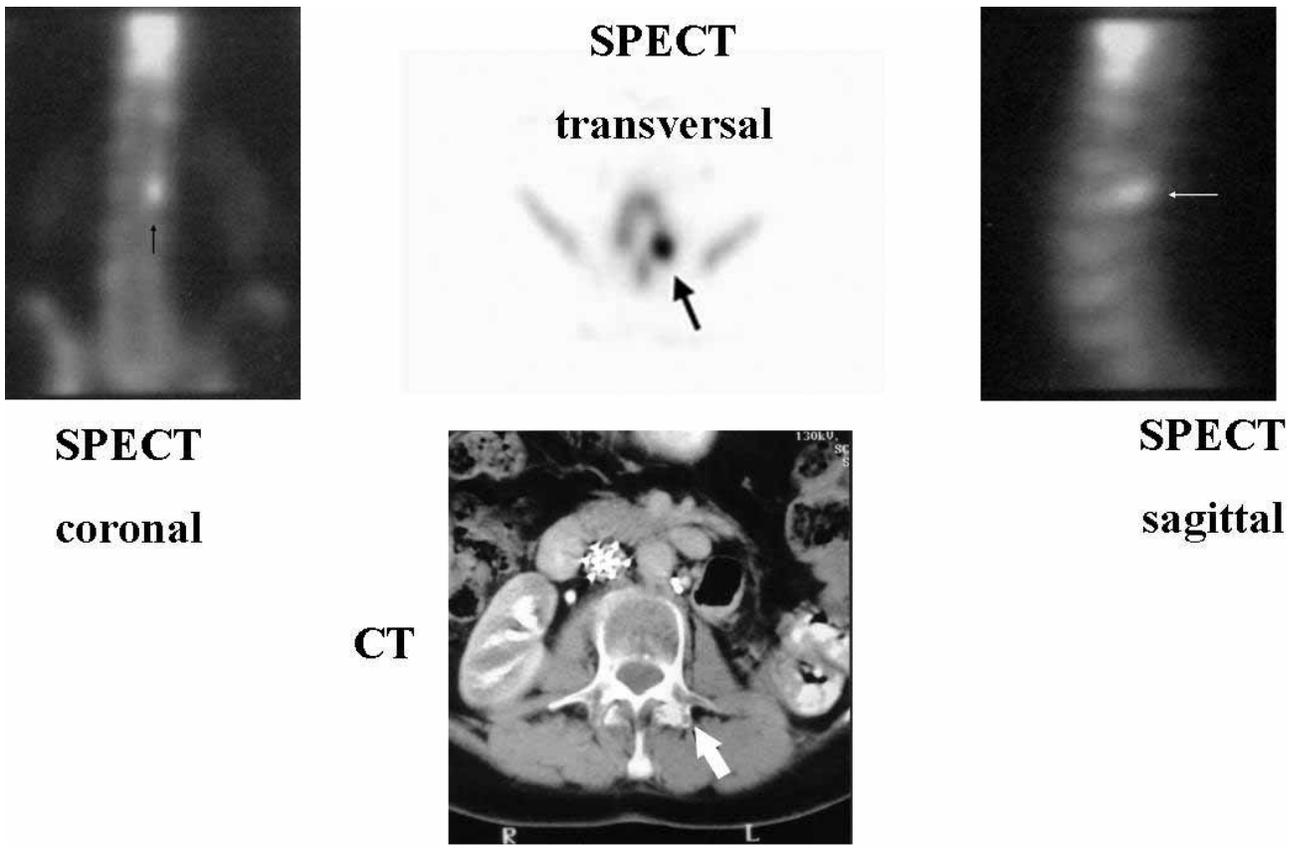
The aim of this retrospective study was to elucidate whether SPECT alone provides sufficient detailed information in patients with suspected spinal malignancies, and whether specific patterns of increased uptake throughout the vertebral body can be correlated to whether a lesion is malignant or benign.

In our study, SPECT provided superior information compared to planar scintigraphy in patients with both malignant and benign degenerative alterations of the spine. SPECT was able to detect 103/115 (89%) degenerative spinal lesions, whereas planar scintigraphy detected only 69 lesions (60%). Similar data were reported elsewhere (14), but only 67% of patients with lesions seen on SPECT had positive planar scans. In our group of patients, lesions were particularly likely to be missed by planar bone scans when they were limited to facet joints, pars interarticularis, pedicles, and the posterior part of the vertebral body. Relatively low uptake in these smaller areas, combined with lower contrast and anatomic clarity of the underlying bone structures is likely to be the main reason for lack of detection. With SPECT, the sensitivity of detection was better when posterior and lateral bone structures were affected.

SPECT correctly diagnosed lesions that were limited to the pars interarticularis, facet joints or costotransversal articulation only. All lesions limited to these areas were



**Fig. (1).** Patient with *metastasis* of the 2<sup>nd</sup> lumbar vertebra seen with increased continuous uptake in the pedicle and MRI alterations, respectively. Due to tumor infiltration, the anterior part of the vertebra is pathologically fractured.



**Fig. (2).** *Spondylarthrotic* lesions limited to the facet joint and pars interarticularis easily can be detected with SPECT as focal uptakes.

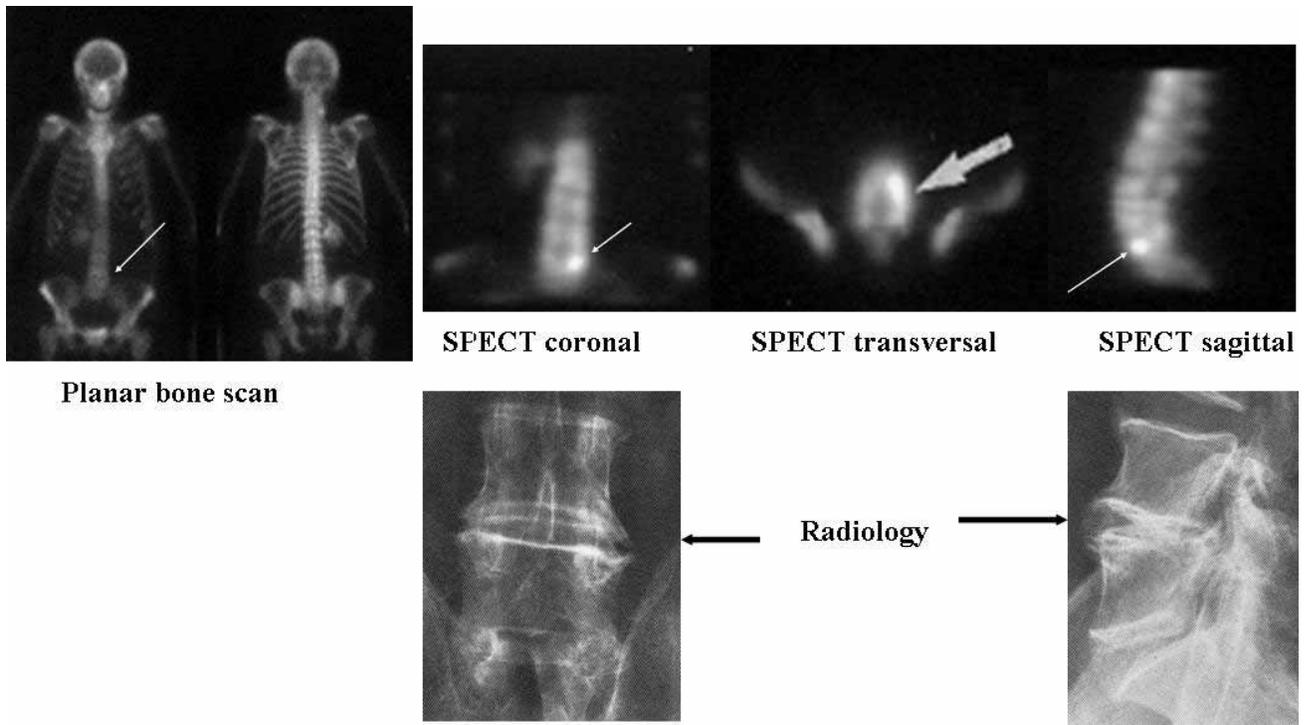


Fig. (3). Patient with lateral spondylophyte. Planar bone scintigraphy shows a slightly increased uptake at the left lateral part of the 5<sup>th</sup> lumbar vertebra. SPECT demonstrates an increased uptake at the lateral part of the vertebra and left pedicle.

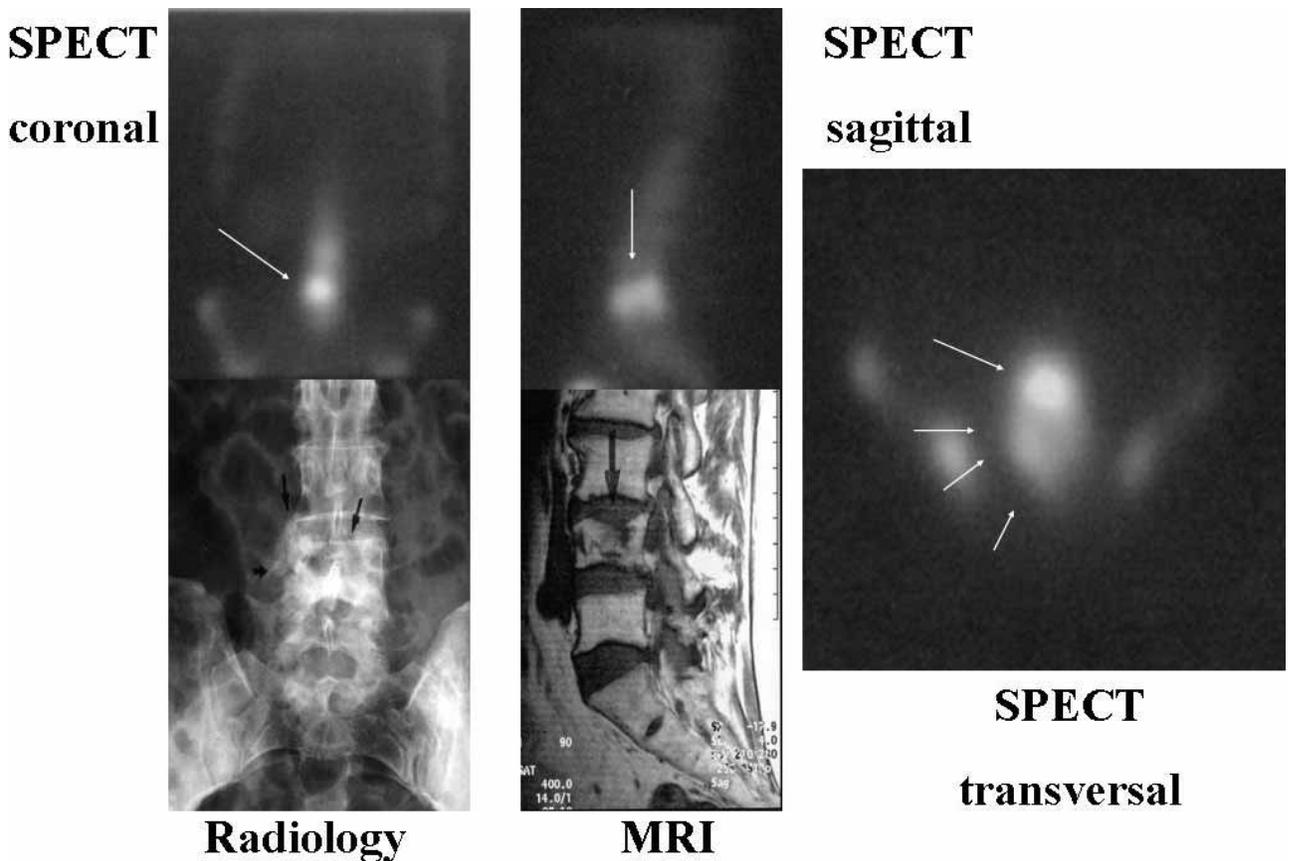


Fig. (4). The osteoporotic bone fracture shows increased uptake in the 4<sup>th</sup> lumbar vertebral body. Changing bone pressure results in very low intensity uptake in the right pedicle. Low intensity of uptake in the pedicle could be indicative of benign lesions.

**Table 2. SPECT Findings with Increased Uptake of the Vertebral Body and Pedicles Associated with the Final Results of Benign Degenerative Alterations Verified by CT, MRI, or Radiography**

Site of SPECT Lesion	Total No. of Lesions	Associated CT Lesions	Number of Associated CT Lesions
Vertebra +1 pedicle	21	New Bone Formation/Osteophytes	14
		Frontal Compression Fracture	5
		Congenital Alteration	4
		Disc Degeneration/ Sclerosis	3
		Osteoid osteoma	1
		Spondylolisthesis	1
Vertebra + both pedicles	17	Disc Degeneration/Sclerosis	9
		Frontal Compression Fracture	5
		Hemangioma	2
		Surgical bone reconstruction	1

**Table 3. Overall Diagnosis of 145 Lesions Found by CT and MRI in the Spine Correlated with Anatomic Location on SPECT Images. Out of These 145 Radiographically Detected Spinal Lesions, SPECT was Able to Find 133**

Bone Uptake	Benign Lesion	Malignant Lesion	Vertebral Osteomyelitis
Diffuse in the body	5	7	1
Focal in the body	12	9	0
Body and pedicle	45	9	1
Anterior part of the body	12	1	0
Lateral part of the body	19	2	0
Facet joints	14	0	0
Pars interarticularis	8	0	0

correctly interpreted as spondylarthrosis or costovertebral arthrosis, owing to the high degree of anatomical resolution. On planar scans, these lesions were seen as areas of mildly increased bone mineralization, but could not be correlated to morphologic structures and dignity of bone alteration. In this location, specificity was dramatically increased with SPECT. Thus, it appears justified to make this specific diagnosis when lesions limited to the pars interarticularis and facet joints are observed by SPECT.

Most publications report SPECT to be superior to planar bone scintigraphy and to yield results comparable to CT and MRI [15, 16]. Data published by Roland *et al.* [15] reported that planar bone scintigraphy in a 45 - year - old pre menopausal woman with breast cancer missed multiple metastatic lesions in the lumbar and thoracic spine, whereas SPECT revealed all lesions with focally increased uptake. Similar results were found in the present study with 9/28 metastases missed with planar scans and confirmed as being suspicious for malignancy by SPECT. In two of these patients, SPECT revealed an additional benign lesion.

In the present study, 9/28 (32%) of metastatic lesions displayed uptake in the vertebral body and the adjacent pedi-

cle. The same pattern was seen in 45/115 (39%) degenerative alterations, and in 1/2 (50%) cases of spondylitis. SPECT sensitivity was achieved, if focally localized uptake between the vertebra and the adjacent pedicle was interpreted as indicative of benign alterations, and continuous uptake was interpreted as malignant. Even-Sapir *et al.* [11] found a continuously increased uptake in the vertebral body and pedicle to be indicative of metastasis in 83% of a similar group of cancer patients with 125 spinal lesions. A possible explanation for our findings is that an increase of uptake in the pedicle may often be due to disproportionate pressure conditions involving the vertebral body. This theory is supported by the fact that this sign was frequently seen in patients with new osteophytic bone formation, disc degeneration, and frontal compression fractures, whereas it was less often seen when the pedicle was infiltrated by metastatic disease. It may also explain why focally localized uptake was observed more frequently in benign spinal alterations. The initial site of metastasis usually involves the posterior part of the vertebral body (> 90%) [17]. From here, the metastasis begins to infiltrate the adjacent pedicle. In our set of data, continuous uptake between the vertebra and the adjacent pedicle was observed particularly in patients whose vertebral metastasis included > 50% of the vertebral body area (as shown by CT). In elderly patients with advanced osteoporosis, only a minor degree of metastatic infiltration is necessary to cause a pathologic bone fracture [18]. Since vertebral bodies tend to fracture in the frontal part (where they physiologically bear increased weight), increased pressure in the posterior part and pedicles has to be expected in compensation. This would explain why the increased focally localized uptake between the vertebral body and the adjacent pedicle was detected more often in elderly patients, particularly postmenopausal females with advanced degenerative alterations.

In a similar patient population recently SPECT/CT data were presented and the authors [19] published similar results as compared with ours. But, several limitations of the study were due to unresolved technical problems, such as potential registration errors in the thorax, which were due to breathing. Because a SPECT scan is an image created with data acquired over many breathing cycles, the fusion of SPECT images with CT images would require respiratory gating of

the SPECT scan. Another limitation of the study was that combined SPECT/CT system was not available and image fusion had to be performed manually. However, the authors came to the conclusion that up to now SPECT / CT was not a promising approach owing to the substantial resultant increase in imaging time.

## CONCLUSION

As long as improved software algorithms imperative to enable automatic and robust image fusion are not commonly available for SPECT/CT and increased costs lead to comparative lack of availability of PET or PET/CT, we believe that SPECT will remain a very reliable imaging modality with high diagnostic confidence for daily routine.

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