Egyptian Journal of Radiology and Nuclear Medicine

RESEARCH Open Access

Diagnostic performance of PET/CT in primary malignant bone tumors

Ahmed Eid Fahim Abdella[1], Khaled Ismail Elshafey[2], Mohammed Fouad Sherif[2] and Hanan Ahmad Nagy[2*]

Abstract

Background: Nowadays, PET/CT plays a substantial role in the diagnosis of different types of tumor by its ability to provide combined functional and anatomic imaging in the same session. The purpose of this study is to evaluate the added value of PET/CT in staging and re-staging of primary malignant bone tumors.

Results: Out of the studied 40 patients, 7 patients were referred for primary staging of different types of histologically proven primary malignant bone tumors, their FDG-PET/CT studies yielded additional diagnostic information in 28.6% of them. Thirty three patients were referred either for assessment of treatment response or for follow-up to detect any viable lesions; FDG-PET/CT was more sensitive and specific than CT in follow-up and assessment of treatment response with PET/CT sensitivity 94.4%, specificity 86.7%, and total accuracy 90.9% and CT sensitivity 88.2%, specificity 81.2%, and total accuracy 84.8%.

Conclusions: PET/CT was an accurate imaging modality in evaluation of primary malignant bone tumors regarding tumor staging, assessment of therapeutic response and detection of metastatic disease as compared to CT.

Keywords: Positron emission tomography/computed tomography (PET-CT), Malignant bone tumors, FDG, Primary satging, SUVmax

Background

Primary malignant bone tumors are fairly rare. The most common primary malignant bone tumors are osteosarcoma, chondrosarcoma, and Ewing's sarcoma. Staging of the disease is necessary for determination of the treatment plan as well as follow-up of the lesion and its response to therapy. This depends on complete imaging and histo-pathological confirmation of the suspected entity [1, 2].

Diagnostic imaging has a master role in evaluation and management of bone cancers. Standard imaging modalities as conventional radiography, computed tomography (CT) scanning, magnetic resonance imaging (MRI) and skeletal scintigraphy cannot reach the accurate staging of the tumor as they depend mainly on morphologic diagnostic criteria and cannot differentiate between post-treatment changes and recurrence or residual tumor due to distortion of the regional anatomy by surgery and/or radiation [3, 4].

Also, positron emission tomography (PET) is limited in this field as it depends only on functional imaging through localization of metabolic activity using various radiopharmaceutical agents with lack of anatomical localization [5].

The introduction of the hybrid 18F-fluorodeoxy-D-glucose positron emission tomography-computed tomography (18F-FDG PET/CT) technique has advanced the knowledge of the pathophysiology of cancers that significantly impacts the evaluation, staging and management of different tumors and thus providing more efficacious treatment, better quality of life, and increased survival [6].

Also, its unique advantages, as high sensitivity and an extremely long scan range provide an opportunity for wider clinical application, including low administered

*Correspondence: hanan.nagy84@hotmail.com
[2] Faculty of Medicine, Tanta University, El-geish Street, Tanta, Gharbya Governorate, Egypt
Full list of author information is available at the end of the article

activity, total-body dynamic scanning, and long acquisition delay [7].

The CT component of this imaging provides important morphologic information which is added to the functional information given by PET scans in the same session [8].

Viable malignant primary bone tumors are usually 18F-fluorodeoxyglucose (FDG) avid. Accumulation of FDG may reflect tumor characteristics based on its metabolic activity providing better characterization of indeterminate lesions and guidance of targeted biopsy of the most metabolically active area within larger tumors especially tumors of mixed grade and/or cell type [9, 10].

FDG-PET is used also for more accurate staging of histologically confirmed tumors, assessment of treatment response to detect disease course and find out any recurrent lesions. It also provides a non-invasive method in estimating tumors grade depending on the amount of FDG uptake; this is an important prognostic factor in most bone tumors and a reliable independent prognostic indicator [11, 12].

The aim of this work is to assess the role of positron emission tomography-computed tomography (PET/CT) in primary malignant bone tumors including the primary staging, assessment of treatment response and detection of residual or recurrent disease.

Methods

Study population

Forty patients (22 males and 18 females) with histologically confirmed diagnosis of primary malignant bone tumor were included in this prospective study. The age of the selected patients ranged from 9 to 67 years with a mean of 35.17 years. They were referred to PET/CT unit in Radio-diagnosis department over a period from March 2020 to March 2021.

Approval of Research Ethics Committee (REC) and informed consent were obtained from all participants in this study after explanation of the benefits and risks of the procedure. Privacy and confidentiality of all patients' data were guaranteed. All data provision were monitored and used for scientific purpose only.

The included criteria were all patients with histologically proven primary bone tumor. No age or gender predilection.

Exclusion criteria were pregnant females, patients with hyperglycemia (blood glucose level ≥ 200 mg/dl), serum creatinine level > 2 mg/dl, recent tumor surgery less than 1 month, radiotherapy within less than 8 weeks, chemotherapy within less than 2 months, or organ failure or active infection, and claustrophobic patients.

All the included patients were subjected to the following

Data collection

- Full medical history, including personal history, history of the current illness; onset, course, and duration of the tumor at time of presentation, biopsy results, received treatment; radiotherapy or chemotherapy or surgical interference, past history of prior bone malignancy and previous imaging. The patients were given the optimum appointment for PET/CT scanning according to these data; one week post-biopsy, 4 weeks post-surgery, 2 to 4 weeks post-chemotherapy, and 1 to 3 months post-radiation.
- Recent creatinine level and history of potential allergies to contrast material.

Patient preparation

All patients were instructed to follow the standard dietary protocol for oncological FDG PET/CT study, and to avoid any kind of strenuous activity 24 h prior to the examination and after injection of the radioisotope to avoid physiologic muscle uptake of FDG.

In case of diabetic patients; they should not have regular insulin administered subcutaneously within 4 h of having FDG administered.

Blood glucose level was checked prior to 18F-FDG injection at PET/CT unit; Target blood sugar was 150 mg/dl.

Dosage administration

A dose of 8 -12 mCi (370 MBq; approximate dose to patient, 3–5 MBq/Kg) 18F-FDG was injected 60 min before examination. Patients stayed comfortable, and relaxed with limited movements to minimize physiologic uptake of FDG into skeletal muscle.

No oral contrast agent was used for the PET-CT examinations.

Image acquisition and reconstruction

PET/CT imaging was performed using a dedicated PET/CT scanner (Biograph, Seimens, Germany) with a 64-detector multislice CT scanner with Time-of-Flight technology.

It was performed from the skull base to the level of mid-thigh (Torso imaging) approximately 1hour after an intravenous injection of FDG. The whole study took approximately 20–35 min.

Patient position

The patients were positioned supine on the PET/CT scanner table with their arms kept overhead, they were informed to remain motionless during the total scanning time to obtain complete scan acquisition. They were reminded to avoid motion between CT and PET components of the study to give accurate co-registration of the CT and PET and avoid substantial attenuation correction artifacts.

CT technique

All the patients in this study were injected with IV contrast material (non-ionic iodinated contrast; Ultravist 300, 80–120 ml) using an automatic injector (Medrad, Germany) with injection rate 3 mL/sec. The CT scan was performed after the bolus delay time (typically 60–65 s) in a cranio-caudal direction with 130 kV, 200–250 mAs, 5-mm slice thickness, field of view 500–600 mm, and voxel size $0.98 \times 0.98 \times 5\text{mm}^3$.

An initial scout image was taken to position the table for the desired axial coverage. The CT continuous scan acquisition was performed during breath-hold and lasted approximately 10–20 s depending on the axial coverage.

PET technique

After CT acquisition, PET scan was performed over the same axial coverage using a series of fixed table positions (approximately 10 to 15 bed positions, 2–5 min per bed position, overlap between each bed position is approximately 50%) with a preferable flat breath to reduce the effect of respiratory motion of the lungs.

PET/CT fusion

CT data were used for attenuation correction of PET emission images. The PET images were reconstructed with and without attenuation correction. The helical CT scans were reconstructed into 512×512 images with a slice thickness to match those of the PET scans (5 mm) to form the fused PET/CT images.

Precautions after PET/CT scan

The patients were advised to avoid close contact with surrounding personnel, especially for children and pregnant women up to 24 h.

Images interpretation

Axial CT images, PET images, fused PET/CT images, and reconstructions of PET, CT, and PET/CT into sagittal and coronal planes as well as the PET maximum intensity projection (MIP) rotating image display were reviewed on a picture archiving and communication system workstation and were interpreted by two radiologists with 9 and 8 years of PET/CT experience, blinded to the clinical data, and final decisions reached by consensus were reported.

Visual assessment and the standardized uptake value (SUVmax.) were used for interpretation of the whole body PET/CT scans to detect metabolically active lesions indicative of the primary tumor, locoregional lymph nodes, loco-regional tumor recurrence or residue, and distant metastases.

The standard reference was the biopsy/histopathological results, and comparison with other imaging modalities performed during follow-up up to 6 months. Histopathological correlation was performed in 3 patients, follow-up by radiological imaging were used in 31 patients, and follow-up PET/CT studies were available in 6 patients. Also, reviewing previous radiological examinations was done in most of the studied patients to correlate recorded lesions.

Statistical analysis

- The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 20 for Windows® (IBM SPSS Inc, Chicago, IL, USA).
- Quantitative data were expressed as mean ± SD (Standard deviation) and range. Qualitative data were represented as frequencies and relative percentages. Pearson Chi square test (χ^2) was used to calculate difference between qualitative variables as indicated.
- The diagnostic ability of quantitative variable in prediction of categorical outcome was calculated.
- Probability: P-value < 0.05 was considered significant.

Results

This current prospective study included 40 patients; 22 of them were males (55%) and 18 of them were females (45%) with their ages ranged from 9 to 67 years with a mean of 35.17 ± 16.76. The majority of patients were at the age group from 10 to 20 years; 11 patients representing 27.5%.

The entire studied patients had primary malignant bone tumor proved by biopsy which revealed osteosarcoma in 12 patients (30% of the patients), chondrosarcoma in 11 patients, Ewing sarcoma in 9 patients, fibrosarcoma in 6 patients and angiosarcoma in 2 patients.

The primary sites of the primary malignant bone tumors in the studied patients were variable, femur was the most affected site as detected in 10 patients (25%), followed by ribs in 7 patients, iliac bone in 5 patients,

tibia in 5 patients, fibula in 4 patients, humerus in 4 patients, scapula in 2 patients, mandible in 1 patient, foot in 1 patient, and wrist in 1 patient.

According to the indication of PET/CT in the current study, the patients were classified into two major groups; pre-treatment group which included 7 patients (17.5%) who had PET/CT studies for a pre-treatment TNM staging of known primary malignant bone tumor as proven by biopsy (Fig. 1).

The other group in this study was the post-treatment group, it included the remaining 33 patients (82.5%). Nineteen of them (47.5% of patients) had PET/CT studies for assessment of treatment response and detection of either local residual lesions or distant metastatic lesions (Figs. 2, 3, 4), and 14 patients (35%) had PET/CT studies performed as routine follow-up to detect any recurrent lesions or after developing positive clinical findings suspicious for local recurrent tumor.

According to the 7 patients who had done PET/CT for primary staging of the tumor, biopsy proved rib chondrosarcoma in 2 patients, iliac chonrosarcoma in 1 patient, humeral Ewing sarcoma in 1 patient, mandibular fibrosarcoma in 1 patient, rib Ewing sarcoma in 1 patient and humeral chondrosarcoma in 1 patient. The results of primary staging in the present study are shown in (Table 1).

Compared with morphological CT findings, the total TNM staging changed in 2 patients (28.6%) whose PET/CT showed downstaging based on metabolic activity. It revealed a metabolically inactive right deep cervical lymph node in a patient with right mandibular fibrosarcoma, and metabolically inactive inguinal lymph nodes in the other patient with right iliac chondrosaroma, these lymph nodes were detected previously by CT and misdiagnosed as malignant lymph nodes.

The post treatment group included 33 patients. Twenty eight patients (84.8% of them) underwent previous surgical excision of the tumors; 15 patients didn't receive post-surgical medical treatment and 13 patients received this treatment after surgery. Five patients (15.2% of them) had received either chemotherapy or radiotherapy without surgery; 2 patients received just chemotherapy and 3 patients received combined chemo-radiotherapy.

Post treatment PET/CT studies for assessment of treatment response in 19 patients were performed between 4 and 13 weeks after completing definitive chemo-radiotherapy according to the protocol of work. We considered post-treatment 18F-FDG PET/CT performed later

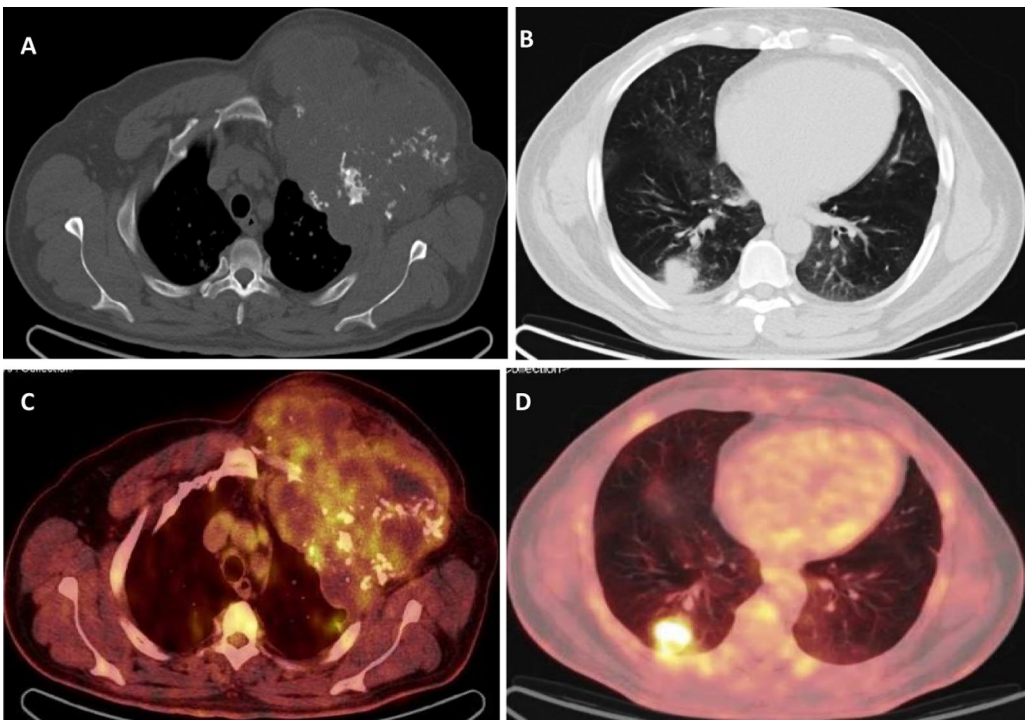

Fig. 1 A 48 years old male patient with biopsy-proven left ribs chondrosarcoma. He was referred for primary staging of the tumor. **A**, **B** Axial CT images and **C**, **D** Axial fused PET/CT images show metabolically active FDG avid large left anterior chest wall heterogenous lesion with dense matrix calcifications and areas of breaking down with SUVmax ~ 10.4, and pulmonary nodule at right lower lung lobe with SUVmax ~ 12. According to AJCC TNM staging system, the case was staged as T2 N0 M1a (group staging IVA)

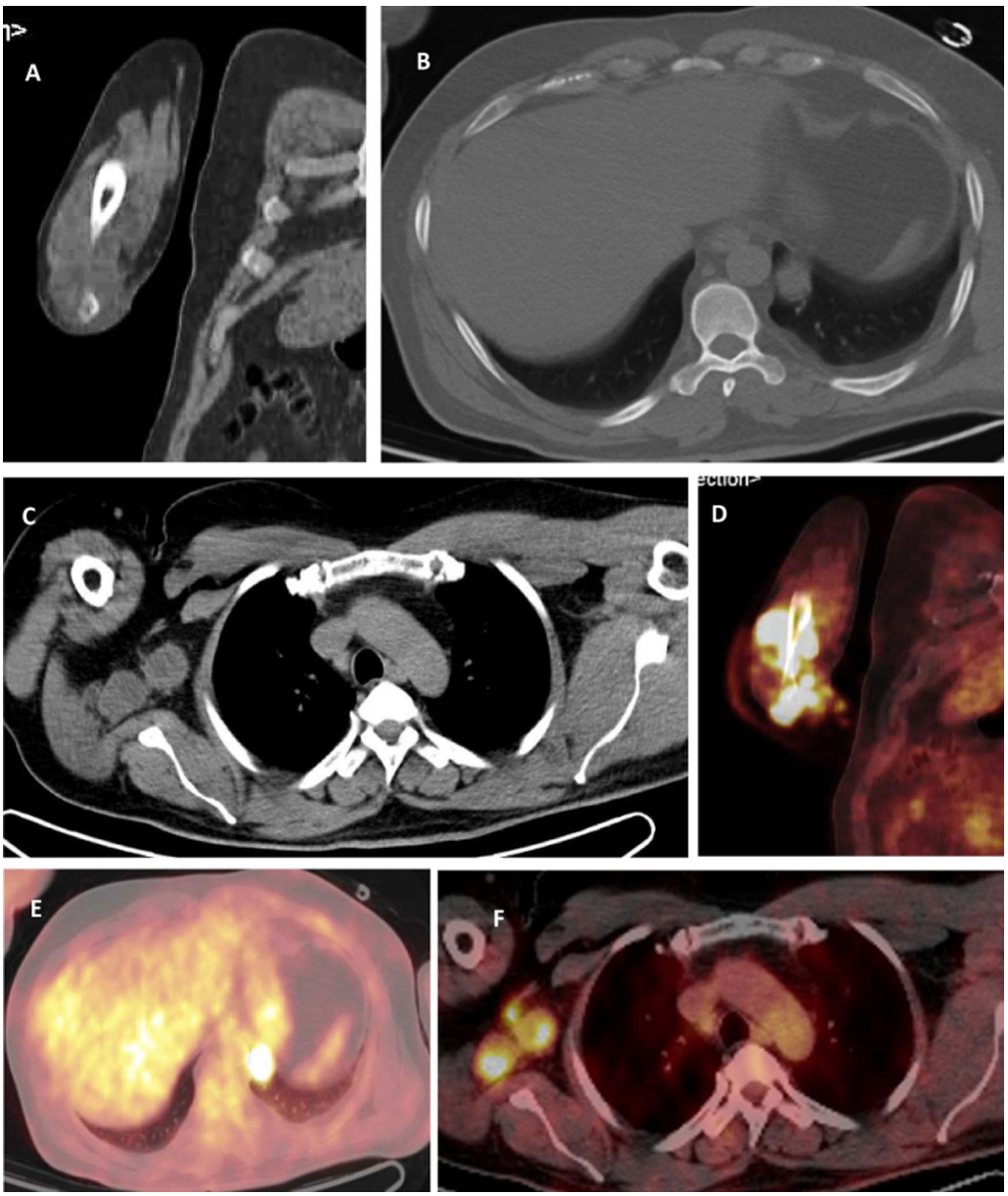

Fig. 2 A 38 years old male patient with biopsy-proven right distal humerus chondrosarcoma. Tumoral excision was done, and the patient was referred for post-operative assessment of any residual tumors. **A**, **B**, **C** Axial CT images and **D**, **E**, **F** Axial fused PET/CT images show extensive FDG uptake at right elbow at the operative bed infiltrating the surrounding muscles with SUVmax ~ 18.2 associated with multiple right axillary and mediastinal retrocaval lymphadenopathy with corresponding increased FDG uptake (SUVmax ~ 12.9 and 3.5 respectively) as well as metabolically active left lung basal deposit with SUVmax ~ 16.3 denoting local tumoral residue/recurrence, locoregional lymph nodes and distant metastases. Twenty months later, the patient was referred again after total right upper limb amputation for follow-up and detecting any viable tumors. **G** Coronal CT, and **H** Coronal fused PET/CT images show significant progression in size, number and metabolic activity of the pulmonary nodular deposits and mediastinal lymphadenopathy with SUVmax reaching up to 18.2 and 9.1 respectively

than 3 months from the completion of therapy as follow-up rather than post-therapy assessment.

Regarding to the final outcome of the reviewed 33 PET/CT studies depending on the criteria accepted as standard reference including histopathological results, follow-up by radiological imaging over 6 months, or available follow-up PET/CT studies in 6 patients, or comparison with previous radiological examination, CT defined 18 positive studies (54.5%) and 15 negative studies (45.5%); there were 15 true positive, 3 false

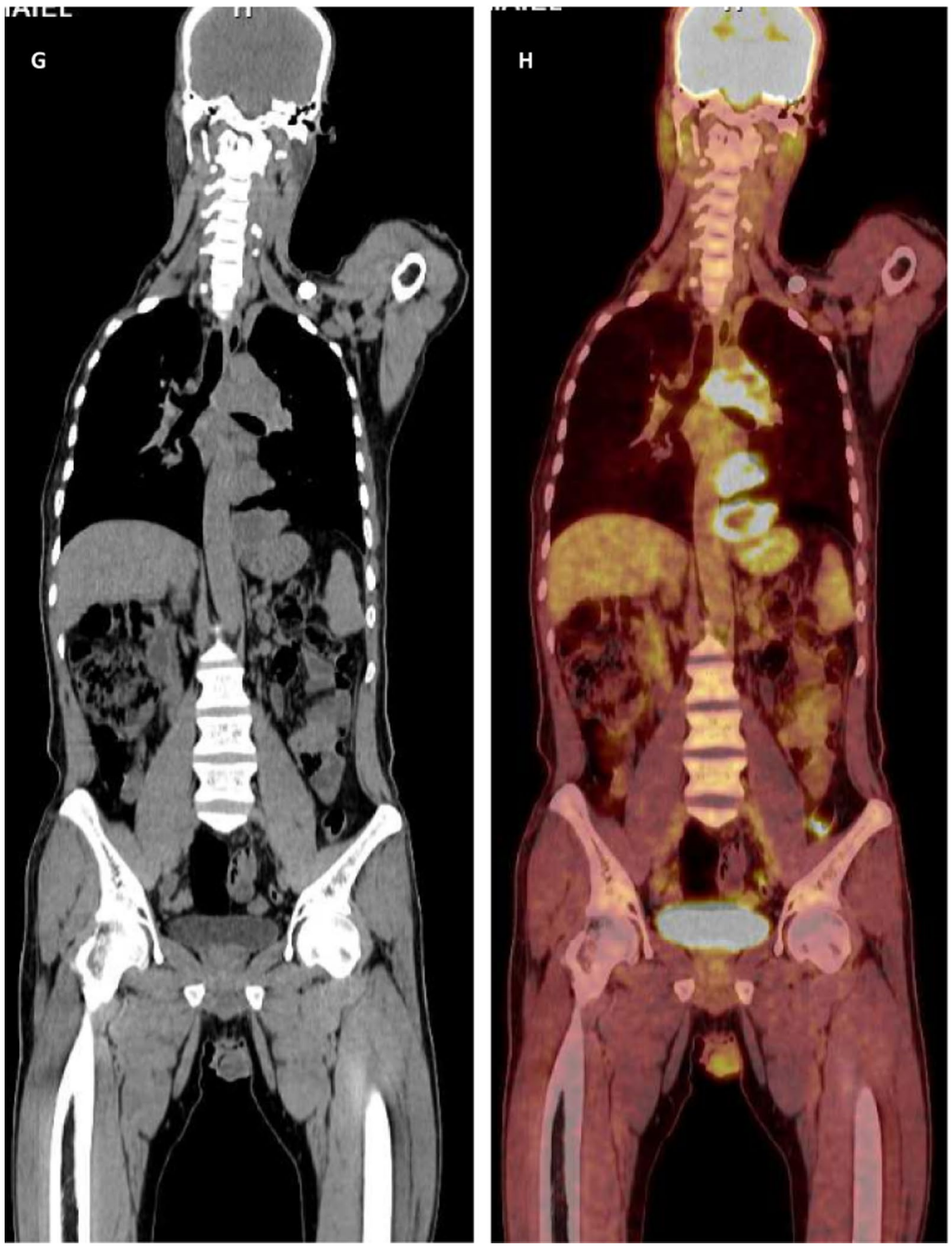

Fig. 2 continued

(See figure on next page.)

Fig. 3 A 67 years old male patient with biopsy-proven right distal femoral osteosarcoma. He was referred after an above-knee amputation for post-operative assessment of any residual tumors. **A** MIP image show multiple areas of increased FDG uptake at the operative bed and other sites all over the surveyed body denoting local recurrence with distant metastatic lesions. **B**, **C**, **D** Axial CT, and **E**, **F**, **G** Axial fused PET/CT images show multiple metabolically active FDG avid osseous deposits with SUVmax ~ up to 19.2 with no corresponding significant CT structural changes

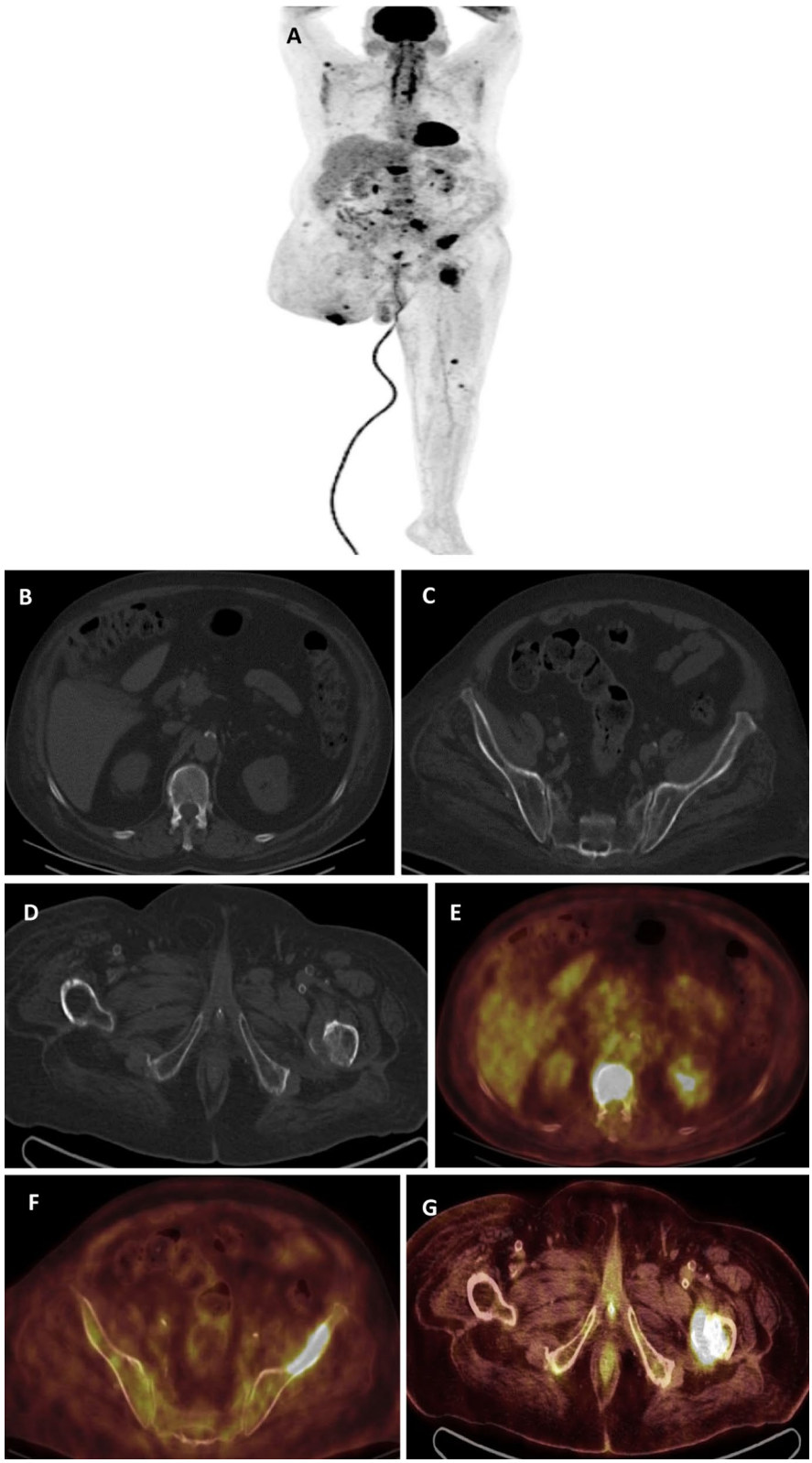

Fig. 3 (See legend on previous page.)

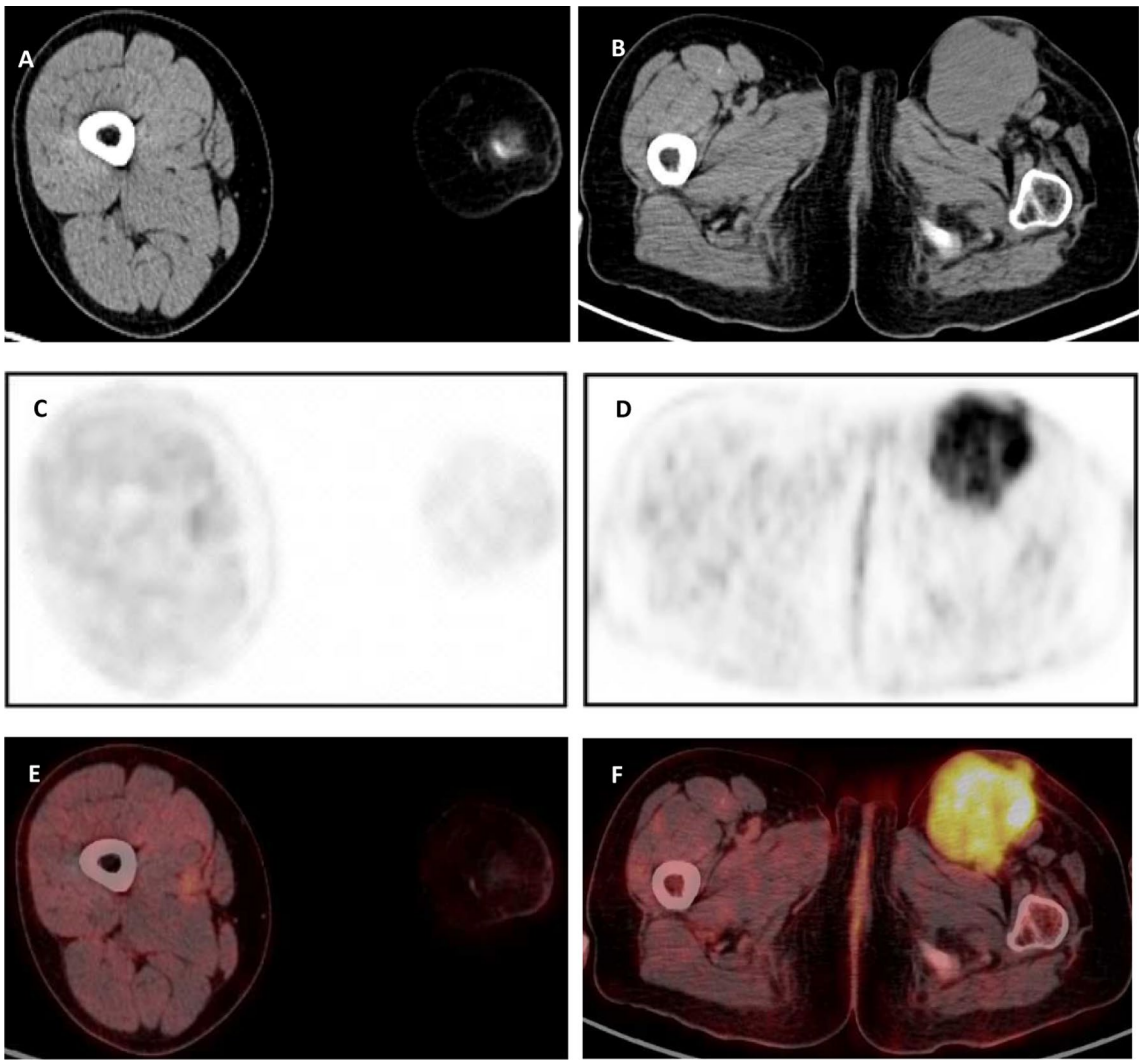

Fig. 4 A 33 years old female patient with biopsy-proven left tibial Ewing sarcoma. She underwent an above-knee amputation and received chemo and radiotherapy that ended 1 year ago. The patient was referred for follow-up and detecting any viable tumors. **A**, **B** Axial CT, **C**, **D** Axial PET, and **E**, **F** Axial fused PET/CT images show no metabolically active local recurrent tumor at the operative bed, but a metabolically active FDG avid left femoral large lymph node is seen with SUVmax ~ 6.48

positive, 13 true negative, and 2 false negative studies (Table 2). On the other hand, PET/CT defined 19 positive studies (57.6%) and 14 negative studies (42.4%); there were 17 true positive, 2 false positive, 13 true negative, and 1 false negative studies. The Pearson Chi-Square value was 22.06 and the *P* value was < 0.001 denoting strong agreement between the PET/CT findings and the standard of references (Table 3).

The diagnostic accuracy of the CT and PET/CT for the study-based statistical analysis is shown in (Table 4).

One false positive study was that of a patient with left scapular chondrosarcoma. PET/CT study was performed 3 months after left upper limb amputation and left scapulectomy and revealed FDG avidity at the operative bed with associated cystic lesion having active margin with SUVmax ~ 4.1, this lesion was thought to be residual/recurrent tumor. However, it was confirmed by CT scan that it is post-operative sequel. Follow-up PET/CT study of the same patient revealed resolution of this lesion.

The other false positive study was that of a patient with right femur osteosarcoma. PET/CT study was performed 4 months after surgical removal of the tumor

Table 1 Results of primary staging in the studied 7 patients with primary malignant bone tumors

Type of tumor	PET/CT findings	TNM staging	Group staging
Left rib chondrosarcoma	Metabolically active left chest wall mass > 8 cm (SUVmax ~ 10.4) with pulmonary metastases and hilar LNs metastases (SUVmax ~ 12 and 7.2 respectively)	T2 N1 M1	IVB
Right rib chondrosarcoma	Metabolically active right 6th rib expansile lesion (SUVmax ~ 5.6)	T1N0 M0	IA
Right distal humerus chondrosarcoma	Metabolically active distal humerus mass > 8 cm (SUVmax ~ 12.2) with axillary LNs, mediastinal LNs and lung metastases (SUVmax ~ up to 4.9, 6.4, and 2.7 respectively)	T2 N1 M1a	IVB
Right iliac chondrosarcoma	Metabolically active tumor confined to right iliac bone > 8 cm with extraosseous soft tissue component (SUVmax ~ 11.8)	T2 N0 M0	IIB
Right mandible fibrosarcoma	Metabolically active tumor confined to right mandible < 8 cm (SUVmax ~ 6.8)	T1 N0 M0	IA
Right humerus Ewing sarcoma	Metabolically active mottled osseous texture of right humeral head and neck > 8 cm (SUVmax ~ 7.3) with lung metastases (SUVmax ~ up to 3)	T2N0M1a	IVA
Left iliac chondrosarcoma	Metabolically-active left iliac lesion > 8 cm (SUVmax ~ 8.3) with multiple lytic bone metastases and lung metastases (SUVmax ~ up to 12.4 and 6.8 respectively)	T2N0M1b	IVB

Table 2 Comparison between the results of the CT findings and those of a reference standard in the post-treatment group

Cases	A reference standard results				χ^2	*P*-value
CT results	− ve		+ ve			
	No	%	No	%		
− ve	True − ve		False − ve		16.07	< 0.001*
	13	39.4	2	6.1		
+ ve	False + ve		True + ve			
	3	9	15	45.5		

χ^2, chi-square test; *P*-value, probability

*Significant *P* value (< 0.05)

Table 3 Comparison between the results of the 33 PET/CT studies and those of a reference standard in the post-treatment group

Cases	A reference standard results				χ^2	*P*-value
PET/CT results	− ve		+ ve			
	No	%	No	%		
-ve	True − ve		False − ve		22.06	< 0.01*
	13	39.4	1	3		
+ ve	False + ve		True + ve			
	2	6.1	17	51.5		

χ^2, chi-square test; *P*-value, probability

*Significant *P* value (< 0.05)

and revealed metabolically active FDG avid right inguinal lymph nodes with SUVmax ~ 3.9, however, these lymph nodes had benign looking on localization CT. Three months later, follow-up CT scan revealed nearly total resolution of the lymph nodes with no treatment.

The false negative study was that of a patient with right tibial angiosarcoma. PET/CT study was performed 1 month after right lower limb amputation and revealed low grade FDG avidity at the amputation stump with SUVmax ~ 2.4, it was considered post-operative changes. Two months later, follow-up PET/CT study revealed evident soft tissue lesion at the operative bed with increased FDG avidity (SUVmax ~ 4.6) denoting tumor recurrence.

Regarding to the final outcome of the 33 PET/CT studies depending on the standard reference, residual/recurrent disease was found in 17 patients (true positive

Table 4 Diagnostic accuracy of PET/CT versus CT in the studied 33 patients with primary malignant bone tumors in the post-treatment group dependent on statistical analysis

Statistical analysis	PET/CT (%)	CT (%)
Sensitivity	94.4	88.2
Specificity	86.7	81.2
PPV	89.5	83.3
NPV	92.8	86.6
Accuracy	90.9	84.8

cases) varying from locoregional tumor residual/recurrent lesions in 5 patients, locoregional lymph nodes in 2 patients and distant metastatic lesions in 13 patients.

The distant metastatic lesions in 13 patients were variable according to the site of metastases; pulmonary (8 patients), osseous (4 patients), nodal (3 patients), and muscular deposits (1 patient) and all lesions were confirmed by imaging.

According to the detected metastatic osseous lesions in the post-treatment group, all the lesions were FDG avid with an average SUVmax. 10.59 ± 5.31 (ranged from 3.9 to 19.2). The lesions were lytic in nature on CT images in 3 patients. In only 1 patient with right distal femoral osteosarcoma, follow up PET/CT study revealed recurrent tumor at the operative bed in addition to FDG avid metastatic osseous lesions with no CT structural bony changes (Fig. 3) denoting PET/CT superiority to CT in detecting early bony lesions before appearance of anatomical changes.

Among the detected metastatic pulmonary lesions, there were many pulmonary nodules with no FDG avidity on PET/CT study especially those with size less than 1 cm.

Discussion

Primary malignant bone tumors have an elevated rate of glycolysis and, consequently, a high uptake of ^{18}F-FDG in malignant cells. Yet, FDG uptake alone is not adequate for characterization of primary bone tumors. Also, CT modality relies on morphological criteria as size and contrast enhancement pattern that does not accurately reflect the presence of active malignant conditions. The hybrid imaging modality PET/CT allows assessing molecular as well as morphologic information at the same time. So, PET/CT represents an efficient tool for whole-body staging and re-staging within one imaging modality [13, 14].

After random selection of the 40 patients in this study, they were categorized according to the indication of PET/CT study into pre-treatment group (7 patients) for primary staging of the tumor and post-treatment group (33 patients) either for detection of recurrent tumor in 14 patients or assessment of treatment response in 19 patients.

El-Galaly et al. [15] considered that the advantages of PET/CT in the diagnosis of different stages of bone tumors were accurate localization of the lesion, detection of the smaller lesion, and differentiating the benign, malignant and different stages of the tumor.

In the pre-treatment group in our study, PET/CT had an effective role in changing the total TNM staging in 2 patients (28.6%) with sarcomas; CT scan defined lymph nodes that were considered malignant while PET/CT revealed no corresponding FDG avidity; PET/CT provides a non-invasive method for well-characterization of the lesions that help in systemic therapeutic decision-making [16].

In a study performed by Tateishi et al. [17] on 50 patients with histologically proven bone sarcomas, nodal metastasis was correctly assessed in 48 patients (96%) with PET/CT, in contrast to 46 patients (92%) with CT. By adding information from conventional imaging to the PET/CT findings in another study by Tateishi et al. [18], they could achieve accurate staging in 60 of 69 patients (87%), upstaging in (12%) and downstaging in (1%) of sarcoma patients.

In this study, PET/CT studies were performed in 33 patients after treatment, either radiation, chemotherapy, combined chemo-radiotherapy or surgery, to exclude the presence of any viable tumor; recurrent/or residual lesions, locoregional lymphadenopathy and distant metastatic lesions and also to assess the treatment response. Twenty eight patients (84.8% of them) underwent previous surgical excision of the tumors as the first choice of treatment of malignant bone tumors is surgical whether it is followed by medical treatment or not [19].

FDG-PET-CT is highly useful for monitoring response to therapeutic interventions. It can identify response to therapy earlier than any other imaging modality improving patient management by allowing termination of ineffective and toxic therapies. It allowed better evaluation of anatomic regions that have been previously treated by surgery or radiation in which the differentiation between post-treatment scar and recurrent tumor may be a big challenge [20].

We reported higher sensitivity of PET/CT compared to CT in detection of local tumor recurrence/residue, it has higher ability to differentiate between post-surgical tissue changes and early local recurrences, and also it was not affected by metallic artifacts which degraded the CT quality of image.

This study demonstrated PET/CT sensitivity of 94.4% and specificity of 86.7% with accuracy of 90.9% compared to CT sensitivity of 88.2% and specificity of 81.2% with accuracy of 84.8%. These results were comparable to those of Liu et al. [19] in their meta-analytical study of twenty six studies in the effectiveness of PET/CT in recurrence and metastases formation observations of osteosarcoma that reported PET/CT sensitivity of 91%, specificity of 90%, and accuracy of 94%.

Our results matched also with those of Schulte et al. [21] who studied 44 patients with malignant bone tumors showing PET/CT sensitivity of 93%, specificity of 76.7%, and accuracy of 81.7% in detecting recurrent disease and re-staging patients with primary bone tumors.

One of the false positive results in the present study was in the form of post-operative changes that was misdiagnosed as recurrent tumor, but resolved on follow-up. Kumar et al. [22] realized that post-surgical inflammatory oedema, scarring and granulation tissue can cause increased FDG uptake making the interpretation of PET/CT studies very difficult. Also, even if PET/CT is obtained after 12 weeks following completion of chemoradiation, false-positive findings may still occur and are caused by post- chemo-radiation, inflammation, oedema, hyperaemia, fibrosis and loss of tissue planes and the presence of post-treatment inflammatory tissue can cause increased FDG uptake which may be misdiagnosed as residual tumor [23].

In one case in our study, multiple bone deposits have been developed in the form of FDG avidity with no corresponding anatomical changes on localization CT. In their study on the efficiency of PET/CT in evaluation of skeletal deposits, Wafaie et al. [24] detected a considerably large number of missed (false negative) lesions on CT images due to absence of any detectable structural abnormalities with a high metabolic activity of such lesions on fused PET/CT images. This is attributed to the ability of PET to detect bone marrow based metastases early and in the absence of morphologic changes on CT images; thus improving CT sensitivity.

Also, a lesion based analysis was performed in detailed retrograde matter for a total of 386 detected osseous lesions in a study performed by Ali and Abd Elkhalek [25] that showed higher sensitivity of PET/CT study than CT study alone (100% and 93.9% respectively) in detection of osseous metastases due to the presence of active osseous deposits without structural abnormalities, that were falsely interpreted as negative by CT.

In patients with bone sarcoma, the lungs are at highest risk for distant metastases. Franzius et al. [26] stated that PET alone is not sufficient for detection of small lung metastases likely due to respiratory movements during the PET acquisition. Other causes are that FDG-negative lung metastases can be small in size and have decreased FDG avidity.

According to the detected metastatic pulmonary nodules in this study, multiple nodules especially smaller than 1 cm were beyond PET resolution and had no corresponding FDG uptake and thus the PET-only scans were inferior to diagnostic CT for detecting lung lesions. So, the PET/CT protocol should include a diagnostic lung CT in bone tumors patients [27].

London et al. [28] compared PET/CT with conventional imaging (CT, MRI, ultrasound, and bone scan) in a study that included 314 lesions on 86 scans, they reported that PET/CT had a higher sensitivity (98% vs 83%) and specificity (97% vs 78%) than did conventional imaging for detecting distant metastases, with the exception of pulmonary nodules; regarding pulmonary nodules, PET/CT was found to have a higher specificity (96% vs 87%) but lower sensitivity (80% vs 93%) than did conventional imaging.

In those who underwent medical treatment in the present study, PET was able to detect regression in FDG avidity and decreased SUV in one patient with left iliac Ewing sarcoma which showed no CT morphological changes. Rashad et al. [29] in their study which performed FDG PET in 18 pediatric sarcoma patients prior to and after neoadjuvant chemotherapy that an overall tumor SUV and SUVmax. on post-treatment 18F-FDG PET/CT scans were more accurate for the assessment of treatment response than changes in tumor size.

This is considered one of the powerful advantages of FDG PET/CT; it can determine therapeutic response through early identification of bad responders [30]. This gives the chance to modify or extend preoperative chemotherapy while overcoming any delay related to surgery or histopathologic analysis of the resected specimen.

The main limitation in this study was the relative small number of included subjects that might cause some missed diagnosis and misdiagnosis not giving full idea about the diagnostic efficacy of PET/CT. Also, statistical tests could not be able to identify significant relationships within various data set, as the relationship between PET/CT findings and different types of primary malignant bone tumors.

Conclusions

Combined PET/CT facilitated localization of bone tumors, bone tumors metastases and differentiation between benign and malignant lesions depending on provided combined metabolic and morphologic data and thus it was important in diagnosis, primary staging and restaging of primary malignant bone tumors.

We recommend close or long time follow-up of the disease by PET/CT with histologic correlation to all lesions to get more benefit from SUVmax. in evaluation of tumoral lesions, loco-regional lymph nodes or distant metastatic lesions.

Abbreviations
18F: Fluorine-18; CT: Computed tomography; FDG: Fluorodeoxyglucose; MIP: Maximum intensity projection; PET: Positron emission tomography; SUVmax: Maximum standardized uptake value.

Acknowledgements
To all the participants for their cooperation and patience.

Authors' contributions
KI suggested the research idea and ensured the original figures and data in the work, minimized the obstacles to the team of work, correlated the study concept and design and had the major role in analysis, AE collected data in all stages of manuscript, performed data analysis. HA supervised the study with significant contribution to design the methodology, manuscript revision and preparation. MF correlated the clinical data of patient and matched it with the findings, drafted and revised the work. All authors read and approved the final manuscript for submission.

Funding
No funding. Not applicable for this section.

Availability of data and materials
The author's confirm that all data supporting the finding of the study are available within the article and the raw data ad data supporting the findings were generated and available at the corresponding author on request.

Declarations

Ethics approval and consent to participate
Informed written consents taken from the patients, the study was approved by ethical committee of Tanta university hospital, faculty of medicine. Committee's reference number: 33664/1/20.

Consent for publication
All patients included in this research gave written informed consent to publish the data contained within this study. In case of patients less than 16-year-old, written informed consent for the publication of this data was given by their parents.

Competing interests
The authors declare that they have no competing of interests.

Author details
[1]Nasser Institute for Research and Treatment, El-geish Street, Tanta, Gharbya Governorate, Egypt. [2]Faculty of Medicine, Tanta University, El-geish Street, Tanta, Gharbya Governorate, Egypt.

Received: 2 July 2021 Accepted: 20 September 2021
Published online: 27 September 2021

References

1. Kumar N, Gupta B (2016) Global incidence of primary malignant bone tumors. Curr Orthop Pract 27(5):530–534
2. Kindblom LG (2009) Bone tumors: epidemiology, classification, pathology. In: Davies AM, Sundaram M, James SJ (eds) Imaging of bone tumors and tumor-like lesions: techniques and applications, vol 1. Springer, Berlin, pp 1–15. https://doi.org/10.1007/978-3-540-77984-1
3. Biermann JS, Chow W, Reed DR et al (2017) NCCN guidelines insights: bone cancer, version 2.2017. J Natl Comp Cancer Netw 15(2):155–167. https://doi.org/10.6004/jnccn.2017.0017
4. Mittra E, Iagaru A (2010) 18F-FDG-PET and PET/CT for evaluating primary bone tumors. Pet Clin 5(3):327–339. https://doi.org/10.1016/j.cpet.2010.04.004
5. Behzadi AH, Raza SI, Carrino JA et al (2018) Applications of PET/CT and PET/MR imaging in primary bone malignancies. PET Clin 13(4):623–634. https://doi.org/10.1016/j.cpet.2018.05.012
6. Choi YY, Kim JY, Yang SO (2014) PET/CT in benign and malignant musculoskeletal tumors and tumor-like conditions. Semin Musculoskelet Radiol 18(2):133–148. https://doi.org/10.1055/s-0034-1371016
7. Tan H, Yusen Gu, Haojun Yu et al (2020) Review. Total-body PET/CT: current applications and future perspectives. Am J Roentgenol 215:325–337. https://doi.org/10.2214/AJR.19.22705
8. Tian R, Su M, Tian Y et al (2009) Dual-time point PET/CT with F-18 FDG for the differentiation of malignant and benign bone lesions. Skeletal Radiol 38(5):451–458. https://doi.org/10.1007/s00256-008-0643-0
9. Lakkaraju A, Patel CN, Bradley KM et al (2010) PET/CT in primary musculoskeletal tumours: a step forward. Eur Radiol 20(12):2959–2972. https://doi.org/10.1007/s00330-010-1862-z
10. Hirata K, Tamaki N (2021) Quantitative FDG PET assessment for oncology therapy. Cancers (Basel) 13(4):869. https://doi.org/10.3390/cancers13040869
11. Hillner BE, Siegel BE, Liu D et al (2008) Impact of positron emission tomography/computed tomography and positron emission tomography (PET) alone on expected management of patients with cancer: initial results from the National Oncologic PET Registry. J Clin Oncol Off J Am Soc Clin Oncol 26(13):2155–2161. https://doi.org/10.1200/JCO.2007.14.5631
12. Lim HJ, Johnny Ong CA, Tan JWS et al (2019) Utility of positron emission tomography/computed tomography (PET/CT) imaging in the evaluation of sarcomas: a systematic review. Crit Rev Oncol Hematol 143:1–13. https://doi.org/10.1016/j.critrevonc.2019.07.002
13. Vercher-Conejero JL, Cenzano GC (2016) 18F-FDG positron emission tomography in oncology: main indications. Radiologia 58(4):303–319. https://doi.org/10.1016/j.rx.2016.03.007
14. Becker J, Schwarzenböck SM, Krause BJ (2020) FDG PET hybrid imaging. Recent Results Cancer Res 216:625–667. https://doi.org/10.1007/978-3-030-42618-7_19
15. El-Galaly TC, Gormsen LC, Hutchings M (2018) PET/CT for staging; past, present, and future. Semin Nucl Med 48:4–16. https://doi.org/10.1053/j.semnuclmed.2017.09.001
16. Von Eisenhart-Rothe R, Toepfer A, Salzman M et al (2011) Primary malignant bone tumors. Orthopade 40(12):1121–1142. https://doi.org/10.1007/s00132-011-1866-7
17. Tateishi U, Hosono A, Makimoto A et al (2007) Accuracy of 18F fluorodeoxyglucose positron emission tomography/computed tomography in staging of pediatric sarcomas. J Pediatr Hematol Oncol 29(9):608–612. https://doi.org/10.1097/MPH.0b013e318142b5ab
18. Tateishi U, Yamaguchi U, Seki K et al (2007) Bone and soft-tissue sarcoma: preoperative staging with fluorine 18 fluorodeoxyglucose PET/CT and conventional imaging. Radiology 245:839–847. https://doi.org/10.1148/radiol.2453061538
19. Liu F, Zhang Q, Zhou D et al (2019) Effectiveness of (18)F-FDG PET/CT in the diagnosis and staging of osteosarcoma: a meta-analysis of 26 studies. BMC Cancer 19(1):323. https://doi.org/10.1186/s12885-019-5488-5
20. El-Qassas NFA, Maarouf RA, Salama AMM (2021) 18F-FDG PET/CT for monitoring of treatment response in breast cancer. Med J Cairo Univ 89:473–479. https://doi.org/10.21608/mjcu.2021.167785
21. Schulte M, Cross B, Heymer B et al (2000) Grading of tumors and tumor-like lesions of bone: evaluation by FDG PET. J Nucl Med 41(10):1695–1701
22. Kumar V, Abbas AK, Aster JC (2017) Inflammation and repair. In: Kumar V, Abbas AK, Aster JC (eds) Robbins basic pathology, 10th edn. Elsevier Saunders, Philadelphia, pp 29–74
23. Schöder H (2013) Head and neck cancer. In: Strauss HW, Mariani G, Volterrani D, Larson SM (eds) Nuclear oncology: pathophysiology and clinical applications, vol 10. Springer, New York, pp 269–295
24. Wafaie A, Kassem H, Kotb M et al (2014) Evaluation of the efficiency of FDG PET/CT in detection and characterization of skeletal metastases.

Egypt J Radiol Nucl Med 45:181–190. https://doi.org/10.1016/j.ejrnm.2013.11.007
25. Ali AS, Abd Elkhalek YI (2016) Added value of combined 18F-FDG PET/CT fordetection of osseous metastases in cancer patients. Egypt J Radiol Nucl Med 47:453–458. https://doi.org/10.1016/j.ejrnm.2016.03.006
26. Franzius C, Daldrup-Link HE, Sciuk J et al (2001) FDG-PET for detection of pulmonary metastases from malignant primary bone tumors: comparison with spiral CT. Ann Oncol 12(4):479–486. https://doi.org/10.1023/a:1011111322376
27. Strobel K, Fischer DR, Stumpe KDM et al (2012) Imaging primary musculoskeletal tumors: role of 18F-FDG-PET/CT. Imaging Med 2(1):87–98. https://doi.org/10.2217/IIM.09.28
28. London K, Stege C, Cross S et al (2012) 18 F-FDG PET/CT compared to conventional imaging modalities in pediatric primary bone tumors. Pediatr Radiol 42(4):418–430. https://doi.org/10.1007/s00247-011-2278-x
29. Rashad AM, Abougabal AM, Fadel SH et al (2019) Value of 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) in assessment of response to preoperative chemotherapy in pediatric sarcoma. Egypt J Radiol Nucl Med 50:24. https://doi.org/10.1186/s43055-019-0025-8
30. Abdoli M, Dierckx RAJO, Zaidi H (2012) Metal artifact reduction strategies for improved attenuation correction in hybrid PET/CT imaging. Med Phys 39(6):3343–3360. https://doi.org/10.1118/1.4709599

Publisher's Note