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# **RESEARCH- ARTICLE**



# The Role of Susceptibility Weighted Magnetic Resonance Imaging in Differentiation between Lytic and Sclerotic Spine Metastatic Bone Lesions

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#### Abstract

**Background:** About 30–70% of the diseased patients due to cancer have spinal metastases at postmortem examination and about 14% of the patients with spinal metastases will develop symptomatic lesions during their illness. The morbidity associated with metastatic spinal disease is significant. Aim and objectives: To evaluate the diagnostic performance of susceptibility-weighted magnetic resonance imaging (SWMR) for the differentiation between lytic and sclerotic spine metastatic bone lesions compared to compute tomography (CT). **Subjects and methods:** A prospective comparative study was conducted at the Diagnostic Radiology department, Suez Canal University hospital, Ismailia, Egypt, including 84 participants. Results: Our study showed a promising diagnostic performance of different MRI techniques including the newly introduced susceptibility weighted MRI sequence for identification of lytic bony lesions with a diagnostic accuracy of 96.43%, sensitivity of 100%, specificity of 92.31%, and positive predictive value of 93.75% and negative predictive value of 100%. The study showed impressive diagnostic performance of different MRI techniques including the susceptibility weighted sequence for detection of sclerotic bony lesions with a diagnostic accuracy of 89.29%, sensitivity of 90.91%, specificity of 88.24%, and positive predictive value of 83.33% and negative predictive value of 93.75%. We found that using either inverted magnitude MRI sequence alone, phase contrast MRI sequence alone or combining both techniques resulted in similar diagnostic performance with diagnostic accuracy of 89.29%, sensitivity of 90.91%, specificity of 88.24%, positive predictive value of 83.33%, and negative predictive value of 93.75%. Conclusion: we concluded that the susceptibility weighted MRI enables proper differentiation between lytic and sclerotic bony lesions with higher sensitivity and specificity compared to conventional MRI sequences

Keywords: Susceptibility, SWMR, CT

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## 1 | INTRODUCTION

The bony skeleton is one of the most common sites for metastatic lesions owing to high blood flow in the red marrow. The growth of disseminated tumor cells in the skeleton requires bone marrow infiltration, from which they stimulate local bone cell activity (1).

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The spine is the third most common site for metastatic disease, following the lungs and liver. Spinal metastases are the most common spinal tumors. Metastatic disease to the spine can involve the bone, epidural space, leptomeninges and spinal cord (2).

Approximately 30–70% of the diseased patients due to cancer have spinal metastases at postmortem examination and about 14% of the patients with spinal metastases will develop symptomatic lesions during their illness. The morbidity associated with metastatic spinal disease is significant; more than half of these patients will require radiotherapy or surgical intervention for spinal cord or nerve root compression (3).

Bone metastasis can be either osteolytic or osteoblastic in nature. The phenotypes of bone destruction and bone formation vary in clinical features, including incidence, prognosis, skeletalrelated events and bone biomarkers (4).

Magnetic resonance (MR) imaging is a widely available modality for the evaluation of suspected spinal metastasis, as it offers unparalleled visualization of the spinal column and cord. It provides superior imaging of bone marrow infiltration, allows characterization of the levels of involvement, and can delineate the associated cord compression and extraosseous soft tissue component of a neoplasm (5).

Susceptibility weighted imaging (SWI) is a highresolution 3D MRI sequence that highlights changes of magnetic susceptibility. Diamagnetic calcified (e.g. lesions, bone minerals), paramagnetic (e.g. ferritin, deoxy-haemoglobin) ferromagnetic substances and distort the magnetic surrounding field. Diamagnetic substances align opposite and paramagnetic compounds line up with the external magnetic field (6).

SWI has gradually developed into a useful clinical tool in the field of cerebrovascular diseases. It has been applied widely for detection of cerebral hemorrhage, hemorrhagic transformation, cerebral venous thrombosis and assessment of brain tissue at risk for infarction (7).

It seems that the role of CT may decline if the differentiation between the two main types of osseous metastases can be made with

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weighted MRI. susceptibility-Susceptibility weighted MRI may help us to assess the risk of pathologic fracture for any given lesion. This risk assessment would prove to be crucial from the quality of life and treatment regimens standing point of views as only 50% of the pathological fractures will spontaneously heal. Osteolytic metastasis represents higher risk for pathological fracture than the sclerotic metastasis. Many believe these pathologic fractures begin the "end of life cascade" in patients with metastatic disease. CT remains the mainstay for that assessment in the meantime. But perhaps in the near future, MRI techniques such as susceptibility-weighted MRI may overtake the CT for that matter.

#### 2 | SUBJECTS AND METHODS

#### Study setting and Study population

A study was prospective comparative conducted at the Diagnostic Radiology department, Suez Canal University hospital, Ismailia, Egypt. No specific interval time was determined between the CT (reference standard) and the MRI. The patients were randomly selected from the attendants of the oncology clinic in the Suez Canal university hospitals for their routine examination and follow up, as well as those who present to the radiology department (CT and MRI units) for their scheduled imaging follow up.

#### **Inclusion criteria**

- Adult patients ( $\geq$  18-year-old).
- Patients with established diagnosis of lytic or sclerotic spine metastatic bone lesions in the lumbar spine, proved by CT (reference gold standard)

**Supplementary information:** The online version of this article (https://doi.org/10.52845/ (<u>rrarjmcs/</u> 2023/9-3-1) Contains supplementary material, which is available to authorized users.

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- Patients with devices that are incompatible with MRI (such as pacemakers, metallic stents, internal fixation... etc.)
- Patients with bone metastasis that extensively involve all examined vertebral bodies sparing no healthy vertebral body bone marrow as a reference to compare to
- Females who are pregnant or breast feeding
- Invisibility of the metastasis findings in CT (no reliable delineation in the standard exam).
- Upper dorsal and cervical spine metastatic lesions were excluded due to artifacts in the phase images which prevented proper diagnostic interpretation

#### Study design

It was a prospective comparative study

#### Sample Size Justification

The estimated sample size was 84 patients.

## **3 | Data collection procedure**

## **Imaging Protocol**

All cases were examined by multi-detector CT scan of the affected part of the spine using (Activion 16 model TSX-031A-2012 with standard accessories – Toshiba medical system) and (Alexion model TSX-032A with standard accessories – Toshiba medical system).

All the cases performed the standard MRI assessment of the lower dorsal and lumbosacral spine as well as the susceptibility weighted MRI sequence

## MRI imaging protocol (8)

All patients were examined on a 1.5 Tesla MRI (Philips Medical Systems, Achieva), using superconductive coil (a standard body coil for the lumbar spine).

For the lumbar spine, sagittal T1 SE, T2 TSE and axial T2 TSE sequences were acquired with the following imaging parameters:

Additionally, a 3D-fast low-angle gradient-echo sequence (SWMR) was performed for the lumbar spine. The SWMR magnitude image derives from ARJMCS 09 (3), 1098–1106 (2023) a velocity-compensated 3D-GRE sequence, which is part of the SWMR. This sequence is comparable to standard GRE sequences for the detection of T2\*-time shortening lesions. Reconstruction of phase information was also done.

## Image analysis

Analysis was carried out with a picture archiving and communication system workstation - PACS (FUJIFILM Medical systems, USA). A combination of all available imaging modalities, including CT and standard spine MRI sequences, were used to document and identify bone metastasis.

In the first step of the MR analysis, spine metastases on standard MR images were classified visuallv predominantly osteoplastic as osteocytes. Metastases that will be predominantly hypo intense on T1-weighted images and hyper intense on T2 weighted images will be stated as predominantly osteocytes. Spine metastases that will be predominantly hypo intense on T1weighted and T2-weighted images will be stated as predominantly osteoplastic. Based on other previous studies, the reliance on the conventional MR sequences to determine the nature of the lesions is very limited.

On susceptibility-weighted MR images, metastases were stated as predominantly osteoplastic if they were hyper intense on inverted magnitude images and hypo intense on phase images and as osteocytes if they were hypo intense on inverted magnitude images and hyper intense on phase images.

As for the objective analysis of the lesions of concern on MRI, metastatic to vertebral body ratio (MVR) was calculated in CT, phase contrast images and inverted magnitude images using region of interest (ROI) – plotted by the first reviewer on the lesion and again on the reference normal surrounding bone marrow. Creation of cut-off value for both lytic and sclerotic bone lesions help the radiologist achieving both subjective and objective analysis of the examined bone lesions. MVR was calculated according to the following equation: signal (metastasis)/ signal (vertebral body) = S (M)/S (VB) = MVR. (9)

#### 4 | RESULTS

Table (1).	Clinical	characteristics	of studied	patients
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Variables	( <b>n=84</b> )
Age (years), mean ± SD	$56.25 \pm 13.74$
Gender, n (%)	
Male	39 (46.4)
Female	45 (53.6)
Primary tumor, n (%)	
Breast cancer	39 (46.4)
Prostate cancer	27 (32.1)
Cancer Colon	6 (7.1)
Bronchogenic carcinoma	6 (7.1)
Multiple myeloma	3 (3.6)
Unknown primary	3 (3.6)

Table 1 summarizes the baseline characteristics of the studied patients. The mean age of the patients was 56.25  $\pm$  13.74 years. Females formed about 53.6% of the sample. The most frequent primary tumor was breast cancer (46.4%), prostate cancer (32.1%) and cancer Colon (7.1%) (Figure 1)



Figure (1). Percentage of primary tumor among the patients

Table	(2).	Comparison	hetween (	CT	morphology	and	primarv	source	of t	he metastatic	lesions
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Primary tumor, n (%)	Hypodense lesion (Lytic) (n=45)	Hyperdense lesion (Sclerotic) (n=33)	Mixed lesions (n=6)	Test value	p-value
Breast	30 (66.7)	3 (9.1)	6 (100)		
Prostate	3 (6.7)	24 (72.7)	0 (0)		
Colon	6 (13.3)	0 (0)	0 (0)	12.2	0 16 <sup>a</sup>
Bronchogenic	0 (0)	6 (18.2)	0 (0)	15.5	0.10
Multiple Myeloma	3 (6.7)	0 (0)	0 (0)		
Unknown	3 (6.7)	0 (0)	0 (0)		

<sup>a</sup> p-values are based on Fisher Exact Test. Statistical significance at P < 0.05

Table 2 shows that there is no statistically significant difference between the type of the metastatic bony lesion based on CT morphology and the origin of the primary tumor.

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Table (3). Radiological features of metastatic bony lesions

Variables	( <b>n=84</b> )
CT, n (%)	
Hypodense lesions (Lytic)	45 (53.6)
Hyperdense lesions (Sclerotic)	33 (39.3)
Mixed lesions	6 (7.1)
MRI, n (%)	
T1Wis	
Hypointense lesion	60 (71.4)
Isointense lesion	3 (3.6)
Hyperintense lesion	21 (25)
T2Wis	
Hypointense lesion	27 (32.1)
Isointense lesion	9 (10.7)
Hyperintense lesion	36 (42.9)
Heterogeneous lesion	12 (14.3)
Inverted Magnitude	
Hypointense lesion	48 (57.1)
Hyperintense lesion	36 (42.9)
Phase Contrast	
Hypointense lesion	30 (35.7)
Hyperintense lesion	48 (57.1)
Heterogeneous lesion	6 (7.1)

Table 3 shows the radiological features of metastatic bony lesions. Regarding CT morphology, 53.6% of cases were lytic metastatic bony lesions. Conventional MRI assessment showed 71.4% of lesions were hypointense in T1WIs and 42.9% were hyperintense in T2WIs. Susceptibility-weighted magnetic resonance imaging (SWMR) MRI sequences showed hypointense lesion in 57.1% of Inverted Magnitude images and hyperintense lesion in 57.1% of Phase-contrast images.

Table (4). Subjective assessment based on MRI features of metastatic bony lesions

Variables	( <b>n=84</b> )
Observer 1	
Lytic	48 (57.1)
Sclerotic	36 (42.9)
Observer 2	
Lytic	48 (57.1)
Sclerotic	36 (42.9)

Table 4 Subjective assessment based on MRI features of metastatic bony lesions where both observers consider 57.1% of cases as lytic bony lesion and 42.9% of cases as sclerotic bony lesions.

 Table (5). Comparison between CT and MRI morphology of the metastatic lesions

	CT morphology				
MRI morphology, n (%)	Hypodense (Lytic) (n=45)	Hyperdense (Sclerotic) (n=33)	Mixed (n=6)	Test value	p-value
T1WIs					
Hypointense	24 (53.3)	30 (90.9)	6 (100)		
Isointense	0 (0)	3 (9.1)	0 (0)	9.5	<b>0.01</b> <sup>a</sup>
Hyperintense	21 (46.7)	0 (0)	0 (0)		
T2WIs					
Hypointense	9 (20)	12 (36.4)	6 (100)		<b>0.03</b> <sup>a</sup>

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Isointense	0 (0)	9 (27.2)	0 (0)	11.2	
Hyperintense	30 (66.7)	6 (18.2)	0 (0)		
Heterogeneous	6 (13.3)	6 (18.2)	0 (0)		
IM					
Hypointense	45 (100)	3 (9.1)	0 (0)	26.2	<0.001 <sup>a</sup>
Hyperintense	0 (0)	30 (90.9)	6 (100)	20.3	
Phase Contrast					
Hypointense	0 (0)	30 (90.9)	0 (0)		
Hyperintense	45 (100)	3 (9.1)	0 (0)	24.3	<b>&lt;0.001</b> <sup>a</sup>
Heterogeneous	0 (0)	0 (0)	6 (100)		

a p-values are based on Fisher Exv act Test. Statistical significance at P < 0.05

Table 5 shows comparison between CT and MRI morphology of the metastatic lesion. Conventional MRI sequences, T1WIs and T2WIs, were seen statistically associated with CT morphology with bony lesions, (p=0.01) and (0.03) respectively. Meanwhile, in Phase-Contrast MRI sequence lytic bony lesions were statistically associated with hyperintense signal and sclerotic bony lesions were associated with hypointense and isointense signals (p<0.001). On the other hand, in Inverted Magnitude MRI sequence lytic bony lesions were associated with hypointense signal and sclerotic bony lesions were statistically associated with hypointense signal and sclerotic bony lesions were statistically associated with hypointense signal and sclerotic bony lesions were statistically associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hypointense signal and sclerotic bony lesions were associated with hyperintense signal (p<0.001).



**Figure (2).** L3 lytic lesion. The white circle in all 5 images refer to L3 vertebral body lesion – demonstrated in CT (A), T1WI (B), T2WI (C), Inverted Magnitude (D) and Phase Contrast images (E).

It appears hypodense in the reference gold standard CT– **lytic lesion:** It appears hyperintense in T1 weighted images (B) and T2 weighted images (C) It appears hypointense in relation to the bone marrow in IM images (D) It appears hyperintense

in phase contrast images in relation to the normal bone marrow (E)



**Figure (3).** L4 sclerotic lesion. The white circle in all 5 images refer to L4 vertebral body lesion – demonstrated in CT (A), T1WI (B), T2WI (C), Inverted Magnitude (D) and Phase Contrast images (E). It appears hyperdense in the reference gold standard CT – **sclerotic lesion** (A). It appears hypointense in T1 weighted images, T2 weighted images (B&C). It appears hyperintense in IM images in relation to the surrounding normal bone marrow signal intensity (D). It shows noisy hypointense signal in phase contrast images in relation to the normal bone marrow (E)

#### 4 | DISCUSSION

Radiography, CT, MRI and nuclear imaging techniques are currently used for the detection and characterization of bone metastases. The accuracy of radiography depends on different factors, including size and location of metastases. In general, up to 30%–50% loss of bone density must

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occur before metastases can be reliably detected on plain X-ray (9).

Computed tomography is more sensitive than radiography in the detection of bone metastases; however, it also relies on changes in the matrix of the bone. The sensitivity and specificity of CT for detection of bone metastasis is 74% and 56%, respectively (10)

Our present study aimed at exploring the added value of susceptibility-weighted magnetic resonance imaging (SWMR) in differentiation between lytic and sclerotic spine metastatic bone lesions compared to the gold standard computed tomography (CT). This study was designed as a prospective comparative study including 84 patients with spine metastatic bone lesions. The mean age of the patients was  $56.25 \pm 13.74$  years. Females formed about 53.6% of the sample. The most frequent primary tumor was breast cancer (50%), prostate cancer (32.1%) and cancer Colon (7.1%).

Lange et al. conducted a study of 187 tumors. They reported bone osteolytic lesions in 105 tumors, osteoblastic lesions in 23 tumors and mixed lesions in 59 tumors. Our present study was in agreement with the larger Lange et al. study, regarding the most common types of primary malignancy encountered during the data collection. In our study, we found that prostate and breast cancer cases accounted for almost 80% of our cases. Meanwhile, Lange et al. found that prostate cancer and breast cancer were the most frequent types of cancer, accounting for almost 70 % of all tumors (11)

The identification of the origin of the primary tumor plays an important role in choosing the proper diagnostic modality to screen for bone metastasis. A method such as bone scan solely reflects bone metabolism at sites with active bone mineralization, such as sclerotic lesions, making it of particular importance in prostate cancer and of limited use in predominant osteolytic lesions such as multiple myeloma (12). Hence, we decided to assess the correlation between the type of bone metastasis and the type of the primary tumor. Surprisingly, there was no significant statistical correlation between the type of the primary tumor and the type of metastatic bony lesions based on the CT morphology in our current study. We actually couldn't fully understand the reason behind this lack of association.

In the present study, regarding CT morphology, 53.6% of metastatic bony lesions were lytic in nature. Subjective assessment of metastatic bony lesions based on MRI features in different sequences including SWI by both reviewers (each separately) labeled 57.1% of total cases as lytic bony lesions and 42.9% of total cases as sclerotic bony lesions. Our success rate in correct subjective identification of the type of metastasis based on MRI findings was very comparative to Böker et al. In the study conducted in 2019, Böker et al. analyzed 64 spine lesions in 53 study participants. Similarly, they used CT as the reference standard, with a sensitivity of 100% and a specificity of 96% identifying osteoblastic for lesions using susceptibility-weighted MRI. On the basis of susceptibility-weighted MRI, 25 of the 26 osteolytic metastases were correctly classified as osteolytic (96%). In the classification of osteolytic metastases, susceptibility-weighted MRI achieved a sensitivity of 96% (25 of 26; 95%) and a specificity of 100% (38 of 38; 100%). This is notably better than the combination of T1- and T2weighted MRI sequences alone achieving a lower performance with sensitivity of 73% (19 of 26) and a specificity of 92% (35 of 38) (13)

On the same note, our study showed impressive diagnostic performance of different MRI techniques including the susceptibility weighted sequence for detection of sclerotic bony lesions with a diagnostic accuracy of 89.29%, sensitivity of 90.91%, specificity of 88.24%, and positive predictive value of 83.33% and negative predictive value of 93.75%.

Compared to Böker et al 2019, we found that the sensitivity and specificity of the MRI regarding the differentiation between lytic and sclerotic lesions are considerably high in both studies. There was a slight difference between both studies that came to our attention; our study was more successful and accurate regarding identification of lytic lesions. Meanwhile, Böker et al study was more reliable when it comes to sclerotic lesions identification. MANUSCRIPT CENTRAL-

Both studies used CT as gold standard and both described same MRI signal intensities in inverted magnitude and phase contrast sequences. The larger sample of Böker et al 2019 cannot explain the differences. Böker et al calculated the sensitivity and specificity of the conventional MRI sequences (T1 and T2) separately and compared them to the newly added inverted magnitude and phase contrast. Unlike Böker et al, our reviewers didn't interpret the T1 and T2 images separately. Instead we interpreted all sequences together, inverted magnitude alone, phase contrast alone and both inverted magnitude and phase contrast together. This could have added further depth and strength to the diagnostic preformance of SWI sequences regarding the differentiation of both types of lesions. However, we tested our results against the already low sensivitty and specificity numbers of T1 and T2 weighted images regarding this matter, mentioned previously in other studies (13, 14)

## 5 | CONCLUSION

Based on our study results, we concluded that susceptibility-weighted MRI enables the reliable differentiation between predominantly osteosclerotic and osteolytic spine metastases with a higher accuracy compared to standard spine MRI sequences.

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## **Personal Information**

A skilful Diagnostic Radiology specialist with over 10 years of clinical experience

A member of the european society of Radiology

A holder of the european diploma in Radiology (EDiR)

A holder of a master degree in Diagnostic Radiology

A member of the PAIRS with credited skills in body interventional radiology

#### About My Work

I'm glad to submit my work to your journal. Hopefully, it will represent a corner stone for more work to come in the field of bone imaging. It is an authentic work made with percision. It aims at improving clinical practice in the field of diagnostic radiology and oncology.

I wish this work would be the first of many more researches to come.

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