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The added value of positron emission tomography/computed tomography (PET/CT) in assessment of treatment response of secondary malignant osseous lesions: our experience

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Abstract

Background: Bone metastasis can be noted in the course of many primary malignant neoplastic lesions; breast and prostate cancers are the most frequent, but lung, kidney, and thyroid malignancies frequently metastasize to bones. Secondary osseous lymphomatous infiltrations is relatively uncommon and mainly noted in patients with non-Hodgkin lymphoma (NHL). By adding the metabolic changes to the conventional CT morphologic changes, combined positron emission tomography (PET) and computed tomography (CT) may offer clinically useful addition in assessment of treatment response of these lesions and offer helpful judgment for the different oncologic therapeutic regimens.

Results: The study included 45 patients, 24 females (53.33%) and 21 males (46.66%). Showing bone dominant or isolated bony secondary malignant infiltrations. The study included 24 patients with history of breast cancer (53.33%), 12 patients with history of lymphoma (26.66%), and 9 patients (20%) with history of lung cancer. All the bony lesions included in the study were multiple lesions in each patient, classified into mixed lytic and sclerotic bony lesions in 21 patients (46.66%), sclerotic lesions in 12 patients (26.66%), and radiologically occult lesions or osteopenic areas in 12 patients (26.66%). The most accurate SUV max cut-off value among studied cases was 4, taking the lesion with highest SUV max value as the reference standard, with measurements taken before and after the medical regimen with six months interval. Confirmation of PET/CT results was done by serial post management follow up at 6 months interval and 1 year interval.

Conclusion: PET/CT study is an effective tool for assessment of treatment response for ossoues secondary malignant lesions.

Keywords: Positron emission tomography, Computed tomography, Bone deposits treatment response, Secondary osseous neoplastic lesions

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Background

Secondary malignant bony lesions can occur in patients with advanced cancer and can cause signifiacnt morbidity and disability. Pain, mechanical disability, spinal cord compression, and pathological fractures could occur as a sequel to bone secondary malignancies [1]. Secondary bony lesions could be classified into lytic, sclerotic or radiologically occult, or mixed according to its morphology [2].

Evaluation of treatment response as early as possibe is mandatory to make the correct treatment decisions; accurate techniques are needed for monitoring the treatment response [3].

Although bone scintigraphy was the imaging modality of choice for decades for evaluation of bony secondary neoplastic lesions, yet it has limitations in its sensitivty and specificity and limitation in assessment of treatment response with poor anatomical details [4, 5]. Computed tomography (CT) assessment misses the early bone marrow lesions with negative CT morphological changes; CT also is limited in differntiating the active metastatic sclerotic bony lesions from the healed sclerotic ossoeus lesions with the same morphological pattern [6].

By adding the functional metabolic data to the morphological data obtained in the fused PET/CT images, advance in secondary osseous malignant lesions knowledge can be achieved including its detection, characterization, and assessment of teatment response [7].

Methods

This is a retrospective analysis of 45 patients with primary malignancies developed secondary osseous lesions.

The visual assessment method and semi-quantitative analysis were used with measuring the standard uptake value (SUV) max and the normal would be the normal blood pool liver SUV max.

Inclusion criteria

- Patients with primary malignant lesions with bone dominant or isolated bony metastatic disease
- Patients with history of non Hodgkin lymphoma developed secondary osseous infiltrations

Exclusion criteria

- Primary malignant ossoeus lesions
- Bone deposits due to primary prostate malignant lesion
- Pediatric population

Technique

A hybrid PET/CT scanner (Siemens Biograph 64 PET/CT scanner) was used in this study. Before the examination by 6 h, the patients were instructed to fast, except for water. Avoidance of (extreme) exercise for at least 6 h before the study was asked to minimize ^{18}FDG uptake in muscles and to reduce the false positive results. The allowable blood glucose level for the study was of < 150 mg/dL. Voiding of urine was done before injection, and then approximately 5 MBq/kg body weight of ^{18} FDG was injected. Further, 60–90 min later, the data were acquired [8]. The patients then were kept lying comfortably and were asked not to talk to avoid false positive uptake. A noncontrast-enhanced CT from mid-thigh to the skull was obtained 60 min after the tracer injection. Nuclear medicine consultant and radiology consultant interpreted the data at Siemens work station.

The lesion with the highest SUVmax was taken and studied befroe and after the treatment algorithm

Ethics approval and consent to participate

All the patients included in this study gave written informed consent to publish the data contained within this study. Approval for this study was obtained from the Research Ethics Committee of our medical institute. All study procedures were carried out in accordance with the Declaration of Helsinki regarding research involving human subjects.

Table 1 Distribution of the studied patients according to different parameters

	Number of the patients (*n*: 45)	Percentage
Sex		
Females	24	53.33%
Males	21	46.66%
Primary malignancy		
Breast	24	53.33%
Lymphoma	12	26.66%
Lung	9	20%
Location of the highest SUV max lesion		
Spine	18	40.04%
Sternum	6	13.33%
Iliac bones	15	33.33%
Shoulder girdle	3	6.65%
Proximal femur	3	6.65%
CT pattern of the lesions		
Sclerotic	12	26.66%
Mixed lytic and sclerotic	21	46.66%
Radiologically occult	12	26.66%
Response to systemic treatment		
Responders	36	80%
Non responders	9	20%

Results

The study included 45 patients, 24 females (53.33%) and 21 males (46.66%). Showing bone dominant secondary malignant infiltrations (Table 1).

The study included 24 patients with history of breast cancer (53.33%), 12 patients with history of lymphoma (26.66%), and 9 patients (20%) with history of lung cancer lung (Table 1); all with osseous dominant metastatic disease.

All the bony lesions included in the study were multiple lesions in each patient.

The lesions are classified according to the CT morphology into mixed lytic and sclerotic bony lesions in 21 patients (46.66%) (Fig. 1), radiologically occult lesions in 12 patients (26.66%) (Fig. 2), and sclerotic lesions in 12 patients (26.66%) (Fig. 3).

The most accurate SUV max cut-off value among studied cases was 4, taking the lesion with highest SUV max value as the reference standard, with measurements taken before and after the medical regimen with six months interval.

The lesions were classified according to the PET/CT results in to two groups: responder in 36 patients with appreciable decrease in the SUV max after treatment (80%) and non responders in 9 patients (20%) with notification of denovo osseous lesions (Table 1).

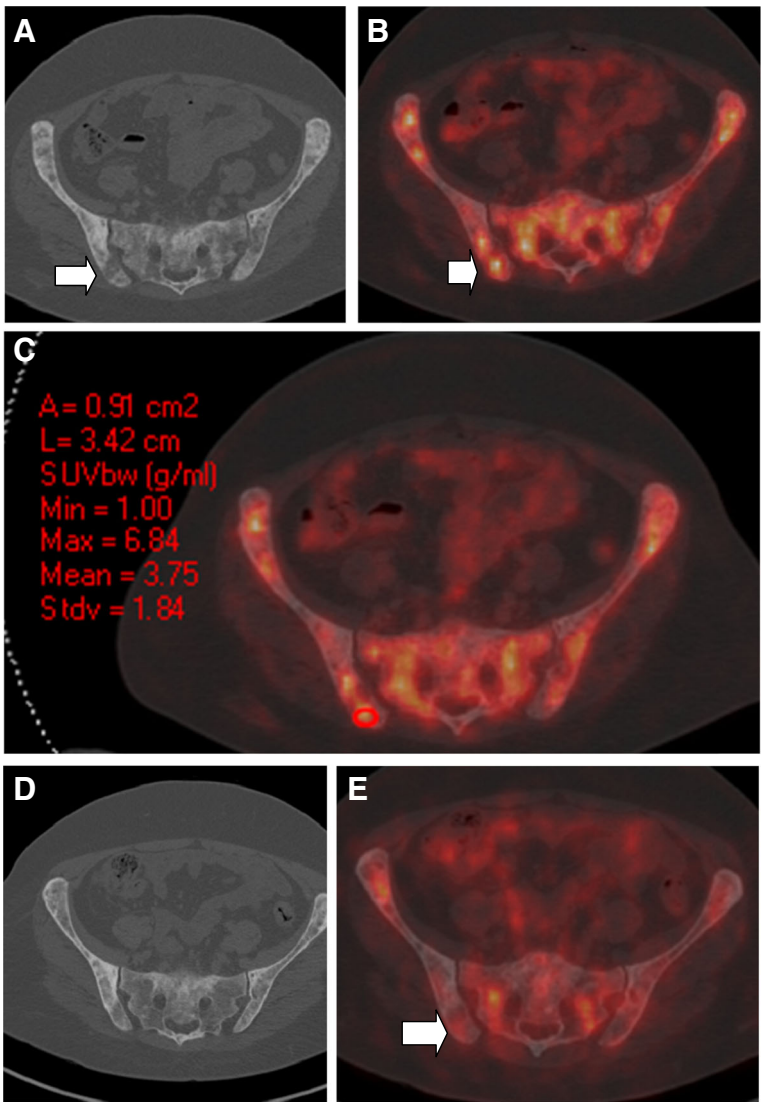

Fig. 1 Follow up post chemotherapy regimen for patient with cancer breast and isolated bony metastatic disease **a** axial CT bone window and **b, c** corresponding PET/CT fused image showing multiple iliac and sacral lesions, the lesion with highest SUV max value was the lytic lesion targeting the posterior asepct of the right iliac bone SUV max: 6.8 (arrow in **b**). **d** Axial CT pelvis and **e** corresponding PET/CT fused image 6 months following the chemotherapy; the lesion shows relative increase density in the CT image and signifnact decrease in FDG uptake (arrow); the SUV max value reaching 2 treatment responder

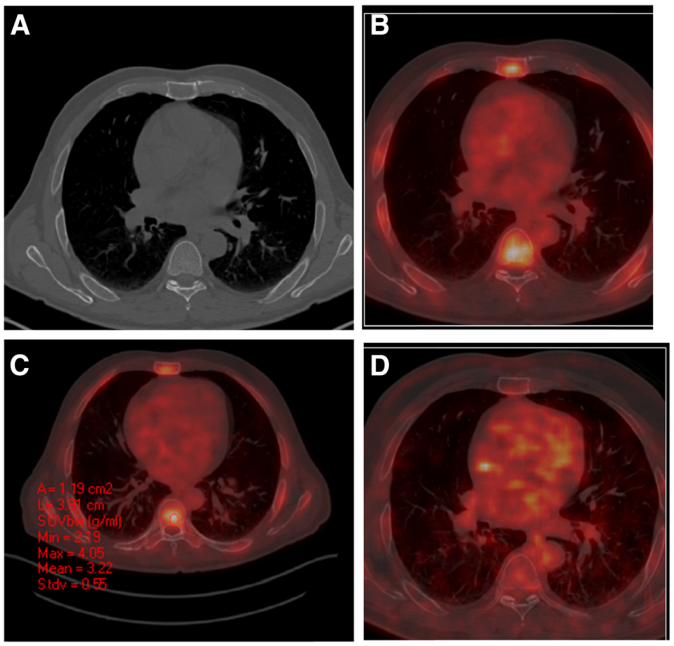

Fig. 2 A 56-year-old male patient with history of NHL. **a** Conventional CT study showing no gross lytic or sclerotic lesions noted within the sternum and DV5 body. **b, c** Corresponding PET/CT fused image shows focal FDG uptake in the sternum and DV5 vertebral body matching with radiologically occult bone marrow infiltration, SUV Max of the vertebral lesion: 4.05 **d** 7 months post treatment PET/CT fused image showing complete metabolic response with disappearance of the metabolically active bone marrow lesions by the visual assessment method

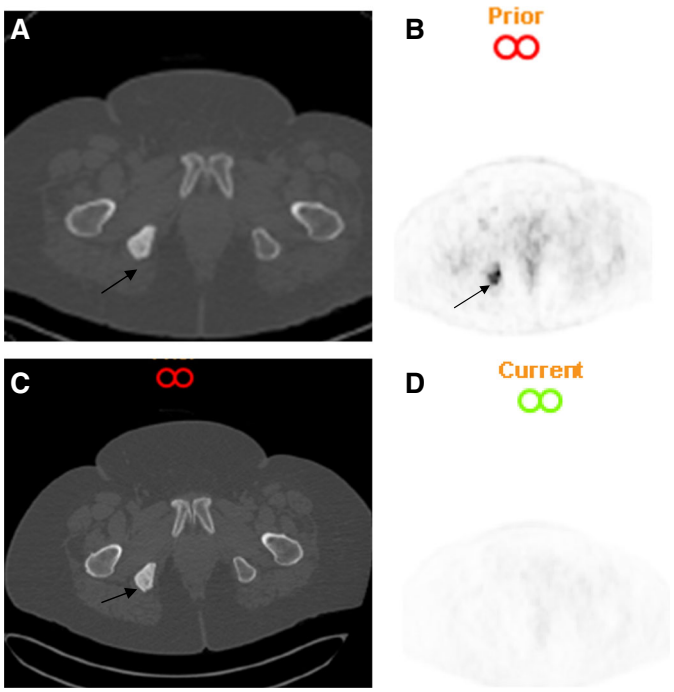

Fig. 3 Assessment of treatment response of patient with history of cancer breast and isolated bony metastatic disease with sclerotic metastatic lesions. **a** Axial CT bone window setting with sclertoic lesion noted in the rigth ischium (arrow). **b** Corresponding PET image showing avid uptake in the right ischium anatomical site. **c** Axial CT pelvis 6 months post treatment PET/CT study with sclerotic morhpolgy of the right ischium could represent sclerotic metastatic lesion or healed lesion. **d** Corresponding PET image shows no uptake within the lesion impressive of complete metabolic response

Confirmation of PET/CT results was done by serial post management follow up at 6 months interval (Fig. 4).

Discussion

A weakness point of conventional imaging techniques is its inability to early measure the effect of treatment upon the isolated or dominant bony secondary malignant lesions, an area where functional imaging may be of benefit for response assessment [9].

Our study suggested that ^{18} FDG uptake by the ossoeus lesions reflect the metabolic neoplastic activity of the lesions regardless of its CT morphological pattern either lytic or sclerotic or radiologically occult.

Generally, there is no universally accepted technique for assessment of treatmane response of bone deposits. A combination of imaging, laboratory, and clinical symptoms assessment (pain relief, movement limitations improvement) for response assessment are used. Bone scan was the imaging modality of choice for assessment of bone deposits for decades yet limited by the poor spatial resolution, as well as false positive results. Flare phenomenon occurs within 2 weeks to 3 months post treatment that describes the avid uptake of the tracer during the healing process of the metastatic lesion which could be falsely intepreted as progressive disease [9–11].

Whole-body diffusion magnetic resonance imaging (WB-DWI) is a well-established technique with multiple advantages: no exposure to ionizing radiatation, no injection of radioactive agents with its pre-injection and post injection precautions, even with no contrast material injection. In his study, Padhani et al. [12] concluded that it can make signifiacnt impact on therapy assessment. The disadvantages of the technique is relative limitations in assessment of mineralized lesions and sclerotic deposits [12].

In this study, ^{18}FDG was used in the PET/CT study; it is widely used radioactive agent yet with limitation in uptake in certain malignancies like cancer prostate. Cook G et al. [13] supported the use of other PET/CT agents for cancer prostate bone deposits assessment; Choline, labeled either with 11C-carbon or 18F-fluorine, has become a standard clinical tracer for staging high-

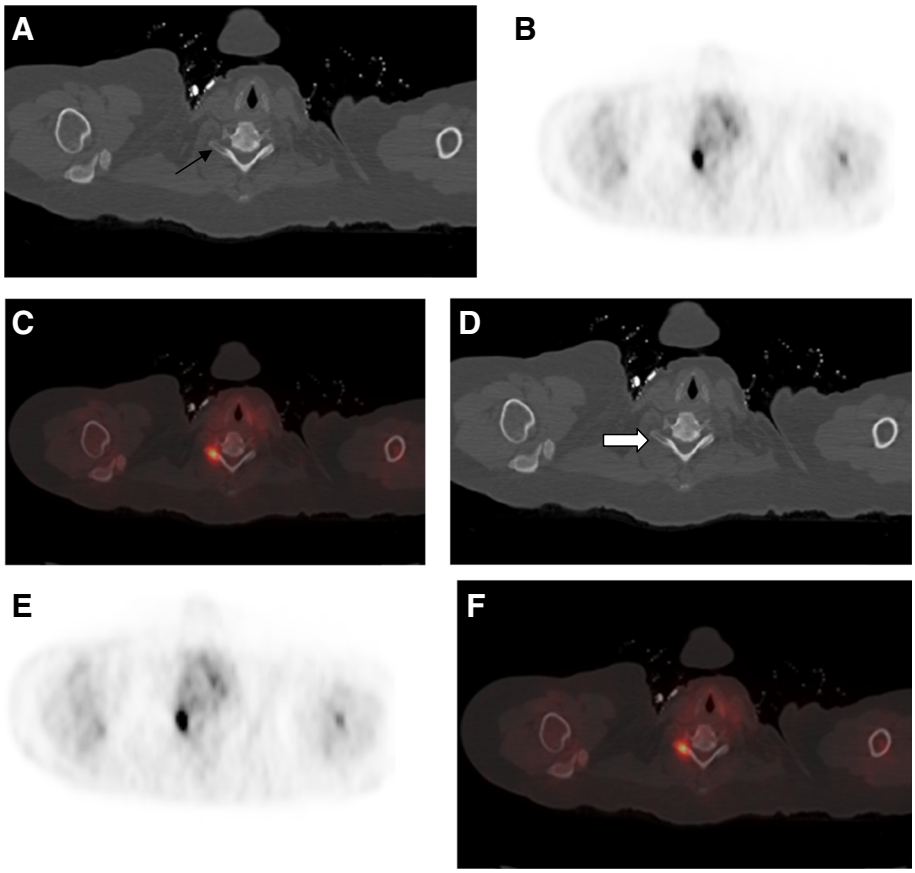

Fig. 4 Follow up post chemotherapy regimen for patient with history of breast cancer. **a** Axial CT bone window showing isolated lytic ossoeus lesion targeting CV7 right pedicle.**b** Correponding PET axial image. **c** Corresponding PET/CT fused image showing avid uptake within the lesion by visual assessment method, SUV max: 7. **d** Axial CT bone window 6 months post chemotherapy regimen. **e** Corresponding PET axial image and **f** fused PET/CT image showing no appreciable interval changes. Non responder

risk prostate cancer and patients with biochemical recurrence [13].

The SUV max cut-off value among studied cases was 4 , we used in this study the SUV max unit , Wahl et al. [14] used the SUL peak unit based on the lean body mass (total body weight minus the body fat weight), Cronin et al. [15] in the other hand depended mainy in his study upon the visual assessment with taking hepatic FDG uptake as the reference standard.

Considerations about cost-effectiveness have not been part of this study but will be necessary, as they will play an increasing role in the near future as the clinical utility of PET/CT will lead to a change in the diagnostic and management strategy of cancer patients [16–18].

Conclusion

PET/CT is essential for assessment of treatment response of lytic and sclerotic bony lesions and can directly improve or refine the oncologic management plan.Further studies designed for comparison between PET/CT and whole body diffusion MRI is advised.

Abbreviations

PET: Positron emission tomography; CT: Computerized tomography; SUV: Standardized uptake value; SUL: Standardized uptake value corrected to lean body mas; WB-DWI: Whole body diffusion-weighted magnetic resonance imaging

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None.

Authors' contributions

MA reported the cases. WO reported the cases and helped to draft the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

A written informed consent was obtained from all patients included in this study to publish this study data. Approval for this study was obtained from the Research Ethics Committee of our medical institute (IRB: 00012098) (FWA: 00018699). All study procedures were carried out in accordance with the Declaration of Helsinki regarding research involving human subjects.

Consent for publication

All the patients included in this study gave written informed consent to publish the data contained within this study.

Competing interests

There are no conflicts of interests. The authors declare that they have no competing interests.

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