

## ORIGINAL ARTICLE

## Bone SPECT-CT in the diagnosis and staging of osseous metastases

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### Abstract

**Aims** The combined application of baseline whole-body bone scan (WBBS), followed by more specific techniques such as SPECT-CT fusion is an advanced approach for the diagnosis, differential diagnosis and staging of osseous metastases. The purpose of this work was to assess SPECT-CT images in diagnosis of suspected bone metastases in patients with oncological diseases.

**Methods** This study included 89 patients (54 females, 35 males aged 18-92 yrs) with different types of tumours. All patients underwent routine WBBS with <sup>99m</sup>Tc-MDP as well as target SPECT-CT imaging using a double-headed SPECT-CT camera coupled with a 2-slice CT scanner.

**Results** The skeletal findings with previously uncertain character were classified as definitely

benign, indeterminate or definitely malignant. These included: 1) 33% benign degenerative lesions, 2) 28% single osseous metastases, 3) 10% direct bone infiltration, 4) 15% cold or osteolytic bone lesions, 5) 12% mixed type lesions and 6) 2% single extraosseous lesions.

**Conclusion** The most important clinical application of bone SPECT-CT imaging is for differential diagnosis between degenerative and metastatic foci with abnormal tracer uptake and similar scintigraphic appearance on the WBBS.

**Key words:** SPECT-CT, whole-body bone scan, bone metastases

### Introduction

Metastatic involvement is a common occurrence in patients with oncological diseases. Skeletal metastases are clinically important because of the associated symptoms and complications leading to bone pain and cancer-induced bone disease and their profound significance for staging, treatment and prognosis [1, 2]. The frequency with which metastases are detected varies considerably with the type of primary tumor and with the methodology utilized for detection [3, 4].

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Whole-body bone scintigraphy (WBBS) is the most sensitive method for the early detection of secondary skeletal lesions; it is positive with an infiltration of 5-15 % of the trabeculae. The specificity of this technique is however low due to the fact that increased mineral metabolism is observed in a number of benign diseases of degenerative, inflammatory or traumatic nature [5,6].

The combined application of baseline WBBS, followed by more specific techniques such as SPECT-CT fusion is an advanced approach for the diagnosis, differential diagnosis and staging of osseous metastases [7,8].

The purpose of this study was to assess the role of SPECT-CT images in diagnosis and differentiation diagnosis of suspected bone metastases in cancer patients.

## Patients and methods

The study included 89 patients (54 female, 35 male; aged 18-92 yrs) with different types of tumours including 35 patients with breast cancer, 22 with prostatic cancer, 11 with lung cancer, 10 with renal cancer, 4 with colorectal cancer, 4 with urinary bladder cancer and 3 with multiple myeloma.

In a small proportion of the cases, WBBS was routinely carried out as part of a postoperative protocol for active follow-up of cancer patients. The other patients were directed to the nuclear medicine department due to some subjective complaints (e.g. discomfort or pain in some parts of the skeleton) or because of abnormal laboratory indices such as increased levels of alkaline phosphatase or some tumour markers (CA 15-3, PSA, CA 19-9, etc).

All patients underwent routine WBBS with  $^{99m}\text{Tc}$ -MDP as well as targeted SPECT-CT imaging. The field-of-view of the SPECT-CT images correlated with scintigraphically

visualized bone foci with abnormal tracer uptake and uncertain or equivocal appearance, with an aim to differentiate metastatic from degenerative skeletal lesions. A double-headed SPECT camera with 2-slice CT scanner (Symbia T2, Siemens) was used. SPECT images were obtained at 128x128 matrix; 64 projections were acquired at 60 intervals with 20-sec per projection.

Low-dose CT scanning (130 kV; 30mA; 5-mm reconstruction) was performed in the helical mode. CT images were reconstructed with a standard reconstruction algorithm at 512x512 matrix, 35-40 cm field-of-view for image fusion and 50 cm field-of-view for attenuation correction.

## Results & Discussion

After a retrospective review of the WBBS and the SPECT-CT fused images, 141 bone lesions in 89 pts were analyzed (Table 1). The skeletal findings with previously uncertain character were classified as definitely benign, indeterminate or definitely malignant.

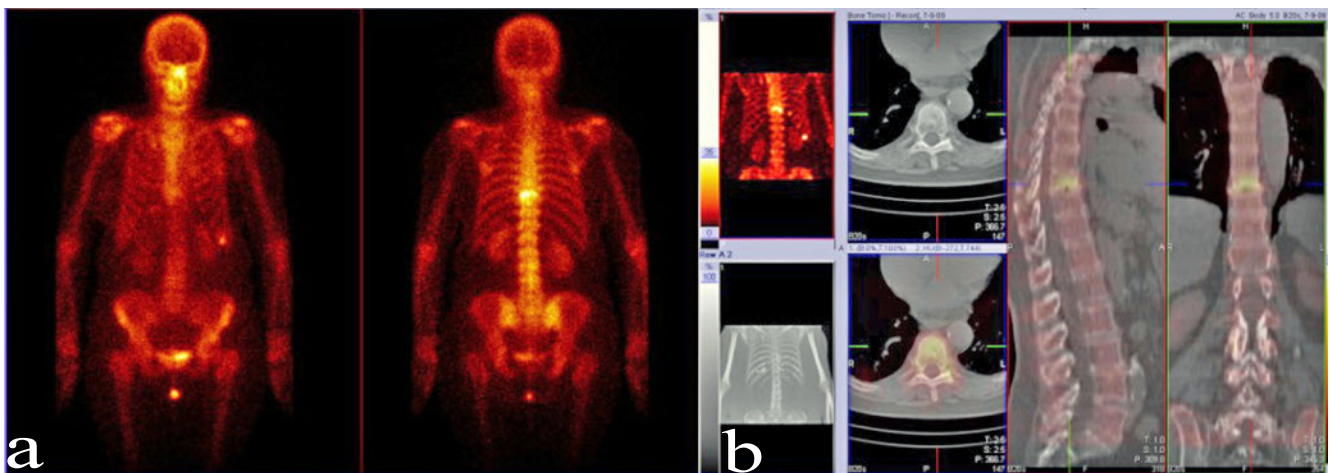
A total of 47 (33%) of all lesions in 36 patients could be correlated with benign degenerative findings on the SPECT-CT images. 5 (3%) lesions in 3 of these patients were indeterminate on the SPECT-CT images. They were localized to the articular parts and corpus of the thoracic vertebra and the ribs. After additional MR examination and 6-month follow-up these changes were considered degenerative.

Localized increased uptake of the radiotracer was visualized mostly in the thoracic and the lumbar vertebrae and in the thoracic costovertebral articulations, with CT characteristic consistent with osteophytes and the presence of spondyloarthritis and osteochondrosis (Figure 1).

In some patients the WBBS showed collapse of the lumbar vertebrae. Targeted CT scan made it possible to further clarify the nature of the uncertain scintigraphic findings and the anatomic details of the bony and cartilaginous

**Table 1** SPECT-CT location of 139 analyzed bone foci with abnormal/uncertain tracer uptake on the WBBS in 87 patients (2 with 2 extraosseous lesions)

Anatomic Region	Benign (n)	Malignant (n)
1. Cranium	1	5
2. Cervical spine	1	1
3. Thoracic spine	12	10
4. Lumbar spine	11	9
5. Rib	5	6
6. Sternum	3	7
7. Sternoclavicular joint	0	4
8. Clavicle	0	3
9. Pelvis	14	41
10. Femur	0	5
11. Shoulder	0	1



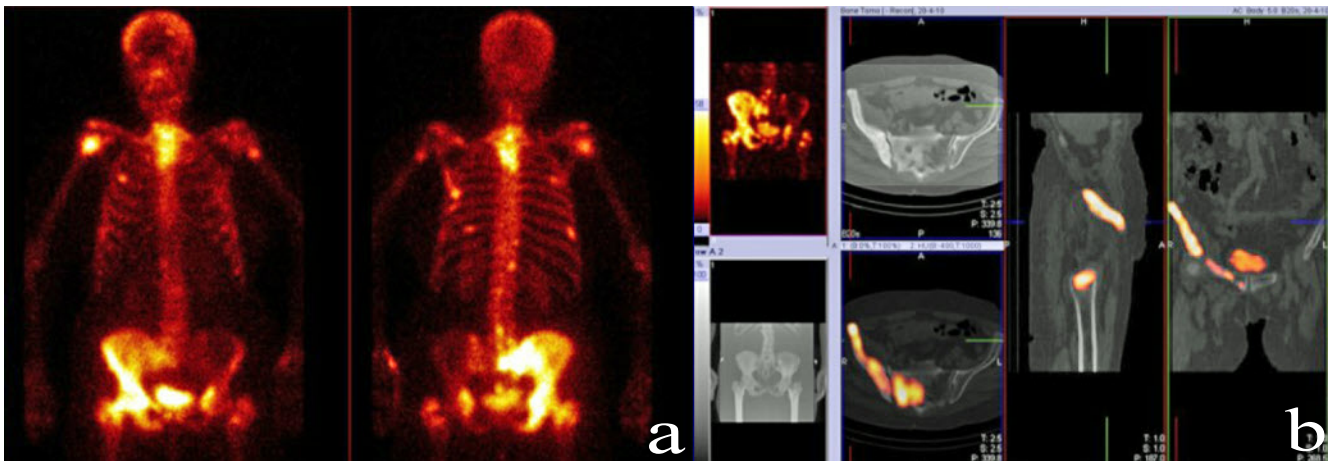
**Figure 1** A 68-year-old female with breast cancer after left mastectomy and combined therapy. Intensive tracer uptake was observed in the region of 9th and 10th thoracic vertebrae and the anterior side of the left 8th rib on the WBBS (a). Fusion SPECT-CT images showed degenerative changes due to osteochondrosis and trauma (b)

destruction. The observed changes were compression fractures due to advanced osteoporosis [2, 9]. These patients were those with prolonged hormone or chemotherapy.

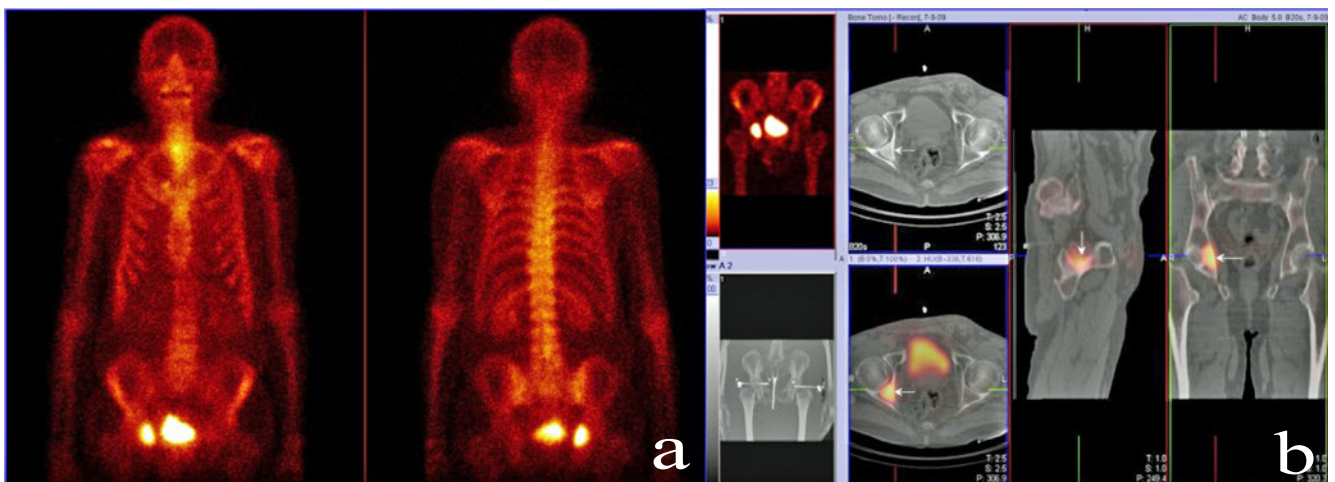
There were 14 benign lesions seen on the WBBS in the region of the pelvic joint and bone structures due to chronic inflammatory disease of the coxofemoral articulation, coxarthrosis and aseptic necrosis of the femoral head. In some patients with colorectal or endometrial cancer, intensive <sup>99m</sup>Tc-MDP accumulation was shown in one or both sacroiliac joints after post operative

radiotherapy because of sacroiliitis. The scintigraphic images of metastatic or degenerative pelvic bone and articular changes had very similar characteristics on the WBBSs. CT is valuable method for discriminating between benign and malignant pelvic osseous lesions [10, 11].

In some cases increased mineral metabolism was observed on the WBBS in the region of the ribs or the sternum after post-traumatic fractures or surgical intervention due to osteoblastic regeneration. Differential diagnosis



**Figure 2** A 72-year-old female with breast cancer after right mastectomy and combined therapy. Multiple "hot" spots suspicious for metastases were visualized in the regions of the pelvis, thoracic vertebrae, ribs, shoulders and calvarium on the WBBS (a). Fusion SPECT-CT images showed hyperplastic and asymmetrical degenerative osseous changes due to Paget's disease (b)



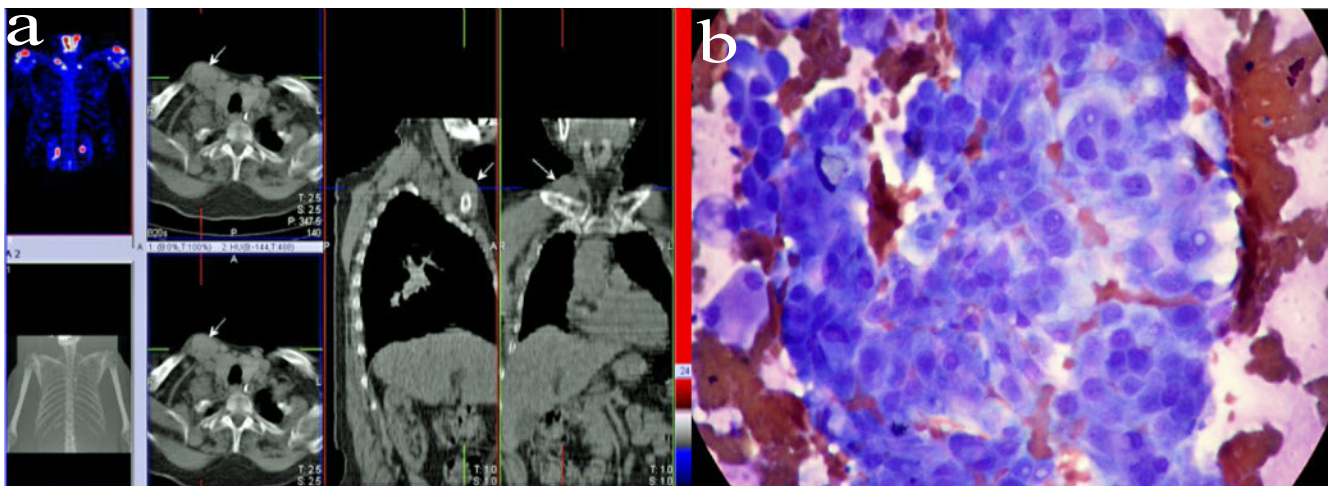
**Figure 3** A 68-year-old male with prostatic cancer. Single "hot" spot was observed in the region of the right coxofemoral joint on the WBBS (a). Fusion SPECT-CT images showed an osteosclerotic metastatic lesion in the right acetabulum (b)

with secondary lesions was made on the fused SPECT-CT images.

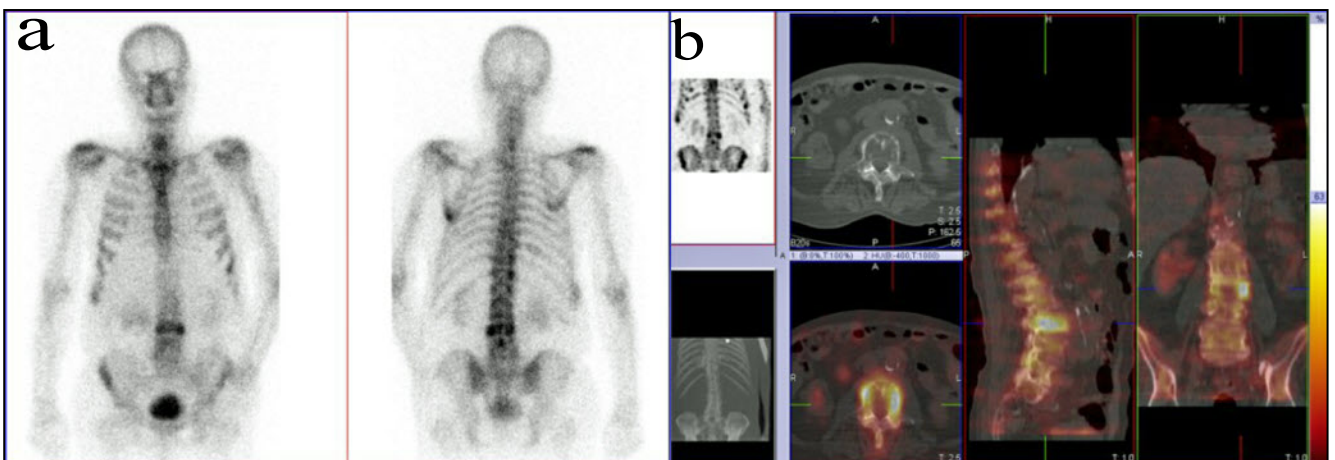
In one woman with breast cancer, multiple hot spots, suspected for bone metastases, were visualized on the WBBS. Fused SPECT-CT images showed hyperplastic degenerative lesions in the skeleton and asymmetrical pelvic bone structures due to Paget's disease (Figure 2).

A total of 41 (28.1%) single osseous metastatic hot spots (up to 3 foci considered as "single" as per staging classification of bone metastases) were scanned in 31 patients. They were localized mostly to the vertebrae, the flat bones of the pelvis (Figure 3) or the sternum, i.e. in those parts of the skeleton characterized with active myelopoiesis.

There were 13 (10%) lesions caused by direct infiltration of bone structures observed in 6



**Figure 4** A 70-year-old female with breast cancer after right mastectomy and combined therapy. A suspicious hot spot was seen in the right clavicle with increased uptake in the right sternoclavicular joint on the <sup>99m</sup>Tc-MDP WBBS. Fusion SPECT-CT showed soft-tissue metastatic mass infiltrating the right clavicle and the sternoclavicular joint (a). Biopsy was significant for tumoral cells from metastatic right supraclavicular lymph node (b)

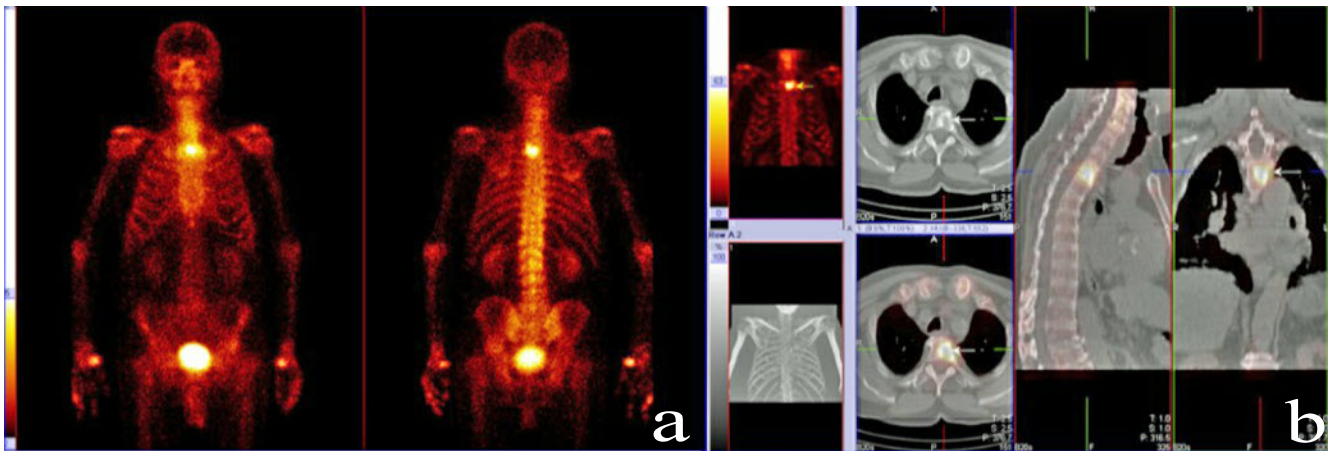


**Figure 5** A 74-year-old male with cancer prostate. Increased tracer uptake with non-specific appearance was observed in the region of L3 and the posterior side of the right 9th rib on the WBBS (a). Fusion SPECT-CT images showed osteolytic secondary lesions in these bone structures (b)

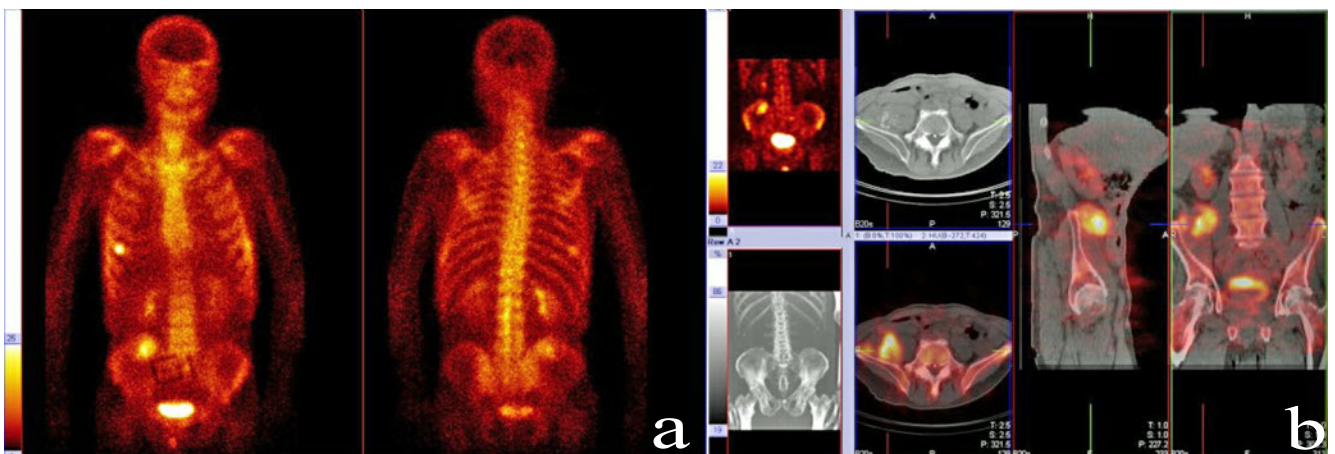
patients, as a result of proximity to the neoplastic recurrent or metastatic process localized in the surrounding soft-tissues, in contrast to the haematogeneous type of dissemination of tumour cells in the skeleton (Figure 4).

In 2 of these, one with renal cancer and the other with multiple myeloma, SPECT-CT was applied after a stabilizing operation

(laminectomy carried out due to pathological fracture of thoracic and lumbar vertebrae). Locally advanced metastatic disease with expansion of preexisting soft-tissue metastatic lesions to the infiltrated bones was found in 6 patients with breast cancer and multiple myeloma. These results determined correct radiotherapy planning or the volume of surgical intervention.



**Figure 6** An 80-year-old male with cancer prostate after hormonal and therapy with Zometa. Single "hot" spot in the region of the T3 observed on the WBBS (a). Fusion SPECT-CT images showed "mixed" osteolytic consolidated metastatic lesion with osteosclerotic periphery in the body of T3 (b)



**Figure 7** 75-year-old male with rectal cancer after surgery. "Hot" spot seen in the region of the right iliac bone on the WBBS (a). Fusion SPECT-CT showed recurrent soft-tissue formation with calcifications - calcifoid metastasis below the right kidney (b)

There were 21 (15%) "cold" osteolytic lesions with prevailing soft-tissue component observed in 16 patients with renal, lung, colorectal or urinary bladder cancer. They were not visualized clearly on the WBBS because of the absence of osteoblastic reaction associated low tracer uptake [11] (Figure 5). SPECT-CT was applicable for exact localization of abnormal "cold" lesions in the bones, their morphological type, size and extension, especially in cases with superposed activity from the urinary bladder

over the pelvic structures [12].

There were 17 (12%) "mixed-type" lesions (osteolytic and osteosclerotic) seen in 15 cases with breast and prostatic cancer after complex treatment [3, 11, 13]. In some of these patients bone metastases were visualized as lesions with "cold" (osteolytic) central part with "hot" (osteoblastic) peripheral accumulation of <sup>99m</sup>Tc-MDP due to consolidation after therapy, very well demonstrated on the CT component of the fusion images (Figure 6).

CT is a valuable method for characterizing destruction of the spongy bone lesions, their consolidation or calcium accumulation. This fact allows differentiation of the osteolytic metastases from the sclerotic and mixed ones. This is possible because of the good differentiating ability of CT [2, 7, 8]. It has a direct relationship to the therapeutic approach of tumour-induced bone disease by determining the necessity of prescribing diphosphonate medication or metabolic radiotherapy [3, 13].

There were 2 patients with 2 (1.9%) "single" extraosseous lesions including one with myositis ossificans in the region of the right femur and the other with a soft-tissue calcified metastasis in the right abdomen due to rectal cancer (Figure 7).

WBBS is technically easy-to-perform and a reliable imaging modality for examination of bone and joint structures with comparatively low radiation exposure of the body. In most patients bone scintigraphy makes it possible to document the presence of foci with increased mineral metabolism, and to determine their location and distribution. This is of particular importance for the timely diagnosis and staging of osseous metastases [10, 12]. SPECT-CT allows a significant increase in diagnostic accuracy, mainly because of the improvement in specificity determined by CT, by merit of its capability to differentiate as "definitely benign" or "definitely malignant" in more than 90% of the abnormal findings that had been classified as indeterminate on planar scans [6, 11, 14]. Hybrid SPECT-CT technique may also improve on WBBS sensitivity because it may be possible to detect "cold" or osteolytic lesions with soft-tissue component, which usually do not show tracer uptake on the bone scintigraphy [11, 15].

## Conclusion

The most important clinical application of bone SPECT-CT imaging is the differential diagnosis between degenerative and metastatic foci with abnormal tracer uptake and similar scintigraphic appearance on the WBBS.

Anatomical cross-sectional CT data enables differential diagnosis of most uncertain bone lesions, reducing false-positive and inconclusive studies and thus increasing specificity and sensitivity of bone scintigraphy, which is very important for future management of cancer patients. WBBS followed by SPECT-CT is a very effective diagnostic approach for the follow-up of patients with osseous metastatic lesions after complex therapy in order to assess the therapeutic response.

## References

1. Coleman R. Incidence and distribution of bone metastases. In: Metastatic bone disease. Diel I, Kaufmann M., Basrert G (Eds). Springer Verlag 1994: 20-21.
2. Braunstein EM, Kuhns LR. CT demonstration of spinal metastases. *Spine* 1983;8:912-915.
3. Sergieva S., Kirova G., Dudov A. Current diagnostic approaches in tumor-induced bone disease. *J BUON* 2007; 12:493-504.
4. Jonsson B., Petrn-Mallmin M., Anderson I et al. Pathological and radiographic findings in spinal breast cancer metastases. *Acta radiologica* 1991;23:219-223.
5. Utsunomiya D., Shiraishi S, Imuta M., Tomiguchi S., Kawanaka K., Morishita S., Awai K., Yamashita Y. Added value of SPECT-CT fusion in assessing suspected bone metastases. *Radiology* 2006;238(1):264-271.
6. 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. *J Nucl Med* 2006;47:1102-1106.
7. Israel O, Goldsmith S. Hybrid SPECT-CT imaging in clinical practice. 2006. Taylor & Francis Group.
8. Horger M., Bares R. The role of Single-Photon Emission Computed Tomography/ Computed Tomography in Benign and Malignant Bone Disease. *Semin Nucl Med* 2006; 36: 286-294.

9. Mariani G., Bruselli L., Kuwert T., Kim E.E., Flotats E., Israel O., Dondi M., Watanabe N. A review on clinical uses of SPECT-CT. *Eur J Nucl Med Mol Imaging* 2010; 37: 1959-1985.
10. Cuccurullo V, Cascini G, Rossi A, Tamburrini O, Rotondo A, Mansi L. Pathophysiological premises to radiotracers for bone metastases. *Q J Nucl Med Mol Imaging*. 2011 Aug;55(4):353-73.
11. Palmedo H1, Marx C, Ebert A, Kreft B, Ko Y, Türler A, Vorreuther R, Göhring U, Schild HH, Gerhardt T, Pöge U, Ezziddin S, Biersack HJ, Ahmadzadehfar H. Whole-body SPECT/CT for bone scintigraphy: diagnostic value and effect on patient management in oncological patients. *Eur J Nucl Med Mol Imaging*. 2014;41(1):59-67.
12. Cuccurullo V, Cascini GL, Tamburrini O, Rotondo A, Mansi L. Bone metastases radiopharmaceuticals: an overview. *Curr Radiopharm*. 2013 Mar;6(1):41-7.
13. Franca Dore, Luca Filippi, Matteo Biasotto, Silvia Chiandussi, Fabio Cavalli, Roberto Di Lenarda. Bone Scintigraphy and SPECT/CT of Bisphosphonate-Induced Osteonecrosis of the Jaw. *J Nucl Med* 2009; 50(1):30-35.
14. Michael H Carstensen, Mashael Al-Harbi, Jean-Luc Urbain, Tarik-Zine Belhocine SPECT/CT imaging of the lumbar spine in chronic low back pain: a case report Carstensen et al. *Chiropractic & Manual Therapies*. 2011;19:2-7.
15. Fanti S, Farsad M, Mansi L. Atlas of SPECT-CT. Springer Verlag Berlin 2011:108-118.