ORIGINAL ARTICLE

SPECT-CT in Differentiating Metastatic and Degenerative Lesions of the Spine

Khadijah Abdul Hamid[1], Sazilah Ahmad Sarji[2], Mohammad Nazri Md Shah[2], Ibrahim Lutfi Shuaib[1]

[1] Oncological and Radiological Sciences Cluster, Advanced Medical and Dental Institute, Universiti Sains Malaysia, 13200 Kepala Batas, Penang, Malaysia
[2] Department of Biomedical Imaging, University Malaya Medical Centre, Lembah Pantai, 59100, Kuala Lumpur, Malaysia

ABSTRACT

Introduction: The purpose of this study was to determine the usefulness of SPECT-CT in differentiating metastatic and degenerative disease of the spine. **Methods:** Twenty-eight patients aged 50 years and above diagnosed with various cancers were referred for whole body (WB) planar bone scintigraphy. Those with a maximum three foci of tracer uptake in the spine were selected for the study. SPECT-CT of these areas of uptake was performed and the lesions were classified as degenerative, indeterminate or metastasis. A repeat study (WB planar bone scintigraphy and SPECT-CT) was performed between 3 to 12 months later. These areas of uptake were reassessed and compared with the first WB planar bone scintigraphy and SPECT-CT. The second SPECT-CT was used as the standard for the diagnosis. **Results:** Thirty-seven lesions in 28 patients were assessed. The sensitivity of the first WB planar bone scintigraphy, second WB planar bone scintigraphy and first SPECT-CT is 75%, 62.5% and 75% respectively. The specificity of the first WB planar bone scintigraphy, second WB planar bone scintigraphy and first SPECT-CT is 86%, 93%, 90% respectively. There was 2.7% of 'indeterminate lesion' in the first WB planar bone scintigraphy, 5.4% in the second WB planar bone scintigraphy, and 5.4% in the first SPECT-CT. The indeterminate lesions were resolved in the second SPECT-CT. **Conclusion:** SPECT- CT is useful in differentiating degenerative disease from metastatic lesions in the spine.

Keywords: SPECT-CT, Bone scan, Bone metastasis, Degenerative, Indeterminate lesions

Corresponding Author:
Khadijah binti Abdul Hamid, MMed Nuclear Medicine
Email: khadijah@usm.my
Tel: +604-5622414

INTRODUCTION

Nuclear medicine studies are used for decades in diagnostic imaging, providing functional information about our body. This includes function of certain organs such as liver, kidney, or spleen. Functional information regarding bone is done by using whole body bone scintigraphy. It is known to have sensitivity of above 90% (1). Unfortunately, it lacks specificity. Interpretation of the scans need to be evaluated by expert nuclear physicians looking at both clinical and anatomical context. Ideally it is best compared and correlated with other imaging modalities for the most accurate assessment.

In normal healthy bone, continuous remodeling is the product of the balanced interaction between two types of bone cells, osteoclasts and osteoblasts. Osteoclasts are responsible for bone resorption and osteoblasts for bone formation (2). In bone metastasis, there is imbalance between osteoclastic and osteoblastic activity, leading to either excess bone destruction or bone formation. On bone scintigraphy it is seen as increased uptake ('hot' lesions) or reduced uptake ('cold' lesions) of radioactive tracer. The human eyes are trained to see bright spots, thus higher the level of osteoblastic activity, the more sensitive the scan.

Low specificity of bone scintigraphy results in difficulty in interpretation of the scan. Benign processes such as inflammation, degenerative activity, fracture and Paget disease will show hot lesions. Primary malignant and benign bone tumours will also show similar apperances, i.e increase in radiotracer uptake.

Single photon emission computed tomography (SPECT) is used in addition to planar scintigraphy to enhance the findings in the vertebral column, ribs and pelvis. SPECT allows better anatomical localisation of the lesions and can help to differentiates benign and malignant lesions. Previous study has shown there will always be indeterminate findings on the SPECT scan especially in the spine (3). Recent technology of SPECT combined with low dose CT scan is now available, allowing more efficient and accurate diagnosis of bone lesions in single examination. SPECT in combination with CT (SPECT-CT) enables a direct correlation between anatomical

localisation and bodily function. This will reduce patient anxiety, waiting time and time of making the diagnosis.

MATERIALS AND METHODS

Study design

It was a prospective study of all newly diagnosed cancer patients referred to the Nuclear Medicine Unit of University Malaya Medical Centre (UMMC) for bone scintigraphy over a period of 24 months.

Patient selection criteria

Patients aged 50 years old and above, who had maximum three uptake in the spine and five uptakes in the whole-body planar bone scintigraphy were selected in this study. SPECT-CT examination was performed on the spine lesions. A repeat whole-body (WB) planar bone scintigraphy and SPECT-CT of the same area were performed between 3 to 12 months to compare the findings.

Whole body (WB) planar bone scintigraphy

WB planar bone scintigraphy was performed 2-3 hours after intravenous injection of 1,100MBq (30 mCi) Tc-99m-methylene diphosphonate (MDP) with dual headed Brightvew SPECT or Brightview XCT gamma camera (Philips Medical Systems (Cleveland),Inc). These gamma cameras are equipped with low energy high resolution (LEHR) collimator. For WB planar bone scintigraphy, counts from energy windows of 140 keV ± 20% were acquired into 128x128 matrix. The scan speed was 15 cm/min.

SPECT-CT

A total of 68 patients went for SPECT-CT study with Brightview XCT gamma camera (Philips Medical Systems (Cleveland), Inc). From these numbers, only 28 patients returned for a repeat study. For SPECT acquisition, counts from energy windows of 140 keV ± 20% were acquired into 128 x 128 matrix. A CT using a flat panel detector with the same field of view. The CT parameters used were 120 kV and 247.34 mAs. It was reconstructed into 1 mm thick. The matrix size was 512 x 512. Standard filtered back projection was used to filter all CT images. For fused images, the accuracy of the matching between the SPECT and CT images was verified.

Imaging analysis

A radiologist and a Nuclear Medicine physician interpreted all images. Both were blinded to the patient's clinical information. The reviewers read planar and SPECT-CT in sequence. Each image was interpreted as benign, indeterminate or metastasis. For SPECT-CT images, if the CT showed either osteolytic, osteoblastic or mixed osteolytic-osteoblastic changes, it would be considered as metastasis. The area of intense uptake was also important. The diagnosis of metastasis was made if an abnormal MDP uptake was seen involving the vertebral body and/or pedicle of the vertebra. If the CT showed degenerative changes, such as osteosclerosis, osteophyte, or end plate changes a diagnosis of degenerative lesion was made. If the lesion was in between the two CT segments and appeared uncertain, the diagnosis of indeterminate was made.

Statistical analysis

All the collected data was entered and analysed using SPSS Statistic for Mac version 20.0. Descriptive analysis was used for ethnic group, age group, gender, and type of cancer. Crosstab was used in differentiating the findings from planar WB scintigraphy and SPECT-CT, versus the final diagnosis, to compare the accuracy of planar WB scintigraphy versus SPECT-CT.

RESULTS

Demography

Twenty-eight patients were included in this study. There were 19 (67.9%) females and 9 (32.1%) males. The age range was between 50-86 years. As shown in Table I, 17 (60.7%) patients had breast cancer and 5 (17.9%) patients had prostate cancer. The rest made up 21.4%. Twenty patients had degenerative spine disease (71.4%) and 8 patients had metastasis spine disease (28.6%).

Table I: Type of cancer referred for bone scintigraphy

Type of cancer	Number of patients (N)	Percentage (%)
Breast	17	60.7
Prostate	5	17.9
Colon	2	7.1
Renal Cell Carcinoma	1	3.6
Sarcoma	1	3.6
Others	2	7.1
Total	28	100.0

Outcome for both studies

Table II shows the percentages of indeterminate, degenerative and metastasis in first WB planar bone scintigraphy, second WB planar bone scintigraphy, first SPECT-CT and second SPECT-CT. One indeterminate lesion was diagnosed in the first WB planar bone scintigraphy (2.7%) and 2 indeterminate lesions were diagnosed in the second WB planar bone scintigraphy (5.4%). The single indeterminate lesion in the first WB planar bone scintigraphy was confirmed to be degenerative in the first SPECT-CT and 2 indeterminate lesions in the second WB planar bone scintigraphy were confirmed to be degenerative in the second SPECT-CT. Two indeterminate lesions were diagnosed in the first SPECT-CT and were confirmed to be one degenerative and one metastasis in the second SPECT-CT. There was no indeterminate lesion diagnosed in the second SPECT-CT. Out of the 30 lesions that were reported as degenerative on the second WB planar bone scintigraphy, 3 (10%) were confirmed to be metastasis on the second SPECT-CT. Nine lesions that were reported as metastasis on the first WB planar bone scintigraphy were confirmed to be

Table II: Outcome for both planar and SPECT-CT

Imaging type	Diagnosis n, (%)			Total
	Indeterminate	Degenerative	Metastasis	
Planar 1	1 (2.7)	27 (73.0)	9 (24.3)	37
Planar 2	2 (5.4)	30 (81.1)	5 (13.5)	37
SPECT-CT1	2 (5.4)	28 (75.7)	7 (18.9)	37
SPECT-CT2	0	29 (78.4)	8 (29.8)	37

degenerative in 2 (22.2%) on the first SPECT-CT [Figure 1(a) and 1(b)], while 2 (22.2%) became indeterminate. Following the second WB planar bone scintigraphy and second SPECT-CT examinations, 3/37 lesions were upgraded from degenerative to metastasis (8.1%). For metastatic lesions seen on the second WB planar bone scintigraphy, there was 100% agreement between the two examinations. All indeterminate lesions were resolved in the second examinations [Figure 2(a) and 2(b)]. The sensitivity of the first WB planar bone scintigraphy, second WB planar bone scintigraphy and first SPECT-CT is 75%, 62.5% and 75% respectively. The specificity of the first WB planar bone scintigraphy, second WB planar bone scintigraphy and first SPECT-CT was 86%, 93%, 90% respectively.

Agreement between the first and second WB planar bone scintigraphy

Out of the 27 lesions (73%) that were reported as degenerative in the first WB planar bone scintigraphy, 1 lesion (3.7%) was upgraded to metastasis in the second WB planar bone scintigraphy. The single indeterminate lesion in first WB planar bone scintigraphy was decided to be degenerative in the second WB planar bone scintigraphy. Of the 9 lesions (24%) that were reported as metastasis in first WB planar bone scintigraphy, 4 (44.4%) were downgraded to degenerative, while 1(11.1%) became indeterminate in the second WB planar bone scintigraphy. In total 29 (78%) of 37 lesions on the second WB planar bone scintigraphy agreed with the first WB planar bone scintigraphy findings. The agreement between the first WB planar bone scintigraphy and the second WB planar bone scintigraphy was shown in Table III.

Table III: Agreement between the first WB planar bone scintigraphy and the second WB planar bone scintigraphy

Planar 1	Planar 2 n, (%)			Total
	Degenerative	Indeterminate	Metastasis	
Degenerative	25 (92.6)	1 (3.7%)	1 (3.7)	27 (100)
Indeterminate	1 (100)	0	0	1 (100)
Metastasis	4 (44.4)	1 (11.1)	4 (44.4)	9 (100)

Agreement between the first and second SPECT-CT

All patients underwent two SPECT-CT examinations. All 27 degenerative lesions in the first SPECT-CT were confirmed in the second SPECT-CT. Two indeterminate findings (5.4%) on the first SPECT-CT were confirmed to be one degenerative and one metastatic lesion in the second SPECT-CT. All 7 metastatic lesions in the first SPECT-CT were confirmed on the second SPECT-CT. There was no indeterminate finding on the second SPECT-CT. Comparison of findings between the two SPECT-CT examinations were shown in Table IV.

Table IV: Agreement between the first and the second SPECT-CT

SPECT-CT1	SPECT-CT2 n, (%)			Total
	Degenerative	Indeterminate	Metastasis	
Degenerative	28 (100)	0	0	28(100)
Indeterminate	1 (50)	0	1 (50)	2 (100)
Metastasis	0	0	7 (100)	7 (100)

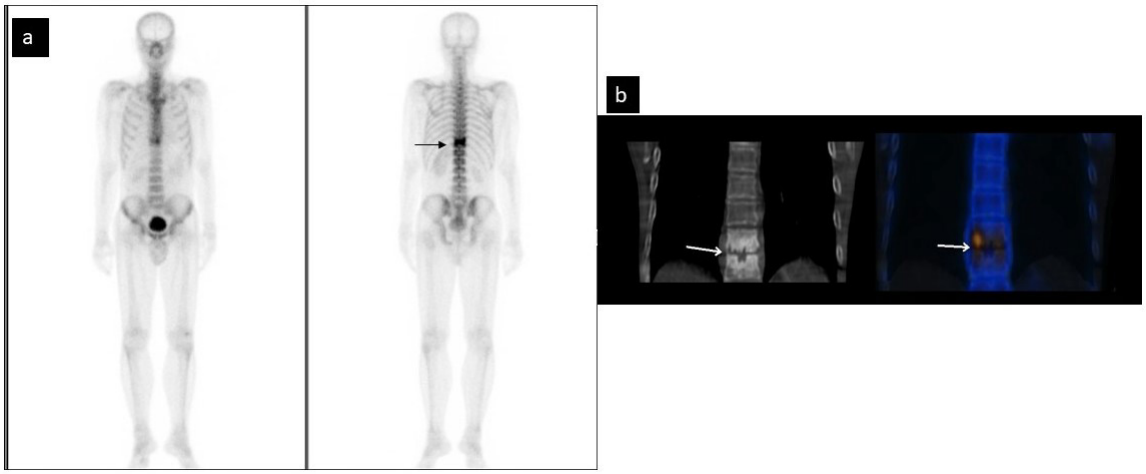

Figure 1: (a) WB planar bone scintigraphy (anterior and posterior views) with intense tracer uptake in T10 or T11 vertebral body posteriorly (black arrow), likely a metastatic lesion. (b) CT and SPECT-CT at the level of T10/T11 in coronal plane showing spondylodiscitis of T10/T11 corresponding to area of intense uptake (white arrows)

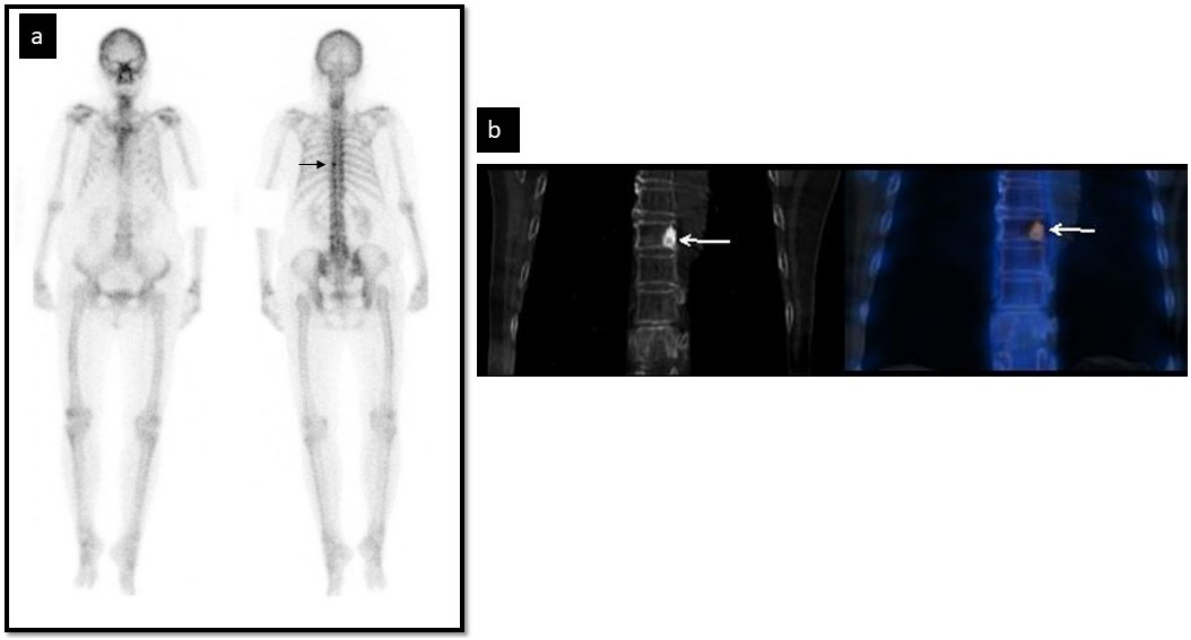

Figure 2: (a) WB planar bone scintigraphy (anterior and posterior views) showing moderately increase tracer uptake on left side of T9 vertebral body (black arrow), which looks like a degenerative lesion. (b) CT and SPECT-CT at the level of T9 vertebral body in coronal plane showing a sclerotic lesion in the left side of body of T9, corresponding to area of intense uptake (white arrows) in keeping with sclerotic metastasis

DISCUSSION

Skeletal metastasis is not uncommon. It occurs in approximately 30% of all patients with cancer (4). Plain radiography, CT scan, MRI, PET-CT and WB planar bone scintigraphy has been used to diagnose bone metastasis (5). Bone scintigraphy presently is the most sensitive tool in detecting bone metastases. However, increase tracer accumulation may occur in the skeleton with variety of reasons of increase bone turnover, thus bone scintigraphy may be non-specific to diagnose bone metastases. This has led to indeterminate finding in bone scintigraphy reports, especially when reporting the spine of elderly cancer patients. SPECT in combination with CT increase the sensitivity and specificity of WB bone scintigraphy in detecting bone metastases (6). SPECT-CT enables a direct correlation between anatomic and functional information. This results better localisation and gives more values of WB planar scintigraphic findings (7).

Patients aged 50 years old and older were chosen for this study and the rationale behind it was to differentiate whether uptake in the spine could be due to degenerative disease or metastases. This would be seldom a problem in young patients with cancer although disc degeneration could start as early as 30 years old. At 50 years old, the changes were more prominent (8).

The incidence of solitary bone scan abnormalities were only 8-15% (9). Due to this reason, we chose the maximum of three spine uptake and the maximum of five uptake throughout the skeleton for our study. We selected patients with maximum of three areas of uptake in the spine to ensure reliability of the study. Patients with extensive or multiple bone metastases would not require a SPECT-CT to differentiate between metastatic or degenerative disease, as the overall management of the patients would not be affected as in change of treatment.

Our patients underwent their second WB planar bone scintigraphy and SPECT-CT of the same area within one-year interval. The shortest period of interval was 3 months. The findings from the second SPECT-CT were considered the standard for this study. A similar study was done by Iqbal and coworkers whereby they assessed the value of SPECT-CT in solitary spine lesion, using Infinia Hawkeye low dose SPECT-CT (GE Healthcare)(10). From the results of their study, there was a good agreement between both the WB planar bone scintigraphy examinations in deciding the areas of uptake which were due to degenerative changes in the spine.

Planar scintigraphy has the advantage of offering a whole-body image of the skeleton in one examination, economical and has a high sensitivity. Only 5% changes in bone turnover rate is needed for a positive uptake in a bone scintigraphy, whereas in plain radiographs, 40-50% of bone change is needed to be able to detect any lucency in the bone (11). WB planar bone scintigraphy provides visualisation of the skeletal system from head to toe with sensitivity rates of 62-100% in the detection of bone metastases (12).

There were 2 (5.4%) indeterminate lesions in the first SPECT-CT. The first WB planar bone scintigraphy only showed one indeterminate lesion, but there were

uptakes which were downgraded and upgraded by the SPECT-CT. Although the first SPECT-CT had 2 indeterminate lesions, this was due to technical errors, where the location of the lesions was in between the two CT segments. Brightview XCT gives CT images in segments, where one segment is equal to 14.4 cm of the patient. Occasionally, during scanning the patient moves, and these segments were not fused properly and created a gap in between the images. These cases were then required a follow up images, either CT scan, MRI or a repeat WB bone scintigraphy with SPECT-CT of the area of interest. First and second WB planar bone scintigraphy had good agreement in degenerative disease but not seen in metastasis. The effects of treatment changes in these patients were not included in this study.

Following the second WB planar bone scintigraphy and second SPECT-CT examinations, 3/37 lesions were upgraded from degenerative to metastasis (8.1%). This changed the overall management of the patients. For metastatic lesions seen on the second WB planar bone scintigraphy, there was 100% agreement between the two examinations. All 'indeterminate lesions' were resolved in the second examinations. There was 100% agreement in deciding on degenerative and metastastic lesions between the first SPECT-CT and the second SPECT-CT. This showed that the SPECT-CT was more superior in diagnosing degenerative and metastatic disease of the spine than the WB planar bone scintigraphy. Previous studies also supported this finding (3, 13).

Accuracy was determined between SPECT-CT and WB planar bone scintigraphy. For this, the indeterminate lesions were reclassified as metastatic lesions. We found that the sensitivity of the first WB planar bone scintigraphy was 75% and the specificity was 86%. The second WB planar bone scintigraphy shows sensitivity of 63% but specificity increased to 93%. This showed that a repeat WB planar bone scintigraphy was good in detecting a true negative finding, but true positive finding might be missed. Therefore, a repeat WB planar bone scintigraphy of suspected lesions in the spine as a follow up study in a cancer patient might not be necessary. Sensitivity of the first SPECT-CT was 75%, similar to the first WB planar bone scintigraphy. The second planar had a lower sensitivity of 62.5%. This result showed that WB planar bone scintigraphy was not more sensitive as SPECT-CT in detecting true metastatic lesions. The specificity of the first SPECT-CT (90%) was higher than the first WB planar bone scintigraphy (86%) and lower than the second WB planar bone scintigraphy, which was 93%. Overall, there was no significant difference in specificity of WB planar bone scintigraphy and SPECT-CT. This was due to the small sample size of our study. Although accuracy showed no significant difference between WB planar bone scintigraphy and SPECT-CT, we emphasised that there was 100% agreement between both SPECT-CT examinations in deciding degenerative and metastatic findings.

A study by Strobel et al (2007), on the performance of WB planar bone scintigraphy compared with SPECT and SPECT fused with 64 MDCT showed a sensitivity and specificity of 82% and 94% for WB planar bone scintigraphy and 100% for SPECT fused with CT (14). Their study used clinical follow-up, additional MRI and additional WB planar bone scintigraphy only if needed. Therefore, the ultimate diagnosis was actually the SPECT combined with CT (14). They concluded that SPECT with CT has significantly increased certainties in diagnosis, although WB planar bone scintigraphy may be sufficient enough in differentiating benign and malignant lesions (14). Zhao et.al concluded that SPECT-Spiral CT was useful for the diagnosis of bone metastasis by providing precise anatomical localisation and detailed morphologic characteristics of the bone in cancer patients (15).

SPECT provides superior information as compared to planar scintigraphy for both malignant and degenerative changes of the spine. The sensitivity in detection is better when posterior and lateral bone structures are affected. SPECT-CT is showing better specificity than WB planar bone scintigraphy or SPECT alone. This is proven to be useful in the evaluation of spinal abnormalities in cancer patients (16). Sixty three percent of indeterminate uptake in another study is also shown in the spine area (3).

In a study of 47 cancer patients with 104 equivocal lesions on bone scintigraphy, SPECT-CT provided an 85% correct diagnosis for these lesions as compared to only 36% by using SPECT alone. Over 60% of these lesions were located in the spine (17). Helyar et al (2007) also found the addition of SPECT-CT reduced equivocal reports in prostate cancer study, and also has improved diagnostic confidence as compared to planar and SPECT imaging alone (18). Other indications for SPECT-CT examinations are in localisation of neuroblastoma, parathyroid adenoma, radioiodine and well-differentiated thyroid carcinoma, and prostate carcinoma (19).

In our study, 5 (83.3%) lesions in thoracic spine were metastasis and 10 (100%) of the cervical spine lesions were degenerative in nature. The majority of 18 (90%) lesions in lumbar spine were of degenerative. It was reported that vertebral metastases is 70% more common in thoracic, followed by lumbar and cervical (20).

Study by Iqbal and co-workers found 10% of baseline SPECT-CT was indeterminate lesions, and there was no indeterminate lesion in the follow-up SPECT-CT. Fifty two percent indeterminate lesions were in the planar scan, as compared to only 14% during the follow-up of the planar scan (10). Another study found 8% of indeterminate lesions after SPECT-CT (3). Our findings were 5.4% in the first SPECT-CT and no indeterminate

lesion in the second SPECT-CT that is almost similar to the studies above.

Bone scintigraphy using low dose SPECT-CT is a superior modality in diagnosing bone metastasis in a cancer patient as compared to the combination of multi-planar bone scintigraphy and diagnostic CT scan for a host of reasons. Bone SPECT-CT using brightview XCT increases the level of diagnostic confidence for the interpreting physicians. It is also reducing additional diagnostic imaging studies such as MRI and diagnostic CT scan. Other study is suggesting that SPECT-CT should be done on a patient-by-patient basis (21). In effect, this would greatly help the logistics of doing a diagnostic procedure for both the healthcare side and the patient. From the healthcare side, this would mean one procedure slot as opposed to two that might require separate appointments on different days. From the patients' point of view, it means that they do not have to come back to hospital for another procedure. This would significantly eliminate the problem of patients not complying with appointment times.

CONCLUSION

SPECT-CT is useful in differentiating degenerative and metastatic disease of the spine in a patient with primary malignant disease. Hybrid SPECT-CT can resolve indeterminate lesions in the spine. A second SPECT-CT is only needed if there is 'indeterminate lesions' of the first SPECT-CT.

ACKNOWLEDGEMENTS

This research is done as a partial fulfillment of Master of Medicine (Nuclear Medicine). This work is supported by USM Student Research Grant (USM/IPPT/2000/G-2/xiv).

REFERENCES

1. Palmedo H, Marx C, Ebert A, Kreft B, Ko Y, Türler A, et al. Whole-body SPECT/CT for bone scintigraphy: diagnostic value and effect on patient management in oncological patients. European Journal of Nuclear Medicine and Molecular Imaging. 2014;41(1):59-67.
2. Glaudemans A, Lam M, Veltman N, Dierckx R, Signore A. The contribution of nuclear medicine in the diagnosis of bone metastases. Bone Metastases: Springer; 2009. p. 137-62.
3. Romer W, Nomayr A, Uder M, Bautz W, Kuwert T. SPECT-guided CT for evaluating foci of increased bone metabolism classified as indeterminate on SPECT in cancer patients. Journal of nuclear medicine : official publication, Society of Nuclear Medicine. 2006;47(7):1102-6.
4. Stoker D, Saifuddin A. Bone tumors: malignant lesions. Grainger and Allison's Diagnostic Radiology: A Textbook of Medical Imaging. 2001:1885-6.
5. Rosenthal DI. Radiologic diagnosis of bone metastases. Cancer. 1997;80(S8):1595-607.
6. Utsunomiya D, Tomiguchi S. Bone metastasis: Single photon emission computed tomography/computed tomography. Cancer Imaging: Academic Press; 2008.
7. Buck AK, Nekolla S, Ziegler S, Beer A, Krause BJ, Herrmann K, et al. Spect/ct. Journal of Nuclear Medicine. 2008;49(8):1305-19.
8. Andersson GBJ. 8 What are the age-related changes in the spine? Baillиre's Clinical Rheumatology. 1998;12(1):161-73.
9. Corcoran RJ, Thrall JH, Kyle RW, Kaminski RJ, Johnson MC. Solitary abnormalities in bone scans of patients with extraosseous malignancies. Radiology. 1976;121(3):663-7.
10. Iqbal B, Currie GM, Wheat JM, Raza H, Kiat H. The incremental value of SPECT/CT in characterizing solitary spine lesions. Journal of nuclear medicine technology. 2011;39(3):201-7.
11. Brenner AI, Koshy J, Morey J, Lin C, DiPoce J. The Bone Scan. Seminars in Nuclear Medicine. 2012;42(1):11-26.
12. Even-Sapir E, Metser U, Mishani E, Lievshitz G, Lerman H, Leibovitch I. The detection of bone metastases in patients with high-risk prostate cancer: 99mTc-MDP Planar bone scintigraphy, single-and multi-field-of-view SPECT, 18F-fluoride PET, and 18F-fluoride PET/CT. Journal of Nuclear Medicine. 2006;47(2):287-97.
13. Utsunomiya D, Shiraishi S, Imuta M, Tomiguchi S, Kawanaka K, Morishita S, et al. Added value of SPECT/CT fusion in assessing suspected bone metastasis: comparison with scintigraphy alone and nonfused scintigraphy and CT. Radiology. 2006;238(1):264-71.
14. Strobel K, Burger C, Seifert B, Husarik DB, Soyka JD, Hany TF. Characterization of focal bone lesions in the axial skeleton: performance of planar bone scintigraphy compared with SPECT and SPECT fused with CT. AJR Am J Roentgenol. 2007;188(5):W467-74.
15. Zhao Z, Li L, Li F, Zhao L. Single photon emission computed tomography/spiral computed tomography fusion imaging for the diagnosis of bone metastasis in patients with known cancer. Skeletal radiology. 2010;39(2):147-53.
16. Papathanassiou D, Bruna-Muraille C, Jouannaud C, Gagneux-Lemoussu L, Eschard J-P, Liehn J-C. Single-photon emission computed tomography combined with computed tomography (SPECT/CT) in bone diseases. Joint Bone Spine. 2009;76(5):474-80.
17. Horger M, Bares R. The Role of Single-Photon Emission Computed Tomography/Computed Tomography in Benign and Malignant Bone Disease. Seminars in Nuclear Medicine. 2006;36(4):286-94.

18. Helyar V, Mohan H, Barwick T, Livieratos L, Gnanasegaran G, Clarke SM, et al. The added value of multislice SPECT/CT in patients with equivocal bony metastasis from carcinoma of the prostate. European Journal of Nuclear Medicine and Molecular Imaging. 2010;37(4):706-13.
19. Brandon D, Alazraki A, Halkar RK, Alazraki NP. The Role of Single-Photon Emission Computed Tomography and SPECT/Computed Tomography in Oncologic Imaging. Seminars in Oncology. 2011;38(1):87-108.
20. Harel R, Angelov L. Spine metastases: Current treatments and future directions. European Journal of Cancer. 2010;46(15):2696-707.
21. Franc BL, Myers R, Pounds TR, Bolton G, Conte F, Bartheld M, et al. Clinical utility of SPECT-(low-dose)CT versus SPECT alone in patients presenting for bone scintigraphy. Clinical Nuclear Medicine. 2012;37(1):26-34.