A COMPARATIVE STUDY BETWEEN 18F-FDG-PET/CT AND 99M TC-MDP BONE SCAN IN THE DIAGNOSIS OF METASTATIC BONE LESION IN CANCER PATIENTS

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ABSTRACT

Background: The rate at which bone metastases occur in the general population is unknown. The most reliable method of detection bone metastases in cancer cases is planar ^{99m}Tc-MDP-bone scintigraphy. It has been documented that ^{18}F-FDG-PET/CT is a sensitive instrument for tumor staging in a variety of malignant disorders.

Aim and objectives: to evaluate the comparison Between ^{18}F-FDG-PET/CT And ^{99m} Tc-MDP Bone Scan in The Diagnosis of Metastatic Bone Lesion in Cancer Patients.

Subjects and methods: This prospective study was conducted on 87 adult patients with a biopsy proven primary tumor. Patients were referred to nuclear medicine unit in Maadi Armed Forces medical compound from February 2018 June 2019.

Results: Average age of our group was 52 years (range 27-82) with female predominance (49 female & 38 male patients). The pelvis has the highest number metastatic lesions in 42 out of 103 lesions (40.7%), the spine and ribs have highest number of benign lesions. ^{18}F-FDG PET/CT was better for detection metastatic lesions in the skull, sternum, ribs and spine regions. PET/CT outperformed bone scans in sensitivity, specificity, PPV, NPV, and accuracy.

Conclusion: Cancer patients typically have a ^{99m} Tc-MDP bone scan to identify bone metastases. When it comes to detecting metastatic lesions, particularly those in the bone, ^{18}F-FDG-PET/CT is an extremely sensitive method for tumor staging across a wide range of malignant disorders. Bone scans and PET/CT imaging with ^{18}F-FDG are used together to detect metastatic lesions, such as lytic or osteoblastic ones.

Keywords: 18F-FDG-PET/CT, Tc-MDP Bone Scan, Metastasis, Cancer.

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INTRODUCTION

In fact, behind the lungs and the liver, bone is a typical example of distant metastatic sites **[1].** The prognosis of the disease and the case's quality of life are profoundly affected by the discovery of bone metastases **[2].**

The gold standard for detecting bone metastases in those with cancer is planar ^{99m}Tc-MDP-bone scintigraphy. It has been documented that ^{18}F-FDG-PET/CT is a sensitive instrument for tumor staging in a variety of malignant disorders. However, it has not been contrasted with bone scintigraphy in terms of how well it detects bone metastases **[3].**

Metastatic illness to the skeleton can be detected with the help of a bone scan and 18F-FDG-PET/CT **[4].**

For the identification of bone metastases, ^{18}F-FDG-PET/CT may one day replace ^{99m} Tc-MDP bone scan **[5].**

This study's goals were to determine the relative cost-effectiveness of bone scans contrasted with 18F-FDG-PET/CT for the assessment and treatment of cancer cases, to contrast the diagnostic value of ^{18}F-FDG-PET/CT with the purpose of detecting osteoblastic versus osteolytic osseous deposits, and evaluation of diagnostic utility of ^{18}F-FDG-PET/CT with the purpose of detecting osteoblastic versus osteolytic osseous deposits.

PATIENTS AND METHODS

This prospective research involved 87 cases assigned to the Department of Nuclear Medicine at Maadi Armed Forces Medical

Compound with evidence of confirmed cancer among February 2017 and June 2019. The Oncology and NM department's ethics committee at Cairo University's Faculty of Medicine gave its stamp of approval to the study's protocol .

In consultation with the referring physicians, we retrieved all relevant clinical and histological data from the patient's clinical sheet. Information such as pathological findings, test results & the present rationale for referring you for FDG-PET/CT were all recorded.

Inclusion criteria: Histopathological confirmation of a malignant diagnosis, High-risk patients with clinical suspicion of metastatic bone lesions and all study-related procedures require the patient's written informed permission, and patients must be above the age of 18 to participate.

Cases with high tumor markers, inconclusive CT/MRI results, or a positive bone scan were all enrolled in the PET/CT analysis of metastatic cancer to the bone.

FDG-PET/CT studies were done shortly following appearance of osseous lesions in skeletal scanning in a period not exceeding two weeks and Comparison with other modalities; diagnostic CT/MRI were done whenever possible.

Methodology and data collection

Data was collected for all patients in the department's clinic and completed on the day of the scan.

Technique Of Whole-Body PET/CT Imaging with ^{18}F-FDG: Case Preparation, Dosage Administration, Case position and acquisition and Imaging interpretations.

As regards the analysis of the pathological findings: After defining concordant positive lesions as those with confirmed disease involvement in both PET and CT tests, they were contrasted with results from other methods of diagnosis. Whenever possible, by other imaging modality (magnetic resonance [MR] imaging, and X-ray) or by bone biopsy and Concordant negative lesions if no lesions detected by PET and CT studies.

Technique Of Bone Scan Imaging with 99mTc-MDP: Physician Directive, Dosage Administration, Patient position and acquisition and Images interpretation.

Standard of reference (evidence of metastatic): Suggestive of metastatic osseous lesions by laboratory evidence such as elevated tumor marked and/or radiological evidence in the form of positive findings in CT and or MRI.

Comparison of bone scanning and PET/CT

Analysis of both images for different bone lesions: Positive lesions: in both bone scan and PET/CT is considered as positive for metastatic lesions, Negative lesions: if both skeletal scanning had no evidence of any lesions, False positive lesions: if bone scan showed lesions seen only in CT part of PET/CT as degenerative or traumatic lesions and False negative lesions: if bone scan was negative and positive lesions are seen in PET or PET/CT images.

Statistical analysis

Data that had already been pre-coded were subsequently entered into the statistical analysis tool known as the Statistical Package of Social Science Software, version 21 (SPSS). Upon further clinical and imaging confirmation, true-positive (TP), true-negative (TN), false-positive (FP), and false-negative (FN) findings were found. The sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were the diagnostic performance characteristics that were determined.The nonparametric McNemar test was utilized in order to examine the statistical significance of the variations in sensitivity and specificity (a two-sided P value of less than 0.05 was regarded significance).

RESULTS

Table (1): Distribution of age and sex in 87 cases with possible metastatic lesions.

	No.	%
Sex		
Male	38	43.7
Female	49	56.3
Age (years)		
≤50	41	47.1
>50	46	52.9
Min. – Max.	27.0 – 82.0	
Mean ± SD.	52.55 ± 12.16	
Median	52.0	

Median age of our group was 52 years (range 27-82) with female predominance (49 female & 38 male patients).

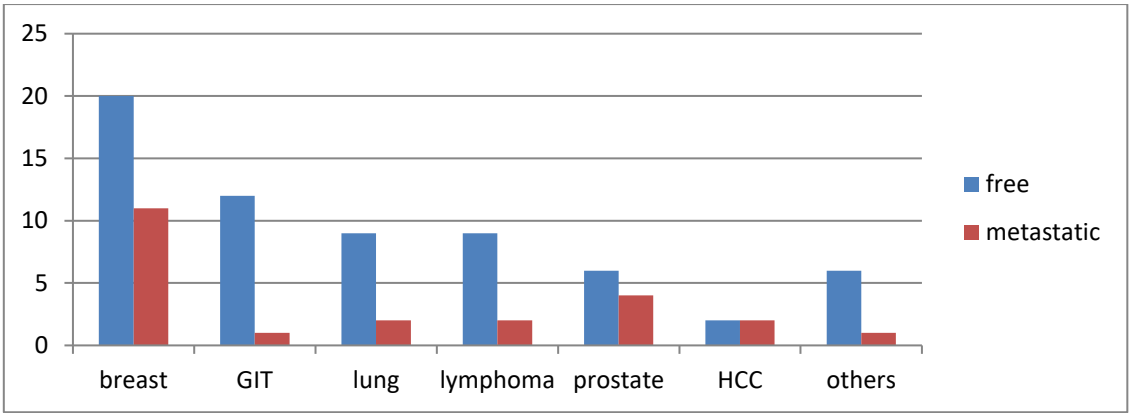

Figure 1: Prevalence of bone metastases among different pathologies in 87 patients with different primary tumors.

Table 2: lesions distribution in different regions of skeletal system by ^{99m}Tc-MDP bone scan.

	Skull	U & L limbs	sternum	Ribs	Spine	Pelvis	Total
Benign	1	3	1	42	55	40	142
Metastatic	5	13	9	18	16	42	103
Total	6	16	10	60	71	82	245

For better assessment of the whole skeleton; the skeleton was divided in 6 regions (skull, upper and lower limbs, sternum, ribs, spine and pelvis). Lesions were grouped in two categories; benign or metastatic. There were 142 benign lesions and 103 metastatic lesions with total number of 245 lesions. The pelvis has the highest number metastatic lesions in 42 out of 103 lesions (40.7%), the spine and ribs have highest number of benign lesions in 55 and 42 lesions (38.7%) and (29.5%)

Table 3: lesions distribution in different regions of skeletal system by 18F-FDG PET/CT scan.

	Skull	U & L limbs	sternum	Ribs	Spine	Pelvis	Total
Benign	4	9	4	49	59	40	165
Metastatic	7	11	13	21	17	34	103
Total	11	20	17	70	76	74	268

Similar to bone scan; the skeleton was also divided into 6 regions; every detected lesion in ^{18}F-FDG PET/CT was categorized to either benign or metastatic. There were 165 benign lesions and 103 metastatic lesions with total 268 lesions. The pelvis has the highest number metastatic lesions (34 out of 103 lesions) (33%); the spine and ribs have highest number of benign lesions (59 and 49 sites) (35.7%) and (29.6%) respectively.

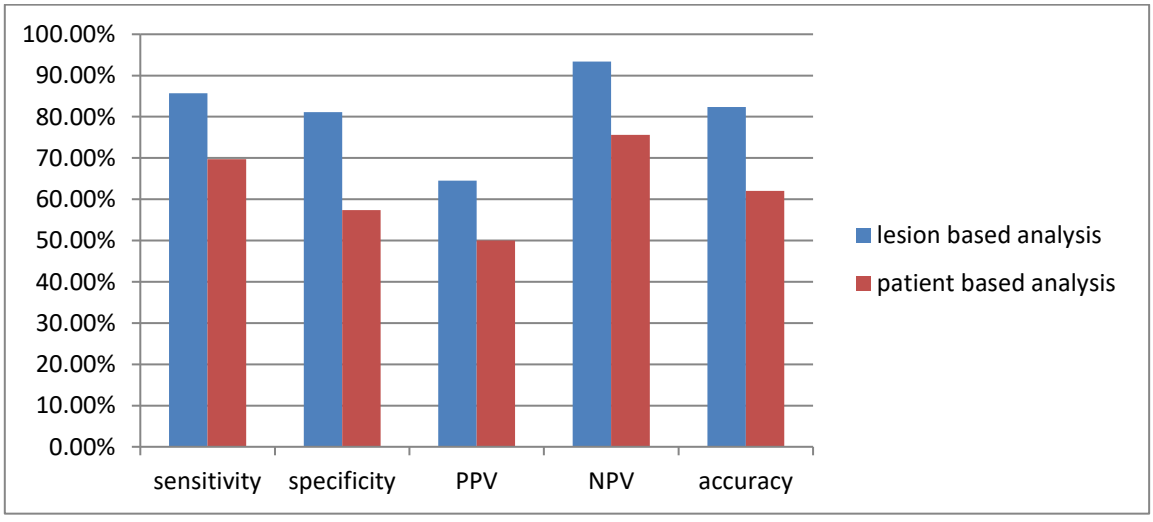

Figure 2: sensitivity, specificity, PPV, NPV and accuracy of bone scanning using lesion and patient-based analysis.

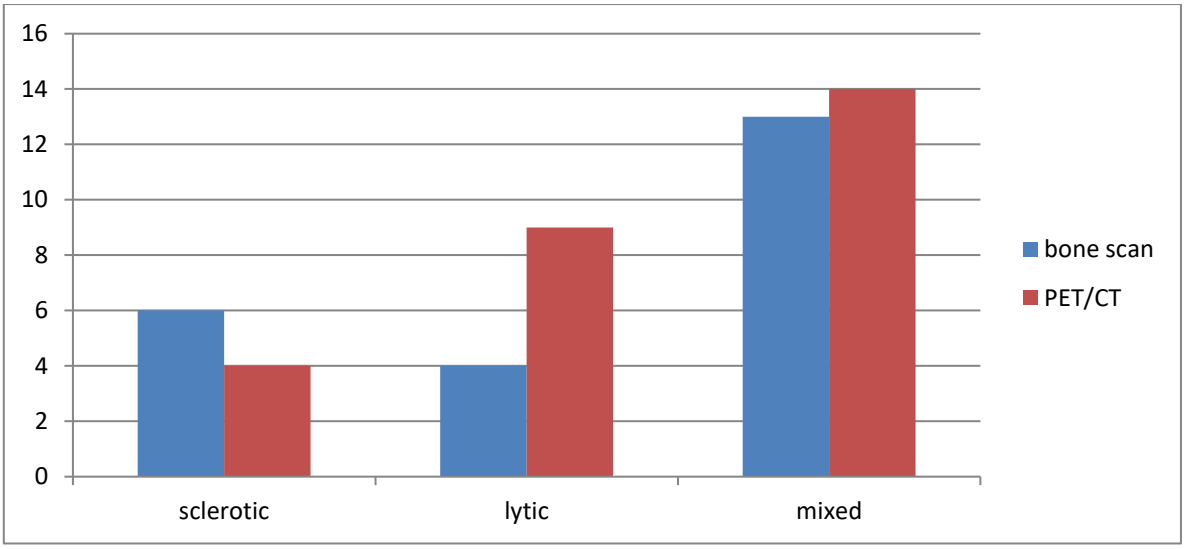

Figure 3: prevalence of true bone deposits with different primary malignancies based on their predominating bone deposits nature.

Table 4: metastatic lesions characterization by ^{99m}Tc-MDP bone scan & ^{18}F-FDG PET/CT scan:

	Skull	U & L limbs	sternum	Ribs	Spine	Pelvis	Total
Bone scan	5	13	9	18	16	42	103
PET/CT	7	11	13	21	17	34	103
Total	12	24	22	39	33	76	206

^{18}F-FDG PET/CT improved detection metastatic lesions in the skull, sternum, ribs and spine regions {7 out of 12 lesions (58.3%), 13 out of 22 lesions (59%), 21 out of 39 lesions (53.8%) and 17 out of 33 lesions (51.5%) respectively}. While the ^{99m}Tc-MDP bone scan improved detection metastatic lesions in upper & lower limbs as well as pelvic regions {13 out of 24 lesions (54.1%) and 42 out of 76 lesions (55.2%) respectively}.

Table 5: benign lesions characterization by 99mTc-MDP bone scan & ^{18}F-FDG PET/CT scan:

	Skull	U & L limbs	sternum	Ribs	Spine	Pelvis	Total
Bone scan	1	3	1	42	55	40	142
PET/CT	4	9	4	49	59	40	165
Total	5	12	5	91	114	80	307

^{18}F-FDG PET/CT and the 99mTc-MDP bone scan were equal in detecting benign lesions in pelvic regions in 40 sites (50%), while ^{18}F-FDG PET/CT improved detection benign lesions in the other regions; skull, upper & lower limbs, sternum, ribs and spine regions {4 out of 5 lesions (80%), 9 out of 12 lesions (75%), 4 out of 5 lesions (80%), 49 out of 91 lesions (53.8%) and 59 out of 114 lesions (51.7%) respectively}

Table (6): sensitivity, specificity, PPV, NPV and accuracy of PET/CT and bone scan

	Sensitivity	Specificity	PPV	NPV	Accuracy
PET/CT	96.4%	84.7%	75%	98%	88.5%
Bone scan	69.7%	57.4%	50%	75.6%	62%

The accuracy, PPV, NPV, sensitivity, and specificity were greater in PET/CT than in bone scan (96.4%, 84.7%, 75%, 98% and 88.5% versus 69.7%, 57.4%, 50%, 75.6% and 62% respectively).

CASE PRESENTATION

Case No. (1)

History:

37-year-old woman, had left breast cancer that had not been surgically removed. **Initial assessment:**

1. **^{99m}Tc-MDP Bone scan:**

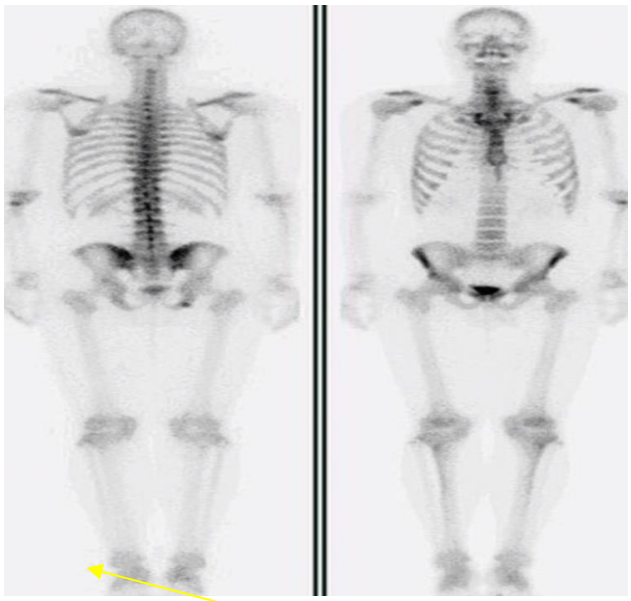

Figure 4: ^{99m}Tc-MDP bone scan for a case with left breast cancer; solitary right ischial osseous deposit.

^{18}F-FDG PET/CT results:

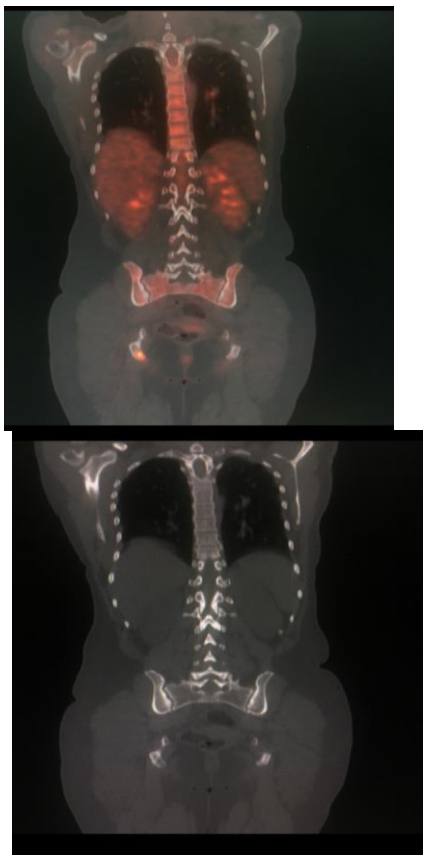

Figure 5: ^{18}F-FDG PET/CT shows FDG uptake at the right ischial bone agreeing with osteolytic lesion in CT cuts; positive for metastatic osseous deposits.

Comment:

This is patient with left breast cancer with solitary osseous metastases detected in both ^{99m}Tc-MDP bone scan & ^{18}F-FDG PET/CT.

Case No. (2)

History:

Prostate cancer was diagnosed in a 65-year-old male patient.

Initial assessment:

1. **^{99m}Tc-MDP Bone scan:**

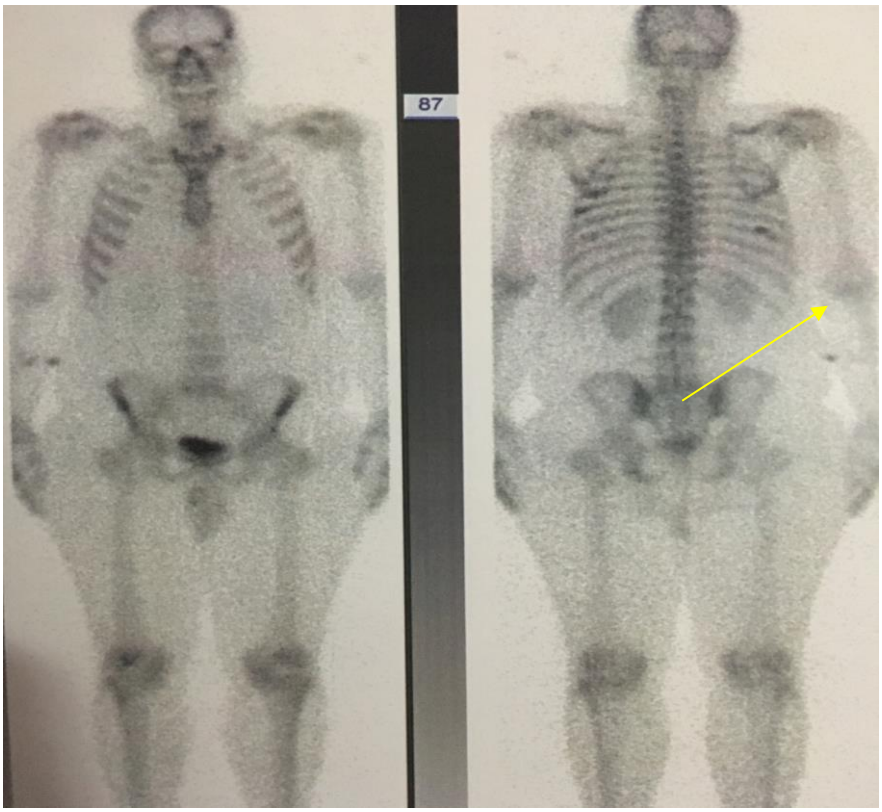

Figure 6: ^{99m}Tc-MDP bone scan for a case with left breast cancer; solitary right 8th rib osseous deposit.

^{18}F-FDG PET/CT results:

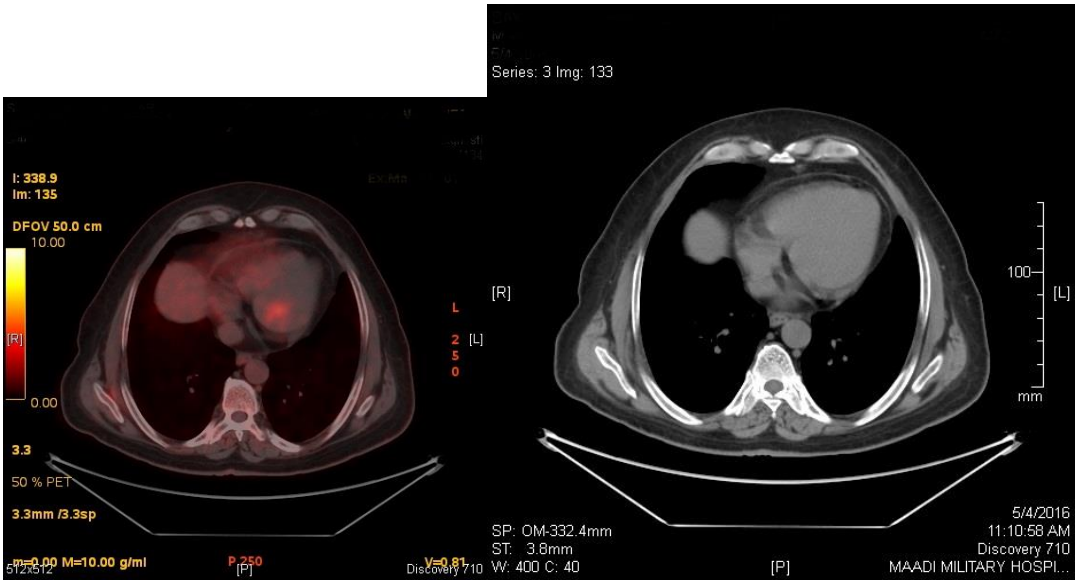

Figure 7: ^{18}F-FDG PET/CT shows normal FDG uptake seen in PET part of study.

Comment:

This is patient with prostatic cancer; solitary traumatic right 8th rib lesion detected in ^{99m}Tc-MDP bone scan & negative ^{18}F-FDG PET.

DISCUSSION

Despite the rarity of primary bone malignancies, metastases from malignant neoplasms are quite common. Bone is the principal location of distant metastasis from primary breast cancer and the third

most frequent organ impacted by metastasis overall. Skeletal metastasis must be detected as soon as possible so that it may be properly staged and treated **[6].**

Macedo et al. found that the frequency of bone metastases is unknown in the general population. Nevertheless, in cases with advanced metastatic illness, the relative frequency of bone metastasis varies widely depending on tumor type, ranging from 65 to 75 percent in breast cancer to 65 to 75 percent in prostate cancer to 60 percent in thyroid cancer to 30 percent in the lungs to 40 percent in the bladder to 20 percent in renal cell carcinoma to 14 percent in melanoma **[7].**

In the present study, the incidence of bone metastases differs according to primary pathological type; 35.6% in breast cancer, 13.8% for GIT and 12.6% in lung cancer. Such difference in incidence is related to being selected group of patients referred for metastatic evaluation.

Cheng et.al. performed meta-analysis in 2011 by reviewing literatures from 2000 to 2010 to assess the sensitivity of ^{99m}Tc-MDP bone scan during detection osseous metastases compared to other modalities. Bone scans had a sensitivity of 70.6% and a specificity of 91.1% for detecting osseous metastases in lung cancer (1340 cases) and other malignancies for which researches were involved in the meta-analysis **[8]**.

In our study, although the sensitivity of the ^{99m}Tc-MDP bone scan was 69.7% and the specificity was 57.4% in patients-based analysis, higher results were seen in lesion-based analysis similar to previous study 85.7% and 81.1 %.

Gurkan et al, reported that Bone metastases distribution comprised the pelvis (24.1 percent), the lower thoracic spine (17.9 percent), the lumbar spine (16.6 percent), the ribs and sternum (10.3 percent), the lower limbs (9.7 percent), the upper thoracic spine (7.6 percent), the upper limbs (4.8 percent , and other regions (9 percent) **[9]**.

In the present study, the sum of all tumors found by the ^{99m} Tc-MDP bone scan was 245 lesions including; 162 lesions considered as negative for metastases 10 lesions of them proved later to be false negative (in the follow up ^{99m} Tc-MDP bone scan) & the remaining 142 lesions proved to be true negative (57.9%). While 93 lesions considered as positive for metastases 33 lesions of them proved later to be FP as proved to be fracture or trauma and the remaining 60 lesions proved to be TP (24.5%).

In this study, the sum of all tumors found by the ^{18}F-FDG PET/CT was 268 lesions including; 170 lesions regarded as negative for metastases 5 lesions of them proved later to be false negative (in the follow up ^{18}F-FDG PET/CT) and the remaining 165 lesions proved to be true negative (61.5%); while 85 lesions considered as positive for metastases 13 lesions proved to be FP (being of traumatic or fracture) and the remaining 85 lesions proved to be TP (31.7%).

Wang et al. stated similar findings in 135 lesions that were discovered by ^{18}F-FDG-PET/CT and the whole-body ^{99m} Tc-MDP bone scan; 121 lesions were proven to be metastatic and 14 were benign. Compared to a full body ^{99m} Tc-MDP bone scan, the ^{18}F-FDG-PET/CT has a statistically significant advantage in terms of diagnostic efficacy. The sensitivity of 18F-FDG-PET/CT was 95 percent (38/40), 90 percent (36/40), and 100% (25/25) for the diagnosis of osteolytic, osteoblastic, and mixed metastatic tumors; the sensitivity of ^{99m} Tc-MDP bone scan was 100% (12/12), 100% (12/12), and 79.55 percent (35/44) for the diagnosis of osteolytic, osteoblastic & mixed metastatic tumors **[10]**.

In our investigation, there was significant difference in the prevalence of metastatic osseous deposits among the different pathological categories. The primary tumors that have mixed osseous deposits have the highest prevalence of osseous metastases among their group (56.6% in bone scan compared to 51.8% PET/CT), the primary tumors that have sclerotic pattern was higher in bone scan than in PET/CT (26% compared to 14.8% respectively) while the primary tumors that have lytic pattern of osseous metastases was higher in PET/CT in 33.3% as compared to 17.4% in bone scan.

Fox et al. also reported that ^{18}F-FDG-PET/CT was TP in 18/19 cases and equivocal (EQ) in 1/19. Results from ^{99m} Tc-MDP bone scans were positive in 6/19 cases, equivocal in 5/19 cases, and negative in 8/19 individuals. There were no more lesions found with the ^{99m} Tc-MDP bone scan compared to the ^{18}F-FDG-PET/CT. Companion CT showed either no abnormalities (13/18) or osteolytic lesions (5/18) for ^{18}F-FDG-PET/CT lesions classified as TP **[11].**

We observed that the ^{18}F-FDG-PET/CT is more effective than the ^{99m} Tc-MDP bone scan. ^{18}F-FDG-PET/CT had a better sensitivity, specificity, PPV, NPV, and overall accuracy than ^{99m} Tc-MDP bone scan (96.4%, 84.7%, 75%, 98%, and 88.5% vs. 69.7%, 57.4%, 50%, 75.6%, and 62%).

Furthermore, Tanaka et al. contrasted ^{99m} Tc-MDP bone scan to ^{18}F-FDG-PET/CT in evaluating skeletal metastases in 51 cases with breast cancer & showed that the ^{99m} Tc-MDP bone scan had a sensitivity of 77.7%, a specificity of 80.9% & an accuracy of 80.3%. 18F-FDG-PET/CT had corresponding findings of 77.7%, 97.6%, and 94.1% for the identification of bone metastases. There was a statistically significant variance in specificity **[12].** bone scan. When it comes to detecting metastatic lesions, particularly those in the bone, ^{18}F-FDG-PET/CT is an extremely sensitive method for tumor staging across a wide range of malignant disorders.

CONCLUSION

The identification of bone metastases in cancer patients is routinely accomplished by a ^{99m} Tc-MDP

Metastasis of several forms, such as lytic or osteoblastic lesions, can be detected with a combined ^{18}F-FDG-PET/CT and bone scan.

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