

Role of 18FDG-PET/CT in evaluation of breast cancer metastasis

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Abstract:

Background: Worldwide breast cancer is the most frequently diagnosed malignancy among women and it is the most common leading cause of cancer death. The main applications of FDG-PET/CT in breast cancer are detection of malignancy, re-staging, detection of metastatic disease and for monitoring treatment response. **Objective:** This prospective study aimed to evaluate the role of (¹⁸FDG- PET/CT) in breast cancer metastasis. **Patients and methods:** Fifty female patients with breast cancer were included in this study. **Results:** PET/CT showed high sensitivity and specificity to detect breast cancer metastasis involving loco-regional metastasis (nodal) and distant metastasis. Bone is the most frequent site of distant metastasis in breast cancer patients. **Conclusion:** PET/CT can detect metastatic spread in breast cancer and monitor therapy response.

Keywords: [18] fluorodeoxyglucose-positron emission tomography /computed tomography (¹⁸FDG - PET/CT); breast cancer; distant metastasis.

Introduction:

Worldwide breast cancer is the most frequently diagnosed malignancy among women and it is the most common leading cause of cancer death with progressive increased incidence over the last few decades [1].

Many risk factors are well-known; however, the exact causes of breast cancer have not been identified. Family history of breast cancer, also genetic mutations are considered to convey a very strong risk factors of developing the disease [2].

Early detection of breast cancer is considered to be an essential milestone in the control of breast cancer. Early diagnosis is crucial in determining the choice of therapy, as well as a patient's prognosis and chances for survival [3].

PET/CT is a new imaging modality in oncology it has re-defined as the gold standard for oncologic imaging compared with other imaging modalities to demonstrate proper extent of the disease and metastatic spread within a single non-invasive investigation [4].

Integrated positron emission tomography (PET) and computed tomography (CT) performed with fluorine 18 (^{18}F) fluorodeoxyglucose (FDG) is one of the functional imaging modalities used to visualize glucose metabolism in living human tissues. Given its high sensitivity in detection of malignancy, FDG PET/CT is increasingly being used in evaluation of oncology patients [5].

PET/CT collect between the CT anatomical information and PET functional information leading to increase the ability in different types of clinical oncology and provides an effective and accurate imaging technique for a variety of diagnostic oncology. In breast cancer, main applications were detection of

the response, restaging, detection of metastatic disease and for monitoring treatment response [6].

PET/CT play a very important role in the diagnosis of locoregional metastasis (including nodal) and distant metastasis in helping to plane surgical and medical treatment as well as monitoring the response to treatment [7].

The aim of this work: The aim of the work is to evaluate the role of FDG PET/CT in evaluation of breast cancer metastasis.

Patients and Methods:

This is a prospective study in which fifty female patients with evidence of proven metastatic breast cancer were referred for PET/CT in Department of Nuclear Medicine in Egyptian Armed Forces Hospitals in the period between November 2015 and December 2020. The mean age of the studied patients was 57 years, with a standard deviation of 13 years. About two-thirds of the patients showed positive family history. Half of the patients (50.0%) had right breast cancer, forty-four percent had left breast cancer, and only 6% had bilateral breast cancer.

The research ethics committee (Faculty of medicine-Benha University) approved the study protocol, and all patients were

enrolled after written informed consent was obtained. Patients were recruited from Radiodiagnosis, Nuclear medicine departments. The regional ethics committee approved the study and written informed consent were obtained from all participants.

Inclusion criteria were: All patients included in the study with PET/CT on account of evaluation of metastatic breast cancer; these were evident by elevated tumor markers, equivocal findings on CT and MRI.

- Initially metastatic breast cancer or relapsed after primary treatment evident by abdominal ultrasound, CT scan, bone scan or elevated tumor markers.
- FDG-PET/CT studies were performed shortly after appearance of clinical, radiological and/or laboratory data warranting restaging and follow up.

Exclusion criteria:

- Patients with strong history of hypersensitivity disorders to the CT contrast agents.
- Patients with renal function impairment (with serum creatinine > 2 mg/dl) because they are liable to contrast nephropathy.

- Pregnant patients as the patient have high dose of radiation exposure.
- Overweight patients that have difficulties in accessing the scanners and table movement.

Contrast-enhanced CT Protocol:

Contrast-enhanced CT of the chest, abdomen, and pelvis was performed by using a 64-detectors CT scanner. Patients were given 200–800 mL of 2% oral contrast material divided at 45 and 15 minutes before the examination [8].

Intravenous bolus injection of a nonionic iodinated contrast material at a dose of 2-3mL/KG of body weight was performed just before initiation of scanning [8].

Scans were acquired from the thoracic inlet to the pelvic floor by using 2.5-mm-thick sections, and contiguous 5-mm axial image reconstruction [8].

Scanning protocols with 120 kVp and effective tube current that varied from 60 to 140 mAs were used [8].

PET-CT Protocol:

Patients fasted for at least 4 hours before the examination, and blood glucose levels were less than 140mg/dL. A dose of (0.18–0.21mCi/kg, minimum 3mCi) FDG was injected intravenously. The patients rested

in a quiet room. After the 45–60-minute uptake period, the patients were taken for the PET-CT study [9].

No oral or intravenous contrast agent was used for the CT part of the PET-CT examination.

A section thickness of 4 mm and a pitch of 1 were used. After CT acquisition, PET acquisition of the same axial range begun with the patient in the same position on the table for 2–3 minutes per bed position PET data were acquired by using a matrix of 128x128 pixels. CT- based attenuation correction of the emission images was used [9].

After PET data acquisition was completed, the reconstructed attenuation corrected PET images, CT images, and fused images of matching pairs of PET and CT images were available for review in axial, coronal, and sagittal planes, as well as in maximum intensity projections and in three-dimensional cine mode [9].

Results:

Statistical methods

Data management and statistical analysis were done using SPSS version 25. (IBM, Armonk, New York, United States). Numerical data were summarized as means and standard deviations or medians and

ranges. Categorical data were summarized as numbers and percentages. CT and PET/CT were compared regarding detection of metastasis in different sites using the McNemar test. The number of metastasis detected by CT and PET/CT in different sites was compared using Wilcoxon signed ranks test. All P-values were two-sided. P values less than 0.05 were considered significant.

Number of metastasis in different sites by CT and PET/CT (Table 1 & Figure 1):

- ***Lymph nodes metastasis***
 - The median number of lymph node metastasis detected by PET/CT was significantly higher (5) than that of CT (3). P-value was <0.001.
- ***Bone metastasis***
 - The median number of bone metastasis detected by PET/CT was significantly higher (12) than that of CT (7). P-value was 0.028.
- ***Liver metastasis***
 - The median number of liver metastasis detected by PET/CT was significantly higher (5) than that of CT (2). P-value was 0.015.
- ***Loco-regional***
 - The median number of locoregional metastasis detected by PET/CT was

significantly higher (4) than that of CT (2). P-value was <0.001.

- **Lung**

- There were no significant differences between CT and PET/CT regarding the number of metastasis detected in the lung (P-value = 0.187) and suprarenal (P-value = 1.0).

- **Suprarenal**

- There were no significant differences between CT and PET/CT regarding the number of metastasis detected in the suprarenal (P-value = 1.0).

(Table 1): Number of metastasis in different sites by CT and PET/CT.

	Median (range)	P value
Lymph nodes		
CT	3 (1 - 15)	<0.001
PET/CT	5 (1 - 42)	
Lung		
CT	4 (1 - 52)	0.187
PET/CT	3 (1 - 38)	
Bone		
CT	7 (1 - 89)	0.028
PET/CT	12 (1 - 59)	
Liver		
CT	2 (1 - 47)	0.015
PET/CT	5 (1 - 30)	
Suprarenal		
CT	1 (1 - 2)	1.0
PET/CT	2 (1 - 2)	
Locoregional		
CT	2 (1 - 4)	<0.001
PET/CT	4 (1 - 9)	

Wilcoxon signed ranks test was used

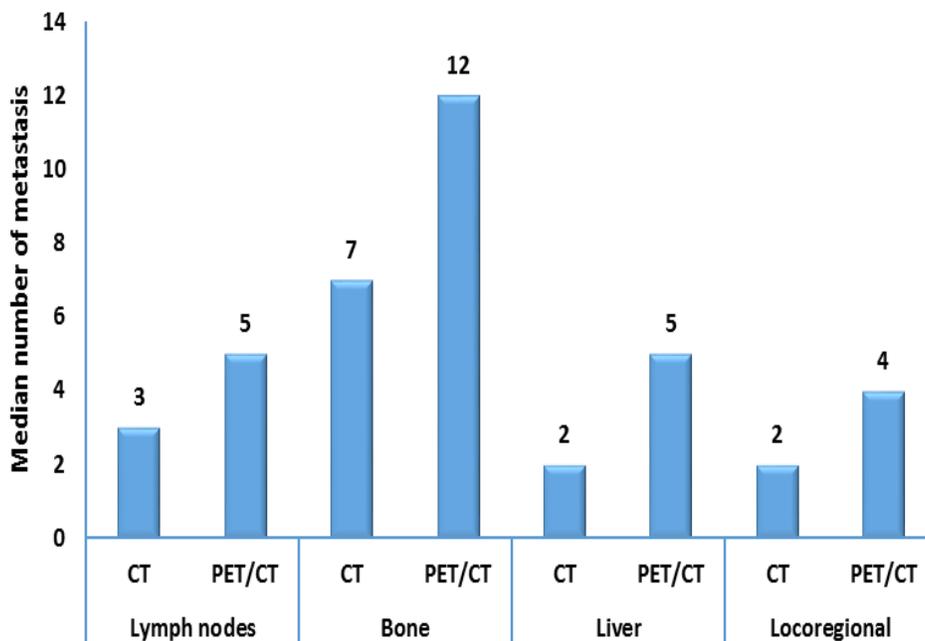


Figure 1: Number of metastasis in different sites by CT and PET/CT.

Discussion:

Worldwide, breast cancer is the most frequently diagnosed life threatening cancer in women and a leading cause of death [10].

Since breast tumors represent a collection of different histopathological types, understanding metabolic differences between molecular subtypes offers a way to identify new subtype-specific treatment strategies, especially if metabolite changes are evaluated in the broader context of the network of enzymatic reactions and pathways [11].

Imaging techniques play an important role in the detection of metastatic spread in breast cancer, such early detection improves patients' prognosis, and has a substantial influence on therapy management, especially using molecular imaging with PET-CT [12].

Also monitoring treatment responses with PET-CT for women with metastatic breast cancer can be difficult and with the goals of therapy focused on improving quality of life and overall survival, finding a test that is

safe, non-invasive and reliable to assess response is a challenge [13].

Although tumor size, lymph node metastasis and tumor grade have been widely accepted in daily clinical practice, the identification of further prognostic indicators. Calculation of metabolic SUV max appears to be useful for selecting patients who have inferior prognosis and need further adjuvant treatment of different breast cancer subtypes [14].

In this prospective study which includes 50 female patients with metastatic breast cancer, we try to detect the diagnostic value of PET/CT in metastatic breast cancer patients. PET/CT was requested for initial staging of the included cases then evaluated qualitatively and semi quantitatively with calculation of SUV max.

A retrospective study was done which included 225 patients with breast cancer patients and compared the sensitivity and specificity of PET/CT and conventional imaging (CT, Ultrasonography, radiography, and skeletal scintigraphy) for the detection of distant metastases and they concluded that, in the detection of such metastases, PET/CT was superior to conventional imaging in terms of both sensitivity and specificity [15].

In the present study, using PET/CT showed high sensitivity and specificity to differentiate between metastatic lesions and this result agrees with the previously reported results.

Regarding bone metastasis, bone is the most frequent site of distant involvement in breast cancer. In our study, the median number of bone metastasis detected by PET/CT was significantly higher (12) than that of CT (7). P-value was 0.028.

Another study was done and in their results Twenty-nine consecutive women with breast cancer were assessed with CT scan, bone scintigraphy and whole-body FDG-PET/CT. The sensitivity of CT scan and bone scintigraphy was 76% (53/70) compared to 96% (67/70) for FDG-PET/CT. The specificity of CT scan and bone scintigraphy and FDG-PET/CT was 95% and 92%, respectively. On a lesion-basis whole-body FDG-PET/CT is more sensitive and equally specific for the detection of bone metastases compared with CT scan and bone scintigraphy [16].

Similarly another reported high sensitivity, specificity and accuracy of 85%, 90% and 88%, respectively for FDG- PET in detection of metastatic spread to lymph nodes in mediastinal and intra-mammary groups. While CT was able to provide

sensitivity, specificity and accuracy of only 54%, 85% and 73% in same patients groups [17].

In our study, the median number of lymph node metastasis detected by PET/CT was significantly higher (5) than that of CT (3). P-value was <0.001.

Also the median number of loco-regional metastasis detected by PET/CT was significantly higher (4) than that of CT (2). P-value was <0.001.

Regarding pulmonary metastasis, diagnostic CT efficiently detected sub-centimetric pulmonary nodules. Whereas in PET imaging in view of partial-volume effect and respiratory movements, PET lacked sensitivity for detecting smaller nodules. Combined PET/CT examination obviously improved the sensitivity of PET/CT in comparison to stand alone PET. There were no significant differences between CT and PET/CT regarding the number of metastasis detected in the lung (P-value = 0.187).

FDG PET/CT had sensitivity for liver metastases slightly higher than that of conventional imaging, PET/CT helped to classify doubtful findings on conventional imaging (angiomas and cysts), as reported in another study on 115 breast cancer patients they found that PET/CT is able to assess primary tumor size and metastatic spread

more accurately than traditional diagnostic methods. It can detect distant metastases in 7-8% of those patients who were declared free of metastasis. PET/CT scan modifies the disease stage determined by traditional diagnostic modalities in almost half of the patients and leads to a change in the treatment plan in every 6th patient [18].

In our study, the median number of liver metastasis detected by PET/CT was significantly higher (5) than that of CT (2). P-value was 0.015.

The FDG uptakes of metastatic sites were evaluated using the SUV max (SUV >2.5 is considered suspicious for malignancy) [19].

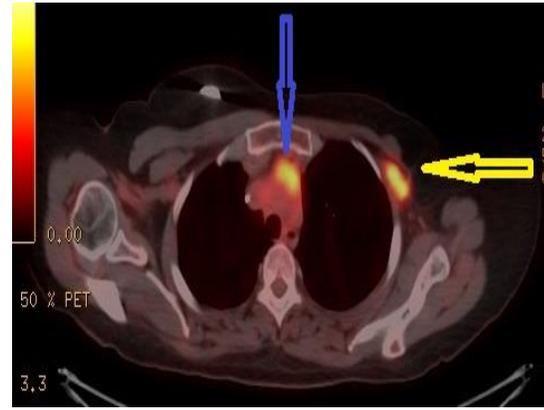
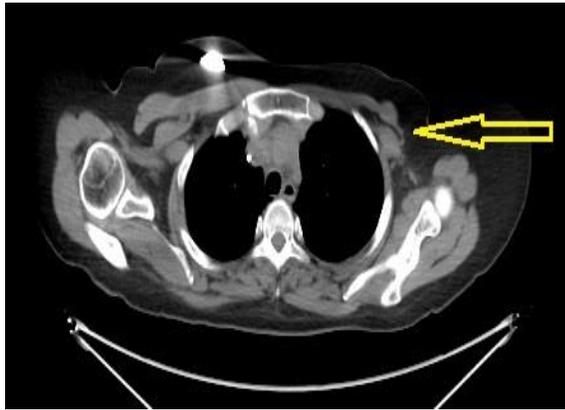
Illustrative cases

Case No. 1

- A 37 years old female patient with history of left breast cancer since April 2013 underwent surgical lumpectomy at September 2014, followed by multiple cycles of chemotherapy and radiotherapy and kept on hormonal therapy.
- Whole body FDG PET/CT was done with multiple metastatic deposits denoted at left sub-pectoral lymph nodes, retrosternal lymph nodes, right hepatic lobe and both iliac bones.

➤ The following images show the sites of

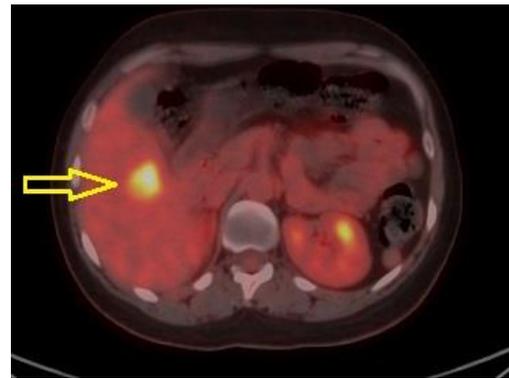
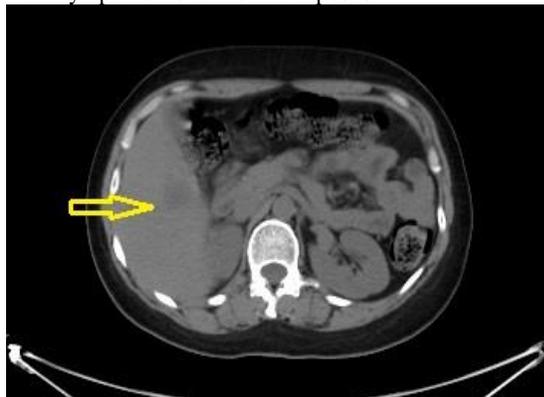
metastatic deposits (Figure 2, 3 & 4).



A

B

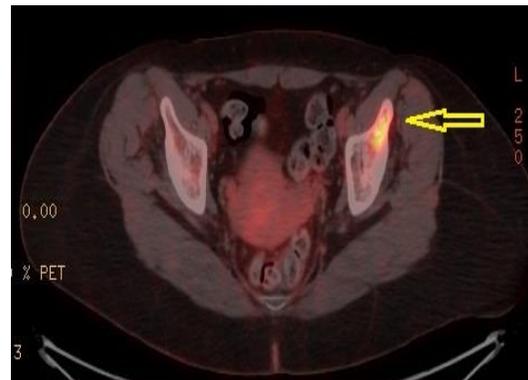
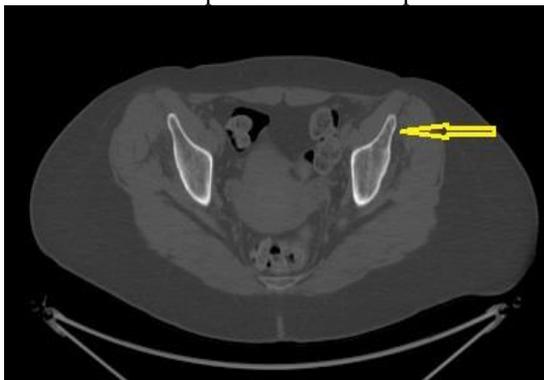
Figure (2): a. CT scan of the chest (soft tissue window axial cuts) showed enlarged left sub-pectoral lymph nodes, the largest measure 25 mm (yellow arrow). **b. PET/CT** (axial images) showed enlarged FDG-avid left sub-pectoral lymph nodes (yellow arrow), its SUVmax = 7.5, also showed enlarged FDG-avid retro-sternal lymph nodes (blue arrow), its SUVmax = 8 ; consistent with lymph nodes metastatic deposits.



A

B

Figure (3): a. CT scan of the abdomen (soft tissue window axial cuts) showed ill-defined hypo-dense right hepatic lobe focal lesion seen at sub-segment V measure about 3.5 x 3 cm (yellow arrow). **b. PET/CT** (axial images) showed FDG avid right hepatic lobe focal lesion seen at sub-segment V with SUVmax = 10.8 (yellow arrow) consistent with hepatic metastatic deposit.



A

B

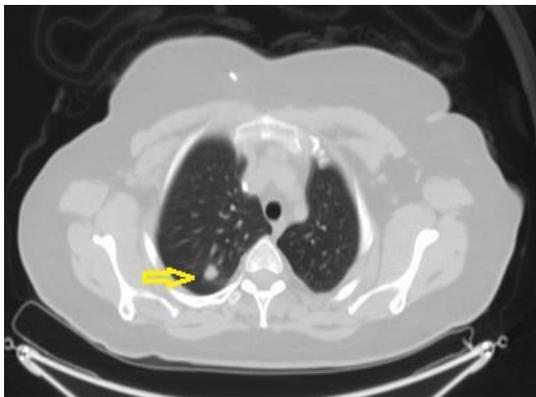
Figure (4): a. CT scan of the pelvis (bone window axial cuts) showed an ill-defined intra-osseous sclerotic bony lesion is seen at the left iliac bone (yellow arrow). **b. PET/CT** (axial images) showed FDG-avid intra-osseous bony lesion is seen at the left iliac bone (yellow arrow) with SUVmax = 5.7 consistent with metastatic bony deposits.

Case No. 2

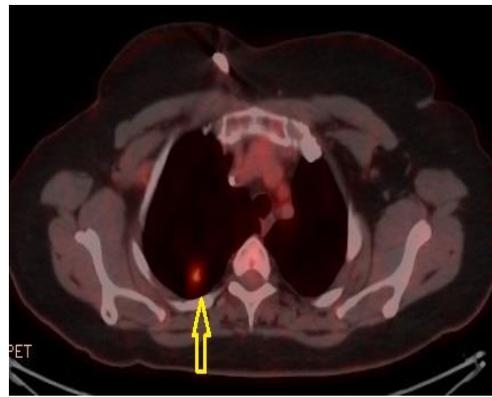
➤ A 52 years old female patient with history of right breast cancer since October 2015 underwent surgical lumpectomy at January 2016, followed by multiple cycles of chemotherapy and radiotherapy.

➤ Whole body FDG PET/CT was done with multiple metastatic deposits denoted at dorsal vertebra, lumbar vertebra, both scapula, both iliac bones, ribs and right upper lung lobe.

➤ The following images shows the sites of metastatic deposits (Figure 5 & 6).

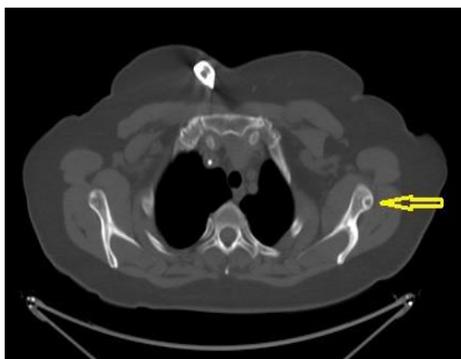


A

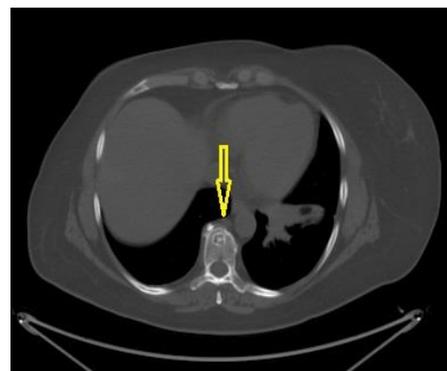


B

Figure (5): a. CT scan chest (lung window axial cuts) showed right upper lung lobe nodule (yellow arrow). **b. PET/CT scan** (axial images) showed FDG-avid right upper lung lobe (yellow arrow) with SUVmax = 4.9, consistent with pulmonary metastatic deposits.



A



B

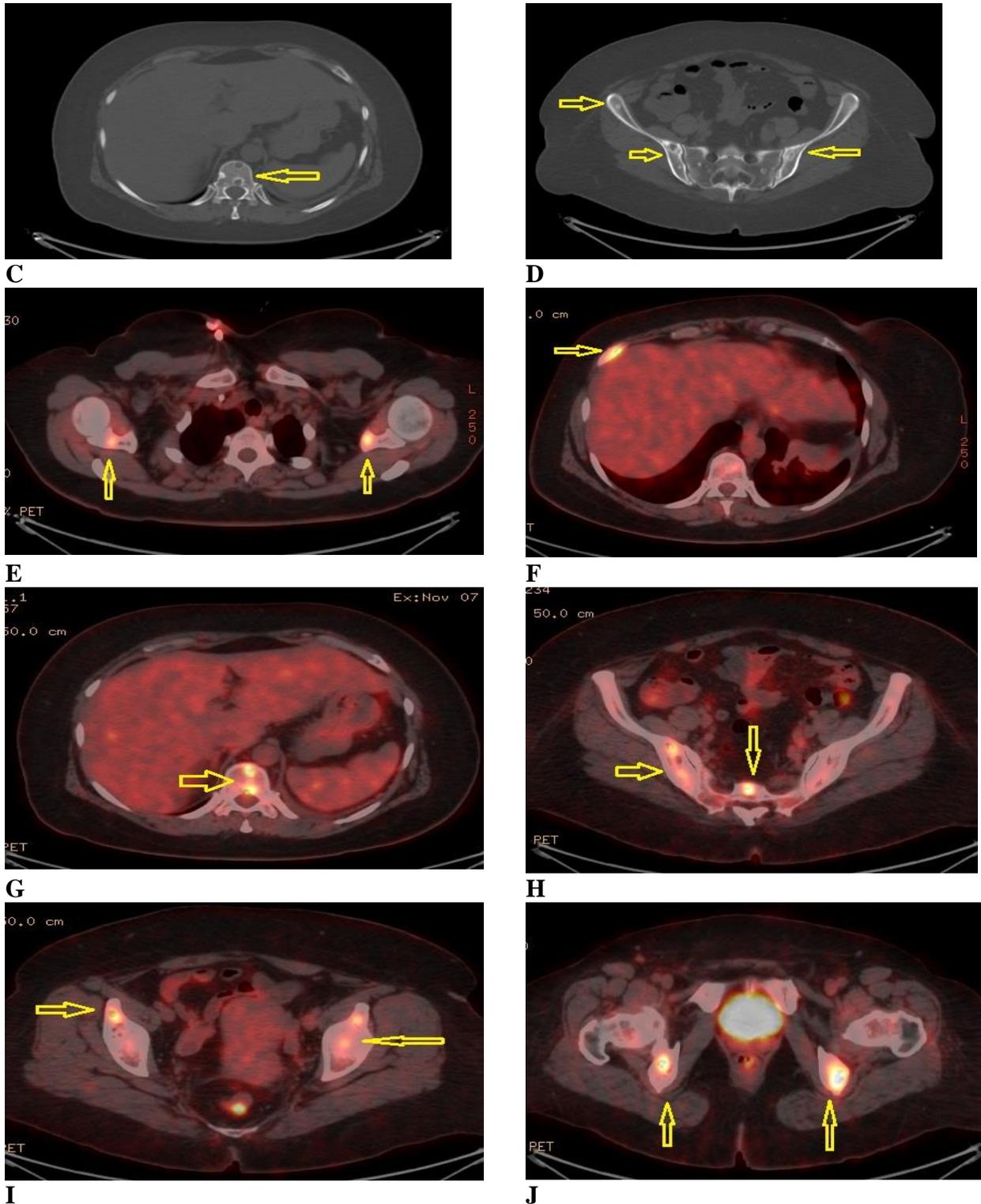


Figure (6): a., b., c. & d. CT scan chest, abdomen and pelvis (bone window axial cuts) showed multiple scattered variable size intra-osseous mixed sclerotic and osteolytic deposits seen at dorsal and lumbar vertebra, scapula, right ribs and both iliac bones (yellow arrows). e., f., g., h., i. & j. PET/CT scan (axial, coronal and sagittal images) showed multiple scattered FGD-avid intra-osseous deposits seen at dorsal vertebra, lumbar vertebra, both iliac bones, both scapula and right ribs (yellow arrows) with SUVmax = 8.1 – 10.5, consistent with multiple metastatic bony deposits.

Case No. 3

- A 42 years old female patient history of left breast cancer since July 2016 underwent modified radical mastectomy at October 2017, followed by multiple cycles of chemotherapy and radiotherapy.

- Whole body FDG PET/CT was done with multiple metastatic deposits denoted at sternum, left sub-pectoral lymph node and both hepatic lobes.
- The following images show the sites of metastatic deposits (Figure 7, 8 & 9).

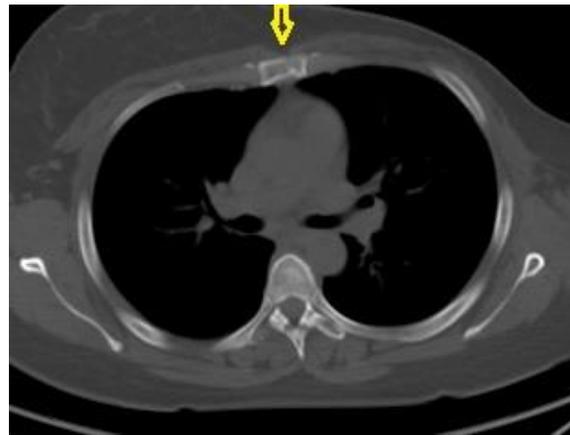


Figure (7): a. PET/CT (axial images) showed FDG-avid intra-osseous bony lesion is seen at the sternum (yellow arrow) with SUVmax = 5.4 consistent with metastatic bony deposits. **b. CT scan** of the chest (bone window axial cuts) showed an ill-defined intra-osseous osteolytic bony lesion is seen at the sternum (yellow arrow).

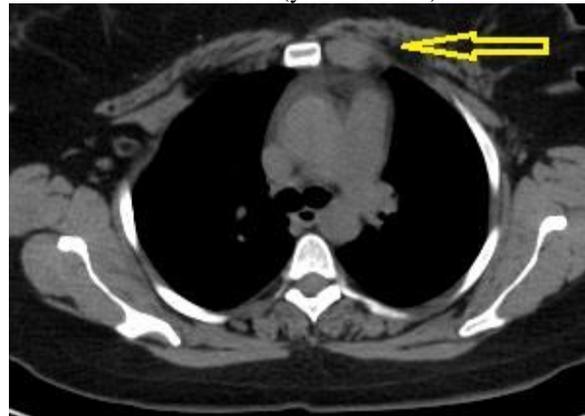
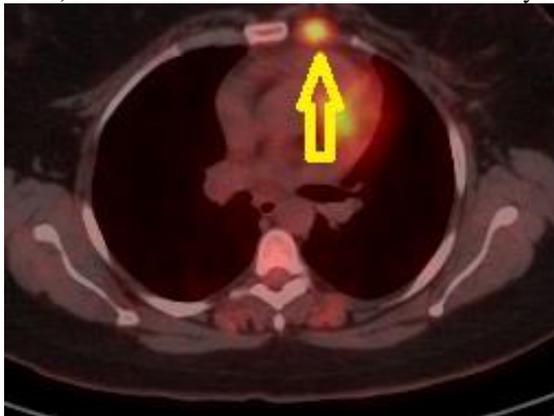


Figure (8): a. PET/CT scan axial cuts showed FGD-avid enlarged left sub-pectoral lymph nodes lymph nodes with SUVmax = 4.7 consistent with metabolically active loco-regional metastatic deposits. **b. CT Scan** of the chest (soft tissue window axial cuts) showed enlarged left sub-pectoral lymph nodes measure 3 x 2 cm (yellow arrows).

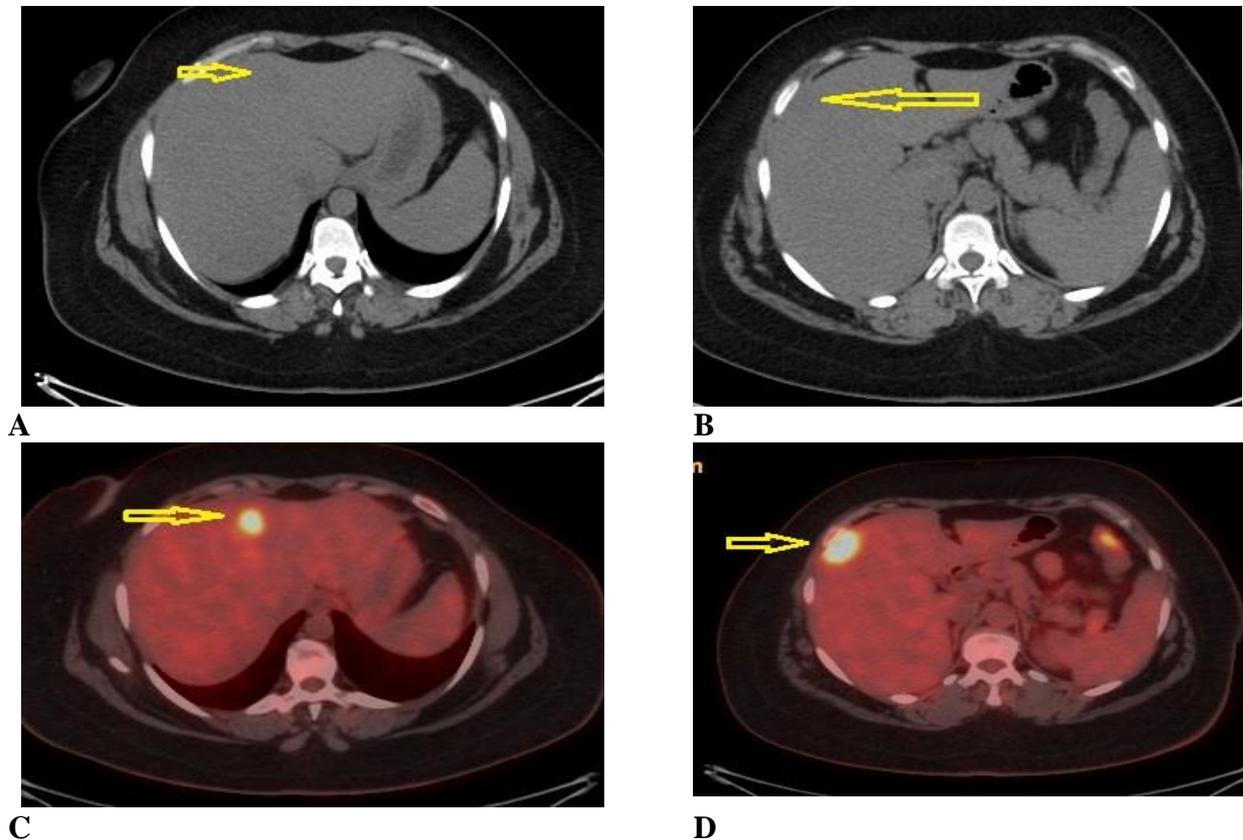
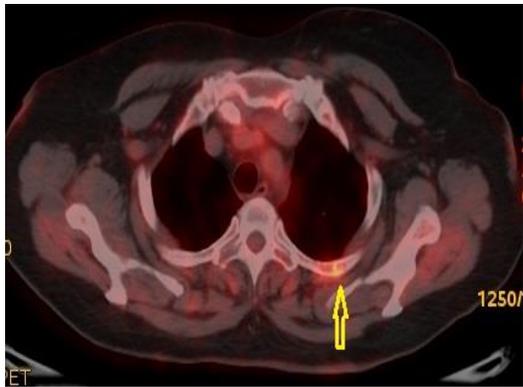


Figure (9): a. & b. CT scan of the abdomen (soft tissue window axial cuts) showed both hepatic lobes ill-defined slightly hypodense lesions, the largest measure 2.5 x 2 cm (yellow arrows). **c. & d. PET/CT scan** (axial images) showed FGD-avid both hepatic lobes lesions (yellow arrow) with SUVmax = 11.2 consistent denoting hepatic metastatic deposits.

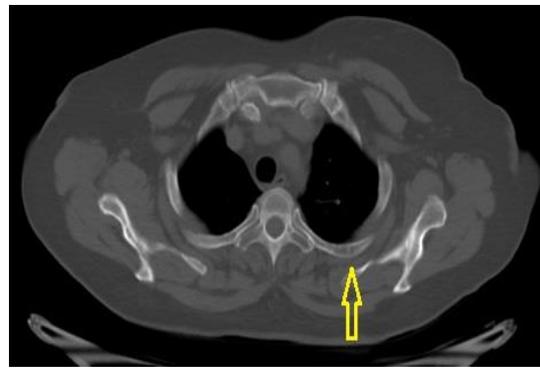
Case No.4

➤ A 70 years old female patient history of right breast cancer since November 2016 underwent lumpectomy at April 2017, followed by multiple cycles of chemotherapy and radiotherapy.

- Whole body FDG PET/CT was done with multiple metastatic deposits denoted at right axillary lymph nodes, left 3rd rib, lumbar vertebra.
- The following images shows the sites of metastatic deposits (Figure 10 , 11 , 12 & 13).

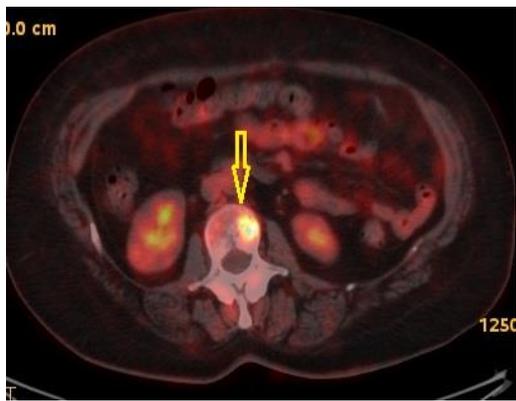


A



B

Figure (10): a. PET/CT (axial images) showed FDG-avid intra-osseous bony lesion is seen at the left 3rd rib (yellow arrow) with SUVmax = 6.7 consistent with metastatic bony deposits. **b. CT scan** of the chest (bone window axial cuts) showed an ill-defined intra-osseous osteolytic bony lesion is seen at the left 3rd rib (yellow arrow).



A

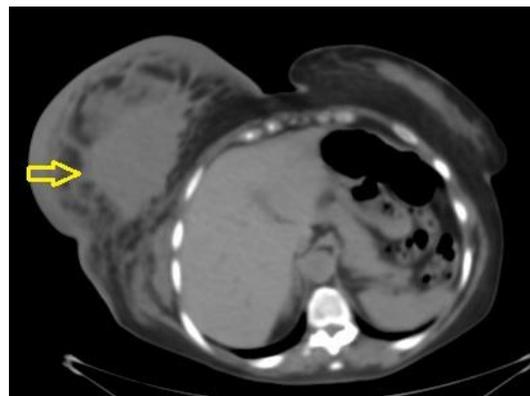


B

Figure (11): a. PET/CT (axial images) showed FDG-avid intra-osseous bony lesion is seen at the 2nd lumbar vertebra (yellow arrow) with SUVmax = 14 consistent with metastatic bony deposits. **b. CT scan** of the abdomen (bone window axial cuts) showed an ill-defined intra-osseous sclerotic bony lesion is seen at the 2nd lumbar vertebra (yellow arrow).

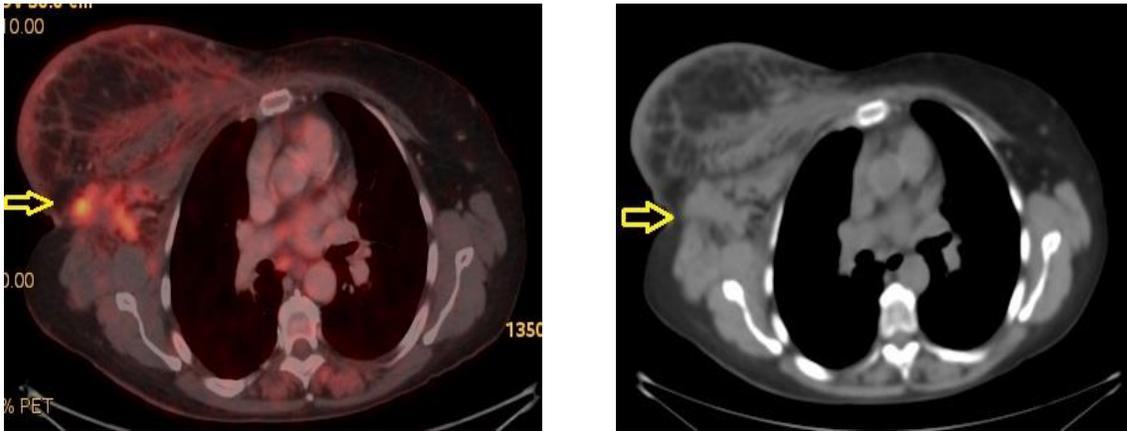


A



B

Figure (12): a. PET/CT scan axial cuts showed FDG-avid parenchymal lesions seen at the right breast with SUVmax = 8 consistent with metabolically active neoplastic tissues with loco-regional metastatic deposits. **b. CT Scan** of the chest (soft tissue window axial cuts) showed diffuse increased skin and subcutaneous tissue thickness of the right breast with diffuse parenchymal heterogeneity as well as ill-defined soft tissue density mass lesion measure 12.8 x 5.9 cm (yellow arrows).



A **Figure (13): a. PET/CT scan** axial cuts showed FGD-avid enlarged right axillary lymph nodes with SUVmax = 5.3 consistent with metabolically active loco-regional metastatic deposits. **b. CT Scan** of the chest (soft tissue window axial cuts) showed enlarged right axillary lymph nodes measure 3 x 5 cm (yellow arrows).

Conclusion:

PET/CT is whole body single imaging which can detect metastatic spread in breast cancer as well as monitoring the therapy response in relation to different molecular subtypes.

¹⁸F-2-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) is able to supply functional information for whole-body tumor staging with higher sensitivity, specificity and accuracy as compared to CT in detection of metastatic spread and follow up after treatment.

PET/CT was requested for initial staging of the included cases then evaluated qualitatively and semis quantitatively with calculation of SUV max.

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