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Role of Positron Emission Tomography/Computed Tomography (PET/CT) in Detection of Bone Metastases

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ABSTRACT

Background and Aim of the Work: Early detection of skeletal metastasis is critical for accurate staging and optimal treatment. Among the various imaging modalities currently available for imaging skeletal metastasis, hybrid techniques which fuse morphological and functional data are the most sensitive and specific, and positron emission tomography (PET)/computed tomography imaging will almost become increasingly important in this regard**.** We tried to assess the efficacy of *fluorine-18 fluoro-deoxy-glucose Positron Emission Tomography/Computed Tomography (PET/CT) ((18) F-FDG-PET/CT) scan* in detecting bone metastases among various primary malignancies. In order to detect accuracy of fused PET/CT in the initial detection & characterization of osseous metastases compared to isolated PET and CT with contrast.

Patients and methods: The study included thirty patients (with a mean age = 27) with various primary malignancies (pathologically proven) to whom PET/CT was done. In this study population, a detailed retrograde lesion based analysis was performed for a total of 80 detected bone lesions on PET, CT and fused PET/CT images. Sensitivity, specificity, PPV and NPV of each modality were calculated. Stastical analysis of the lesions were performed to study the relationship between the lesion's SUV and its corresponding morphologic pattern on CT and to set a reliable SUVmax cut-off value that can predict the presence of malignant lesion.

Results: The calculated fused PET/CT sensitivities and specificities in various malignancies ranged from 95.2% to 99.6% and 75% to 100%, respectively. The combined PET/CT has significantly improved the low CT sensitivity (especially in lymphoma) as well as both separate CT and PET specificities (using SUVmax of 3 as a cut off value for malignant osseous lesions).

Conclusion: Detection of early bone marrow infiltration not apparent on CT, resolution of metabolic activity before definite signs of complete healing on CT, detection of missed sclerotic metastases on PET due to their relatively low metabolic activity, detection of intra and extra osseous recurrence and differentiation of benign from malignant bone lesions.

INTRODUCTION

Positron emission tomography (PET) is a molecular imaging technique most widely applied in oncology, using 18F labeled fluoro-deoxy-glucose (18F-FDG). It provides quantitative and qualitative functional information about tumor cells depending on their increased rate of glucose metabolism. 18F-FDG PET is regarded to be effective in the detection, staging and restaging of malignancies with a remarkably high sensitivity. The combination of PET and computed tomography (CT) represents a unique imaging modality that scans the whole body in the same session, providing functional and anatomic information in fused images. It combines the high sensitivity of PET to the superior anatomical localization by CT resulting in much more accurate detection and staging of malignancies [(1)].

Several studies had illustrated the additional value of PET/CT scan compared to various imaging modalities in the accurate initial staging and follow up of malignancies. PET/CT scan can identify invisible metastatic lesions not yet developing into structural changes. Thereby, a significant change in the management plan might be done [(2)].

Combined PET/CT is widely applied in the evaluation of various malignancies; hence the importance of evaluating its role in the detection and characterization of skeletal metastases. The integration of PET and CT in one modality has improved the diagnostic accuracy of each in the

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evaluation of malignancies& thereby in the evaluation of skeletal metastases [1] .

PATIENTS AND METHODS

The study done on 30 patients at (Oncology Department , Nasser Institute Hospital For Research And Treatment) . The 30 patients were (20 female and 10 male , mean age: 56.13 years ±SD: 13.47)

For all patients, the primary malignancy type has been pathologically proven. The study excluded those who had recent intervention (biopsy) or local external beam radiotherapy or granulocyte colony stimulating factor therapy within 1 month from PET/CT scan.

At referral, medical history, previous investigations and pathology reports were recorded. The patients were followed up after the PET/CT study.

All patients included in the study singed for a consent about the risks of this investigation e.g. Risks of the following

- Injection of the radiotracer may cause slight pain and redness which should rapidly resolve.
- Nuclear medicine diagnostic procedures have been used for more than five decades, and there are no known long-term adverse effects from such low-dose exposure.
- Allergic reactions to radiopharmaceuticals may occur but are extremely rare and are usually mild. Nevertheless, you should inform the nuclear medicine personnel of any allergies you may have or other problems that may have occurred during a previous nuclear medicine exam.
- Women should always inform their physician or radiology technologist if there is any possibility that they are pregnant or if they are breastfeeding. See the Safety page for more information about pregnancy, breastfeeding and nuclear medicine exams.
- For risks of CT exams& radiations .
- Risk of radio-isotope after return back to home to the surrounding persons specially children & pregnant (better not get in close relation with them for at least 2 days .)

All patients will be subjected to the following:

- History taking specially if the patient has any allergies or adverse effect to medications .
- Fasting blood sugar level.
- Serum creatinine level.
- Pregnancy test.

Inclusion criteria

- Cancer patients searching for bone metastases.
- Cancer patients with bony lesions to assess their nature.
- Patients with bone metastases for follow up after treatment.
- Patients with metastases of un-known origin to assess bony primary.
- Cancer patients with bone metastases to assess recurrence or residual.

Exclusion criteria

- Patients with bad general condition.
- Patients with history of previous allergic reaction or adverse effect to medications.
- Patients with high renal function tests.
- Patients with un-controlled diabetes mellitus.
- Pregnant patients.

Among the 30 patients included in the study, (3 had Hodgkin's Disease , 1 had Thyroid Cancer , 1 had Multiple Myeloma (MM) , 8 had Breast Cancer , 2 had Cancer Colon ,1 had Cancer Prostate , 1 had Malignant Peripheral Nerve Sheath Tumor , 2 had Ewing Sarcoma , 1 had Carotid Body Tumor , 1 had Cancer Ovary , 2 had Non Hodgkin Lymphoma , 2 had Neuro-Endocrinal Tumor , 1 had Peri-Ampullary Carcinoma , 2 had Metastatic Of Unknown Origin (MUO) , 1 had Bronchogenic Carcinoma , 1 had Ankle Mass (Poorly Differentiated Malignant Epithelioid Tumor) .

Imaging protocol

PET/CT scanning:

Combined PET/CT scan was performed at Nasser Institute Hospital, using (Siemens Biograph True Point 64; Siemens Healthcare, Erlangen, Germany). The integrated CT system is a 64 multi-slice scanner. The acquisition of co-registered CT and PET images were performed in one session.

Adequate patient preparation rules were strictly followed. Patients were instructed to fast except for glucose-free hydration for 4–6 h before injection of 18F- FDG. The scan was performed

40–60 min after IV injection of (3.7 MBq/Kg; maximum dose 370 MBq) (0.1 millicurie/kilogram (mCi/kg); maximum dose = 20 mCi/kg) of 18F- FDG. The patients were examined in supine position. A whole body examination was performed starting from skull vault to the feet.

A PET emission scan was performed over several bed positions (12 to 14), each with an axial field of view of approximately 15 cm per bed position with an in-plane spatial resolution of 4 mm covering the same field of view as with CT. The acquisition time of emission data was 2 minutes per bed position in the two dimensional mode. The total examination time range between 24 and 38 minutes.

A fully diagnostic CT scan was performed using the following parameters: (350mA, 120 kV, 0.5 second tube rotation time, slice thickness 5mm, 8-mm table feed and 3 mm incremental reconstruction). IV contrast administration (120 mL of a low-osmolarity iodinated contrast agent (Ultravist 300®,Schering, Berlin, Germany) and negative oral contrast agent (water) for bowel were used.

Images were reconstructed and viewed on workstation (Syngo Multimodality Workplace, Siemens Medical Solutions), which provided multi-planar reformatted PET, CT and fused PET/CT images with linked cursors as well as MIP PET images in video mode.

Dual time point imaging was taken by imaging at two time points and evaluating the max. SUV change in between. The time interval between early and delayed scans was 30 minutes or more.

4. Image analysis

PET images and CT images were fused and displayed on a workstation (Siemens, Germany). All PET/CT images were interpreted by an experienced radiologist & an experienced nuclear medicine physician. All images were qualitatively &quantitively interpreted.

Qualitative assessment for presence of hypermetabolic lesions was evaluated on both corrected and uncorrected PET images in the Invert Grey Scale. The criterion for malignancy was [18F] FDG hypermetabolism at the site of pathological changes on CT or marked focal hypermetabolism at sites suggestive of malignancy despite absence of signs of pathology at those sites on CT. The distribution of pathological lesions, a prior knowledge of the pattern of spread of different tumors and the patient's history were taken into consideration.

Quantitive evaluation using Standard Uptake Value (SUV) according to this formula: SUV = (μCi/gram in tissue)/ (total μCi injected) body weight. Max. SUV value of more than 3 was considered significant.

The study was done after approval of ethical board of Benha university and an informed written consent was taken from each participant in the study.

Statistical analysis

Data were statistically described in terms of range, mean ±standard deviation (±SD), median, frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between each modality was done using Kruskal–Wallis analysis of variance (ANOVA) test. For comparing categorical data, Chi square (v2) test was performed. Sensitivity, specificity, positive and negative predictive values, accuracy, P value were calculated to test validity of PET/CT.

Exact test was used instead when the expected frequency is less than 5. P values less than 0.05 were considered statistically significant.

All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY,USA) .

RESULTS

Table 1: Baseline characteristics of patients included in the study.

Variables	**N=30**	
Sex	Male: 10 & Female: 20.	
Age, median	56.13 years	
Mean follow-up duration.	6 months	
Site of primary malignancy on presentation.	Breast cancer	8
	lymphoma	5
	Cancer colon	2
	Neuroendocrinal tumor	2
	Ewing sarcoma	2
	Cancer prostate	1
	Cancer ovary	1
	Metastatic of unknown origin	2
	Multiple myeloma	1
	Bronchogenic carcinoma	1
	Periampullary carcinoma	1
	Thyroid cancer	1
	Malignant peripheral nerve sheath tumor	1
	Carotid body tumor	1
	Poorly differentiated malignant epithelioid tumor	1

Table 2 : CT scores for bone lesions

CT score	Morphologic appearance
1	No morphologic changes
2	Benign looking lesions
3	Equivocal lesions
4	Malignant looking lesions

CT Images :

The whole CT images were reviewed in bone & soft tissue windows. Detected areas of abnormal FDG uptake on PET images were, in particular, further analyzed on CT images. Bone lesions were classified into benign and malignant looking lesions according to their morphologic appearance.Some lesions which did not meet the criteria of either were considered equivocal. Accordingly, a scoring system was also performed for the lesions (Table 2).

Bone lesions were considered *benign* according to the following criteria: being well defined, homogenously and fully sclerotic, and lytic with regular sclerotic margins. Localization to the vertebral end plates or articular surfaces was also considered a benign feature.

Bone lesions were considered *malignant* if appeared ill defined, irregularly or heterogeneously sclerotic, lytic with irregular sclerotic margins, associated with cortical

destruction or extra osseous soft tissue component.At final diagnosis, true positive lesions were those assigned as score 4 and confirmed as active bone metastases by biopsy or on follow up imaging. Lesions with score <4 or have been missed on current scan and proved to be malignant on follow up images, were considered *false negative*.

Lesions with score 1 which show uptake on corresponding fused PET/CT images and proved to be malignant by biopsy or on follow up images were also considered *false negative* lesions.The CT recorded lesions were considered false positive if a malignant looking lesion (score 4) did not show appreciable uptake on corresponding fused PET/CT images and proved to be a healed inactive bone metastasis when correlated to previous scans and follow up images.

True negative lesions were those with score 2 or 3 and proved to be benign on follow up.

Table 3: PET scores for bone lesions

PET score	FDG Uptake
1	No appreciable FDG uptake by visual assessment
2	Notable FDG uptake, SUVmax < liver uptake
3	Notable FDG uptake, SUVmax = liver uptake (±10%)
4	Intense diffuse FDG uptake, SUVmax > liver uptake
5	Intense focal FDG uptake, SUVmax > liver uptake

PET Images :

Analysis of PET images was done via visual and semi quantitative assessment (SUVmax measurement). Positive lesions were recorded at areas of high FDG uptake. The standardized uptake value (SUVmax) was measured at each lesion and compared to background activity. The standard background activity was measured at the liver, right lobe. In patients having diseased liver, the background activity was measured at the mediastinal blood pool. Accordingly a scoring system was applied (Table 3).

At final diagnosis, *true positive* lesions were those with PET score >3 and confirmed as active bone metastases by biopsy or on follow up imaging (whether they show a corresponding morphologic changes on CT or not). Lesions with score 2 or 3, or have been missed on current scan and proved to be malignant as evidenced by progression on follow up images, were considered false negative. Lesions which have been missed being outside PET/CT scan field and detected on other imaging modalities were also considered *false negative*.

PET recorded lesions were considered *false positive* if uptake has been localized extra-osseous on corresponding fused PET/CT images or a lesion with score > 3 appeared to be benign on fused PET/CT images or other imaging modalities and confirmed by biopsy or on further follow up images.

True negative lesions were those lacking appreciable uptake on PET (score 1), though looking malignant on corresponding CT images, and confirmed as healed inactive lesions when correlated to previous scans and follow up images and lesions with score < or = 3 and proved to be benign on fused PET/CT images or other imaging modalities and confirmed on further follow up.

Fused PET /CT Images:

On interpreting fused PET/CT images, lesions were considered positive (active bone metastases) when areas of increased FDG uptake (>liver or mediastinal blood pool) are localized to bone whether showing corresponding morphologic changes or not. Lesions were considered negative for active bone metastases at areas lacking high FDG uptake (< liver or mediastinal blood pool) despite suspicious corresponding CT findings if any.

At final diagnosis, *true positive* lesions were those recognized as active metastases and confirmed by biopsy or on follow up imaging. Lesions which have been missed on current scan and proved to be malignant on follow up images were considered false negative. Lesions which have not been recorded, being outside the scan

field (e.g. calvarial bones or at the extremities), were also considered false *negative lesions*.

Fused PET/CT recorded lesions were considered *false positive* if a lesion has been considered as active metastasis and proved to be benign by biopsy or follow up imaging. True negative lesions were those recognized as benign lesions and confirmed so by different imaging modalities on follow up imaging. Also lesions which have been recognized as inactive healed metastases and confirmed when correlated to previous scans and follow up imaging were also considered *true negative* lesions.

Fused PET/CT images allowed accurate localization of uptake(osseous versus extra osseous), identification of healed bone metastases as such by the absence of uptake as well as allowed detection of early bone marrow infiltration before structural changes are apparent on CT images.

Table 4: Interpretation of the PETCT findings among 30 patients of study group.

PETCT findings	No of patient
True positive	23
False positive	2
True negative	4
False negative	1

Table 5: Sensitivity, specificity, PPV and NPV of FDG-PET/CT in the search for bony mets in various cases of primary malignancies.

Sensitivity	Specificity	PPV	NPP
98.79 %	98.44 %	99.09 %	97.93 %

The relationship between FDG uptake and the morphologic nature of bone lesions. A semi quantitative analysis was performed through measuring SUVmax at each lesion. Lesions having highest average values of SUVmax were lytic bone metastases (8.42) followed by those of no corresponding morphologic changes (8.37). Sclerotic bone metastases showed lower average values of SUVmax (2.37). Sclerotic bone metastases were detectable on PET/CT scan, though showing lower values of FDG uptake yet appreciable visible uptake is noted. The integration of PET and CT further limits the possibility of missing such lesions being readily visible on CT images.

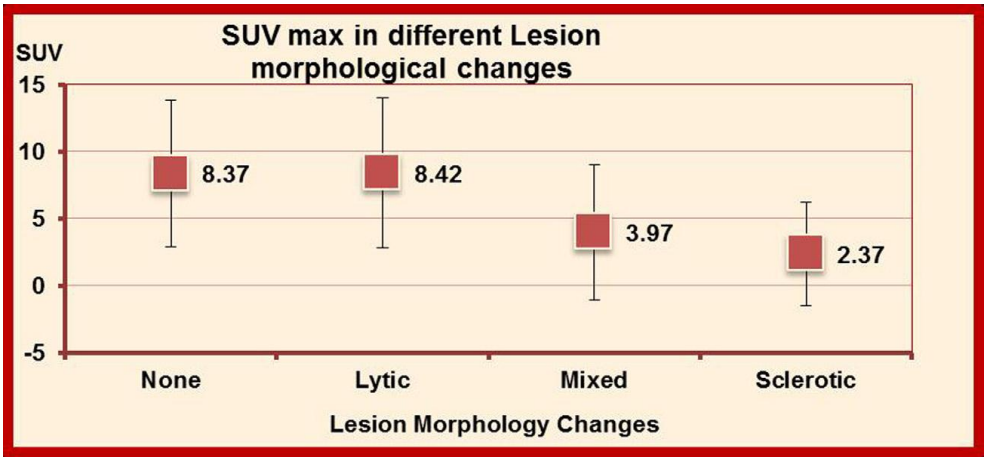

Figure 6: shows the relationships between SUV max of bone lesions on PET and their corresponding morphologic pattern on CT.

Table 6: common Sites of bone metastases in 30 positive patients as detected by PET/CT.

Sites of bone metastases	No of patients	Percentage %
Vertebral column	23	44.8
Pelvic bones	12	31.0
Skull and facial bones	7	7.9
Long bones	7	7.9
Short bones	7	7.9

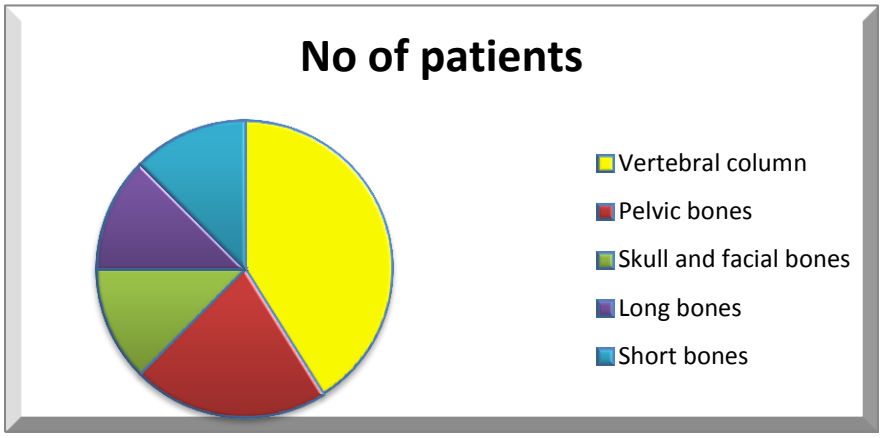

Figure 1: shows common Sites of bone metastases in 30 positive patients as detected by PET/CT. There was statistically significant results in the initial staging PET-CT (P value 0.004)

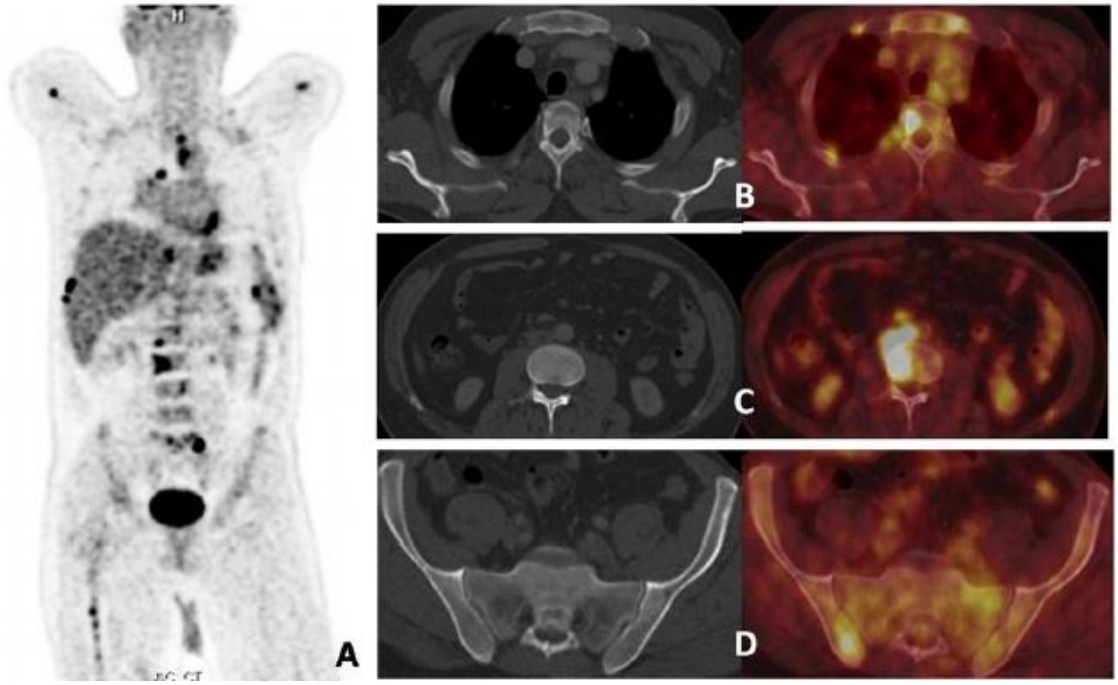

Figure 2: shows a male patient with NHL (A) MIP PET image reveals multiple focal areas of intense uptake denoting lymphomatous infiltrates. The axial CT and fused PET/CT images show: Multiple lymphomatous bony deposits at the sternum, right ribs and dorsal vertebral body with a left paratracheal lymph node (B) lumbar vertebral body with aortocaval and retrocaval lymph nodes (C) and right ischium (D) All the lymphoma bony deposits in this patient did not show any morphologic CT changes.

Table 7 : Distribution of PET/CT and bone scan findings in relation to the final diagnosis

	PET /CT findings		
Final Diagnosis	Positive	Negative	Total
Metastatic	79	1	80
Benign	1	69	70

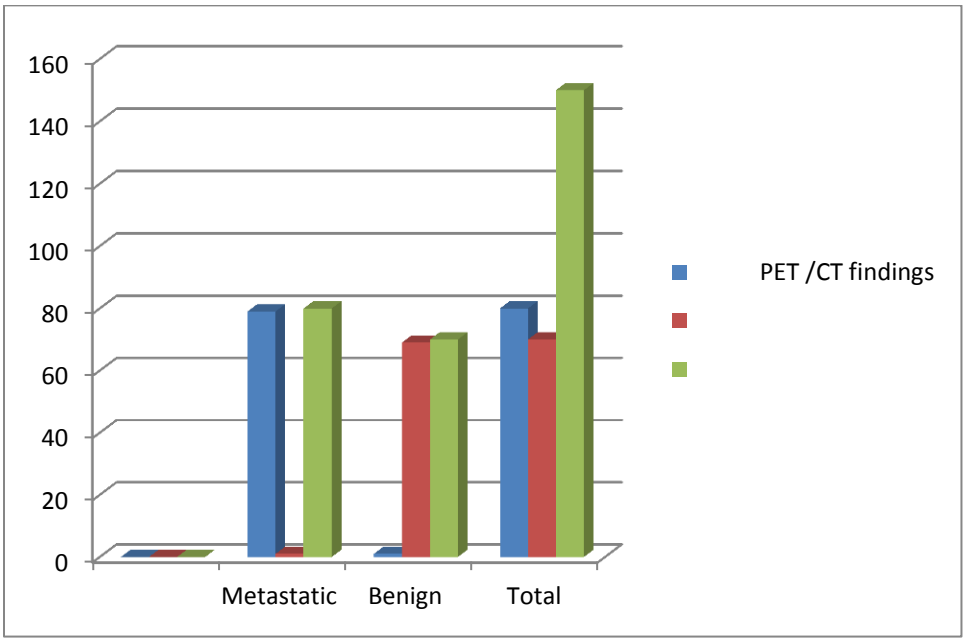

Figure 3: shows Distribution of PET/CT and bone scan findings in relation to the final diagnosis

Table 8: Summary of Factors that May Result in False-Negative and False-Positive Findings

False-Negative Causes	*False-Positive Causes*
Small lesion size	Gastrointestinal and urinary activity
Lesion location	Myocardial activity
Tumor type	Breast, thymus, physis activity
Tumor histologic grade	Autoimmune thyroiditis/parathyroid adenoma
Respiratory motion	Inflammation (infectious and non-infectious)
	Trauma, surgery, fracture
	treatment-related marrow hyperplasia
	Skin contamination (urine) or infiltration (lymph nodes)
	Reconstruction artifacts
	Radiodense and metallic materials (PET-CT)
	Respiratory motion
	Skeletal muscle and brown fat

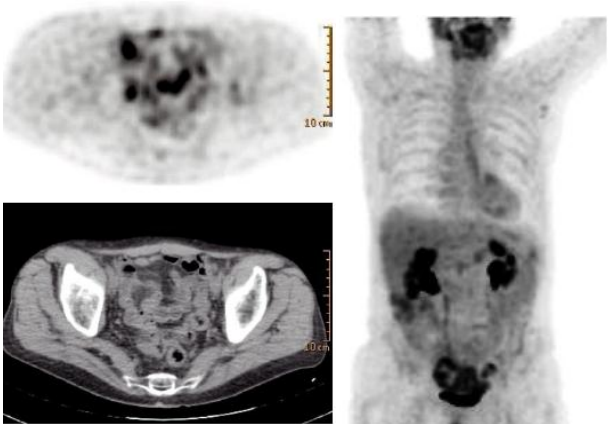

Figure 4: shows Aspecific bowel FDG uptake one of the causes of false positive results [(3)] .

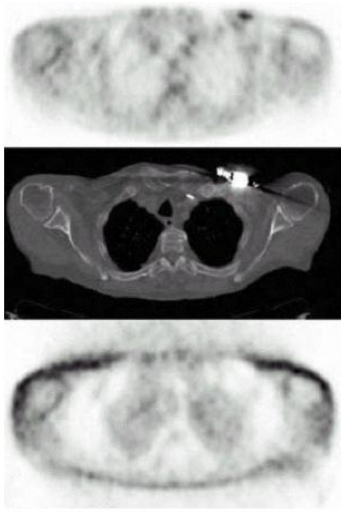

Figure 5: shows Pacemaker Artifact. The top panel shows a CT-corrected PET scan. The middle panel shows the CT scan. The bottom panel shows an uncorrected PET scan. The metal in the pacemaker causes the "hot spot" on the corrected scan [(4)].

DISCUSSION

The results of our study indicated that, FDG PET/ CT was able to detect 78.4 % of bony metastases for various primary malignancies with highest sensitivity (98.79 %), and specificity (98.44%) in comparison to either Bone Scan ,CT alone or PET alone. So PET/ CT in detection of bony metastases of various primary malignancies had a sensitivity ranging from 95.2 % &99.6 % indicating that it is an effective study that the advantage of metabolic information in the search for bony metastases.

PET/CT suggested primary sites in other 4 of 30 patients (13.3%) but none of those patients were confirmed by biopsy or during follow up to be malignant lesions (*false positives*). 4 out of 30 patients (13.3%), proved by PET/CT to be truly negative after clinical, laboratory & radiological follow up for up to 9 months (true negatives).

In the remaining 1/ 30patient (3.3 %) where FDG-PET did not identify the site of bone metastasis, however patient received palliative therapy (*falsenegatives*).

The study performed a separate analysis for data interpreted on PET, CT

and fused PET/CT images in order to evaluate and compare the diagnostic accuracy of each imaging modality and evaluate the added value of combined PET/CT imaging in the detection and characterization of metastatic bone lesions. few studies had performed such a comparative

analysis for the three components in the same study especially regarding the evaluation of CT scan alone [5,6].

The performed CT scoring system in our study categorized the detected lesions according to the diagnostic possibilities (either malignant or not) to obtain a more accurate evaluation of the efficiency of CT in the characterization of lesions in oncology patients. The PET scoring system categorized the lesions according to their visually inspected uptake in comparison to the background uptake and then only those with detectable uptake higher than that of the background were considered definitely malignant. Accordingly, a considerable number of metabolically active bone metastases were missed and have been considered false negative thereby underestimating PET sensitivity. That is why it is worth to mention that when bone lesions having a PET score P = or >3 also recorded as positive; the estimated PET sensitivity was higher but on the expense of lowering PET specificity. The same was also true for equivocal bone lesions having a CT score 3.

Recording such lesions as positive increases the sensitivity of CT but on the expense of lowering the specificity.

In our study, CT shows low sensitivity in the detection of bone metastases, explained by the large number of bone metastases which do not show morphologic changes. This was especially true in *lymphoma* patients, where the estimated CT sensitivities were 6.89% and 17.52% in HD and NHL patients respectively.

The integration of PET and CT has notably improved the sensitivity of CT through detection of high FDG uptake by bone marrow based metastatic cells which are not associated with structural bone changes; neither destructive nor osteoblastic. This goes with the results of previous studies. Nakamoto *et al.*[7] which stated that among true positive bone metastases seen at PET, morphologic changes at CT were observed in only half. Also Evangelista *et al.* [8] stated that PET/CT yielded accurate results in the early detection of bone marrow metastases in breast cancer, lymphoma as well as multiple myeloma. Schaefer *et al.*[9] also encouraged the superiority of PET/CT compared to CT alone or in combination with bone marrow biopsy in lymphoma. The lung cancer group was the only exception in our study where the estimated CT sensitivity is 95.28%. This is actually because all the analyzed bone lesions in this small group of patients had corresponding structural changes either of lytic or mixed pattern.

Regarding CT specificity, almost all false positive lesions on CT images in our study were in fact healed metastases. This was more evident in breast cancer patients, where a large number of this group population was referred for follow up at a regressive disease course explaining the notable low specificity of CT (24.87%) and high specificity of PET (95.33%) in this group. Here the integration of PET and CT significantly improved the specificity of CT and the accuracy of diagnosis through identifying metabolic inactivity regardless the suspicious or malignant looking CT appearance. Or study emphasizing the influence of chemotherapy on the PPV of PET and CT interpretation and the importance of prior knowledge of treatment history [10]. The calculated specificity of CT images alone was 100% in the colon cancer, renal cancer and bronchial cancer groups. It perfectly localized FDG uptake to bone and could identify all benign lesions in these groups. This was a perfect performance compared to the much lower calculated CT specificities in the other groups reflecting the difference in the number of patients in each group and the number of the analyzed bone lesions with a subsequent higher possibility of false positive results in larger groups especially in patients having variably healed metastatic lesions.

Regarding the calculated CT versus combined PET/CT specificities in colon cancer patients, we would like to explain why that of PET/CT was exceptionally lower than CT. This was because of two benign lesions which were accuratelydetected as benign (negative) on CT alone, however according to our methodology we considered lesions with higher uptake than the background to be positive on fused PET/CT ignoring their morphologic CT criteria. The results of our study agree with Yang *et al.* & Liu *et al.* [5, 6] in showing that CT as an imaging modality is more specific than sensitive and that its integration with PET in combined PET/CT improved both its sensitivity and specificity; however variable the calculated

figures are. Yet such improved performance by combined PET/CT is more notable in our results these groups. This was a perfect performance compared to the much lower calculated CT specificities in the other groups reflecting the difference in the number of patients in each group and the number of the analyzed bone lesions with a subsequent higher possibility of false positive results in larger groups especially in patients having variably healed metastatic lesions.

Concordant and Discordant PET and CT findings:

Lesions presenting on PET/CT as sites of increased uptake with normal CT findings (showing neither benign nor malignant changes) were categorized on PET/CT interpretation as inconclusive [11] .

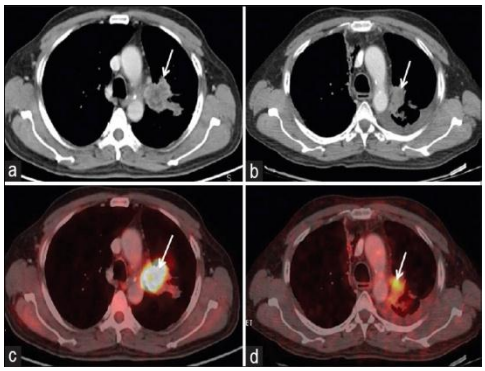

Figure 7: shows Concordance on metabolic and morphological imaging. There is significant reduction in size (1a and, b - arrow) and metabolic activity (max SUV) (1c, and d - arrow) seen on both axial CT component and axial fused PET/CT component, respectively; thus, partial response (PR) on ResponseEvaluation Criteria in Solid Tumor (RECIST) is concordant with partial metabolic response (PMR), according to European Organization for Research and Treatment of Cancer (EORTC) criteria [12].

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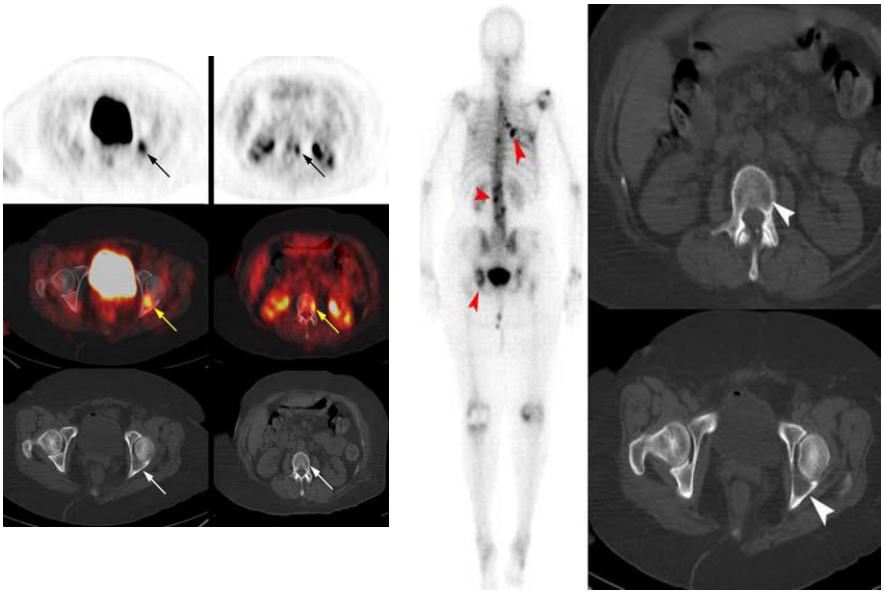

Figure 8: shows Discordant PET/CT findings (true-positive at PET, false-negative at CT) in 72 year old woman referred for lung cancer staging. (A) Transverse PET (top), PET/CT (middle), and CT (bottom) scans show acetabular and spinal metastases identified with PET (black and yellow arrows) that were initially interpreted as negative with CT (white arrows). (B) Follow up bone scan (left) and CT scans (right) obtained 6 weeks later. Posterior planar bone scan helps confirm multiple metastatic foci in the ribs, spine, and pelvis (red arrowheads). Transverse CT scans help confirm lytic metastases in the spine and acetabulum (white arrowheads) [10] .

It was reported the PET and CT interpretations were discordant in 58% of all lesions .This poses a relatively frequent diagnostic dilemma when interpreting these examinations and proved to be a large impetus for deeper analysis of these discordant examinations [10] .

The Positive Predictive Value (PPV) of integrated PET/CT imaging in the evaluation of bone malignancy is very high (98%) when the two portions of the examination are in agreement. However, the PET and CT examinations appear to have discordant findings relatively frequently. When the examinations are discordant, PET is far more accurate than CT in the characterization of bone lesions but is clearly not as accurate as when the two examinations are concordant [10] .

Furthermore, in patients with solitary bone lesions for which the PET and CT findings are discordant, the PPV for integrated PET/CT is even lower (43%) than that in patients with multiple lesions. Thus, an additional adjunctive examination (e.g., MR imaging or biopsy) may be necessary [10] .

Advantages of PET/CT over PET

Image Acquisition :

PET/CT reduces image acquisition times, resulting in patient increased throughput. Conventional PET employs transmission images for photon attenuation correction using an external radiation source. Completion of the transmission scan requires 3–4 min per bed position and thus up to 30 min for whole-body PET studies. PET emission data traditionally have been acquired for 4 min per bed position. Thus, a conventional whole-body PET scan covering 6–8 bed positions requires about 1 h for completion. PET/CT imaging differs in that it utilizes whole-body CT data for attenuation correction. Depending on the number of CT detectors used, attenuation correction is achieved within seconds to slightly >1 min. Thus, the whole-body imaging time is reduced by 50%. With 3-dimensional imaging and lutetium oxyorthosilicate detectors, image acquisition times can be further shortened to <10 min in some patients [13].

Tumor staging and restaging:

Numerous abstracts but few peer-reviewed and published research studies have examined the incremental value of PET/CT over PET alone for staging and restaging of cancer. Preliminary data suggest significant increments in diagnostic and staging accuracy, significant reductions in the number of false-positive and false-negative findings, and an increased reader confidence in PET findings [14] .

Improved lesion localization:

PET/CT facilitates the precise localization of molecular alterations of cancer tissue, which is difficult if not impossible with PET alone. For example, the level of meditational lymph node involvement in lung cancer patients cannot be determined reliably with PET alone. Appropriate localization of hyper metabolic foci to chest wall versus lung, base of the lung versus liver, neck versus superior mediastinum, and in other areas may significantly affect patient management. Judging from our own experience, accurate lesion localization with PET/CT also reduces the number of false-positive and false-negative PET findings [15] .

CONCLUSION

In combined PET/CT, CT images significantly improve PET specificity with better localization of bone metastases and differentiation between benign and malignant lesions. On the other hand, PET can detect bone marrow based metastases early and in the absence of morphologic changes on CT images; thereby improving CT sensitivity. The influence of the integration of PET and CT upon CT specificity is also notable in cases of treated healed metastases which lack metabolic activity in spite of suspicious morphologic appearance.

The estimated fused PET/CT sensitivities and specificities in our study population ranged from 95.2% to 99.6% and from75% to 100%, respectively. The fused PET/CT sensitivities were higher than or equal to PET sensitivities but they were much higher than CT sensitivities especially in the lymphoma groups. The fused PET/CT specificities also showed variably higher values compared to PET and CT, emphasizing the important role of combined

PET/CT in detection and characterization of bone lesions in cancer patients.

Even in false negative cases, FDG PET/CT could detect further unknown metastatic lesions that modifying the disease stage in 40% with positive impact on patients management.

FDG PET/CT is a single modality that has several practical advantages for early detection of bone metastases sites in various primary malignancies compared to multiple investigations. This facilitates early selection of appropriate treatment protocols that will improve patients prognosis

According to our analysis, we used SUV max 3 as a cut off value for malignant osseous lesions. However, it should be used with caution in some limited confusing cases.

(18)F-FDG-PET/CT has the advantage of detecting unknown primary cancers and visceral metastases besides bone metastases.

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