

Additional Value of 99mTc-MDP Single-photon Emission Computed Tomography-computed Tomography for Detection and Characterization of Bone Lesions in Nasopharyngeal Carcinoma Patients

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Abstract

Background: ^{99m}Tc -labelled methylene diphosphonate (^{99m}Tc -MDP) uptake can diagnose bone metastasis in patients. The purpose of our study was to assess the additional value of single photon emission computed tomography/computed tomography (SPECT/CT) over whole-body planar scintigraphy (WBS) and SPECT in detecting bone lesions in nasopharyngeal carcinoma patients.

Methods: Data from 126 patients (169 lesions) with nasopharyngeal carcinoma who underwent WBS, SPECT, and SPECT/CT in this 2-year prospective study. These scans of patients were directly compared for detection and characterization of bone lesions. McNemar's multistep analysis was performed in patient-based and lesion-based.

Results: On patient-based analysis, SPECT/CT significantly reduced the number of equivocal diagnosis than WBS and SPECT ($p=0.004$), and SPECT significantly reduced the number of equivocal diagnosis than WBS ($p=0.004$). The diagnostic coincidence rate of SPECT/CT (90.2%) is significantly higher than WBS (45.5%) and SPECT (61.6%). On lesion-based analysis, SPECT/CT significantly decreased the number of equivocal lesions than WBS and SPECT. SPECT/CT interpretation revealed 98 benign lesions and 37 malignant lesions, more than WBS and SPECT. For all the 112 patients, 32 equivocal patients were diagnosed definitely based on SPECT/CT findings, and received specific treatment and management.

Conclusion: SPECT/CT can add incremental value to whole-body bone imaging by significantly improves diagnostic sensitivity in nasopharyngeal carcinoma patients and decrease the number of equivocal lesions that do not contribute to diagnosis. Moreover, SPECT/CT can contribute to change the clinical management of patient and identify a more accurate metastatic range.

Background

Whole-body bone scintigraphy (WBS) and single-photon emission computed tomography (SPECT) using ^{99m}Tc -labelled methylene diphosphonate (^{99m}Tc -MDP) are recommended in bone metastatic high-risk carcinoma, like prostate cancer, breast cancer and nasopharyngeal carcinoma and lung cancer^[1-2]. But, there are many studies show the specificity is limited to sufficiently characterize a lesion for diagnostic purposes^[3]. The advent of hybrid cameras enabling SPECT to be coupled with CT allows combination of the functional specificity of SPECT and lesion localization by CT. SPECT/CT allows a better characterization of uptake foci, thus improving the specificity and decreasing the number of equivocal lesions^[4-9]. SPECT/CT has gained a wide acceptance for bone scanning, and the role of it in the evaluation of possible bone metastasis is still evolving. The purpose of this study is to assess the incremental value of SPECT/CT, compared to WBS and SPECT in patients with nasopharyngeal carcinoma and the influence on the clinical management of the patients.

Methods

From February 2017 to September 2018 126 patients with histopathologically confirmed nasopharyngeal carcinoma were included in this study which was approved by the Institutional Ethics Committee. Patients with history of known bone metastases were excluded from the study. And the patients with the diagnosis of extensive bone metastases based on WBS only would not undergo further scan. In the study, we consecutively recruited the patients who underwent routine bone scintigraphy in our department. Patients with bone lesions (definitive or equivocal) on WBS were all included.

All patients received intravenous injection of Tc-99m MDP (740 MBq). Patients were asked to void before starting the acquisition. WBS was performed 3 hours after injection in the anterior and posterior projections, with a speed of 20 cm/min, on a double-head gamma camera with a multislice spiral CT scanner installed within the same gantry (SIEMENS Symbia Intevo 16, Germany). The camera heads were equipped with a high-resolution low-energy parallel-hole collimator. Images were acquired on the 140 keV photopeak with a 20% symmetrical window. The matrix size used was 256 × 1024, zoom 1.

All the patients underwent whole-body SPECT with the same gamma camera, whether or not there were suspicious lesions on WBS. The axial field of view of the camera was 38.7 cm (75.4 cm for two SPECT with 2 cm overlap). SPECT data were collected in step-and shoot-mode with a noncircular orbit (auto contouring) and duration of 15 s per step. Images were acquired on the 140 keV photopeak with a 20% symmetrical window. The matrix size used was 128 × 128. After the SPECT data was acquired, the raw data were iteratively reconstructed into trans axial, coronal, and sagittal slices using esoft reconstruction workplace (Siemens Healthcare GmbH and Toshiba Medical, Germany).

The CT component of the whole-body SPECT/CT (from the base of the skull to the proximal femurs, with some slight variations due to patient height) acquired with the exposure of 130 KeV, current 2.5mA, and 512 × 512 matrix. CT-based attenuation correction was used. Processing and fusion of SPECT and CT images were performed by using Syngo MI applications VB10D.

WBS images, SPECT images and the fused SPECT/CT images were randomly and independently interpreted by two nuclear medicine readers with respectively 9–15 years of experience. Third reader would be invited to view the image in cases of discrepancy. Each reader visually accessed bone lesions by a three-point scale: (1) definitely benign; (2) definitely malignant; (3) equivocal.

These patients were followed up for 9–12 months with additional correlative imagings, like magnetic resonance imaging (MRI), plain radiograph, follow-up bone scan, CT. Considering the findings of SPECT/CT compared with the results of clinical follow-up, a final diagnosis as to the true status of lesions was made based on the consensus of the physicians. We evaluated the influence on the management of patient by comparing the final management based on SPECT/CT findings with the management based on WBS alone.

All acquired imaging findings based on WBS, SPECT and SPECT/CT were analyzed. Directly compared the sensitivity and specificity of WBS, SPECT, and SPECT/CT. Patient-based, lesion-based, and patient management analyses were undertaken and incremental values were calculated. Compared the all

acquired data by using McNemar's test with p value of less than 0.05 ($p < 0.05$) considered as statistically significant.

Results

A total of 126 patients (74 males and 52 females) with histologically confirmed nasopharyngeal carcinoma in the age group of 25–73 years were included in the study. 14 patients were lost to follow-up and data from only 112 patients were available for further analysis. There are 57 patients had follow-up bone scan, 8 patients had plain radiography, 28 patients had CT scan, and 19 patients had MRI scan. (Table 1)

Table 1
The number of patients with different follow-up imaging

Modality	Number
Bone scan	57
Plain radiography	8
CT	28
MRI	19
Total	112

Patient-based Analysis

On the whole, the results of 112 patients separately diagnosed by WBS, SPECT and SPECT/CT are detailed in Fig. 1. 62 patients were diagnosed as being equivocal by WBS, while 37 patients were diagnosed as being equivocal by SPECT and only 11 patients were diagnosed by SPECT/CT (Table 2). On comparing, SPECT/CT significantly reduced the number of equivocal diagnosis than WBS and SPECT ($p < 0.05$), and SPECT significantly reduced the number of equivocal diagnosis than WBS ($p < 0.05$). On WBS, there were 51 (21 malignant and 30 benign) patients consistent with final diagnosis. On SPECT, there were 69 (21 malignant and 48 benign) patients consistent with final diagnosis, while there were 101 (20 malignant and 81 benign) on SPECT/CT. The diagnostic coincidence rate of SPECT/CT (90.2%) is significantly higher than WBS (45.5%) and SPECT (61.6%). (Table 3)

Table 2
Comparing WBS, SPECT and SPECT/CT in patient-based analysis of equivocal interpretation

Modality	Number of equivocal lesions (%)	WBS vs SPECT	WBS vs SPECT/CT	SPECT vs SPECT/CT
WBS	62(55.4%)	$P=0.05$	$P=0.05$	$P=0.05$
SPECT	37(33.0%)			
SPECT/CT	11(9.8%)			

Table 3
Diagnose accordance rate of WBS, SPECT, SPECT/CT

Modality	Diagnose accordance rate (%)
WBS	45.5%
SPECT	61.6%
SPECT/CT	90.2%

Lesion-based Analysis

A total of 169 lesions were detected from the 112 patients by SPECT, SPECT/CT, while WBS detected only 153 lesions. Of 169 lesions, SPECT/CT shows a significant reduction in the number of equivocal lesions as compared to SPECT (Table 4, $p=0.05$). SPECT/CT interpretation revealed 97 benign lesions and 42 malignant lesions, more than SPECT. All 153 bone lesions detected by BS were also detected by SPECT and SPECT/CT. On comparing, SPECT/CT significantly decreased the number of equivocal lesions than WBS and SPECT (Table 5, $p=0.05$). SPECT/CT interpretation revealed 98 benign lesions and 37 malignant lesions, more than WBS and SPECT.

Table 4
Proportion of benign, equivocal, and malignant lesions on SPECT and SPECT/CT

	SPECT, n (%)	SPECT/CT, n (%)
Benign	70(41.4%)	109(64.5%)
Malignant	36(21.3%)	39(23.1%)
Equivocal	63(37.3%)	21(12.4%)
Total	169	169

Table 5
Proportion of benign, equivocal, and malignant lesions on WBS, SPECT and SPECT/CT

	WBS, n (%)	SPECT, n (%)	SPECT/CT, n (%)
Benign	38(24.8%)	64(41.8%)	98(64.1%)
Malignant	31(20.3%)	31(20.3%)	37(24.2%)
Equivocal	84(54.9%)	58(37.9%)	18(11.8%)
Total	153	153	153

Of the 169 lesions localization, the most was identified in the spine (87, 51.5%) and the second most was identified in the rib (38, 22.5%) followed by extremities (19, 11.2%).(Table 6, p=0.05) Of the 153 lesions localization, the most was identified in the spine(79, 51.6%) and the second most was identified in the rib (36, 23.5%) followed by extremities (19, 12.4%). Analysis of all lesions indicated that SPECT/CT significantly decreased the number of equivocal lesions as compared to WBS and SPECT. (Table 7, p=0.05)

Table 6
Proportion of equivocal lesions based on location of SPECT and SPECT/CT

	n	SPECT, number of equivocal lesions (%)	SPECT/CT, number of equivocal lesions (%)
Spine	87	32(36.8%)	9(10.3%)
Rib	38	16(42.1%)	7(18.4%)
Pelvis	9	3(30.0%)	0
Scapula	16	8(50%)	3(16.7%)
Extremities	19	4(21.1%)	2(10.5%)
Total	169	63	21

Table 7
Proportion of equivocal lesions based on location of WBS, SPECT and SPECT/CT

	n	WBS, number of equivocal lesions (%)	SPECT, number of equivocal lesions (%)	SPECT/CT, number of equivocal lesions (%)
Spine	79	48(60.8%)	30(38.0%)	8(10.1%)
Rib	36	21(58.3%)	15(41.7%)	6(16.7%)
Pelvis	6	2(33.3%)	2(33.3%)	0
Scapula	13	7(53.8%)	7(53.8%)	2(15.4%)
Extremities	19	6(31.6%)	4(21.1%)	2(10.5%)
Total	153	84	58	18

Patient Management

For all the 112 patients, 32 equivocal patients were diagnosed definitely based on SPECT/CT findings, and received specific treatment and management. All the 32 patients whose diagnosis was altered by SPECT/CT consistent with final diagnosis based on follow-up. Furthermore, the diagnosis of another 4 patients was changed from benign to malignant, while 6 patients were changed from malignant to benign. For those 10 patients, different treatment and management were conducted.

Discussion

WBS is a widely used and highly sensitive imaging modality to detect the bone metastases in cancer patient. However, its specificity is limited in accurately diagnosing a bone lesion due to uptake in other benign conditions (e.g., degenerative changes, fractures, infections, and trauma) ^[11]. SPECT is able to expose accurate localization and characterization of more bone lesions^[2]. Although some patients undergo SPECT scan, there are some lesions still remain equivocal. Combined the anatomical information of CT with functional information of SPECT, SPECT/CT can enable more accurate localization and characterization of lesions using. For the vertebrae where the location of a lesion determines whether it is classified as malignant or benign. The study shows that most of the benign lesions were within the facet joints or at the end plate of the vertebral bodies whereas the malignant lesions were predominantly within the pedicles and vertebral bodies ^[12]. The management of a patient mostly based on diagnosis and clinical staging. But bone metastasis or benign bone disease is detected by bone scintigraphy or other imaging methods may influence the diagnosis and clinical staging of patient. Most of the time, the existence of bone metastasis may result in the change of treatment such as radiotherapy or radionuclide therapy. In our study, the diagnosis of 42(37.5%) patients had been changed based on SPECT/CT, which is also founded by other studies. Thanuja Mahaletchumy et al. ^[13], found 32% patients had their diagnosis altered in their study. Ndlovu et al. ^[14], recorded an alteration of

diagnosis in 40.5% of patients in their study. Meanwhile, 4 patients received chemotherapy for the diagnosis was changed from benign to malignant and 6 patients avoided overtreatment for the diagnosis was changed from malignant to benign (Fig. 2,3). Of the 32 equivocal patients, 21 were found to be benign and 11 were found to be malignant based on SPECT/CT, but only 6 patients received changed treatment plan for other organs metastases. The diagnostic coincidence rate of SPECT/CT is 90.2% when a definitive diagnosis was made. This is lower than a study by Zhao et al. (95.7%)^[15] but higher than the study by Horger et al.^[16](85%).

We observed the role of SPECT/CT in the interpretation of each bone lesion in the lesion-based analysis. Not only SPECT/CT reduced the number of equivocal lesions (12.5%) compared to WBS and SPECT, but also resulted in improved accuracy in the characterization of these lesions, further supporting the value of its clinical application.

And we found that bone lesions commonly affected the spine and ribs, which is corroborated with other studies^[2, 6, 13]. In our study, SPECT/CT significantly decreased the number of equivocal lesions at all bone regions, and the reduction was statistically significant in the proportion of equivocal lesions in the spine ($P < 0.004$)^[14]. These findings suggest that SPECT/CT enhances the confidence diagnosis equivocal lesions which at almost all the bone sites. Specially, using SPECT/CT to scan spine will be most beneficial to patients for degenerative changes frequently occur at this region. This is also found in the study of Thanuja Mahaletchumy et al.,^[13] It's difficult to distinguish the benign changes from bone metastasis by WBS and SPECT alone. In the present study, we found that even though some bone lesions were detected by the CT component of the SPECT/CT which were not seen on WBS and SPECT imaging, it did not change the final diagnosis of the patients.

Many previous studies showed that only one region SPECT/CT commonly used in an area with equivocal lesions found by WBS.^[4,17-18] We performed whole-body SPECT/CT from the base of the skull to the proximal femurs in all the patients no matter they have definite benign or malignant lesions on WBS. For these patients with lesions detected by WBS supporting the diagnosis of benign or malignant bone disease, even we founded additional lesions on SPECT/CT, the overall diagnosis would not be changed. But these findings could help us to confirm the true range of bone metastases. So, not only the equivocal lesions but also the other definitive benign or malignant lesions on WBS could be evaluated by the whole-body SPECT/CT.

Our study has some limitations. First was that the patients did not receive any biopsy of the bone lesions. Theoretically, our study should combine pathologic findings to confirm the diagnoses of malignant or benign lesion, but it's not practical or necessarily ethical to perform bone biopsy for every lesion. Secondly, considering the findings based on MRI, plain radiography, follow-up bone scan, and CT as reference, it's difficult to confirm the common reference standard in patients. Furthermore, the decision on which imaging methods to use as the reference standard in some of the patients was left to the referring physician.

Conclusion

SPECT/CT can add incremental value to whole-body bone imaging by significantly improves diagnostic sensitivity in nasopharyngeal carcinoma patients and decrease the number of equivocal lesions that do not contribute to diagnosis. Moreover, SPECT/CT can contribute to change the clinical management of patient and identify a more accurate metastatic range.

Abbreviations

^{99m}Tc -MDP

^{99m}Tc -labeled methylene diphosphonate; SPECT/CT:Single photon emission computed tomography/computed tomography; WBS:Whole-body bone scans

Declarations

Ethics approval and consent to participate

The current study was approved by the Institutional Ethics Committee of the Sichuan Cancer Hospital & Institute, School of Medicine, University of Electronic Science and Technology of China (No.201609063), and the need for signed informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

The dataset supporting the conclusions of this article is included within the article.Data and materials during the current study are available from the corresponding author upon reasonable request

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Yingzhuo Yang participated in the design of the study, drafted the manuscript and processed the figures, Qiao Wang collected the patients' data. Wen Yang and Wenguo He interpreted the WBS and SPECT/CT images, Bin Shu processed the figures. Yun Duan participated in the design of the study, conceived the study and supervised the project.

All authors read and approved the final version of the manuscript.

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Figures

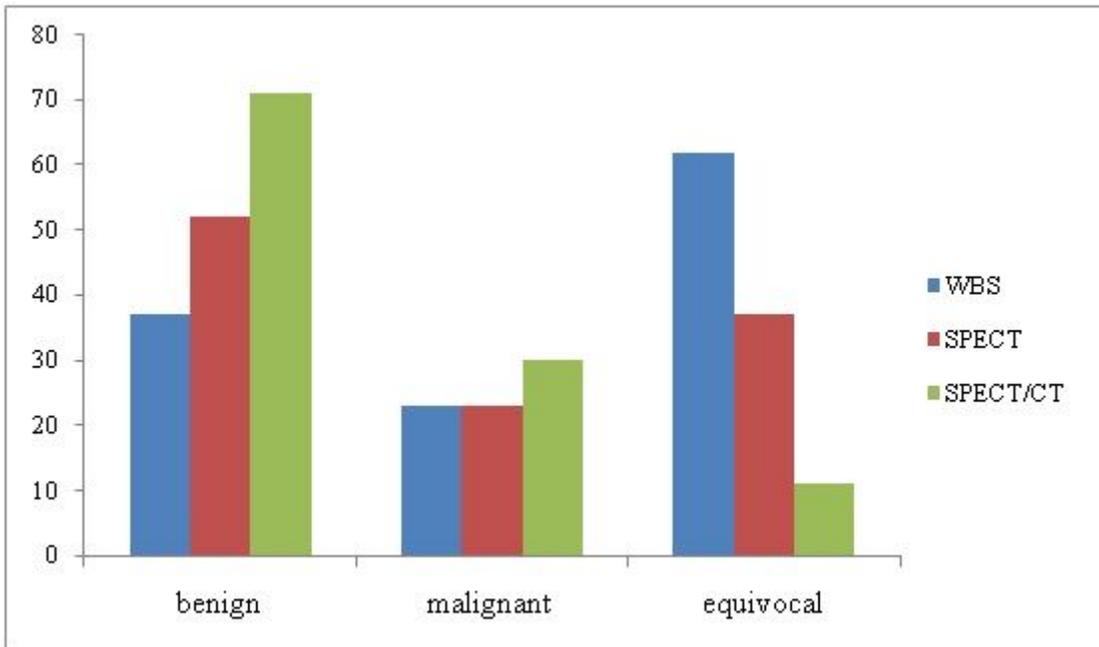


Figure 1

Patient-based analysis interpretation for WBS, SPECT, and SPECT/CT

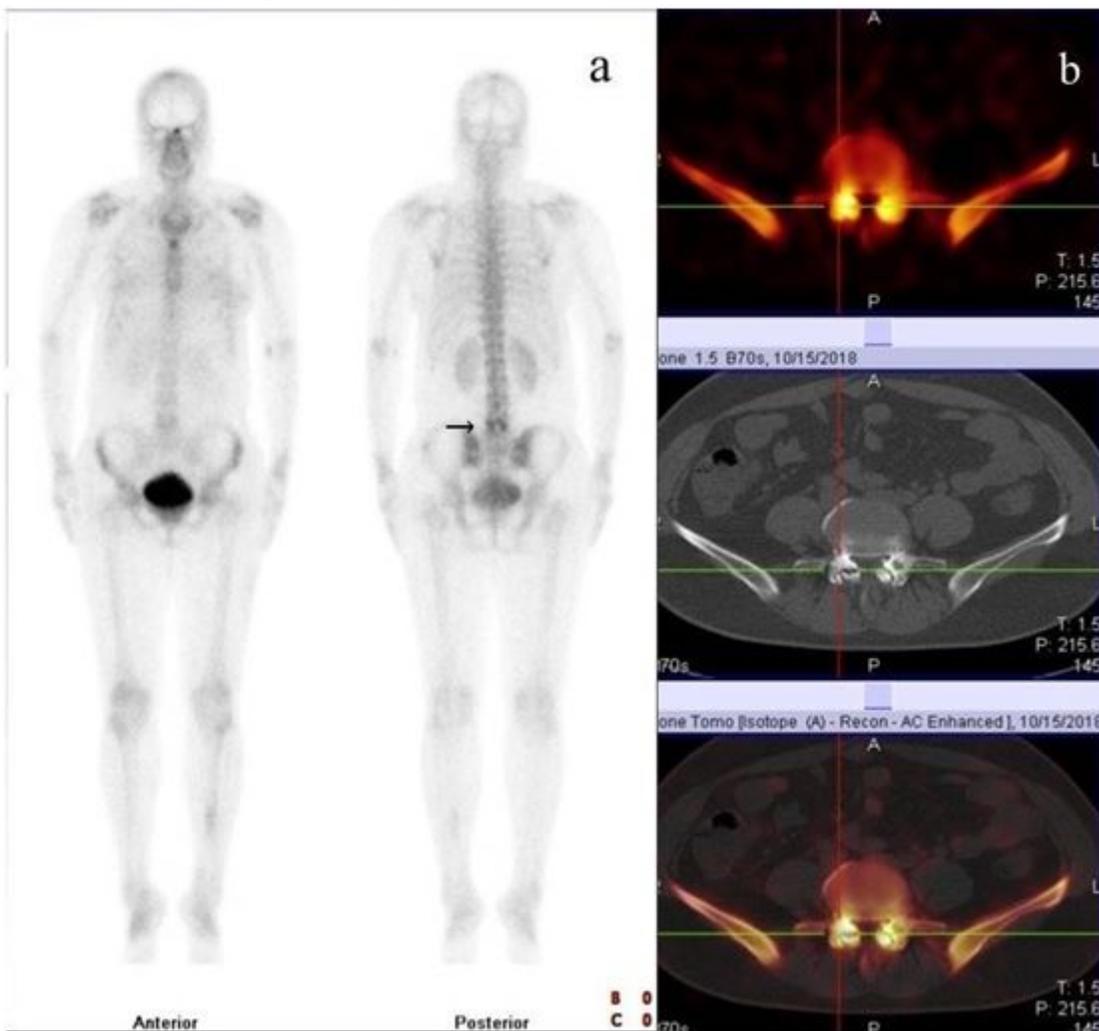


Figure 2

A 43-year-old woman with nasopharyngeal carcinoma.(a) anterior and posterior planar bone scintigraphic images with focal increased uptake at lumbar vertebra(arrow)is equivocal for metastases, (b) single-photon emission computed tomography, computed tomography, and single-photon emission computed tomography-computed tomography images showing hyperostosis and osteosclerosis in bilateral facet joints of L4-L5 vertebrae, based on planar scintigraphy alone it was difficult to determine whether the uptake is at the pedicles or facet joints.

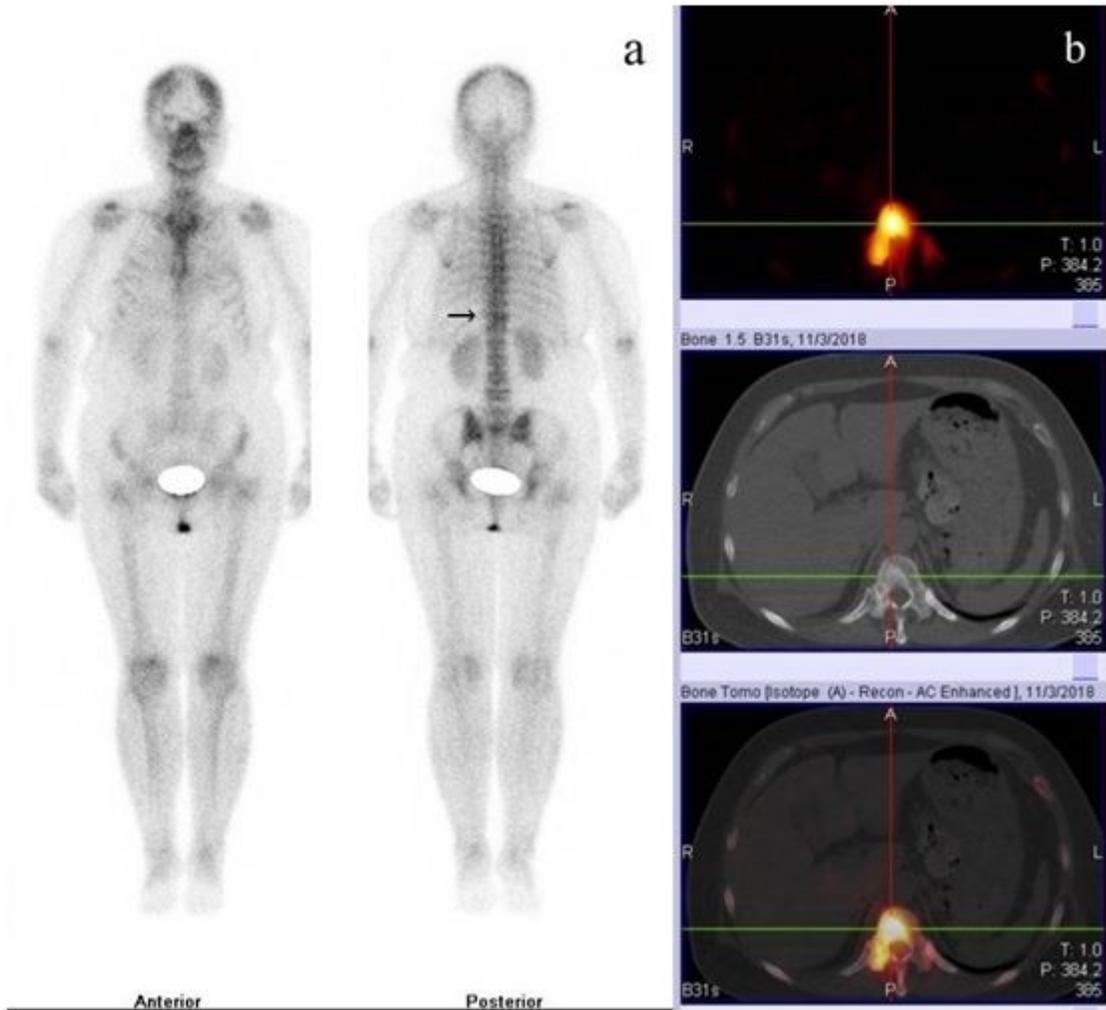


Figure 3

A 68-year-old woman with nasopharyngeal carcinoma.(a) posterior planar bone scintigraphic image showing increased uptake at upper thoracic spine region (arrow), (b) single-photon emission computed tomography, computed tomography, and single-photon emission computed tomography-computed tomography images showing the activity is localized to showing a lytic lesion at the body and right pedicle of T11 vertebra, which was difficult to determine whether the uptake is at the vertebra body or pedicles.