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# Diagnostic Value of Whole-Body Diffusion Magnetic Resonance Imaging (WBD-MRI) in Comparison with PET/CT in Assessment of Multiple Myeloma and Bone Metastasis

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## ABSTRACT

**Background:** Diffusion weighted imaging-Magnetic Resonance Imaging (DWI-MRI) is a functional MRI technique measuring movement of water molecules within tissue. While positron emission tomography computed tomography (PET/CT) is a functional imaging modality reflecting metabolic activity, increase uptake of the radiotracer 18F-fluorodeoxyglucose (FDG) is indicative of viable bone marrow lesion of myeloma and bone metastasis. The aim of this work was to assess diagnostic value of whole-body diffusion (WBD) MRI in comparison to FDG PET/CT in detection diffuse and focal bone marrow involvement of multiple myeloma (MM), as well as bone metastasis.

**Methods:** This prospective study was carried out on 62 patients, 38 patients with MM confirmed by bone marrow aspiration and 24 primary malignancy and metastatic bony lesions.

**Results:** PET/CT can predict MM in skull, thoracic cage, pelvis, spine and long bone respectively (P= 1, 1, 0.625, 1 and 1) with sensitivity 60%, 75%, 66.7%, 85.7% and 66.7%, specificity 66.7%, 66.7%, 66.7%, 66.7% and 50%. In comparison between PET/CT and MRI- WBD, MRI-WBD is better than PET/CT in detection of MM bone marrow lesions and metastatic bony lesions with sensitivity, accuracy, negative and positive predictive value, but have the same specificity.

**Conclusions:** Whole body MRI-DWI and apparent diffusion coefficient values significantly improve the diagnostic accuracy in detection of MM bone marrow lesions and bone metastatic lesions, with relatively higher sensitivity and accuracy than PET/CT study. WBD-MRI seems to be a promising method of imaging in the detection of MM and bone metastasis. Standardization of these protocols is needed.

**Keywords:** *Magnetic Resonance Imaging, Positron Emission Tomography–Computed Tomography, Multiple Myeloma, Bone Metastasis.*

## INTRODUCTION

Multiple myeloma (MM) is the second most common hematologic malignancy in adults, after lymphoma. MM arises from the clonal proliferation of plasma cells, which primarily infiltrate the bone marrow, resulting in widespread lytic lesions in bones but sometimes also clinically presented in the extra-medullary soft tissues [1, 2].

Bone involvement is one of the most prominent features of MM, and imaging has an increasingly important role in the diagnosis, initial staging, and follow-up of MM patients. Other major clinical manifestations may be presented, as chronic anemia, hypercalcemia, proteinuria and renal failure [3].

In routine clinical evaluation, bone marrow aspiration and serum markers are usually used to assess the tumor burden of MM. Serum markers sometimes are not suitable in certain patients with MM, such as patients presented with non-secretory or hyposecretory MM [4].

Conventional skeletal survey was historically used for assessment of bone lesions in patients with MM, due to low costs and widespread availability [5].

Whole-body-MRI is the most sensitive technique for the detection of bone marrow involvement, either diffuse or focal infiltration, before the mineral bone is destroyed [6].

The use of functional MRI sequences further improved the performances of whole-body MRI in the setting of MM. Whole-body diffusion (WBD)-weighted (DW) MRI is the most attractive functional technique and was shown to be superior to positron emission tomography–computed tomography (PET/CT) for bone marrow involvement [7].

Bone metastases produce pain and pathological fractures. Bone metastases are detectable in patients with advanced stages

of breast, prostate, lung, and thyroid cancer [8].

The most useful imaging techniques for the detection of bone metastatic lesions were bone scintigraphy, contrast enhanced CT and 18F- fluorodeoxyglucose (FDG) PET/CT [9].
DW imaging (DWI) is based on the evaluation of microscopic movements of water at the cellular level, providing quantitative such as apparent diffusion coefficient (ADC) band qualitative as signal intensity information, which can be used to distinguish benign from malignant disorders [10].
As well as 18F-FDG PET/CT has gradually become universally available for imaging of suspected bone lesions [11].
The aim of this work was to assess diagnostic value of WBD- MRI in comparison to FDG PET/CT in detection diffuse and focal bone marrow involvement of MM, as well as bone metastasis.

## Patients and Methods:

This prospective study was carried out on 62 patients, 38 patients with MM confirmed by bone marrow aspiration and 24 patients with primary malignancy and metastatic bony lesions. The study was done after approval from the Ethical Committee Tanta University Hospitals, Tanta, Egypt. An informed written consent was obtained from the patients.
Exclusion criteria were WBD MRI: patient with contraindication to MRI examination like patients with any metallic prosthesis or artificial pacemakers and PET/CT: patients with impaired renal function, uncontrolled diabetes mellitus, pregnant and lactating females.
All patients were subjected to complete history taking, clinical examinations, positron emission tomography–computed tomography (PET/CT) and whole-body DWI examination.

### Whole-Body diffusion-weighted imaging Examination:

It was performed using 1.5-Tesla MRI (Siemens) machine. Images are acquired using the integrated body coils and acquired in the coronal plane. By the combination of the moving tabletop, table extender and image-melding software the scan can time is about 25–35 min and total exam time is about 45 min, including patient positioning and survey acquisition.

All patients were prepared by asking patients for presence or absence of cardiac pacemakers, any neurosurgical clips, embedded metal fragments, dental prosthesis. Asking patients to change clothes if having any metallic objects including breast holders, belts or jewels. Informing patients about the knocking sound that is heard during the examination, the relatively longer time of MR examination and instructed to be motion less. Patients were placed in a supine position (the patient head towards the tube) with their arms placed by the sides of the body, and coil elements were positioned from the skull vertex to the knees. Positioning of the upper extremities is dictated by patient habit. In cachectic patients, the arms are easily placed over the thorax and abdomen. In larger patients, the arms are placed above the head, requiring an additional coronal acquisition and an additional 4 min scan time. To cover the whole longitudinal region of interest using the built-in circularly polarized body coil as the patient table entered the magnet and the system-integrated body coil was used with basic adjustment settings provided by the system, or images may be also acquired with multiple array coils that consisted of head coil, body coils, spine coils, and a leg coil. At first three-plane localizer scout view were performed for the region of interest. Pulse sequences used in image acquisition are:

**Whole-body MRI using T1 sequence:**

Whole-body coronal non-fat saturated TIWI in the previous described sites with the following parameters: TR= 400 ms; TE =4 ms; slice thickness, 6= mm; FOV=,300-360 mm and matrix= 256x256.

**Whole-body MRI using STIR sequence**:

Coronal or sagittal STIR images were obtained for the whole body in the previous described sites with the following parameters: TR=3000-5000 ms; TE=70 ms; TI=165 ms; slice thickness= 6mm; FOV = 300-360 mm and matrix = 256x256.

**Diffusion-weighted whole-body imaging background body signal suppression (DWIBS):**

It is performed using the EPI DW technique with a high b value for background suppression. Mostly, using 2 b -values (first between 50–100 s/mm $^2$ and second between 800– 900 s/mm$^2$). Signals from normal tissue such as blood vessels, fat, muscle, and bowel are suppressed. However, other normal structures such as the spleen, prostate, testes, ovaries, endometrium, and spinal cord remain visible.

**Post-imaging processing and image analysis:**

Post processing and interpretation Images of each sequence of body regions (T1, STIR and DWIBS sequences) are then realigned to produce whole-body images using the dedicated software to facilitate instant review at the workstations. Interpretation is done by scrolling through the images at the workstation. Images are well analyzed searching for any soft tissue or bone marrow pathological changes. On visual analysis of the primary lesion on an MRI image, each site of abnormal or focal increase of DWIBS signal intensity not from normal anatomical structure or with unexpected increase of signal intensity was considered as positive findings, such as MM lesion or metastatic deposits.

**Positron emission tomography–computed tomography (PET/CT) examination**

Limited Carbohydrate diet for the previous 24 hours before the examination. Do not eat or drink anything, except water, for 6 hrs before the examination. Avoid strong activity 24 hours prior to imaging. Routine medications may be taken, in diabetic patient, should take their medication (Blood glucose levels confirmed to be < 160 mg/dl). Minimize exposure to cold temperature to avoid brown fat uptake. In additional contrast injection in some situations, should evaluate renal functional test.

PET/CT was performed using Philips 16PET/CT machine. All patients underwent imaging while in the supine position with arms above the head or arms by the sides of the body. The whole-body examinations take nearly about 20 minutes. The patient is intravenously injected with 18F-FDG. The typical dose of FDG is 8-15 mCi injected intravenously. Then, patients will rest for a period of about 60 min in comfortable chair and will be instructed to minimize any talking, chewing, swallowing, or movement of the head to reduce skeletal muscle uptake.

Patients undergo catheterization if necessary, or they void just before being positioned on the PET-CT table. They are positioned either with the arms above the head or with the arms at the side. Except for patients being studied for head and neck cancer, arms above the head are the preferred position to decrease beam-hardening artifact during the CT portion of the examination.

**Positron emission tomography interpretation**

Pitfalls of PET/CT: Physiologic activity, reflecting normal glucose metabolism. Inflammatory processes in many locations are metabolically active, take up FDG. Low Uptake by Malignant Tumors: A number of malignant lesions show low FDG activity and may be missed on PET scans as lobular carcinoma of the breast, low-grade lymphoma, salivary gland neoplasms, and extensively necrotic primary tumors and lymph nodes. Benign tumors may also concentrate FDG. Recent Surgery: FDG accumulates in surgical healing sites; this is related to increased metabolism and the inflammation associated with tissue repair. Fractures demonstrate FDG hyperactivity for weeks while fracture healing occurs. Uptake is related to hematoma resorption, presence of granulation tissue, callous formation, and growth of new bone. Correlation with CT reviewed on bone windows is usually diagnostic. Osteophytes develop in the vertebral column and from joints.

**Sample size:**

The sample size calculation was performed using EpI-Info 2002 software statistical package designed by World Health Organization (WHO) and by Centers for Disease Control and Prevention (CDC). The sample size was calculated based on the following considerations: 95% confidence level and PET sensitivity was 59 % according to a previous study [12] ± 13% confidence limit. Seven cases were added overcome dropout. Therefore, we will recruit 62 cases.

**Statistical analysis**

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD). Qualitative variables were presented as frequency and percentage (%). ROC curve was used for evaluation of diagnostic performance sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

## Results:

This prospective study was carried out on 62 patients, 38 patients with MM confirmed by bone marrow aspiration and 24 patients with primary malignancy and metastatic bony lesions.

Our studied 62 patients are classified in to two groups: the first group was patients had multiple myeloma 38 (61%) and the second group was patients with metastatic bony lesions 24 (39%).

The first group (patients with multiple myeloma) included 38 patients; their ages ranged from 55 to 70 years with a mean of 62 years. There were 28 male & 10 females.

Demographic data, clinical presentation and site and number of MM lesions in both modalities were presented in this table. **Table 1.**

**Table 1: Demographic data, clinical presentation and site and number of MM lesions in both modalities of the studied 38 patients**

| | | |
|---|---|---|
| ➢ | | **N= 38 patients** ➢ |
| **Age (years)** ➢ | | 61 ± 6.49 ➢ |
| **Sex** ➢ | **Male** ➢ | 28 (73.68%) ➢ |
| | **Female** ➢ | 10 (26.3%) ➢ |
| **Clinical presentation** ➢ | **Bone ache** ➢ | 20 (52.63%) ➢ |
| | **Pathological fracture** ➢ | 15 (39.47%) ➢ |
| | **Anemia** ➢ | 15 (39.47%) ➢ |

| | | |
|---|---|---|
| | **Proteinuria** ➢ | 8 (21%) ➢ |
| | **Renal failure** ➢ | 12 (31.7%) ➢ |
| **Site of MM** ➢ | **Skull** ➢ | 8 (21.05%) ➢ |
| | **Thoracic cage** ➢ | 7 (18.42%) ➢ |
| | **Pelvis** ➢ | 12 (31.58%) ➢ |
| | **Spine** ➢ | 18 (47.37%) ➢ |
| | **Long bone** ➢ | 5 (13.16%) ➢ |
| ➢ | | **N = 28 patients** ➢ |
| **Focal lesions** ➢ | **Skull** ➢ | 7 (25%) ➢ |
| | **Thoracic cage** ➢ | 5 (17.86%) ➢ |
| | **Long bone** ➢ | 3 (10.71%) ➢ |
| | **Pelvis** ➢ | 11 (39.29%) ➢ |
| | **Spine** ➢ | 14 (50%) ➢ |
| ➢ | | **N = 10 patients** ➢ |
| **Diffuse lesions** ➢ | **Skull** ➢ | 1 (10%) ➢ |
| | **Thoracic cage** ➢ | 2 (20%) ➢ |
| | **Long bone** ➢ | 2 (20%) ➢ |
| | **Pelvis** ➢ | 1 (10%) ➢ |
| | **Spine** ➢ | 4 (40%) ➢ |

Data are presented as mean ± SD or frequency (%). MM: multiple myeloma.

The PET/CT study revealed multiple focal and diffuse bone marrows lesions, in the following sites: 4 bone marrow lesions in the skull (3 focal and 1 diffuse), 4 bone marrow lesions in the thoracic cage (3 focal and 1 diffuse), 7 bone marrow lesions in the pelvis (6 focal and 1 diffuse), 13 bone marrow lesions in the spine (11 focal and 2 diffuse) and 3 bone marrow lesions in the long bones (2 focal and 1 diffuse).
The MRI-WBD study revealed multiple focal and diffuse bone marrows lesions, in the following sites: 5 bone marrow lesions in the skull (4 focal and 1 diffuse), 5 bone marrow lesions in the thoracic cage (4 focal and 1 diffuse), 8 bone marrow lesions in the pelvis (7 focal and 1 diffuse), 14 bone marrow lesions in the spine (12 focal and 2 diffuse) and 3 bone marrow lesions in the long bones (2 focal and 1 diffuse). **Table 2.**

**Table 2: Focal & diffuse bone marrow lesions detected by PET/CT & MRI-WBD in MM**

| **PET/CT Study .1** | | |
|---|---|---|
| **.2** | **Focal bone marrow lesions .3** | **Diffuse bone marrow lesions .4** |
| **Skull .5** | 3 **.6** | 1 **.7** |
| **Thoracic cage .8** | 3 **.9** | 1 **.10** |
| **Pelvis .11** | 6 **.12** | 1 **.13** |
| **Spine .14** | 11 **.15** | 2 **.16** |
| **Long bones .17** | 2 **.18** | 1 **.19** |
| **MRI-WBD .20** | | |
| **Skull .21** | 4 **.22** | 1 **.23** |
| **Thoracic cage .24** | 4 **.25** | 1 **.26** |
| **Pelvis .27** | 7 **.28** | 1 **.29** |
| **Spine .30** | 12 **.31** | 2 **.32** |
| **Long bones .33** | 2 **.34** | 1 **.35** |

Data are presented as number. PET/CT: Positron emission tomography–computed tomography, MRI-WBD: magnetic resonance imaging- whole-body diffusion, MM: multiple myeloma.

PET/CT can predict MM in skull, thoracic cage, pelvis, spine and long bone respectively (P= 1, 1, 0.625, 1 and 1) with sensitivity 60%, 75%, 66.7%, 85.7% and 66.7%, specificity 66.7%, 66.7%, 66.7%, 66.7% and 50%, PPV 75%, 75%,

85.7%, 92.3% and 66.7%, NPV 50%, 66.7%, 40%, 50% and 50%, and accuracy 62.5%, 71.4%, 66.7%, 82.4% and 60%. There was an agreement between PET/CT and biopsy (Kappa= 0.250, 0.270, 0.273, 0.463 and 0.167).
MRI-WBD can predict MM in skull, thoracic cage, spine and long bone respectively (P = 1) with sensitivity 80%, 100%, 77.8%, 92.9% and 66.7%, specificity 66.7%, 66.7%, 66.7%, 66.7% and 50%, PPV 80%, 80%, 87.5%, 92.9% and 66.7%, NPV 66.7%, 100%, 50%, 66.7% and 50% and accuracy 75%, 85.7%, 75%, 88.2% and 60%. There was an agreement between MRI-WBD and biopsy (Kappa= 0.467, 0.696, 0.400, 0.595 and 0.167). **Table 3.**

**Table 3: PET/CT and MRI-WBD prediction of MM in skull, thoracic cage, pelvis, spine and long bone compared to biopsy**

| | | Biopsy | | Kappa | P | Sensitivity | Specificity | PPV | NPV | Accuracy |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Yes | No | | | | | | | |
| **Skull** | | | | | | | | | | |
| **PET/CT** | **Yes** | 3 | 1 | 0.250 | 1 | 60.0% | 66.7% | 75.0% | 50.0% | 62.5% |
| | **No** | 2 | 2 | | | | | | | |
| **MRI-WBD** | **Yes** | 4 | 1 | 0.467 | 1 | 80.0% | 66.7% | 80.0% | 66.7% | 75.0% |
| | **No** | 1 | 2 | | | | | | | |
| **Thoracic Cage** | | | | | | | | | | |
| **PET/CT** | **Yes** | 3 | 1 | 0.270 | 1 | 75.0% | 66.7% | 75.0% | 66.7% | 71.4% |
| | **No** | 1 | 2 | | | | | | | |
| **MRI-WBD** | **Yes** | 4 | 1 | 0.696 | 1 | 100.0% | 66.7% | 80.0% | 100.0 % | 85.7% |
| | **No** | 0 | 2 | | | | | | | |
| **Pelvis** | | | | | | | | | | |
| **PET/CT** | **Yes** | 6 | 1 | 0.273 | 0.625 | 66.7% | 66.7% | 85.7% | 40.0% | 66.7% |
| | **No** | 3 | 2 | | | | | | | |
| **MRI-WBD** | **Yes** | 7 | 1 | 0.400 | 1 | 77.8% | 66.7% | 87.5% | 50.0% | 75.0% |
| | **No** | 2 | 2 | | | | | | | |
| **Spine** | | | | | | | | | | |
| **PET/CT** | **Yes** | 13 | 1 | 0.463 | 1 | 86.6% | 66.7% | 92.8% | 50.0% | 83.3% |
| | **No** | 2 | 2 | | | | | | | |
| **MRI-WBD** | **Yes** | 14 | 1 | 0.595 | 1 | 93.3% | 66.7% | 93.3% | 66.7% | 88.8% |
| | **No** | 1 | 2 | | | | | | | |
| **Long bone** | | | | | | | | | | |
| **PET/CT** | **Yes** | 2 | 1 | 0.167 | 1 | 66.7% | 50.0% | 66.7% | 50.0% | 60.0% |
| | **No** | 1 | 1 | | | | | | | |
| **MRI-WBD** | **Yes** | 2 | 1 | 0.167 | 1 | 66.7% | 50.0% | 66.7% | 50.0% | 60.0% |
| | **No** | 1 | 1 | | | | | | | |

PET/CT: Positron emission tomography–computed tomography, MRI-WBD: magnetic resonance imaging- whole-body diffusion, MM: multiple myeloma, TH: thoracic cage, NPV: negative predictive value, PPV: positive predictive value.

PET/CT and MRI-WBD can predict MM lesions and bone metastasis respectively (P= 0.388 and 1) with sensitivity 69.2% and 84.6%, specificity 66.7% and 66.7%, PPV 81.8% and 84.6%, NPV 50% and 66.7% and accuracy 68.4% and 78.9%. There was an agreement between PET/CT and MRI-WBD and biopsy (Kappa= 0.329 and 0.513). In comparison between PET/CT and MRI-WBD, MRI-WBD is better than PET/CT in detection of MM bone marrow lesions and metastatic bony lesions with sensitivity, accuracy, PPV and NPV, but have the same specificity (AUC of PET/CT = 0.679 and 0.611) (AUC of MRI-WBD = 0.756 and 0.667). **Figure 1**

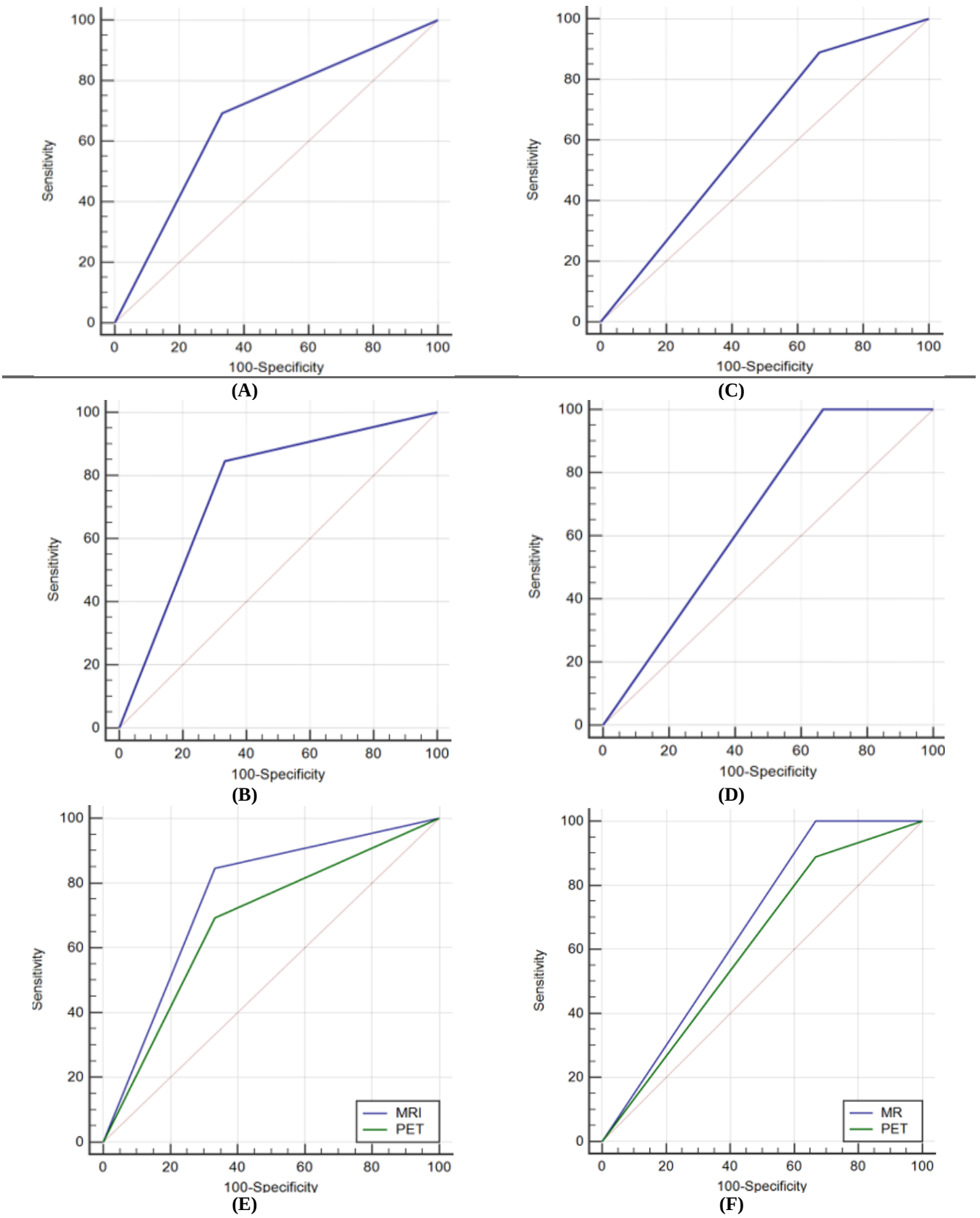


**Figure 1**: ROC curve showing sensitivity and specificity of (A) positron emission tomography–computed tomography and (B) whole-body diffusion magnetic resonance imaging in prediction of multiple myeloma lesions, (C) positron emission tomography–computed tomography in prediction of bone metastasis, (D) whole-body diffusion magnetic resonance imaging in prediction of bone metastasis, comparison between sensitivity and specificity of positron emission tomography–computed tomography and whole-body diffusion magnetic resonance imaging in prediction of (E) multiple myeloma

lesions, (F) bone metastasis

In comparison between PET/CT & MRI-WBD, there was found that MRI-WBD is better than PET/CT in sensitivity & accuracy in detection of multiple myeloma bone marrow lesions, but have the same specificity**, as in Table 4.**

**Table 4: Comparison between PET/CT & MRI-WBD in detection bone marrow lesions of multiple myeloma:**

| ➢ | ➢ **ET/CT** | ➢ **RI-WBD** |
|---|---|---|
| ➢ **ensitivity** | ➢ 9.2% | ➢ 4.6% |
| ➢ **pecificity** | ➢ 6.7% | ➢ 6.7% |
| ➢ **PV** | ➢ 1.8% | ➢ 4.6% |
| ➢ **PV** | ➢ 0.0% | ➢ 6.7% |
| ➢ **ccuracy** | ➢ 8.4% | ➢ 8.9% |

In the second group (patients with metastatic bony lesions): the patients had primary malignancy with metastatic bony lesions at bone scan included 24 patients, their age ranged from 40 to 65 years with a mean of 50 years. There were 11 male & 13 females.

The main complaint was bone ache in 18 patients, then pathological fracture in 15 patients & anemia in 8 patients.

The 24 patients with bone metastasis are identified as: 8(33.3%) patients with breast cancer, 6(25 %) patients with prostatic cancer, 4(16.6%) patients with lung cancer, 2(8.3 %) patients with renal carcinoma, 2(8.3 %) patients with thyroid cancer and 2(8.3%) patients with HCC. **Table 5.**

**Table 5: Identification of the primary malignancy in our patients**

| **.36** | | **N= 24 .37** |
|---|---|---|
| **Primary malignancy .38** | **Breast .39** | 8 (33.3 %) **.40** |
| | **Prostate .41** | 6 (25 %) **.42** |
| | **Lung .43** | 4 (16.6 %) **.44** |
| | **Renal .45** | 2 (8.3 %) **.46** |
| | **Thyroid .47** | 2 (8.3 %) **.48** |
| | **HCC .49** | 2 (8.3 %) **.50** |

Data are presented as frequency (%). HCC: Hepato-cellular carcinoma.

**In comparison between PET/CT & MRI-WBD**, there was found that MRI-WBD is better than PET/CT in detection of metastatic bony lesions with sensitivity, accuracy, PPV & NPV, but have the same specificity, **as showed in Table 6.**

**Table 6: Comparison between PET/CT & MRI-WBD in detection of bone metastasis:**

| **.51** | **PET/CT .52** | **MRI-WBD .53** |
|---|---|---|
| **Sensitivity .54** | 88.9% **.55** | 100.0% **.56** |
| **Specificity .57** | 33.3% **.58** | 33.3% **.59** |
| **PPV .60** | 80% **.61** | 81.8% **.62** |
| **NPV .63** | 50% **.64** | 100.0% **.65** |
| **Accuracy .66** | 75% **.67** | 83.3% **.68** |

**Cases:**

**Case 1:** Male patient aged 55 years, newly diagnosed with MM, (plasma cell percentage 24 %), presented clinically by diffuse bone ache & muscle pain, with disturbance of renal function tests. **Figure 2.**

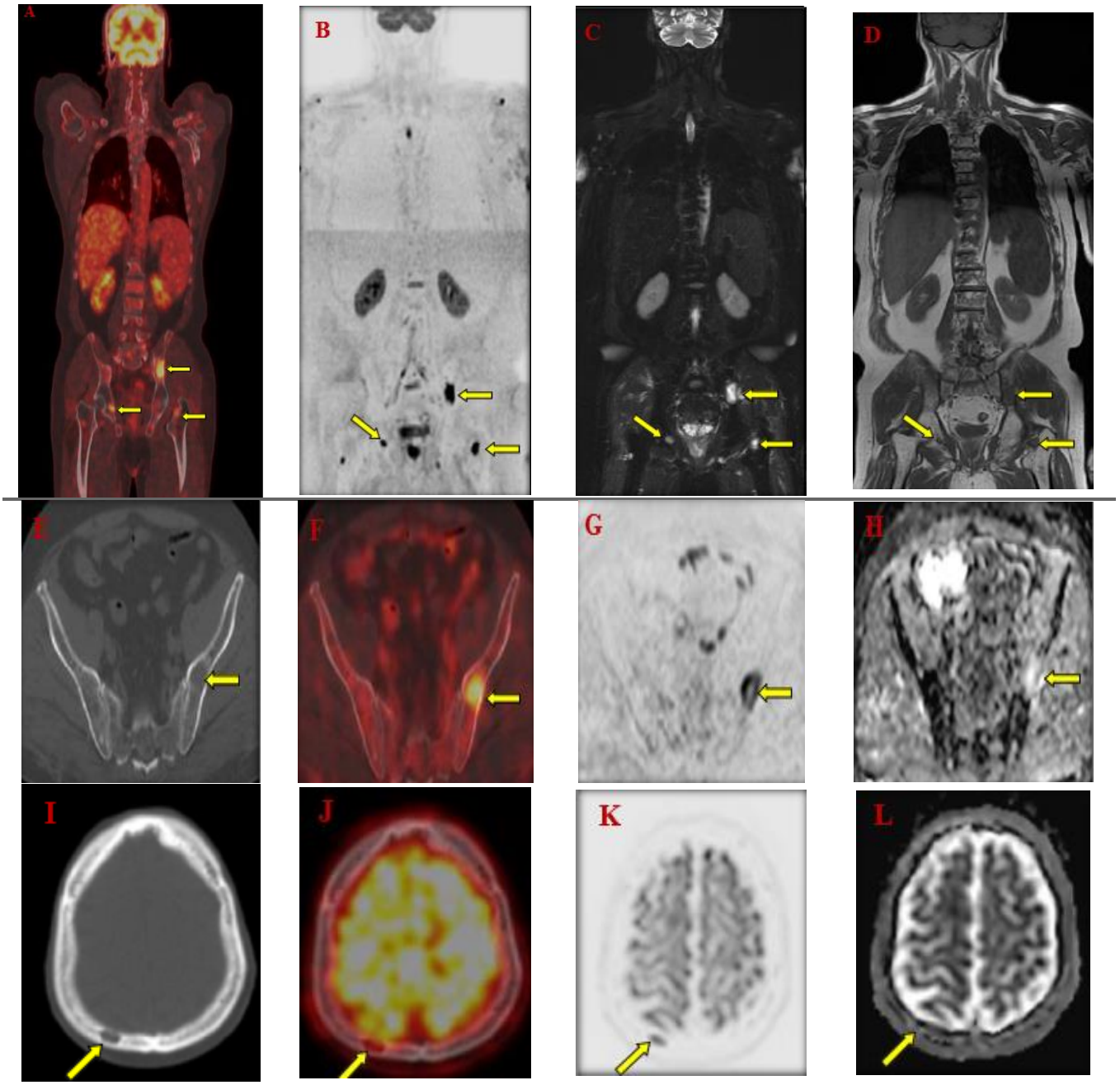


**Figure 2:** (A): PET/CT coronal images showing: multiple focal bone marrow lesions seen involving the left iliac bone, right accetabulum and both femori, displaying increased FDG uptake with SUV for example (SUV in left iliac bone = 6), (B, C and D) MRI with WBD (inverted scale), STIR, T1 WI sequences in coronal sections respectively showing: multiple focal bone marrow lesions seen involving the left iliac bone, right accetabulum and both femori, displaying low SI in TWI and high SI in STIR sequences, with restricted diffusion (high SI) in DWI, (E and F) PET/CT in axial section on the pelvis, showing lytic lesion in the left iliac bone showing increased FDG uptake (SUV = 6), (G and H) MRI-DWI (inverted scale) axial image on the pelvis showing restriction in DWI of the same lesion [Appear high SI in DWI and low SI in ADC image (ADC value = $0.85x10^{-3}$ $mm^2$/sec)], (I and J) PET/CT in axial section on the skull, showing lytic lesion in the right occipital skull bone with no FDG uptake, (K and L) MRI-DWI (inverted scale) axial image on the skull showing restriction in DWI of the same lesion (Appear high SI in DWI and low SI in ADC image (ADC value = $0.62x10^{-3}$ $mm^2$/sec)

**Case 2:** Male patient aged 55 years, diagnosed with lung cancer, presented by bone ache. **Figure 3**

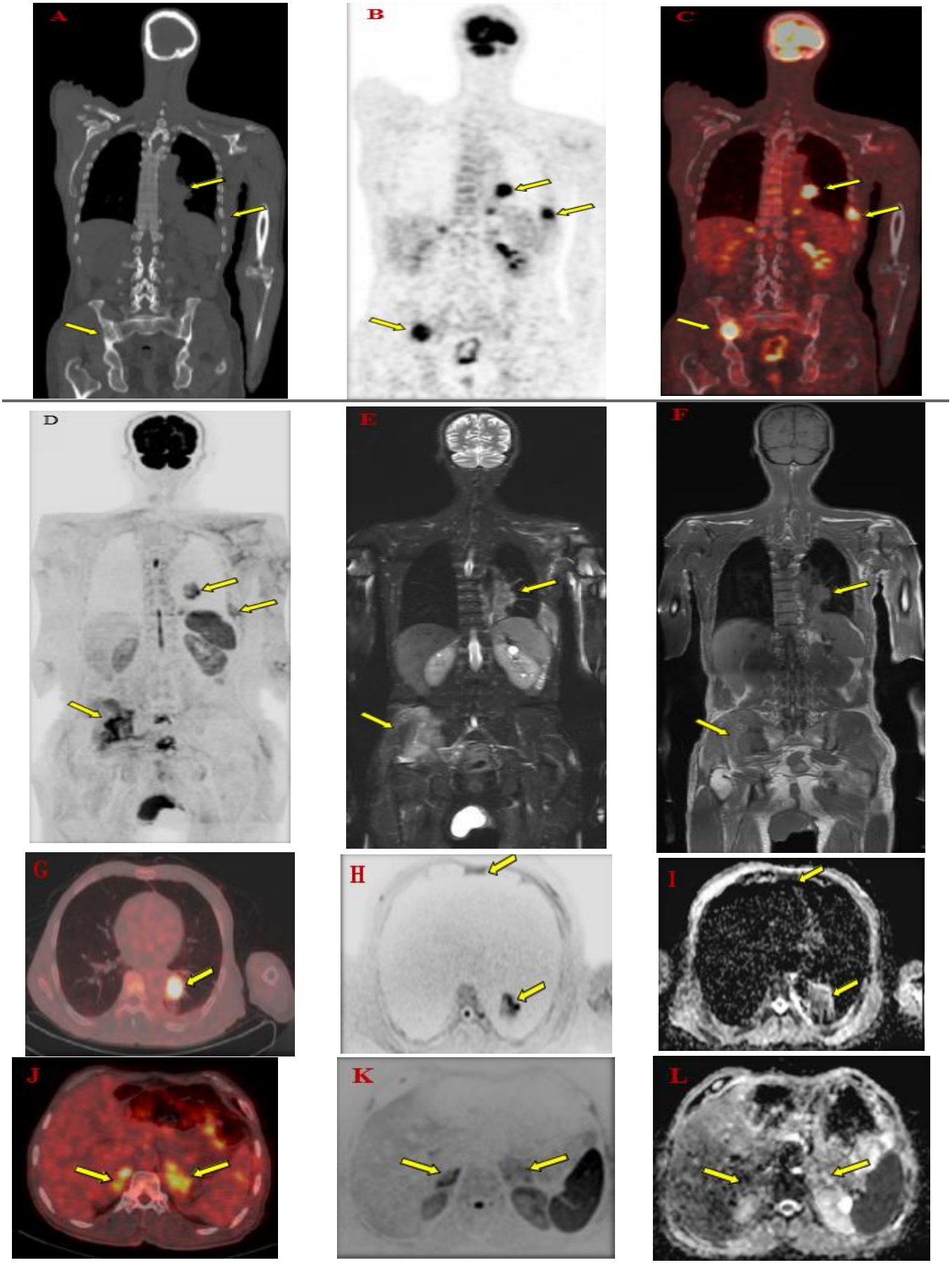
A
B
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**Figure 3:** (A, B and C) PET/CT coronal images showing metabolically active left lower lung lobe speculated soft tissue pulmonary mass (SUV max = 9.5) and metastatic mixed lytic and sclerotic osseous lesions (Left 8th rib with SUV max = 9 and right iliac bone with SUV max = 8.7), (D, E and F) MRI with WBD (inverted scale), STIR, T1 WI sequences in coronal sections respectively showing left lower lung lobe speculated soft tissue pulmonary mass displaying low SI in TWI and mixed iso and high SI in STIR sequences, with restricted diffusion (high SI) in DWI and metabolically active metastatic osseous lesions at left 8th rib and right iliac bone (with infiltration of the adjacent pelvic muscle), displaying low SI in TWI and mixed iso and high SI in STIR sequences, with restricted diffusion (high SI) in DWI, (G) PET/CT (axial section on the chest), showing metabolically active left lower lung lobe speculated soft tissue pulmonary mass (SUV max = 9.5), (H & I) MRI-DWI (inverted scale) and ADC images (axial section on the chest) showing the same left lower lung mass displaying restricted diffusion (Appear high SI in DWI and low SI in ADC image (ADC value = $1.8x10^{-3}$ $mm^2$/sec)) and metastatic bone lesion in the sternum and few bilateral scattered ribs displaying restricted diffusion (Appear high SI in DWI and low SI in ADC image (ADC value = $1.1x10^{-3}$ $mm^2$/sec)) not showing increased FDG in PET/CT, (J) PET/CT (axial section on the abdomen), showing metabolically active bilateral supra renal soft tissue lesions (SUV max = 5.4) likely metastatic and (K and L) MRI-DWI (inverted scale) and ADC images (axial section on the abdomen) showing the same bilateral supra-pubic soft tissue lesions displaying restricted diffusion (Appear high SI in DWI and low SI in ADC image (ADC value = $1.7x10^{-3}$ $mm^2$/sec))

## Discussion

PET/CT for detection of malignant bone involvement in oncologic patients with various human malignant diseases revealed encouraging results. It appeared that PET/CT may take advantage of the high sensitivity, reducing the risk of false positive rate by determining the morphology of the scintigraphy lesions on the CT data of the PET/CT study [13, 14].

In our 38 cases of MM, there was predominance of spine lesion represented 18 cases (47.37%), followed by 12 cases with pelvic lesion (31.58%) then 8 cases with skull lesion (21.05%) then 7 cases with thoracic cage lesion (18.42%) and 5 cases with long bone lesion (13.16%). This is in line with the study of Dimopoulos et al. [15] said that Osteolytic lesions are one of the most common signs of MM and the typical findings at radiological examinations. These lesions are mainly found in the axial skeleton and pelvis bones, less frequently in the arms and legs.

Our study including also 24 patients had primary malignancy with metastatic bony lesions their age ranges from 40 to 65 years with mean of 50 years 13 of them were females and 11 males. 8 of them had primary breast cancer which represent (33.3%) followed by 6 patients had prostatic carcinoma which represent (25%), then 4 patients with lung cancer (16.6%), then 2 patients with renal cancer (8.3%) 2 patient with thyroid cancer (8.3%) and 2 patients with HCC (8.3%). This is in line with the study of O'Sullivan et al. [16] as primary malignant neoplasms such as breast and prostate cancer have a propensity for metastasizing to bone.

In our 38 patients with MM, the PET/CT showing 31 bone marrow lesions, 25 focal bone marrow lesions and 6 diffuse bone marrow lesions, the 25 focal lesions distributed as 3 focal lesions in the skull, 3 focal lesions in the thoracic cage, 6 focal lesions in the pelvis, 11 focal lesions in the spine and 2 focal lesions in the long bones, on the other hand the 6 diffuse bone marrow lesions, distributed as 1 diffuse lesion in the skull, 1 diffuse lesion in the thoracic cage, 1 diffuse lesion in the pelvis, 2 diffuse lesions in the spine and 1 diffuse focal lesion in the long bones.

PET/CT can predict MM in skull, thoracic cage, pelvis, spine and long bone respectively (P= 1, 1, 0.625, 1 and 1) with sensitivity 60%, 75%, 66.7%, 85.7% and 66.7%, specificity 66.7%, 66.7%, 66.7%, 66.7% and 50%, PPV 75%, 75%, 85.7%, 92.3% and 66.7%, NPV 50%, 66.7%, 40%, 50% and 50%, and accuracy 62.5%, 71.4%, 66.7%, 82.4% and 60%. There was an agreement between PET/CT and biopsy (Kappa= 0.250, 0.270, 0.273, 0.463 and 0.167).

MRI-WBD can predict MM in skull, thoracic cage, spine and long bone respectively (P = 1) with sensitivity 80%, 100%, 77.8%, 92.9% and 66.7%, specificity 66.7%, 66.7%, 66.7%, 66.7% and 50%, PPV 80%, 80%, 87.5%, 92.9% and 66.7%, NPV 66.7%, 100%, 50%, 66.7% and 50% and accuracy 75%, 85.7%, 75%, 88.2% and 60%. There was an agreement between MRI-WBD and biopsy (Kappa= 0.467, 0.696, 0.400, 0.595 and 0.167).

Our findings are in line with Mesguich et al. [17] reported in his study on 30 patients with MM. The average numbers of focal patients detected in the whole body were 16.7 for 18F-FDG PET-CT and 23.9 for WB-DWI (P = 0.028). When considering the number of FLs per skeletal region, the average number of FLs detected was significantly greater for WB-DWI than 18F-FDG PET-CT. Pawlyn et al. [18] said that We have compared matched simultaneous assessments of myeloma using FDG PET–CT and WB-DWI and determined the relationship to bone marrow biopsy assessments of disease burden, that supported our study to compare PET/CT and WBD-MRI findings with bone biopsy. Also, our result in agreement with the study of Westerland et al.[19] in which 46 patients showed sensitivity for bone lesions was 69.6% (32/46) for 18F-FDG PET/CT and 91.3% (42/46) for WBMRI.

In our study, we revealed that the most common number of bone marrow lesions detected in anatomical region by PET/CT and WBD-MRI was spine, pelvis, skull, thoracic cage and long bones respectively, that in agreement with the study of Dyrberg et al. [20] said that anatomical distribution of the MM focal lesions classified into (spine, skull, pelvis, long bones, ribs and others) and WBD-MRI detected focal lesion more than PET/CT in different anatomical sites.

Twelve patients from 38 patients were presented with combined focal lesions in two sites, 5 focal lesions of long bones (3 of them are combined with focal lesions in the pelvis and 2 of them are combined with focal lesions in the thoracic cage)

and 7 focal lesions of spine (5 of them are combined with focal lesions in the pelvis and 2 of them are combined with focal lesions in the skull). Most of our cases with focal lesions were presented with number of focal lesions between 2 to 10 lesions in each patient and few of them were presented with more than 10 focal lesions in each patient, the size of the focal lesions ranging from 3mm to 12mm. These findings are in line with Messiou et al.[21] reported that 20% of his cases showed multiple focal lesions of MM were combined with two or more anatomical regions as skull, spine and pelvis, as well as most of the focal lesions their size was above 10mm.

PET/CT and MRI-WBD can predict bone metastasis (P= 1 and 0.500) with sensitivity (88.9% and 100%), specificity (33.3% and 33.3%), PPV (80% and 81.8%), NPV (50% and 100%) and accuracy (75% and 83.3%). There was an agreement between PET/CT and bone scan (Kappa= 0.250 and 0.429). Our results match Stecco et al. [22] reported as WB-MRI-DWI allows qualitative and quantitative evaluation of focal lesions through signal intensity evaluation on DWI images and the reconstruction of the ADC map. The WB-MRI-DWI shows a higher sensitivity when compared to 18F-FDG PET/CT in bone metastasis (epically in bone metastasis of lung and thyroid tumors) and WB-MRI-DWI in prostate and breast cancer, is useful in assessing the response of bone lesions to therapy. With a standardization of the WB-MRI-DWI protocol, this method seems to play an important role in the diagnosis of bone solid tumor metastases. Morone et al. [23] reported that Whole-body MRI is an attractive tool with marked advantages, including its high soft tissue contrast and lack of radiation exposure. It shows mild high sensitivity and accuracy than PET/CT and bone scan in some bone metastasis of primary malignancy and have the same sensitivity and accuracy as PET/CT and bone scan in others. Takenaka et al. [24] reported that whole-body MRI with DWI was found to be more specific and accurate than FDG-PET/CT and bone scintigraphy. In addition to lack of radiation exposure of whole-body MRI DWI.

Limitations of the study included that the sample size was relatively small. The lack of an ideal reference standard is a limitation in diagnostic studies. Ideally, biopsies of all suspected myeloma bone lesions (and theoretically of non-involved bone too) should be performed to histologically confirm the image findings. However, this was neither practically nor ethically possible. In this study, all image findings are considered indicative of myeloma bone disease and detection rates are compared as in previous studies. Red marrow has an altered diffusion signal compared to yellow marrow and therefore detection of marrow disease in younger patients can be challenging. However, this is rarely problematic for myeloma as the incidence is strongly related to age and the MM is more evident in middle to old age. PET/CT has low spatial resolution that may interfere with precise anatomic localization of findings. Recent chemotherapy or radiotherapy can make interpretation difficult.

## Conclusions:

Whole body MRI-DWI and ADC values significantly improve the diagnostic accuracy in detection of MM bone marrow lesions and bone metastatic lesions, with relatively higher sensitivity and accuracy than PET/CT study. WBD-MRI seems to be a promising method of imaging in the detection of MM and bone metastasis. Standardization of these protocols is needed.

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