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ORIGINAL RESEARCH

To compare the MRI findings of suspected metastatic lesions of the vertebral bone marrow with bone scan

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Abstract
Introduction – Accurate evaluation of the presence and extent of malignant bone tumors, both primary and metastatic, is crucial to the proper staging and treatment of these diseases. Bone scan was used initially but now a day's MRI is the first choice. The present study was conducted to compare the MRI findings of suspected metastatic lesions of the vertebral bone with bone scan.
Material and methods- The observational prospective study conducted in the department of Radiodiagnosis, Shri Balaji Action Medical Institute and Action Cancer Hospital among 40 patients undergoing MRI spine and bone scan for one year. The clinical and radiological findings were recorded and results were analyzed using SPSS version 24.0
Results – Out of 40 patients, 22 (55%) were females and 18 (45%) were males. Maximum subjects were from the age group of 51-60 years (35%). Most common malignancy was Ca Breast (35%) followed by Ca Prostate (20%) and Ca lung (15%). MRI reported lesion location at cervical, thoracic, lumbar and sacral spine among 35%, 70%, 70% and 40% of the subjects respectively, while the same was revealed by bone scan in 20%, 55%, 40% and 25%. The number of vertebrae involved in cervical, thoracic, lumbar and sacral vertebrae were 35, 98, 64 and 25 on MRI respectively and 19, 98 , 38 and 13 on bone scan respectively with statistically significant difference as $p<0.05$.
Conclusion- Our study demonstrates that MRI is a better modality than bone scan on both per-patient and per-lesion basis in detection of vertebral metastasis. With advancements in technology such as whole body MRI and faster imaging sequences, role of MRI is set to increase further.
Keywords- bone marrow, lesion, metastatic, MRI, scan

Introduction

Currently, cancer is one of the major public health problems; it is the third leading cause of death worldwide and is responsible for approximately 13% of all deaths worldwide.[1] The World Health Organization estimates 15 million new cancer cases by 2020.[2,3] Cancer is a term for diseases in which abnormal cells divide without control and can invade nearby tissues. Metastatic spread is a key event in the evolution of cancerous disease by transforming a curable, localized illness into a more difficult to control systemic disease.[4] In addition,

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metastatic disease may remain confined to the skeleton with the decline in quality of life and eventual death almost entirely due to skeletal complications and their treatment.[5]
Metastasis to the spine can involve the bone, epidural space, leptomeninges, and spinal cord. After the lung and the liver, the spine is the third most common site for metastatic disease. Spinal metastasis is present in approximately 60-70% of patients with systemic cancer. However, only 10% of these patients are symptomatic. The prognosis for patients presenting with bone metastasis is poor.[6]
Accurate evaluation of the presence and extent of malignant bone tumors, both primary and metastatic, is crucial to the proper staging and treatment of these diseases. Plain film radiographs, CT, scintigraphy, and MR imaging among others are the various imaging techniques that are available for the evaluation of bony metastasis.[7] Although computed tomography (CT) may be helpful in excluding a marrow-based lesion, beam hardening and streak artifacts arising from adjacent dense cortical bone may limit the sensitivity of CT to marrow lesions. Sensitivity may also be diminished by very small differences in X-ray attenuation between infiltrating neoplasms and normal bone.
Scintigraphy is the most commonly used imaging technique for the staging and evaluation of bone metastasis.[7] The mechanism of abnormal Tc-99m MDP uptake shown in bone scan is complex. Abnormal radionuclide uptake is generally believed to increase with regional bone–blood flow, bone remodeling, formation of new bone, and increased bony matrix turnover. Bone scintigraphy is sensitive for detecting areas of bone remodeling associated with metastatic deposits. Scintigraphy may reveal bony metastasis up to 18 months before radiography shows them and has a 50–80% greater sensitivity.[8]
MR imaging has recently been shown to be a sensitive technique for the detection of tumor involvement within the bone. MR imaging is a sensitive method of detecting intramedullary metastasis to those bones with large marrow cavities such as vertebral bodies. With increased capability for scanning the whole body with fast imaging techniques, screening the bone marrow cavities can be cost-effective. MR imaging is not cost-effective in examining bones with small cavities such as ribs because it cannot globally examine the entire skeletal system as bone scintigraphy can. Therefore, in general, the role of MR imaging in the examination of suspected bone metastasis is limited to those bones with large bone marrow cavities such as the spine or proximal extremities and is complementary to other imaging methods[9-11]. Because the vertebral body has a relatively large marrow cavity, early or small metastasis tend to be intramedullary lesions without cortical involvement and may not cause sufficient bony remodeling to be detected on bone scans.[12]
The detection rates of vertebral metastasis can be different between these two modalities and may cause a clinical dilemma in patient treatment, however, only a few studies have compared the findings on scintigraphy with those on MR imaging.[13] Hence the present study was conducted to compare the MRI findings of suspected metastatic lesions of the vertebral bone with bone scan.

Material and methods

This was an observational prospective study conducted in the department of Radiodiagnosis, Shri Balaji Action Medical Institute and Action Cancer Hospital for patients undergoing MRI spine and bone scan for one year duration after approval from ethics committee. Patients were asked to sign an informed consent form before commencement of study.

Sample size

The study of Ortiz Gomez observed that incidence of vertebral body metastasis was 30.6%. Taking this value as reference, the minimum required sample size with 15% margin of error

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and 5% level of significance is 37 patients. To reduce the margin of error sample size taken was 40.

Formula used is:-

$N \geq ((i(1 -i))/(ME/z\alpha)^2$

Where Zα is value of Z at two sided alpha error of 5%, ME is margin of error and I is incidence rate.

Calculations:- Margin of error=15%

n>=((.306*(1-.306))/(.15/1.96)2=36.26=37(approx.)

Patients were selected on the basis of following eligibility criteria

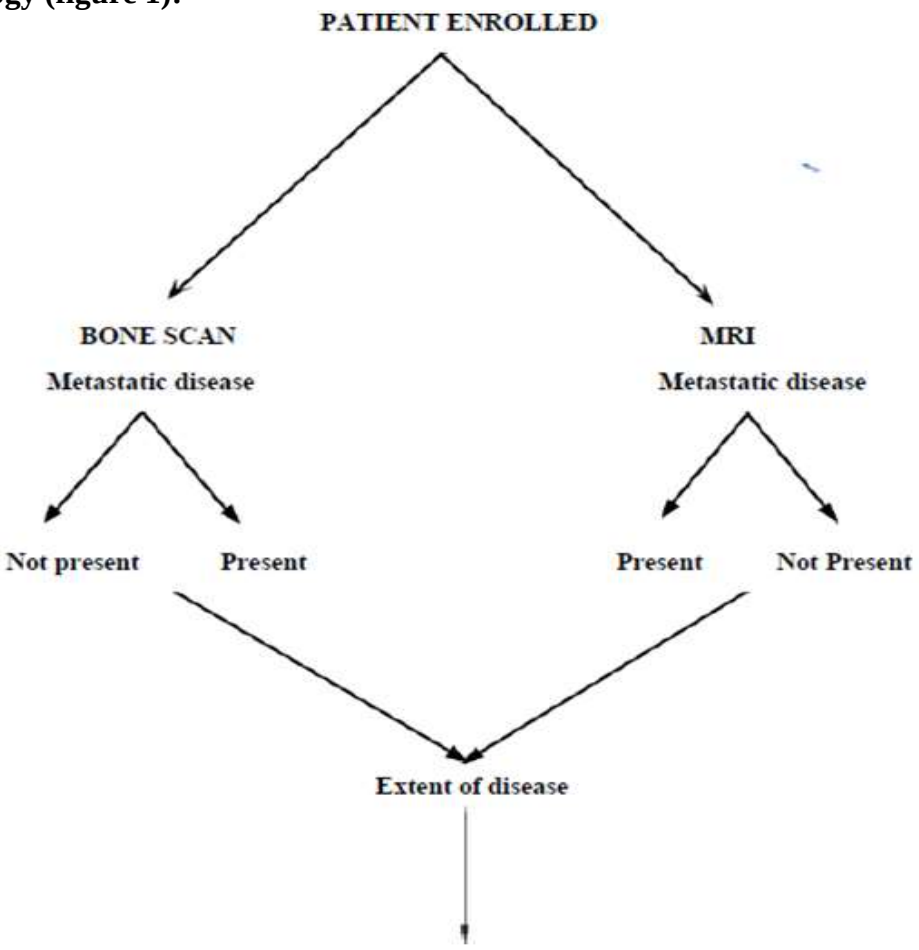
Inclusion criteria

1. Age >18.
2. Patients with proven primary malignancy who have undergone spinal MRI and bone scan.
3. Patients with suspected metastatic lesions of the vertebral bone who have undergone spinal MRI and bone scan.

Exclusion criteria

1. All patients in whom MRI/bone scan is contraindicated.
2. Patients already undergoing treatment with radiation at the time of bone scan or MRI.

Methodology (figure 1):



Equipment: GE Signa HTXD 1.5T. Standard phased array 4 channel dedicated spine coil was used for acquisition of images, GAMMA INFINIA machine for Bone scan.

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Sequences: T1WFSE, T2WFRFSE, STIR imaging, post contrast fat-sat in cases where contrast study is done.

Criteria for mri diagnoses of vertebral metastasis[6]

1. On T1W images – Focal or diffuse area of low signal intensity which is lesser than disc or muscle.
2. T2W images – Lesions which are diffusely hyperintense or show rim of hyperintensity.
3. STIR images – Lesions are hyperintense.
4. Lesions which are hypointense on all sequences are sclerotic metastasis.
5. Post contrast – Enhancement of lesions are noted if contrast study is done.

Criteria for bone scan diagnoses of vertebral marrow metastasis

Focal areas with increased accumulation of tracer which are asymmetrical and non-physiological (hotspots) after administration of Tc-99MDP intravenously.[6]

Based on the above criteria for vertebral metastasis, metastatic lesions were identified by both the modalities. The number of patients and the extent of the disease in each patient with both modalities were compared.

Statistical analysis

Data so collected was tabulated in an excel sheet, under the guidance of a statistician and was analysed using SPSS 24.00 for windows; SPSS inc, Chicago, USA. Difference between the two groups was determined using chi square test and the level of significance was set at $p < 0.05$.The chi-squared test was used to determine whether there is a significant difference between the expected frequencies and the observed frequencies in one or more categories.

Results

Out of 40 patients, 22 (55%) were females and 18 (45%) were males. Maximum subjects were from the age group of 51-60 years (35%) followed by >70 years (27.5%) and 61-70 years (22.5%). Minimum subjects were from the age group of 31-40 years (2.5%) followed by 21-30 years (5%) and 41-50 years (7.5%) as shown in table 1.

Table 1 distribution of patients on the basis of gender and age.

Variable		N (%)
Gender	Female	22 (55.0)
	Male	18 (45.0)
Age Group (in years)	21-30	2 (5)
	31-40	1 (2.5)
	41-50	3 (7.5)
	51-60	14 (35)
	61-70	9 (22.5)
	>70	11 (27.5)

Most common malignancy was Ca Breast (35%) followed by Ca Prostate (20%) and Ca lung (15%). Least reported malignancies were Adenoid Cystic Ca, Giant Cell Tumour, Renal Cell Ca and Testicular Ca as shown in figure 1.

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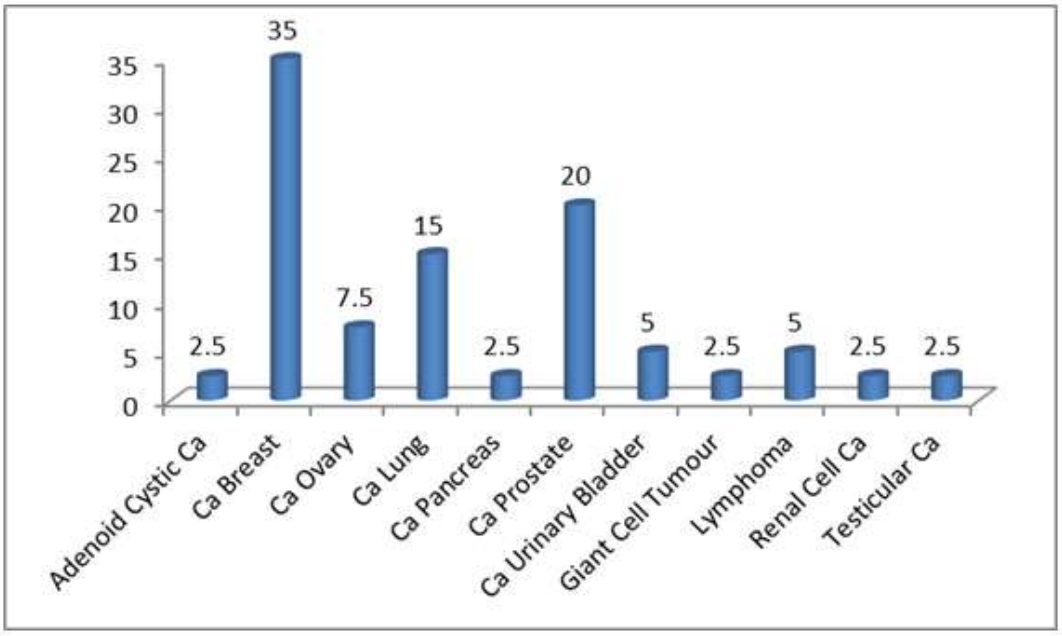
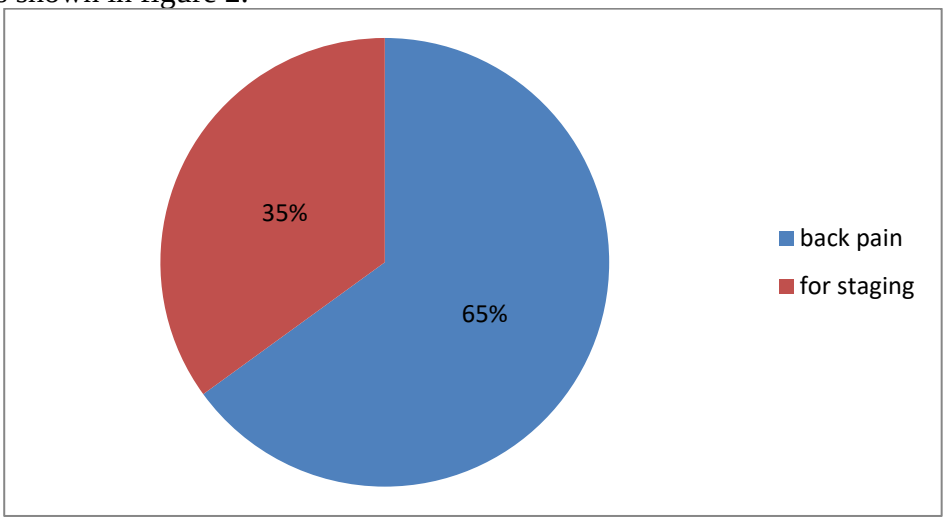
Figure 1 Primary malignancy among the study subjects (in percentage)



Most common indication among the study subjects was back pain, revealed in 65% of the subjects as shown in figure 2.



MRI reported lesion location at cervical, thoracic, lumbar and sacral spine among 35%, 70%, 70% and 40% of the subjects respectively, while the same was revealed by bone scan in 20%, 55%, 40% and 25% of the 40 subjects respectively. MRI detected vertebral metastasis in all the patients whereas bone scan was not able to locate any lesion among 6 (15%) subjects. When lesion location was compared statistically among MRI and bone scan, it was found to be statistically significant as $p<0.05$ as shown in table 2 a and 2 b.

Table 2(a): Number of patients with lesions at below mentioned sites on MRI and Bone scan

Location	MRI		Bone Scan		p value
	N	%	N	%	
Cervical Spine	14	35	8	20	0.007*
Thoracic Spine	28	70	22	55	0.04*
Lumbar Spine	28	70	16	40	<0.01*
Sacral Spine	16	40	10	25	0.004*

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Table 2(b) Number of patients with vertebral metastasis on MRI and Bone scan

	Total Patients	
	N	%
MRI	40	100
Bone Scan	34	75

The number of vertebrae involved in cervical, thoracic, lumbar and sacral vertebrae were 35, 98, 64 and 25 on MRI respectively and 19, 98 , 38 and 13 on bone scan respectively with statistically significant difference as $p<0.05$ as shown in table 3.

Table 3 No of vertebrae involve in cervical, dorsal, lumbar and sacral vertebrae on MRI and Bone scan

No	MRI	Bone Scan	p value
	N	N	
Cervical Vertebrae	35	19	<0.01*
Dorsal Vertebrae	98	50	<0.01*
Lumbar Vertebrae	64	38	<0.01*
Sacrum Vertbrae	25	13	<0.01*

The comparison of prevalence of positive and negative regions by MRI and Bone Scan in breast and prostate cancer was done. MRI found one positive region in both breast and prostate cancer patients among all the subjects while the same was reported by Bone scan among 92.86% and 62.5% of the subjects respectively as shown in table 4.

Table 4: Comparison of prevalence of positive and negative regions by MRI and Bone Scan in breast and prostate cancer

Cancer	N_1	MRI		Bone Scan	
		N_2	%	N_3	%
Breast Cancer (At Least 1 Positive Regions)	14	14	100	13	92.86
Prostate Cancer (At Least 1 Positive Regions)	8	8	100	5	62.5

N_1 – Number of patients with the primary malignancy mentioned N_2 – Number of patients showing vertebral metastasis on MRI
N_3 – Number of patients showing vertebral metastasis on Bone Scan

Discussion

Bone scintigraphy is the method of choice for initial detection of metastasis, as well as the staging of patients with cancer. Additional imaging with conventional roentgenograms, CT (when bone scan findings are inconclusive) and more recently MRI, are being utilized to add specificity to the scintigraphic findings. In particular settings, such as in myeloma, in very aggressive lesions and in lesions confined to the marrow, bone scans have low sensitivity while fractures, degenerative changes and many other benign active disorders of the bones and joints may produce false positive readings. The increasing availability of MRI has prompted its complementary use along with radionuclide scans in the detection of skeletal metastasis[14].

The detection rates of vertebral metastasis can be different between these two modalities and may cause a clinical dilemma in patient treatment. However, only a few studies have compared the findings on scintigraphy with those on MR imaging[15-18]. Hence the present study was conducted to compare the MRI findings of suspected metastatic lesions of the vertebral bone with bone scan.

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In our study female 22 (55%) were higher as compared to males 18 (45%). Maximum subjects were from the age group of 51-60 years (35%). Toshiaki Taoka et al. in their study revealed that there were 42 males and 32 females with mean age of 59 years.[13] In a study by Pipat Chiewvit et al., there were 25 men and 23 women, with mean age 61 years.[5] Our results were similar to the above mentioned studies except gender distribution, as in our study, there were more females while in other studies, there were more males. This difference may be due to difference in the study area.

The most common indication among the study subjects was back pain, revealed in 65% of the subjects. Similar findings were seen in a study by Toshiaki Taoka et al. where they found that back pain was the most frequent initial complaint in patients with spinal metastatic disease, because lesions invaded the richly innervated periosteum with or without detected invasion, possibly through the cortex via the haversian canals.[13]

The most common malignancy in present study was Ca Breast (35%) followed by Ca Prostate (20%) and Ca lung (15%). Least reported malignancies were Adenoid Cystic Ca, Giant Cell Tumour, Renal Cell Ca and Testicular Ca. In a study by Pipat Chiewvit et al., primary neoplasms included breast cancer (n = 11), colorectal cancer (n = 7), lung cancer (n = 6), prostate cancer (n = 5).[5] The most prevalent cancer was breast cancer in both studies.

MRI reported lesion location at cervical, thoracic, lumbar and sacral spine among 35%, 70%, 70% and 40% of the subjects respectively while the same was revealed by bone scan in 20%, 55%, 40% and 25% of the subjects respectively. Bone scan was not able to locate any lesion among 6 (15%) subjects while MRI located minimum one location among all the subjects. When the lesion location was compared statistically among MRI and bone scan, it was found to be statistically significant as $p<0.05$ in this study. Avrahami et al. studied 40 patients with histologically proven primary tumor referred for MRI examination due to progressive back pain. All patients had normal findings on radionuclide bone scan. Twenty-one of these patients had abnormal MRI findings.[17] Delbeke et al. found additional metastatic vertebral sites by MRI in 18% of the 56 patients with known malignancy studied by MRI and bone scan with an overall discordance rate of 23%.[19] Similarly in our study as well, MRI was found to detect metastatic lesions in additional number of patients.

In our study, number of metastatic cervical vertebrae, thoracic vertebrae, lumbar vertebrae and sacral vertebrae were 35, 98, 64 and 25 respectively on MRI and 19, 50, 38 and 13 respectively on bone scan. Number of metastatic vertebrae located on cervical, dorsal, lumbar and sacral spine were found to be higher in MRI as compared to bone scan with statistically significant difference. Similar to our study, Paul R. Algra in their study found that MR imaging showed more abnormal vertebrae than did bone scintigraphy in 49 patients.[20]

In our study, MRI found at least one positive lesion in patients with breast and prostate cancer among all the subjects while the same was reported by Bone scan among 92.86% and 62.5% of the subjects respectively. Approximately similar findings were reported by Edward Gosfield et al. in their study in which they divided the spinal vertebrae of each patient into six regions. Amongst the patients with breast cancer, 75% had at least one region which was positive on bone scan in comparison with MRI. Of the prostate cancer patients, 69% had at least one region which was positive in comparison with MRI.[14]

A number of explanations may account for the increased detection of vertebral metastasis on MRI than bone scan. Hematogenously seeded intramedullary metastasis may produce lesions by marrow replacement detectable on MRI before adequate reaction takes place in the adjacent cortex to be detected scintigraphically or radiographically.[20] The high contrast between fat and metastasis allows early demonstration of metastasis on MRI as soon as macroscopic lesions have been developed in the marrow. However, osteoblastic response is necessary for metastasis to result in increased activity on bone scan.[21] This is a relatively slow process and may require several weeks before it can be visualized on bone scan. In

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addition, the avidity of bone for radionuclide depends on the local metabolic state which is influenced by the activity of the disease and the balance of blastic versus clastic reaction. In addition to the reduction of uptake in response to therapy, there may be a reduction of tracer uptake in rapidly progressive disease where there is little chance for new bone formation.[22]
Limitations of the study were – small sample size, short duration of the study was small and subjects cannot be generalized to whole population due to involvement of Berkesonian bias.

Conclusion

Our study demonstrates that MRI is a better modality than bone scan on both per-patient and per-lesion basis in detection of vertebral metastasis. However, due to its high cost, longer acquisition time and inability to image the entire skeleton, MRI is reserved for cases with equivocal or normal findings on bone scan but high clinical suspicion for vertebral metastasis and cases with positive bone scan but low clinical suspicion for vertebral metastasis. Bone scan is the initial imaging modality of choice due to its low cost, ability to scan the entire skeleton and overall high detection. With advancements in technology such as whole body MRI and faster imaging sequences, role of MRI is set to increase further.

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