THE INCREMENTAL VALUE OF SPECT/CT IN CHARACTERISING
SOLITARY SPINE LESIONS

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Foot line: SPECT/CT in solitary spine lesions
Abstract

Purpose The purpose of this study was to investigate the incremental value of single photon emission computed tomography / computed tomography (SPECT/CT) in patients who had a solitary spinal lesion on bone scan and its impact on the diagnosis.

Methods A prospective study of 80 patients (50 with known cancer) who underwent 99mTc-methylene diphosphonate (MDP) whole-body planar bone scintigraphy and had a solitary spinal lesion. These lesions were then further evaluated using SPECT/CT.

Results Lesions were localized to the vertebral body in 38 (47.5%) of patients, pedicle in 15 (18.8%), facet joint in 15 (18.8%), transverse process in 2 (2.5%), spinous process in 2 (2.5%), lamina in 3 (3.8%) and the end plates in 5 (6.2%). While the specificity of planar bone scans was excellent (100%), the addition of SPECT/CT improved sensitivity from 6.1% in the planar review to 78.8% following SPECT/CT. The results provide evidence that there is a substantial incremental increase in diagnostic accuracy employing SPECT/CT over planar alone for patients in whom a solitary spinal lesion is noted.

Conclusion The addition of SPECT/CT resulted in a significant reduction false negative scans and increase in the number of true positive studies. SPECT/CT also reduced the number of equivocal reports; a definitive diagnosis was given in the majority of the patients due to the improved diagnostic confidence compared to planar imaging alone in patients with solitary spinal lesions.

Key words: bone scan; SPECT; spine lesion; SPECT/CT; metastases
Introduction
Bone scintigraphy has provided a highly sensitive, reliable, non-invasive method in the detection of focal bone pathology for a number of decades (1). These attributes are complimented by its widespread availability, well established safety record, moderate costs, extensive clinical experience, and well documented efficacy in a broad range of pathologies. Advances in instrumentation (resolution and sensitivity) and techniques (single photon emission computed tomography [SPECT] and more recently SPECT/CT), combined with the limitations in other imaging modalities (e.g. cost, availability, radiation dose, lack of physiological detail) have ensured bone scintigraphy remains the preferred procedure in the diagnostic algorithms for detection and characterization of bone lesions of various pathological origins.

Skeletal Metastasis
Bone metastases are by far the most common malignant bone tumors seen in adults (2). Bone metastases may occur with virtually all malignancies, but they are most common in carcinomas of the breast (47–85%), lung (32%), prostate (54–85%), kidney (33–40%), or thyroid (28–60%) (2). The spine is the most common site of skeletal metastases (39%) because of the abundant vascularization and red bone marrow (2).

Most bone metastases result from hematogenous dissemination of cancer cells. Micro-metastases are present in the bone marrow in 25-75% of patients with common malignancies (3). The mechanism of development and growth of bone metastases is a multi-step process, which requires complex interactions between the metastatic cells and the tissue. Metastases do not affect all the bones with the same pattern and frequency, but, generally, prefer the spine and pelvis. Besides molecular and biologic characteristics of both neoplastic and normal cells, other factors may play a role in the skeletal localization of malignant cells, such as the vascular ways of spreading, the speed and the amount of blood flow towards specific areas (3). Bone constitutes a well-defined micro-compartment supplied primarily by the bloodstream. In this structure, most of the bone marrow is found, where the particular capillary structures and the reduction of the speed of blood may favor the seeding of metastatic cells. Vascular sinusoids are lined by endothelial cells with 60 A fenestrae and they lack a basement membrane (3).
As the spine represents the preferential site of metastatic skeletal spread, it is important to know how the blood supply is distributed to the vertebral bone through the vertebral arterial and venous plexuses. Batson et al. (4) first described the evidence of a venous connection between the peri-prostatic and lumbar plexuses in 1940. The author evidenced the existence of a network of longitudinal, valueless vessels, running parallel to the vertebral column and forming countless anastomoses to the sinusoidal structure of the vertebral marrow and epidural venous channels. The evidence suggested that, under increased abdominal pressure, metastatic prostate cells could reach the axial skeleton by retrograde hematogenous spreading, thus, without passing the first anatomic filter (the lungs). More recently, Suzuki et al. (5) established the exact intra-abdominal hemodynamic pressure necessary to make blood, draining the prostate, flow into the vertebral veins in animal models. Other studies have reported that this network of venous vessels may be wider and involve more blood areas. Indeed it is possible to show the presence of links between Batson's plexus and azygos, hemiazygos system and internal mammary system, by means of lateral thoracic and intercostal veins (3). This could explain the possibility to metastasize to the spine even for tumor cells deriving from organs other than the prostate, like breast and lung (3).

Role of Bone Scanning
In the nuclear medicine department, bone scans are typically used for assessment of skeletal metastases using a whole-body sweep technique with gamma camera systems equipped with high or ultra-high resolution collimators and this allows excellent image quality. In the case of detection of a suspicious focal abnormality, additional static projections or SPECT may be indicated to better delineate the lesion (6).

SPECT enables more accurate localization of tracer accumulation, especially in anatomical regions that are otherwise difficult to interpret because of complex architecture of skeletal structures (such as the spine, pelvis, or skull) or due to under or over lying structures. Moreover, the ability to view biodistribution in multiple sections (eg. transverse, sagittal and coronal) means that more precise definition of the location and extent of lesions can be determined; in particular in relation to traversing joints. Furthermore, tracer uptake on planar images may appear similar for different malignant and benign conditions and, thus, SPECT affords the potential to improve diagnostic specificity on the basis of more accurate differentiation of causal pathology (1). Nonetheless, in many instances (eg. solitary lesions in the axial skeleton) correlation with high-quality anatomic images (eg. CT) may be required.
for diagnosis. Visualization of exact anatomical localization and morphology of underlying bone pathology may improve the specificity of bone scans considerably.

**Combined Anatomical and Physiological Imaging**

Extensive work has been carried out on image fusion software during the past 20 years (7). Although accurate image fusion is relatively easy with the rigid structures in the brain and extremities it is more challenging in the thorax and abdomen (7). Patient motion, organ motion, and particularly in the context of bone imaging, differences in the curvature and shape of imaging tables may lead to different positioning of the spine and other structures. Several initial reports on fusion imaging addressed the benefit of the fusion of SPECT data with computed tomography (CT) performed on a separate camera at a different point of time. In theory, the concept of software fusion is fascinating, but in practice, image fusion may be difficult to achieve. In some situations, in particular if patients present with coexisting pathology (eg, degenerative bone disease, inflammation, metabolic disease), the results may be unsatisfactory. SPECT/CT on a hybrid system, even with low-dose CT scanning, overcome many of these limitations by scanning the patient sequentially on the same imaging table to improve diagnostic and localization accuracy.

Detection of skeletal metastasis is clinically important because of associated symptoms, complications (eg, pathologic fractures) and significance for staging, treatment and prognosis. Differentiating benign and metastatic bone lesions, however, can be difficult with planar scintigraphy alone (8). SPECT increases image contrast and improves lesion detection and localization compared with planar scintigraphy (9).
Methodology
The aim of the investigation was to assess the benefit of combined SPECT/CT for classification of solitary lesions in the vertebra. The investigation was approved by an institutional ethics committee.

The prospective study included patients who were referred for a bone scan during 2008 and who were diagnosed with a solitary lesion in the vertebrae on the planar images. All patients also underwent SPECT/CT data acquisition on the same day as the planar study. A follow-up planar and SPECT/CT bone scan was performed three months later and the results were used as reference standard.

Lesions were classified as being consistent with the appearances of either benign or malignant disease on the basis of the criteria described in table 1. Lesions which were not categorizable as either benign or malignant were classified as intermediate. Each study was independently interpreted by two nuclear medicine physicians who were blinded to the patients’ clinical history and test results. Interpreting physicians were also blinded to one another’s interpretation and discordant classification was determined to be intermediate. Interpretation was undertaken for planar and SPECT/CT images separately and sequentially.

All patients were scanned using a GE Infinia Hawkeye low dose (2.5kVa) SPECT/CT. Following whole body sweep acquisitions, planar imaging of the spine was performed using a 256x256 matrix for 1000K counts. SPECT/CT was performed supine through 360 degrees using 3 degree angular sampling, a 128x128 matrix and 15 seconds per step. Data was reconstructed using iterative reconstruction with CT based attenuation correction.
Results
A total of 80 consecutive patients fulfilled entry criteria. Fifty had known cancer (oncology cohort). Of those, 26 (52%) had breast cancer, 12 (24%) had prostate cancer, 6 (12%) had lung cancer, 2 (4%) had uterine cancer, 1 (2%) had bladder cancer, 1 (2%) had facial cancer and 2 (4%) had an unknown primary. The other thirty patients had no prior history of cancer (non-oncology cohort). Of those, 15 (50%) presented with backache, 7 (23.3%) trauma, 5 (16.7%) infection and 3 (10%) were classified as miscellaneous. Lesions were localized to the vertebral body in 38 (47.5%) of patients, pedicle in 15 (18.8%), facet joint in 15 (18.8%), transverse process in 2 (2.5%), spinous process in 2 (2.5%), lamina in 3 (3.8%) and the end plates in 5 (6.2%). The results of image interpretation of the initial planar and SPECT images are summarized in Table 2.

In the oncology cohort (n = 50), the 3 month follow-up provided improved demarcation of disease. Progression of disease was noted in 23 (46%) of the patients, no change or the same disease pattern was seen in 17 (34%) of the patients and a change in intensity of the lesion was noted in 10 (20%) patients. The relative improvements in both planar and SPECT can be noted in table 3 and analysis of performance is summarized in table 4.

In the 30 non-oncology patients, SPECT/CT provided a diagnosis in 24 (80%) of patients including 8 cases of osteomyelitis, 5 post traumatic injuries, 4 cases of spondylosis, 3 of spondylolisthesis and 2 each for facet joint osteoarthritis and metastasis. Planar did not perform nearly as well with just 5 (17%) diagnoses (table 5). If we assume, for the purposes of comparison, that SPECT/CT had no false positive or false negative results (unlikely to be true), then we can determine that, relative to 100% sensitivity and specificity of SPECT/CT that planar would have a 20.8% sensitivity and a 100% specificity.
Case Studies

The following cases are representative cases of the entire sample and provide an insight into the important role of SPECT/CT of the spine. More specifically, these cases highlight the advantage of SPECT/CT in more definitive pathology identification and differentiation of various pathologies. Importantly, the cases provide examples where suspected pathology was both upgraded to and downgraded from sinister pathology (ie. to or from metastatic disease).

Patient 1 is a 45 year old female with a history of breast cancer, 1 month of back pain, no history of trauma and a normal x-ray. Planar bone scanning demonstrated a subtle area of tracer accumulation in the region of the 4th lumbar vertebra which may have been degenerative in nature (figure 1). SPECT/CT indicated focal accumulation in the body of the vertebrae consistent with early metastatic disease (figure 2). Three month follow-up imaging demonstrated advancement of disease including multiple spine, skull and pelvic lesions confirming the original SPECT/CT findings.

Patient 2 was an 80 year old male with a history of prostate cancer and lower backache for 15 days. The patient had a PSA of 727ng/dL. The planar bone scan demonstrated some mild changes suggestive of degenerative changes (figure 3), however, the SPECT/CT revealed early metastases (figure 4).

In the both the first and second cases, when looking at the planar scans, the lesions could have readily been dismissed as degenerative in nature due to their sites and location, however, in both cases SPECT/CT resulted in a change in diagnosis which affected patient management.

Patient 3 presented with suspected post traumatic or degenerative change in the spine on planar images (figure 5) which was shown on CT to be multiple lytic lesions in multiple vertebrae (figure 6) that was correlated with fusion (figure 7) to reveal metastatic collapse of vertebrae in multiple myeloma. The skull x-ray showed a typical ‘pepper pot’ appearance. In this case, the patient presented with long standing backache and the planar bone scan was relatively unremarkable with findings consistent with early degenerative changes. SPECT/CT, however, revealed a more sinister pathology that was shown to be multiple myeloma.

Patient 4 is a 70 year old male with a history of prostate cancer and trauma presenting with back pain. L2 radiopharmaceutical uptake on the planar bone scan (figure 8) is shown to be a
post traumatic vertebral body fracture on SPECT/CT (figure 9). In this case, given the patient’s age, history and the pattern of the disease on the bone scan, metastasis was a consideration on the planar study. SPECT/CT allowed delineation of less sinister pathology; post-traumatic changes.

The final patient is a 52 year old woman with lower back pain and no history of trauma. The planar bone scan shows diffuse radiopharmaceutical uptake in L2 and L3 vertebrae (figure 10) that was suggestive of pathology secondary to osteoporosis. This was revealed as intra-vertebral disc infection on SPECT/CT (figure 11). Subsequent work-up revealed it to be tuberculosis.
Discussion

Our study results demonstrated an improvement in diagnostic efficacy of the bone scan with the addition of SPECT/CT, for the investigation of solitary vertebral lesions. Specifically, the indeterminate outcome was reduced from 63.8% with planar to 13.8% for SPECT/CT. The most important outcome was the improved characterization of spine lesions with an increase in sensitivity from 6.1% to 78.8%; despite a decrease in specificity from 10% to 88.2% for planar and SPECT/CT respectively. One of the key observations was the 46% of oncology patients noting disease progression during the 3 month follow-up. While this advocates the role of bone scan in monitoring disease progression it also provides a clear indication for the need for accurate and early diagnosis on the initial scan, since disease progression and prognosis may change substantially in a short period of time.

Sedonja et al. (10) performed planar scintigraphy and SPECT on 37 patients with lower back pain without known malignant lesions and on 38 patients with confirmed malignant disease. Overall, significantly more metastatic lesions were detected with SPECT (SPECT, 58 of 64 lesions; planar scintigraphy, 42 of 64 lesions; p < 0.01).

Incidental focal tracer accumulation in patients with known malignancy can pose clinically significant diagnostic dilemma, especially when there is only a solitary lesion (1). In a study at Department of Nuclear Medicine, University Hospital Zurich, Switzerland, of the 42 lesions that were studied (in 37 patients) a specific diagnosis was made with planar scintigraphy in 64% of cases, SPECT in 86%, and SPECT fused with CT in all cases (8). This observation is likely to account for the greater improvement reported in our investigation over that reported by Sedonja et al. (10), highlighting the incremental benefit of SPECT/CT over SPECT alone against planar bone scan imaging.

The results summarized in table 4 provide evidence that there is a substantial incremental increase in diagnostic accuracy employing SPECT/CT over planar imaging for patients in whom a solitary spinal lesion is noted. SPECT/CT in cases where there is some diagnostic ambiguity (especially where the spine is involved) can prevent misdiagnosis and, therefore, improve patient management. The regular use of SPECT/CT in such cases is further supported by the case examples provided. Nonetheless, the study and results are limited by a relatively small population and the lack of a histological gold standard. These limitations should be addressed in future research, including more rigorous cost effectiveness analysis.
Conclusion
Our study results indicate that the addition of localized SPECT/CT for the assessment of indeterminate foci both enables a definitive diagnosis in most cases and improves diagnostic confidence. The results would encourage future research to assess the relative cost effectiveness of SPECT/CT over planar or SPECT bone scintigraphy in the evaluation of solitary vertebral lesions among oncologic patient population.
References


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Table 1: Criteria for lesion characterization.
Table 2: Comparative results for both study populations at the initial imaging session.
Table 3: Outcomes for baseline and follow-up planar and SPECT/CT in the oncology cohort.
Table 4: Performance analysis for planar and SPECT/CT in the oncology cohort.
Table 5: Comparison of outcomes planar and SPECT/CT in non oncology studies.
Figure legends

Figure 1: Baseline planar spine.

Figure 2: Baseline SPECT/CT.

Figure 3: Bone scan with L5 degenerative changes.

Figure 4: SPECT/CT reveals an early metastasis.

Figure 5: Bone scan suggestive of post traumatic or degenerative change.

Figure 6: CT scans shows multiple lytic lesions.

Figure 7: SPECT/CT highlighting metastatic disease.

Figure 8: Bone scan with L2 lesion.

Figure 9: SPECT/CT showing vertebral body fracture.

Figure 10: Planar bone scan.

Figure 11: SPECT/CT revealing intra-vertebral disc infection.
Table 2: Criteria for lesion characterization.

<table>
<thead>
<tr>
<th>BENIGN</th>
<th>MALIGNANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Facet joint</td>
<td>▪ Body and pedicle</td>
</tr>
<tr>
<td>▪ Costa-vertebral Joint</td>
<td>▪ Photon deficient area (lytic area)</td>
</tr>
<tr>
<td>▪ Involving two adjacent vertebrae or endplates of the vertebrae</td>
<td></td>
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Table 2: Comparative results for both study populations at the initial imaging session.

<table>
<thead>
<tr>
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<th>Indeterminate</th>
<th>Benign</th>
<th>Malignant</th>
<th>Total</th>
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<tbody>
<tr>
<td>Planar</td>
<td>51 (63.8%)</td>
<td>27 (33.8%)</td>
<td>2 (2.5%)</td>
<td>80</td>
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<tr>
<td>SPECT/CT</td>
<td>11 (13.8%)</td>
<td>39 (48.8%)</td>
<td>30 (37.5%)</td>
<td>80</td>
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Table 3: Outcomes for baseline and follow-up planar and SPECT/CT in the oncology cohort.

<table>
<thead>
<tr>
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<th>Benign</th>
<th>Malignant</th>
<th>Total</th>
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<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Planar</td>
<td>26 (52%)</td>
<td>22 (44%)</td>
<td>2 (4%)</td>
<td>50</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Planar</td>
<td>7 (14%)</td>
<td>20 (40%)</td>
<td>23 (46%)</td>
<td>50</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECT/CT</td>
<td>5 (10%)</td>
<td>17 (34%)</td>
<td>28 (56%)</td>
<td>50</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECT/CT</td>
<td>0 (0%)</td>
<td>17 (34%)</td>
<td>33 (66%)</td>
<td>50</td>
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Table 4: Performance analysis for planar and SPECT/CT in the oncology cohort.

<table>
<thead>
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<th>Baseline Planar</th>
<th>Baseline SPECT/CT</th>
<th>Follow-up Planar</th>
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<tbody>
<tr>
<td>True Negative</td>
<td>17</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>False Negative</td>
<td>31</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>True Positive</td>
<td>2</td>
<td>26</td>
<td>23</td>
</tr>
<tr>
<td>False Positive</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Sensitivity (TPR)</td>
<td>6.1%</td>
<td>78.8%</td>
<td>69.7%</td>
</tr>
<tr>
<td>Specificity (TNR)</td>
<td>100%</td>
<td>88.2%</td>
<td>100%</td>
</tr>
<tr>
<td>Prevalence</td>
<td>4%</td>
<td>66%</td>
<td>46%</td>
</tr>
<tr>
<td>PVP</td>
<td>100%</td>
<td>92.9%</td>
<td>100%</td>
</tr>
<tr>
<td>PVN</td>
<td>35.4%</td>
<td>68.2%</td>
<td>63.0%</td>
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</table>

PVP = positive value of a positive result
PVN = positive value of a negative result
Table 5: Comparison of outcomes planar and SPECT/CT in non oncology studies.

<table>
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<tr>
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<th>Diagnosed</th>
<th>Undiagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planar</td>
<td>5 (17%)</td>
<td>25 (83%)</td>
</tr>
<tr>
<td>SPECT/CT</td>
<td>24 (80%)</td>
<td>6 (20%)</td>
</tr>
</tbody>
</table>
Figures
Figure 2
Figure 6
Figure 7
Figure 8
Figure 10
Figure 11