

Original Article

WHOLE BODY MRI VERSUS 99M TC-METHYLENE DIPHOSPHONATE SCINTIGRAPHY IN DETECTION OF SKELETAL METASTASES

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ABSTRACT

Background: Skeletal metastases have a drastic impact on the staging, treatment and quality of life of cancer patients; Being the most common malignant bone tumor, affecting at least two thirds of the cancer patients

The aim of this study is to compare ability of whole body MRI, with routine 99mTc-phosphonate scintigraphy to detect skeletal metastases in cancer patients.

Patients and methods: 23 patients with pathologically proven primary malignant tumors were examined in the Radiology Department, National Cancer Institute, Cairo University. The patients were subjected to both Whole-Body MRI (WB-MRI) and 99m Methylene Diphosphonate bone scintigraphy (BS).

WB-MRI was mainly obtained using 4 contiguous coronal stations for body coverage using the body coil, and 2 contiguous sagittal stations for the spine with the CTL Coil, using both Fast Spin Echo Inversion Recovery (FSE-IR) and T1-Weighted Fast Spine Echo (T1w-FSE) sequences for each station, in a total acquisition time of ~28 min, and In-Out time of ~40 min. Bone Scan (BS) imaging was completed in 20 min after 2 hours of tracer administration using dual headed gamma camera with low energy general purpose collimator (LEGP).

Results: 15 out of 23 cases had skeletal metastases, while 8 cases were free from metastases. Comparison between the results obtained by each modality was done.

An excellent overview of the skeletal system was obtained in all cases and the results showed that WB-MRI had higher overall sensitivity, specificity, positive predictive value, negative predictive value, accuracy than bone scan, as it could detect all of the 15 metastatic cases, while bone scan characterized only 11 cases.

Although BS showed higher lesion detection in the ribs and the shoulders, but WB-MRI was superior in the spine, pelvis and extremities, and both were equal in the skull. In addition WB-MRI can also detect the extra-skeletal tumor complications (e.g. lung metastases), which gives the clinician an idea about the total tumor burden, aiding in earlier staging and treatment of the patients.

Conclusion: WB-MRI is powerful and effective tool that showed higher sensitivity, specificity and accuracy than BS in various types of primary tumors and in various situations including solitary metastatic focus, diffuse extensive metastases and skeletal metastases from a second primary.

Although WB-MRI showed better results, but we believe that BS would

remain the standard procedure for evaluation of bone metastases for quite sometime due to its easiness, simplicity, much lower cost and better tolerance by patients.

Key Words: *Skeletal scintigraphy, Bone metastases, Whole body MRI.*

INTRODUCTION

In patients with primary tumors that potentially metastasize to bone, diagnosis of bone metastasis is crucial to determine the prognosis and to optimize therapy.

Introduction of new chemotherapy protocols, which include both marrow and stem cell transplantation, has increased the demand for accurate and early detection of skeletal metastases, particularly metastases to marrow.

^{99m}Tc-Phosphonate-based skeletal scintigraphy is the standard method for the initial staging of bone tumors. However, it depicts bone metastases when osteoblastic host reaction to tumor deposits has already occurred.

Other radiologic methods of detecting skeletal metastases have limitations. Metastases to bone only become apparent on radiographs after the loss of more than 50% of bone mineral content at site of disease. Although CT allows earlier detection of cortical destruction by imaging in contiguous tomographic slices, its ability to detect early deposits in marrow is limited.

Since cellular bone marrow is the initial site of metastatic seeding to bone, MRI can detect metastatic lesions at an early stage, before changes of the bone metabolism occur that make lesions detectable on bone scan. Same studies have reported that positive MR imaging findings and negative findings on bone scan can occur in patients with vertebral body metastases. Further, Whole body

MRI had a higher skeletal metastases detection compared to bone scan in spine, pelvis, limb bone, sternum, scapula and clavicle. This renewed the interest in MR imaging as a potential whole body-screening tool.

In addition, whole body MRI is an effective method for evaluating not only bone marrow involvements of the entire skeleton but also other systemic involvement such as lymph nodes in patients with malignant lymphoma. [1-7].

Aim of work:

Is to compare ability of whole body MRI, with standered ^{99m}Tc-phosphonate scintigraphy to detect skeletal metastases in cancer patients.

PATIENTS AND METHODS

Patients:

This study included 23 patients (8 Males, 15 Females), their age ranged between (39-78 years) with a mean age of 53 years. Patients were referred from different medical, surgical, radiotherapy and nuclear medicine departments, with pathologically proven primary malignant tumors with suspected skeletal metastatic disease. Whole body MRI was performed to:

Detect skeletal metastatic lesions.

Reveal the nature of vague bone scintigraphy detected lesions

To evaluate the extent and predict the prognosis of proved lesions

Detect any extra-skeletal lesions or complication of the primary tumor.

Pathology of the 23 patients, 12 patients had breast cancer (11 invasive and one lobular), 3 had prostatic adenocarcinoma, 4 had bladder (2 squamous and 3 transitional) cell cancer, 1 had thyroid cancer, 1 had large cell Lung cancer, 1 had Nasopharyngeal cancer and 1 had Hepatocellular cancer.

Methods:

All patients were subjected to:

- Full history taking,
- Technetium 99m MDP Planer scintigraphy ,
- Whole body MRI.
- (MRI and scintigraphic examinations were performed within 6 weeks of each other).

A) Technique of Whole body MRI:

MRI examination was performed using a super conducting 1.5 Tesla (T) magnet units. The whole body was covered using both FSE-IR (Turbo-STIR) and T1-weighted FSE sequences in 4 coronal stations and 2 sagittal stations. We used body coils for the coronal stations and CTL (cervical, dorsal and lumbar) phased array coil for sagittal stations.

Planes of examination:

Body coverage was achieved using a maximum of four overlapping coronal body coil acquisitions. In each patients coronal images were obliqued to the long axis of the spine.

Position of the upper extremities was dictated by patient's habitués, in large patients, the arms were placed above the head, requiring an additional coronal acquisition.

Spine was imaged in 2 overlapped sagittal stations parallel to the long axis of the spine in the coronal locator using the CTL coil. The 1st station included the cervical and upper dorsal vertebrae. The 2nd station included the lower dorsal and lumbo-sacral vertebrae.

Stations and parameters:

A three-plan localizer scout view of the region of interest was performed for localization of the region to be scanned. 5 locators were taken before each of the 6 stations (only one locator for the spine), in a total of 2:20 minutes.

Coronal Body Stations:

1st Station was used to cover the head, neck, upper chest, proximal upper limb, and cervical and upper dorsal spine. 2nd Station used to examine the lower chest, abdomen, upper pelvis, distal upper limb, lower dorsal and lumbo-sacral spine, using the same parameters as the 1st station and 3rd Station was used to examine the lower pelvis and thigh. 4th Station, used to examine the tibia, fibula and foot.-Additional station was taken some times to scan the upper limbs in obese patients. (Fig. 1A).

Sagittal Spine Stations:

- 1st Station used to examine the sternum, cervical and upper dorsal spine,
- 2nd Station: used to examine the lower dorsal, and lumbo-sacral spine.

Patients in and out time were also calculated and it ranged from 36-42 with an average time of 39 minutes.

B) Technique of Tc 99m MDP Scintigraphy:

All patients should be well hydrated before scanning. They were asked to remove any metallic objects and void immediately before scanning. Standard skeletal scintigraphy was performed using a planar one-phase technique (delayed phase). The Examination was done 2-3 hours after intravenous (IV) injection of 555-925 MBq of technetium 99m labeled Methylene Diphosphonate (99m Tc-MDP). Images were collected using Dual head whole body gamma camera interfaced with recent version of computer system for imaging aquisition. Anterior and posterior images of the whole body were obtained in a single pass in about 20 minutes. If necessary, additional spot views were taken for suspicious or symptomatic areas. Patients were encouraged to void urine frequently following the examination.(Fig. 1B).

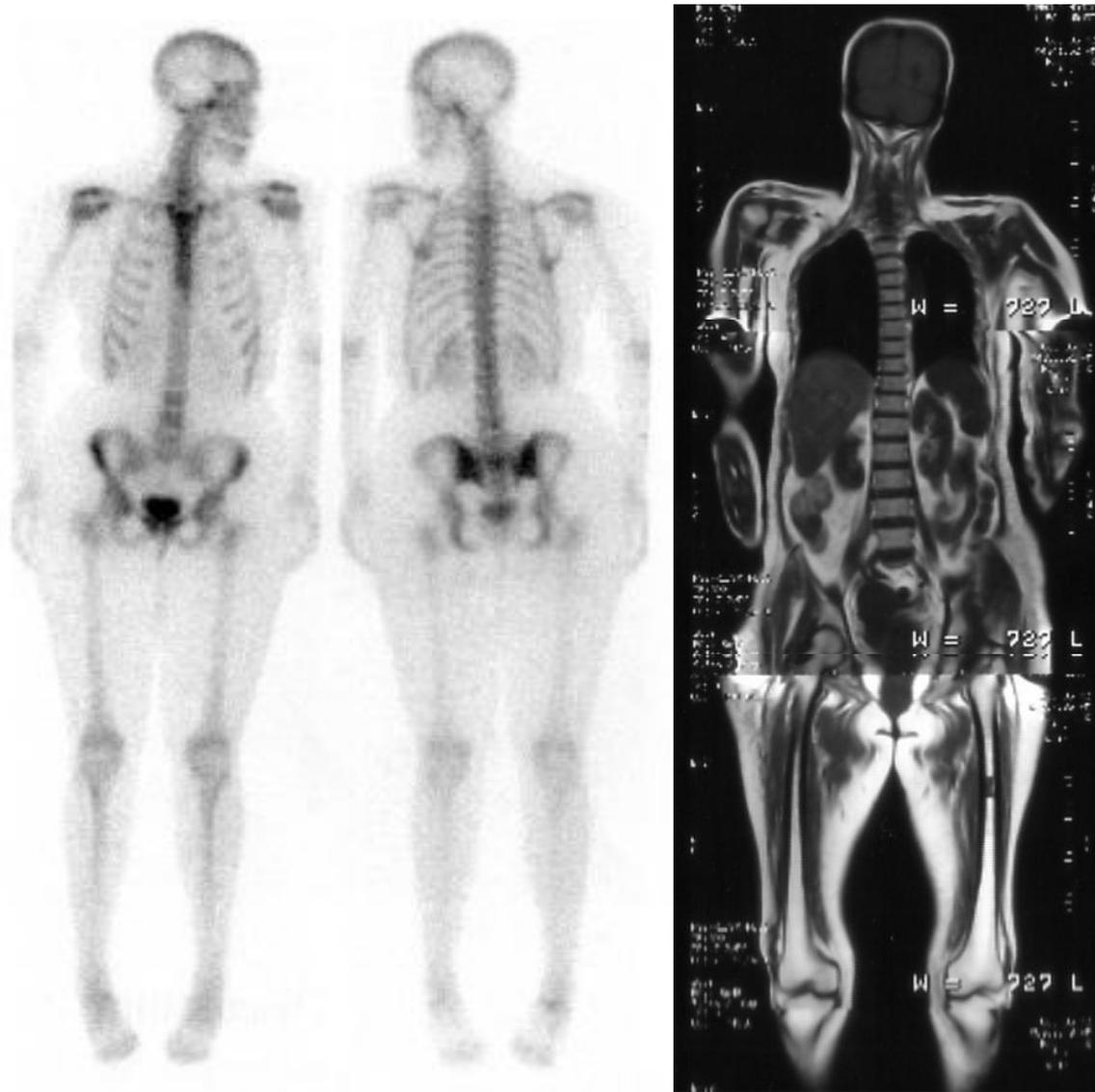


Fig. 1: showing

A) Normal Bone scan image.

B) Normal WB-MRI in 4 coronal stations.

C) Interpretation:

Each case of Whole body MRI were analyzed in consensus by 2-experienced radiologist and correlation was subsequently made with bone scintigraphy evaluated independently by 2 experienced nuclear medicine physicians. Reviewers were blinded to the results of the other imaging modalities. Clinical data such as the primary tumor, age, sex, treatment status of the patient were available for all reviewers.

In both Modalities, each lesion was assessed for the following:

Location: To determine the diagnostic potential of both modalities in different anatomical regions, the skeletal system was divided into 11 anatomic regions including the skull, shoulder girdle, upper limb, sternum, ribs, pelvis, lower limb, cervical vertebrae, dorsal vertebrae, lumbar vertebrae and sacral vertebrae.

Character: whether benign, uncertain or metastatic, according to

Number, lesions,

Pattern whether focal or diffuse. ,

(extra-skeletal abnormalities were also documented and classified into tumor related and non-tumor related.) .

Criteria of characterization of the lesions:

I) In Whole body MRI lesions were analyzed as follows:

Lesions were considered *metastatic* if there is diffuse or focal hypointense bone marrow signal intensity relative to adjacent or contra-lateral normal marrow, in T1 weighted FSE sequences. To differentiate metastatic from benign lesions, additional criteria like the bull's eye sign and halo sign were considered. For the spine, additional criteria for malignant infiltration included bulging of the posterior margin of the vertebral body, signal intensity changes extending into the pedicles and Para osseous tumor extension.

Lesions were considered as *uncertain*, when differentiation between a metastatic and benign process, such as osteoporotic fracture or bone marrow reconversion, was not possible.

The lesion was considered *benign* when it was located directly adjacent to degenerative changes of the vertebral end plates or near joint surfaces or when the lesion displays high T1 signal intensity.

II) In Bone scintigraphy:

An area of focal or diffuse, increased or decreased uptake, relative to the adjacent and contra-lateral normal bone uptake not located in a region of physiologically increased uptake, or affected by degenerative changes or trauma, were considered *metastatic*.

A lesion was regarded to be of *benign and degenerative* origin when focal tracer uptake occurred adjacent to joint surfaces. Well-circumscribed linear tracer uptake involving the spine or active spots of increased tracer uptake at adjacent ribs was considered to be benign caused by osteoporotic or traumatic fractures.

When a differentiation between degenerative, posttraumatic, or tumorous origin of tracer accumulation was impossible, the lesion was considered as *uncertain*.

The gold standard:

In this study, the final result was achieved by strict adherence to the criteria of characterization mentioned above. Discrepancy between WB-MRI and BS was resolved using further regional imaging modalities (regional CT, contrast enhanced MRI).

The region was considered free from metastases (True negative), if it was negative by both modalities, or if the regional imaging diagnosed a discrepant lesion as non-metastatic (benign or degenerative in nature).

For obvious ethical and practical reasons, we did not pursue for histological proof of many foci of the skeletal metastases, most of which were asymptomatic.

RESULTS AND DATA ANALYSIS

This study involved 23 patients with pathologically proven primary malignant tumors. 15 (65%) patients were females and 8 (35%) males, their mean age was 53 years, the youngest was 39 years and the oldest 78 years.

Regarding the primary tumors that were included in this study, most of the patients referred with breast cancer followed by bladder cancer, and prostatic carcinoma.

Table (1): Distribution of patients according to the primary malignant tumor.

Primary malignant tumor	No. Of cases	Percentage
Breast cancer	12	53%
Bladder cancer	4	18%
Prostatic carcinoma	3	13%
Thyroid cancer	1	4%
Hepatocellular cancer	1	4%
Lung cancer	1	4%
Nasopharyngeal carcinoma	1	4%

All cases were undergoing metastatic work up, 10(6wt) of 23 cases complained of pain, (6 of them had generalized bone aches, 4 with back pain). 5 were asymptomatic. 4 had (17%)of 23cases had manifestations of cord compression, 2 with paraplegia and 2 with Para paresis.

Acceptability, Timing and Filming:

Both Whole-body MRI (WB-MRI), and Bone scintigraphy (BS) were tolerated by all patients. MRI was achieved in 39+/- 3 minutes in/out time. This time included 28:00 minutes as acquisition time and 8 to 14 minutes for patient positioning and changing the MR coil. The extra upper limb station was done in 2 cases, rising the time to 44 minutes.

Bone scintigraphy was achieved in 20+/- 5 minutes, after an average of 2 hour waiting time.

Data Analyses based on Patient-by-Patient Comparison:

Three of the 23 patients were concordantly found to be totally free by both WB-MRI and BS, leaving 20 patients which were analyzed as follows:

WB-MRI: - 15 had *skeletal metastases*, 5 had *benign* lesions (degenerative discs, traumatic fractures..ect.) and *no* patients were found to be *uncertain*.

Bone scan showed 11 had *skeletal metastases*, 2 had *benign* findings, and 7 patients were found to be *uncertain* necessitating further radiological and MRI correlation to confirm the nature of the lesion. (Table 2, fig. 2)

Data Analyses based on Region-by-Region Comparison

In this category we compared corresponding anatomical regions in WB-MRI and BS, including the skull, shoulder, sternum, ribs, upper limbs, lower limbs, cervical, dorsal, lumbar vertebrae and sacrum. This was done to asses the sensitivity of both techniques in these regions. Each region was assessed whether affected or not, and then we calculated the sensitivity, specificity, positive and negative predictive values and accuracy in each region as compared to the true positive and negative values. (table 3)

Table (2): WB-MRI and BS finding in 23 patients according to their primary malignant tumors, as well as their final diagnosis.(F: Free, B: Benign, U: Uncertain, M: Metastatic).

Malignant Tumor	1ry Modality	Whole-body MRI (WB-MRI)								Bone scintigraphy (BS)								Total No. of True Metastatic Cases
		F	%	B	%	U	%	M	%	F	%	B	%	U	%	M	%	
Breast cancer		1	8.3	1	8.3	-	-	10	83.3	1	8.3	1	8.3	2	16.6	8	66.6	10 Of 12
Prostatic carcinoma		-	-	1	33.3	-	-	2	66.6	-	-	-	-	1	33.3	2	66.6	2 Of 3
Bladder cancer		-	-	2	50	-	-	2	50	-	-	-	-	3	75	1	25	2 Of 4
Thyroid cancer		-	-	-	-	-	-	1	100	-	-	-	-	1	100	-	-	1 Of 1
Hepatocellular cancer		-	-	1	100	-	-	-	-	-	-	1	100	-	-	-	-	0 Of 1
Lung cancer		1	100	-	-	-	-	-	-	1	100	-	-	-	-	-	-	0 Of 1
Nasopharyngeal carcinoma		1	100	-	-	-	-	-	-	1	100	-	-	-	-	-	-	0 Of 1
Total No. Of cases		3	13	5	21.7	-	-	15	62.2	3	13	2	8.6	7	30.5	11	47.8	15 Of 23

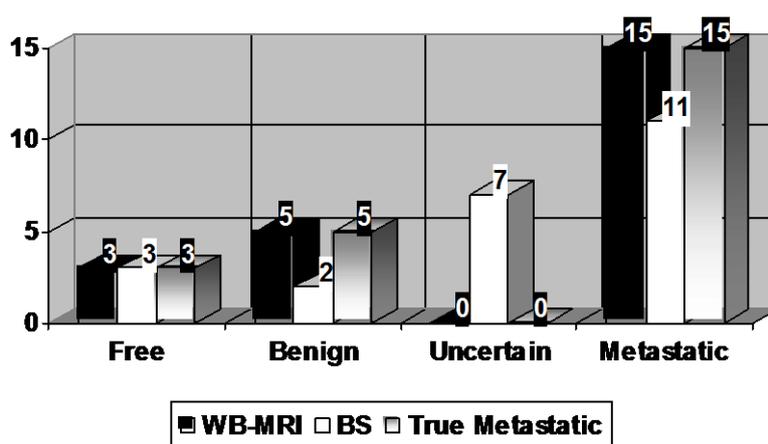


Fig. (2): Final diagnosis of each of the 23 cases by WB-MRI and BS.

Table (3): Number of free & affected regions by WB-MRI, BS

Region	Modality	Affected Regions	Free Regions
Skull	WB-MRI	4	19
	BS	4	19
	Reference	5	18
Shoulder	WB-MRI	2	21
	BS	3	20
	Reference	4	19
Sternum	WB-MRI	5	18
	BS	4	19
	Reference	5	18
Ribs	WB-MRI	5	18
	BS	6	17
	Reference	7	16
Upper limb	WB-MRI	9	14
	BS	5	18
	Reference	9	14
Pelvis	WB-MRI	10	13
	BS	7	16
	Reference	10	13
Lower Limb	WB-MRI	8	15
	BS	5	18
	Reference	8	15
Cervical Vertebrae	WB-MRI	6	17
	BS	2	21
	Reference	6	17
Dorsal Vertebrae	WB-MRI	10	13
	BS	5	18
	Reference	10	13
Lumber Vertebrae	WB-MRI	8	15
	BS	2	21
	Reference	8	15
Sacrum	WB-MRI	6	17
	BS	2	21
	Reference	6	17
Total	WB-MRI	73	180
	BS	45	208
	Reference	78	175

A total of 253 regions were surveyed in both modalities, 78 regions out of them were metastatic, and 175 regions were free of metastases (this number includes those regions which were diagnosed as benign or uncertain).

WB-MRI found 73 of the 78 metastatic regions, with positive predictive value of 100%. It showed 180 areas to be free of metastases, with 5 false negative areas, negative predictive value 97.2%, its accuracy was 98%.

BS found 45 of the 78 metastatic regions, and 2 falsely positive regions, with a positive predictive value of 95.7%. It showed 206 areas to be free of metastases, with 31 false negative areas, making its negative predictive value 83.4% its accuracy was 86.1%.

Data Analyses based on Number of Lesions Detected by Both Modalities:

In each of the 23 patients, lesions were counted and classified as benign, uncertain or metastatic in both modalities.

Table (4): Number and site of lesions detected by both modalities.

Sequence Region	Whole Body MRI (WB-MRI)			Bone Scintigraphy (BS)		
	Benign	Uncertain	Malignant	Benign	Uncertain	Malignant
Skull	-	-	8	-	1	7
Shoulder	-	1	6	-	-	4
Sternum	-	-	9	-	-	6
Ribs	-	-	7	-	3	13
Upper Limbs	-	-	14	-	-	7
Pelvis	2	-	41	-	2	15
Lower Limbs	13	2	27	5	-	10
Cervical Spine	16	-	10	-	1	3
Dorsal spine	17	-	27	8	2	8
Lumber spine	44	-	21	2	4	6
Sacrum	-	-	13	-	1	3
Total	92	3	183	15	14	82

Table (5): Number of lesions detected in different body regions as compared to their sensitivity, and positive predictive values.

Sequence Region	Whole Body MRI (WB-MRI)			Bone Scintigraphy			No. of True Positive lesions
	Number of lesions	Sensitivity	Positive Predictive Value	Number of lesions	Sensitivity	Positive Predictive Value	
Skull	8	72.7%	100%	7	63.6%	100%	11
Shoulder	6	66.6%	100%	4	44.4%	100%	9
Sternum	9	100%	100%	6	66.6%	100%	9
Ribs	7	50%	100%	13	92.8%	100%	14
Upper Limbs	14	100%	100%	7	50%	100%	14
Pelvis	41	100%	100%	15	36.5%	83.3%	41
Lower Limbs	27	100%	100%	10	37%	100%	27
Cervical Spine	10	100%	100%	3	30%	100%	10
Dorsal Spine	27	100%	100%	8	29.6%	100%	27
Lumber spine	21	100%	100%	6	28.5%	100%	21
Sacrum	13	100%	100%	3	23%	100%	13
Total	183	93.3%	93.5	82	41.8%	96.4%	196

These findings confirm the previous findings of the superiority of WB-MRI on BS as reflected by the total number of lesions detected by WB-MRI, 183 of 196 lesions with a sensitivity of 93.5%, it also confirmed the higher sensitivity of WB-MRI in the spine, pelvis and extremities, in addition to the skull and shoulder.

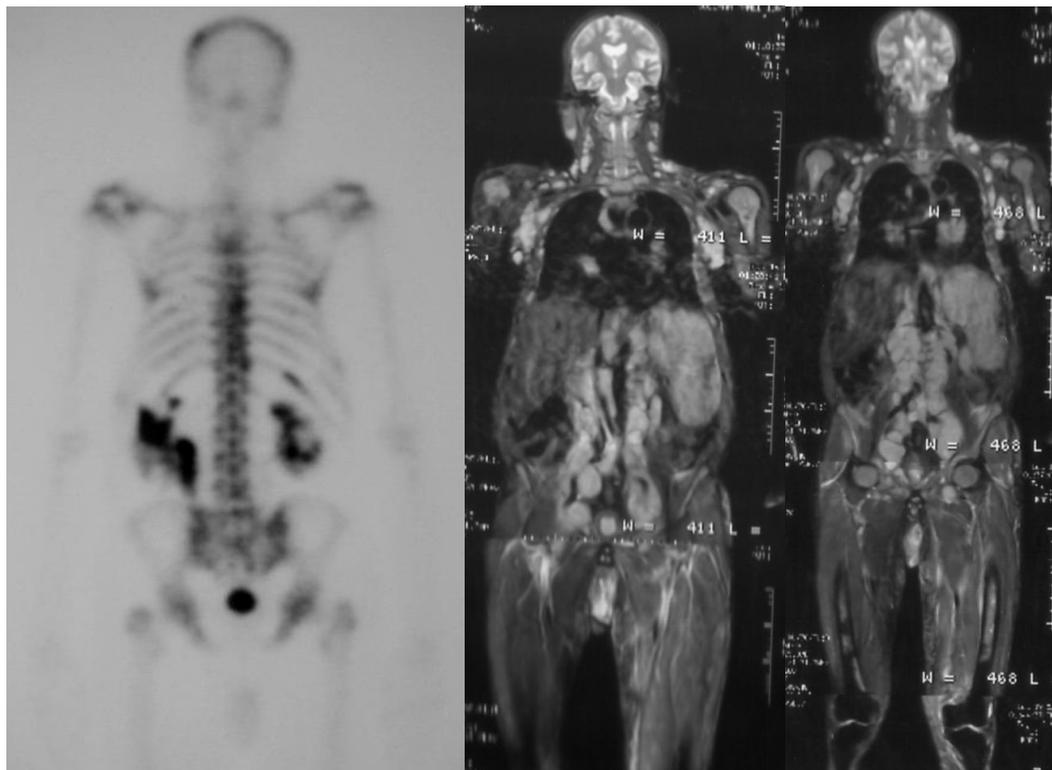
Positive predictive values of WB-MRI was 100%, and that of BS was 96.4%, as there were 3 false positive lesions detected at the pelvis, 2 of which were revealed to be sacroilitis (WB-MRI showed bilateral, symmetrical affection & was confirmed by regional Gd-enhanced MRI), and one was degenerative hip changes (WB-MRI showed normal marrow signal and hip effusion).

Pattern of WB-MRI detected lesions, out of the 183 lesions, 97 (53%) lesion were focal and 86 (47%) lesions were diffuse.

Extraskelatal Lesions:

Whole body MRI elucidated 59 tumor related extraskelatal lesions, including 5 primary detection, 1 chest wall recurrence in a case of breast cancer, 2 cases with bilateral lung metastases not discovered before WB-MRI. Bone scintigraphy only detected 2 tumor related extra-skeletal lesions, which were bilateral hydro-nephrotic renal changes complicating bladder cancer.

Whole body MRI detected 35 tumor non related extraskelatal lesions, the most serious of which was hydronephrotic changes, plural effusions, thyroid nodules and degenerative cord compression.



**Fig. (3): A) Metastatic bone scan with hydronephrotic kidneys.
B) Multiple enlarged LNs above and below the diaphragm indicating
second malignancy proved to be NHL.**

DISCUSSION

It is well recognized that metastases to the skeleton is by far the most common type of malignant bone tumors. The presence of bone metastases significantly impairs quality of life as a result of pain, reduced mobility and bone weakness, predisposing to pathological fractures, epidural compression and bone marrow failure. Thus the detection of bone metastases has a considerable effect on the quality and length of a patient's life and influences the choice of therapy.

Conventional plain radiography provides important information about cortical and trabecular bone, but little information regarding the presence of lesions confined to the bone marrow. The detection of lytic skeletal metastases on plain film radiographs requires loss of up to 50 % of bone mineral content. While a

minimum of 30% increase in bone mineral content is necessary to appreciate sclerotic lesions which may limited value in early detection of skeletal metastases. [8-11]

Scintigraphy using ^{99m}Tc -methylene Diphosphonate is sensitive a technique to detect bone metastases up to 18 months before radiography shows them. It lacks diagnostic specificity; and in many cases further imaging is required to characterize regions of documented abnormality.

Several studies have compared scintigraphy with MR imaging in tumor detection and characterization. Although most of these studies of localized areas conclude that MR imaging is both more sensitive and more specific than scintigraphy, its use as an alternative to scintigraphy for whole-body imaging has been limited by cost,

acquisition time, and convenience. [12-14].

Krishnamurthy et al., reported that appendicular skeleton was involved site of bone metastases in 17% of the patients.

In the contrary we were able to demonstrate 14 upper limb lesions with a sensitivity of 100%. This maybe due to the extra-upper limb station that we added to our protocol in large patients which resulted in only ~3 min in acquisition as a time penalty. No metastatic lesions were encountered in the feet by both modalities. [15-16].

- Assessment of WB-MRI:

Of the 253 regions that we surveyed, 58% (45 of 78 regions) were located in the axial skeleton (Skull, spine and pelvis) and 42% (33 of 78 regions) in the appendicular skeleton (sternum, ribs, shoulders and extremities). Although this percents reflect the predominance of metastases in the axial skeleton due to its higher content of red marrow, however this percent was different than that detected by *Steinborn et al*, who found 73.6% (159 out of the 216 lesions) in the axial skeleton and 26.4% in the appendicular skeleton. The reason for this may be due to that our protocol included upper limb as additional image.

In concordance with previous studies comparing bone scintigraphy (BS) and whole-body MRI (WB-MRI), our technique permitted equivalent or improved evaluation of the skeleton relative to scintigraphy, allowing for both detection and clear anatomic localization of skeletal metastases. WB-MRI showed accuracy of 100%. However BS had an accuracy of 78.2%, when comparison was made on patient-by-patient bases. [17-21]. This difference is explained by improved spatial and contrast resolution, improved anatomic detail, and direct visualization of marrow and tumor using MRI.

The higher sensitivity and specificity of WB-MRI over bone scan was also emphasized when comparison was made on region-by-region bases.

These findings are consistent with those of *Daldrup-Link et al.*, who found 51 lesions in 21 cases, WB-MRI showed a sensitivity of 82% for detection of bone metastases, significantly higher than the sensitivity of 71% for BS, with most of the false negative findings located in small or flat bones. BS showed most of false negatives in the spine. [22-24].

Similarly, in our study WB-MRI was superior to BS at the spine (19 more affected regions), lower limbs and pelvis (3 more affected regions), upper limb (4 more affected regions) and sternum (1 more affected region). Whereas, BS was superior at the ribs and shoulder (1 more affected region), while both were equal at the skull.

Taoka et al. explained the reason for the vast superiority of WB-MRI at the region of the spine. They stated that MRI is a sensitive method of detecting early or small intramedullary metastases to those bones with large marrow cavities. And because the vertebral bodies have a relatively large marrow cavity which may not cause sufficient bony remodeling to be detected by bone scans. [25].

An important aspect of this study is that with bone scintigraphy, significantly more lesions were graded as uncertain in origin. On patient-to-patient bases, 7 cases were uncertain, which were diagnosed by MRI to be 4 metastatic and 3 benign. On the other hand, no cases were diagnosed as uncertain by WB-MRI.

The same results were reached when cases were analyzed on lesion-to-lesion bases. Only 3 lesions were deemed uncertain by WB-MRI, while on BS 14 lesions were uncertain, most of them in the spine (8 lesions). The same finding was reached by *Steinborn*

et al., who deduced that this finding proves that the morphologic information provided by MRI is of great value for the differentiation between benign and malignant lesions.

In addition WB-MRI has detected and explained 78 benign skeletal lesions, able to elucidate 59 tumor-related extra skeletal manifestations, which had a great impact on the staging and management of the patients. This meaning was clearly demonstrated in one of our male patients who suffered from pathologically proven adenocarcinoma of the prostate. The striking finding in this case was not only the patchy pattern of bone marrow involvement, but also the hugely enlarged cervical, axillary, mediastinal, abdominal, pelvic and inguinal lymph nodes, associated with hepatosplenomegaly. These findings suggested that a second primary of lymphoma rather than bone metastases from prostatic carcinoma is the most likely diagnosis. Pathology of this case was diffuse large cell non-Hodgkin lymphoma. Fig 6-B.

When comparing the costs of whole-body MRI which is more than double bone scintigraphy, one has to consider that results of nuclear medicine studies often require additional examinations like plain films, CT, or even MRI.

Our study is not without limitations, one of which as in others is the lack of histological proof of lesions suspected of being skeletal metastases. For obvious ethical and practical reasons, we did not pursue for histological proof of many foci of skeletal metastases most of which were asymptomatic. Rather, this was substituted by strict adherence to accepted criteria for the diagnosis of bone metastases on both BS and WB-MRI and further regional imaging of discrepant lesions.

Despite obvious enthusiasm, whole-body MR Imaging in its current

form is not without limitations. Poor visualization of the lung parenchyma, bowel, retroperitoneum, and upper extremities are problems that must be addressed if the technique is to be accepted as a viable alternative to scintigraphy. Additionally, it should be remembered that the technique is a screening modality and, although the FSE-IR technique is sensitive to both soft tissue and osseous pathology, the findings are nonspecific.

However we believe that true limitation of this technique would lie in the usual contraindications of MRI (e.g. metallic prostheses). Although this was not encountered in our study, also claustrophobia should be considered, as relative contraindication for this technique requiring patient sedation.

It is our belief that WB-MRI technique that we used is an acceptable alternative to Bone scintigraphy whenever bone scintigraphy is not feasible and in cases of chronic renal failure, which result in sub optimal scintigraphy not when urgent assessment of the skeletal system is needed in a pregnant female. Also in cases with solitary increased uptake detected with bone scintigraphy: these lesions are often diagnosed as uncertain when they are encountered in bone scintigraphy. WB-MRI can effectively diagnose the nature of these lesions by either detecting more lesions, thus revealing the multiple nature of the pathology, or detecting tumefactive behavior such as soft tissue components, or revealing other extra skeletal tumor metastases.

To conclude:

Whole-Body MRI (WB-MRI) is one of the most recent innovations in the field of magnetic resonance imaging. The well established high contrast and spatial resolution of MRI in imaging bone marrow, however, due to its ability to image the whole body with high sensitivity at a reasonable cost and time,

skeletal scintigraphy will remain for sometime the method of choice in screening for bone metastases, surpassing both conventional and computed tomography.

REFERENCES

1. Fletcher B. Imaging pediatric bone sarcomas. *Radiol clin North Am*; 35: 1477-1494, 1997.
2. Gold RI, Seeger LL, Bassett LW, Steckel RJ. An integrated approach to the evaluation of metastatic bone disease. *Radial Clin North Am*; 28:471-483, 1990.
3. Flickinger F, Salahattin S. Bone marrow MRI: techniques and accuracy for detecting breast cancer metastases. *Magn Reson Imaging*; 12: 829-835, 1994.
4. Algra PR, Bloem JL, Tissing H, Falke TH, Amdt JW, Verboom LJ. Detection of vertebral metastases: comparison between MR imaging and bone scintigraphy. *Radiographics*; 11:219-232, 1991.
5. Aitchison FA, Poon FW, Hadly MD, Gray HW, Forrester AW, Vertebral metastases and equivocal bone scan: Value of magnetic resonance imaging. *Nucl Med Commun*; 13:429-431, 1992.
6. Chan Y, Chan K, Lam W, Metreweli C. *Chin Med J (Engl)*. Comparison of whole body MRI and radioisotope bone scintigram for skeletal metastases detection. *Jun*; 110(6): 485-9, 1997.
7. Lizuka m, Nagai K, Tamada T, Imai S, Kajihara Y, Fukunaga M, Sugihara T, Yawata Y. Whole-Body MRI in patients with malignant lymphoma. *European Congress of Radiology 2000*.
8. Resnick D, Niwayama G: Skeletal Metastases. In: Donald Resnick (ed): *Diagnosis of Bone and Joint Disorders (4th Edition)*, New York, W.B SAUNDERES COMPANY, 2002.
9. Traill Z, Talbot D, Golding S, Gleeson F. Magnetic Resonance Imaging Versus Radionuclide Scintigraphy in screening for bone Metastases. *Clinical Radiology*; 54, 448-451, 1999.
10. Padhani A and: Bone. In: Husband J, Reznick R and McLean D (eds.): *Imaging In Oncology (1st Edition)*, Oxford, ISIS medical Media, 1998.
11. Van Der Wall H :The evaluation of malignancy: metastatic bone disease. In: *Nuclear Medicine in Clinical Diagnosis and Treatment (2nd edition)*, Murray I, Ell P, Van Der Wall H, Strauss H(eds). Churchill Livingstone, San Francisco, 1998.
12. Moore SG, and Sebag GH. Primary disorders of bone marrow. In: Cohen MD Edward MK (eds.): *Magnetic Resonance Imaging in children*. Philadelphia. BC Becker: 765, 1990.
13. Gosfield E, Alavi A, Kneeland B. Comparison of radionuclide bone scans and magnetic resonance imaging in detecting spinal metastases. *J Nucl Med*; 34:2191-2198, 1993.
14. Delbeke D, Powers TA, Sandler MP Negative scintigraphy with positive magnetic resonance imaging in bone metastases. *Skeletal Radial*; 19: 112-116, 1999.
15. Kavanagh E, Smith C, Eustace S. Whole-body turbo STIR MR imaging: Controversies and avenues for development. *Eur Radiol*; 13: 2196-2205, 2003.
16. Krishnamurthy GT, Tubis M. Hiss J, Bland WH. Distribution pattern of metastatic bone disease: a need for total body skeletal image. *JAMA*; 237:2504-2506, 1977.

17. Steinborn MM, Andreas FH, Reinhold T, Melanie B, Laurie G, Maxmillian FR. Whole-Body Bone Morrow MRI in patients with Metastatic Disease to the Skeletal System. *J Comput Assist Tomogr* Jan-Feb; 23(1): 123-9, 1999.
18. Walker R and Eustace S. Whole-body Magnetic Resonance Imaging: Technique, Clinical Indications, and Future Applications. *Semin Musculoskelet Radiol*; 5-20, 2001.
19. Walker R and Eustace S. Whole-body Magnetic Resonance Imaging: Technique, Clinical Indications, and Future Applications. *Semin Musculoskelet Radiol*; 5-20, 2001.
20. Daldrop-Link HE, Franzius C, Link TM, Laukarup D, Sciuk J, Jurgens H, Schober O, Rummeny EJ. Whole-Body Mr Imaging for Detection of Bone Metastases in Children and Young Adults: Comparison with skeletal Scintigraphy and FDG PET. *AJR* Jul; 177(1): 229-36, 2001.
21. Lauenstien T, Freudenberg L, Goehde S, Ruehm S et al. Whole-body MRI using a rolling table platform for the detection of bone metastases. *Eur Radiol*; 12:2091-2099, 2002.
22. Eustace S, Tello R, De Carvalho v, Carey J, Wro JT, Melhem ER, Yucel EK. A Comparison of whole-body turbo STIR MR imaging and planar ^{99m}Tc-methylene Diphosphonate scintigraphy in the examination of patients with suspected skeletal metastases. *AJR* Dec; 169(6): 1655-61, 1997.
23. Vogler JB III, Murphy WA: Bone marrow imaging. *Radiology* 168:679, 1988.
24. Thrall J and Ziessman H : Skeletal System : In. *Nuclear Medicine: The Requisites*: Thrall J and Ziessman H (eds): Mosby: Chicago:1995.
25. Taoka T, Mayr NA, Lee HJ, Yuh WT, Simonson TM, Rezaik, Berbaum KS. Factors Influencing Visualization of Vertebral Metastases on MR Imaging Versus Bone Scintigraphy. *AJR* Jun; 176(6): 1523-30, 2001.
26. Frank JA, Ling A, Patronas NJ, et al. Detection of malignant bone tumors: MR imaging vs scintigraphy. *AJR*; 155:1043-1048, 1990.