Zagazig University Medical Journal
www.zumj.journals.ekb.eg

https://doi.org/10.21608/zumj.2024.234154.2873 Volume 30, Issue 1.7, Oct. 2024, Supplement Issue

Manuscript ID: ZUMJ-2302-2757 **Doi: 10.21608/zumj.2023.196337.2757**

ORIGINAL ARTICLE

Added Value of Metastasis to Vertebral body Signal Ratio in Susceptibility Weighted Magnetic Resonance Imaging in Differentiation between Lytic and Sclerotic Metastatic Vertebral Lesions

Tarek H. Khalil[1],Ahmed F. Elserafi [1,] Walid Mosallam [2] , Ibrahim S. El Sayed[3*]

[1]Radiology Department, Faculty of Medicine, Suez Canal University, Ismailia, Egypt
[2]Radiology Department, Faculty of Medicine, Suez Canal University, Ismailia, Egypt
[3*]Radiology Department, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

Corresponding author*
Ibrahim Shokri Ali El Sayed

E-mail:
Isf141988@gmail.com

Submit Date 03-03-2023
Revise Date 28-03-2023
Accept Date 29-03-2023

ABSTRACT

Objectives: Background: Spinal metastasis represents a global medical concern. It causes significant clinical problems in almost one fifth of cancer patients. It is associated with significant morbidity and mortality in almost 60% of cancer patients. Lytic bone metastasis is associated with greater risk of disability and associated pathological fractur thansclerotic bony lesions.

Aim : To calculate reliable metastatic to vertebralbody signal-ratio cut-off points in susceptibility-weighted magnetic resonance sequences (SWMR) for the differentiation between lytic and sclerotic spine metastatic vertebral lesions.

methods: A prospective comparative study was conducted at the Diagnostic Radiology department, Suez Canal University hospital, Ismailia, Egypt, including 84 participants.

Results: Our ROC curve analysis of metastases to vertebral body signal-ratio (MVR) indicates that a value of (>1.18) is the best cut-off point to predict the sclerotic bony lesions in inverted magnitude sequence, with sensitivity = 90.91% and specificity = 88.24%. Meanwhile, a value of (<1.45) was found to be the best cut-off point to predict the sclerotic bony lesions in phase contrast sequences, with sensitivity = 90.91% and specificity = 88.24%. As for lytic lesions, a value of (<1.18) was found to be the best cut-off point to predict the lytic bony lesions in inverted magnitude sequence, with sensitivity =100% and specificity =92.31%. On the same note, a value of (>1.45) was found to be the best cut-off point to predict the lytic bony lesions in phase contrast sequences, with sensitivity = 100% and specificity = 92.31%.

Conclusion: we were able to calculate the cut-off value for metastasis to vertebral body signal-ratio in both inverted magnitude and phase contrast MR sequences which would enable radiologists to properly differentiate between lytic and sclerotic bony lesions with high sensitivity and specificity.

Keywords: Metastasis to vertebral body ratio (MVR), Susceptibility, SWMR, CT

INTRODUCTION

Skeletal metastasis is the most common bone tumors. It occurs in approximately 50% of all patients with cancer [1].The spine is a very common site for metastatic disease. Spinal

metastasis involves the bone, dural coverings and spinal cord[2].

The spinal metastasis comes with significant morbidity and mortality. The repercussions of this healthcare cancer range from bed-ridden disabilities owing to vertebral bodies destruction to spinal cord compression and resulting paralysis[3].

Computed tomography is currently the modality of choice in identification and differentiation between lytic and sclerotic bony lesions [4].

Magnetic resonance (MR) imaging is a superior bone marrow imaging modality, providing better characterization of spinal cord, dural involvement and soft tissue masses [5].

The 3D susceptibility weighted imaging (SWI) is used widely in the neurovascular imaging field. It is the most sensitive magnetic resonance sequence for identification of brain hemorrhage and microbleeds as well as diffuse axonal injuries][٦,٧.

There is a worldwide approach to minimize the usage of CT and other imaging modalities using ionizing radiation if possible and whenever less hazardous alternatives exist. Currently, we still depend on CT and plain radiography to differentiate between lytic and sclerotic bony lesions. The role of CT will only recede if the much safer advanced susceptibility MRI sequences proved to be a reliable replacement. Susceptibility weighted MRI may provide us with both subjective and objective data to assess the type of skeletal metastasis. The clinical importance of this classification is to predict the pathological fracture risk for each lesion, a risk that increases significantly with lytic lesions compared to sclerotic lesions. This would help to establish basis for better quality of life.

The study aimed at calculating the cut-off value for metastasis to vertebral body signal-ratio in both inverted magnitude and phase contrast MR sequences which would enable radiologists to properly differentiate between lytic and sclerotic bony lesions with high sensitivity and specificity.

METHODS

Study design:

A prospective comparative study was conducted at the Diagnostic Radiology department, Suez Canal University hospital, Ismailia, Egypt. Adult patients, older than 18 year-old, were randomly selected from the attendants of the oncology clinic in the Suez Canal university hospitals, already diagnosed for bone metastasis, for their routine examination and follow up, as well as those who presented to the radiology department (CT and MRI units) for their scheduled imaging follow up.

Patients with metallic devices that are incompatible with MRI were excluded.

Patients with disseminated metastasis of the spine were excluded.

Ethical considerations:

Our study proposal was agreed initially by the local ethical committee of faculty of medicine in Suez Canal University (File number: 3827 – Date of approval: 07-04-2019). Our work is in accordance with the code of ethics of the world medical association (declaration of Helsinki) for experiments involving humans.

Sample Size Justification

The estimated sample size was 84 patients (Examined one lesion for each patient).

Data collection procedure

MRI imaging protocol and imaging analysis[8].

The conventional CT was done using (Activion 16 model TSX-031A-2012 with standard accessories – Toshiba medical system) and (Alexion model TSX-032A with standard accessories – Toshiba medical system). The susceptibility-weighted MRI, T1-and T2-weighted MRI-sequences were performed using (1.5T - Philips Medical Systems, Achieva). Two radiologists with at least 5 years of diagnostic experience in musculoskeletal imaging reviewed all MR images and were blinded of the CT findings. The signal intensity of the lesions in

different MR sequences was acquired from the first reviewer only (Figures 1, 2 and 3). The 2nd reviewer only gave his final opinion whether the lesion was sclerotic or lytic without detailing his description for each lesion in each available sequence.

Imaging Protocol: (Table 1 in supplementary data)

MRI was performed on a 1.5 Tesla MRI (Philips Medical Systems, Achieva), using a standard body coil for the lumbar spine. To reduce artifacts, a standard ventral saturator was used. Sagittal T1 TSE, T2 TSE or T2 TIRM and susceptibility weighted sequences were acquired. Susceptibility-weighted magnitude-images derive from a velocity-compensated 3D-GRE sequence, which is part of the susceptibility-weighted MRI. In addition to the magnitude-images, susceptibility weighted MRI also includes the reconstruction of phase information. For susceptibility weighted MRI of the lumbar spine, the following imaging parameters were used: Field-of view 280 mm^2, matrix 448, TR/TE = 49/14 msec, 15degree flip-angle, slice-thickness 3 mm.Magnitude-images and phase-images were automatically reconstructed. Acquisition time of the susceptibility-weighted MRI sequence was 9 minutes and 20 seconds. CT was performed on a CT scanner (16 slices) as detailed above.

Imaging Analysis

Region of interest (ROI) was placed in the epicenter of the vertebral lesions as well as in the reference area of normal bone marrow in both phase contrast and inverted magnitude images. Based on these measurements, the "metastases to vertebral body signal-ratio" (MVR) was calculated in both phase contrast and inverted magnitude images. HU value of the vertebral lesions was measured in gold standard CT.

Data obtained from the different MR sequences for each lesion were used collectively to calculate the sensitivity and specificity of the different MRI-sequences in comparison to CT as reference-standard.

RESULTS

The mean age of the studied patients was 56.25 ± 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%). (Table 4 in supplementary data)

The mean MVR of Inverted Magnitude sequence was 1.63 ± 1.25, while the mean MVR of Phase Contrast sequence was 2.03 ± 1.17 (Table 1).

The metastases to vertebral body signal-ratio (MVR) of both inverted magnitude and phase contrast MRI sequences showed statistically significant association with CT density of metastatic vertebral lesions. In pairwise analysis; the MVR of inverted magnitude MRI sequence of the sclerotic lesions (2.69 ± 1.2) was significantly higher than the lytic lesions (0.71 ± 0.15) ($p<0.001$). However, in phase contrast MRI sequence, sclerotic lesions (1.02 ± 0.39) had significantly lower MVR compared to lytic lesions (2.91 ± 0.86) ($p<0.001$) (Figure 4).

There was no significant difference between the MVR in both Inverted Magnitude & Phase Contrast MRI sequences and type of primary tumor, ($p=0.42$) and ($p=0.26$) respectively.

There was a significant negative correlation between metastases to vertebral body signal-ratio (MVR) of Inverted Magnitude & Phase Contrast MRI sequences e ($r = -0.691$) ($p<0.001$) (Table 2).

For inverted magnitude sequence the area under the curve (AUC) was 0.88. A value of (>1.18) was found to be the best cut-off point to predict the sclerotic bony lesions, with sensitivity = 90.91% and specificity = 88.24% (Figure 5). Meanwhile, for phase contrast sequence the area under the curve (AUC) was 0.928. A value of (<1.45) was found to be the best cut-off point to predict the sclerotic bony lesions, with sensitivity = 90.91%

and specificity = 88.24% (Figure 3 in supplementary data).

For inverted magnitude sequence the area under the curve (AUC) was 0.949. A value of (<1.18) was found to be the best cut-off point to predict the lytic bony lesions, with sensitivity =100% and specificity =92.31% (Figure 4 in supplementary data). Meanwhile, for phase contrast sequence the area under the curve (AUC) was 0.987. A value of (>1.45) was found to be the best cut-off point to predict the lytic bony lesions, with sensitivity = 100% and specificity = 92.31%. (Figure 5 in supplementary data)

	Table Name
	Metastasis to vertebral body signal-ratio (MVR) of metastatic vertebral lesions
	Correlation analysis between metastases to vertebral body signal-ratio (MVR) of Inverted Magnitude & Phase contrast MRI sequences

Table (1). Metastases to vertebral body signal-ratio (MVR) of metastatic vertebral lesions

Variables	(n=84)
MVR-Inverted Magnitude	1.63 ± 1.25
MVR-Phase Contrast	2.03 ± 1.17

Table (2). Correlation analysis between metastases to vertebral body signal-ratio (MVR) of Inverted Magnitude & Phase contrast MRI sequences

Variables	MVR-Inverted Magnitude sequences	
	Correlation coefficient (r)	p-value
MVR- Phase Contrast sequence	-0.691	**<0.001** [a]

[a] P values are based on Spearman's correlation test as appropriate.
Statistical significance at P < .05

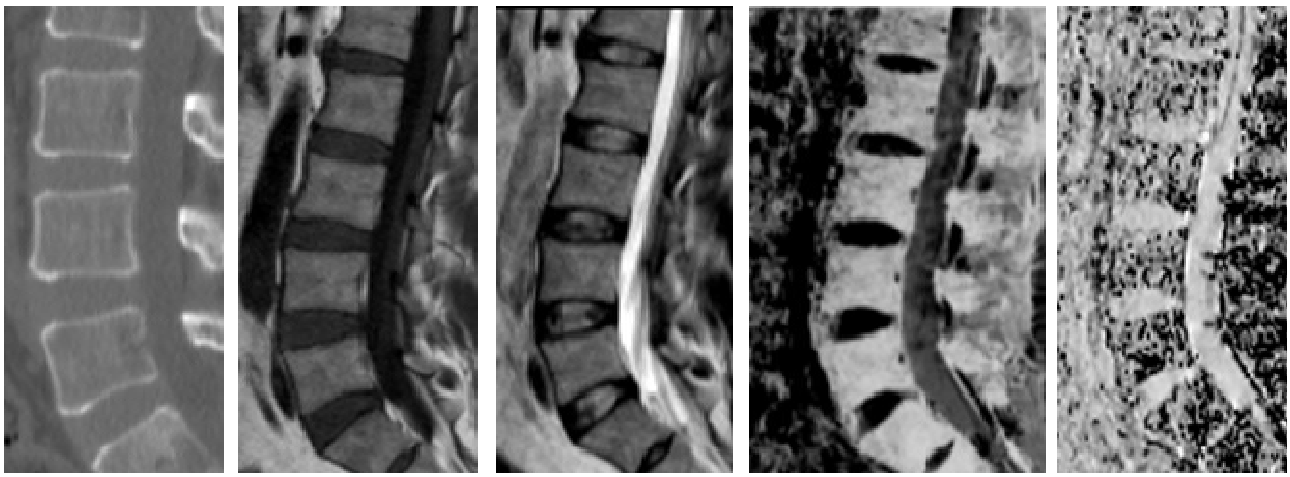

Figure (1): Demonstration of normal bone marrow signal intensity in CT and all used MR pulse sequences. A 32 year-old patient with low back pain presenting for MRI of the lumbosacral spine. The sagittal plain of CT images (A) shows no bony lesions or endplate changes. The T1-weighted and T2-weighted MR images show normal MRI signal intensity (B&C). The inverted magnitude susceptibility MR images show homogenously hyperintense signal intensity of the vertebral bodies with intervening hypointense discs (D). The phase contrast susceptibility MR images show noisy hypointense signal intensity of the vertebral bodies with intervening high signal intensity of the discs (E). The images are acquired after application of IP filter post-processing software.

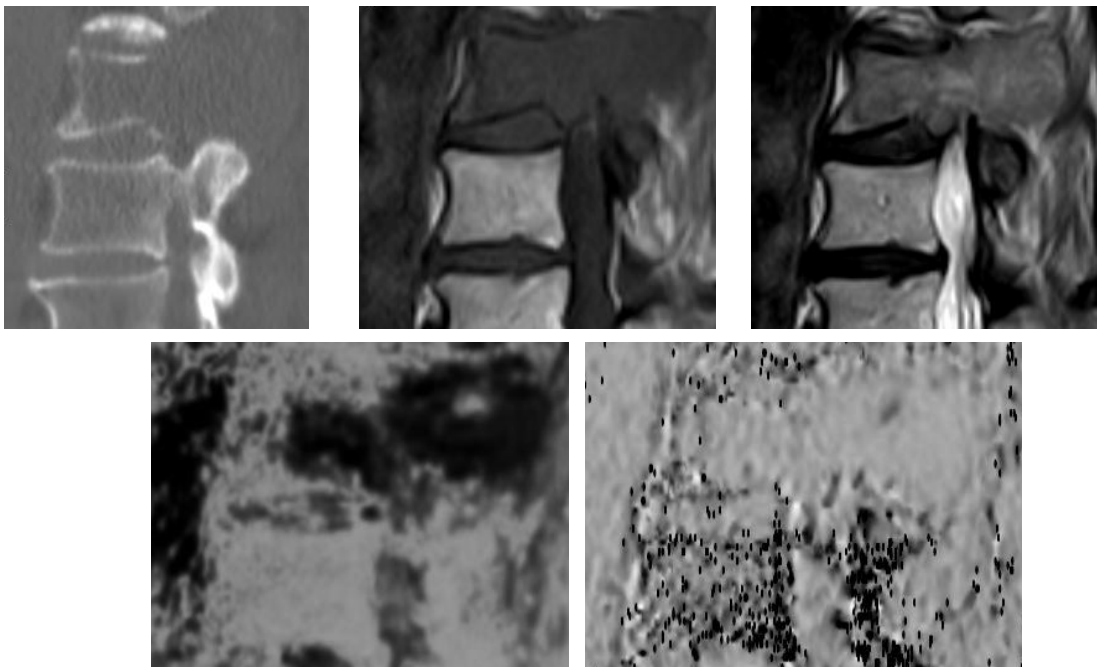

Figure (2): L1 vertebral body destructive metastatic lesion in a 43 year-old male patient with sigmoid cancer. A destructive L1 vertebral body lesion is seen (Arrow) in CT (A), T1-weighted MR image (B), T2-weighted MR image (C), inverted magnitude susceptibility-weighted MR images (D) and phase contrast susceptibility weighted MR images (E). The lesion appears lytic in the gold standard CT images (A). The lesion was correctly classified by a lytic lesion based on conventional and susceptibility weighted MR images. It shows hypointense signal intensity in T1 and T2 images in reference to the normal vertebral bodies bone marrow (B &C). It appears hypointense in inverted magnitude images and hyperintense in phase contrast images (D & E). The dotted red circles in (D) and (E) are corresponding to the site of ROI drawn on the lesion in inverted magnitude and phase contrast images respectively. The dotted blue circles in (D) and (E) are corresponding to the site of ROI drawn on the normal bone marrow in inverted magnitude and phase contrast images respectively. MVR was calculated in both sequences (MVR: 0.3 in inverted magnitude (D) and MVR: 2.9 in phase contrast

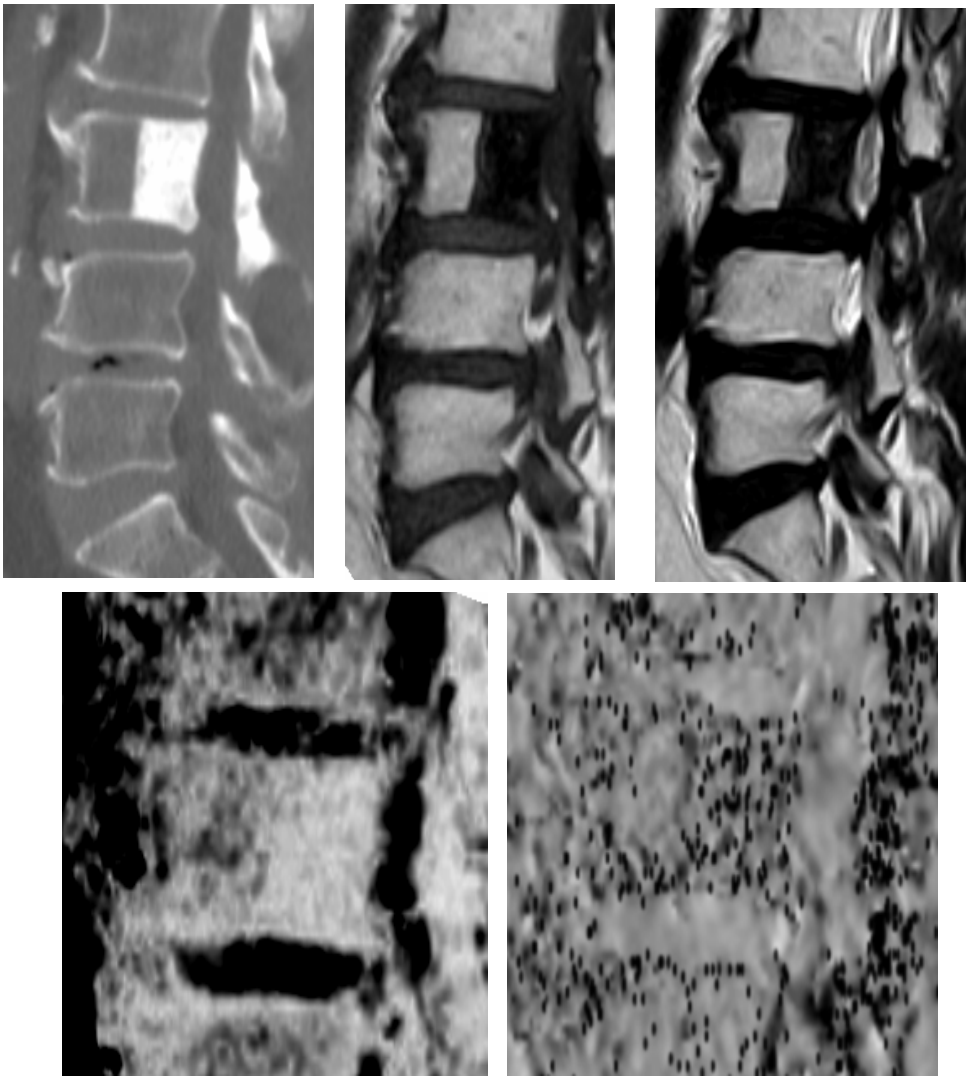

Figure (3): A sclerotic lesion in L3 vertebral body in a known case of prostatic cancer with history of on-going treatment of spine metastasis. The white arrows refer to L3 vertebral body lesion – demonstrated in CT (A), T1-weighted MR images (B), T2-weighted MR images (C), Inverted Magnitude susceptibility MR images (D) and Phase Contrast susceptibility MR images (E). The lesion appears sclerotic in the reference gold standard CT (A). The lesion was correctly classified by the reviewers, who were blinded from the CT images, as a sclerotic lesion. It appears hypointense in both T1 weighted images and T2 weighted images (B & C). It shows significantly hyperintense signal intensity in inverted magnitude images compared to the surrounding bone marrow (D). It shows hypointense noisy signal in phase contrast images in relation to normal marrow (E). The dotted red circles in (D) and (E) are corresponding to the site of ROI plotting on the corresponding lesions in inverted magnitude and phase contrast images respectively. The dotted blue circles in (D) and (E) are corresponding to the site of ROI drawn on the normal bone marrow in inverted magnitude and phase contrast images respectively. MVR was calculated in both sequences (MVR: 1.9 in inverted magnitude and MVR: 0.55 in phase contrast).

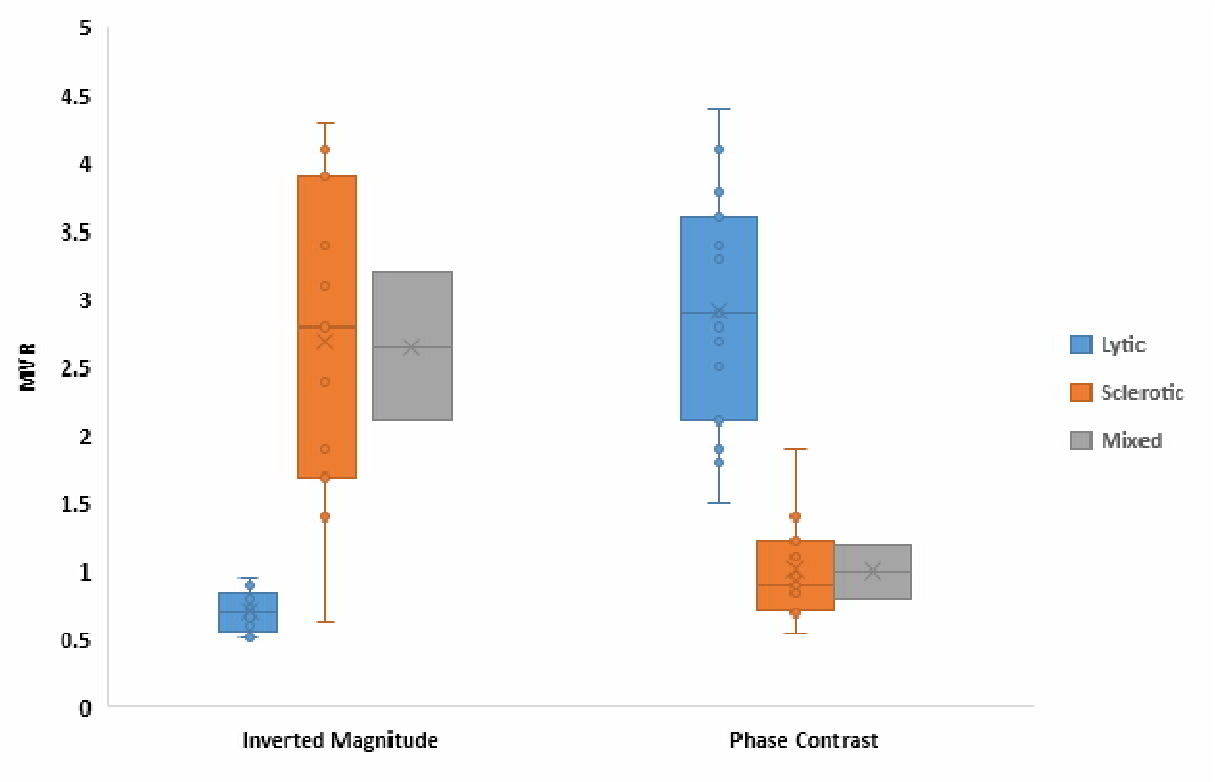

Figure (4). Comparison between CT density and MVR of the Metastatic bony lesions

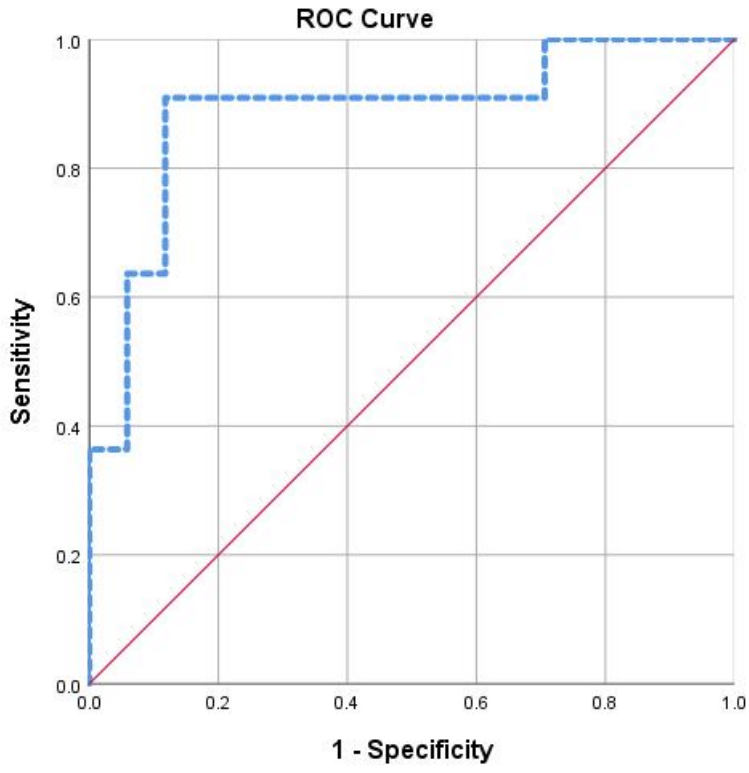

Figure (5). Receiver operator (ROC) curve for prediction of sclerotic bony lesion through MVR in IM sequence

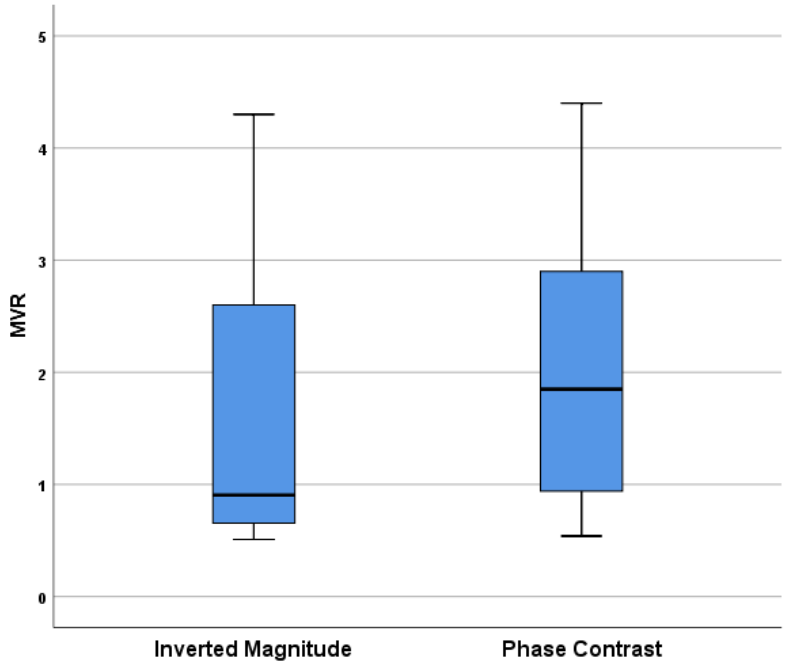

FIGURE (1). MVR of metastatic vertebral lesions of IM and Phase Contrast of MRI sequences

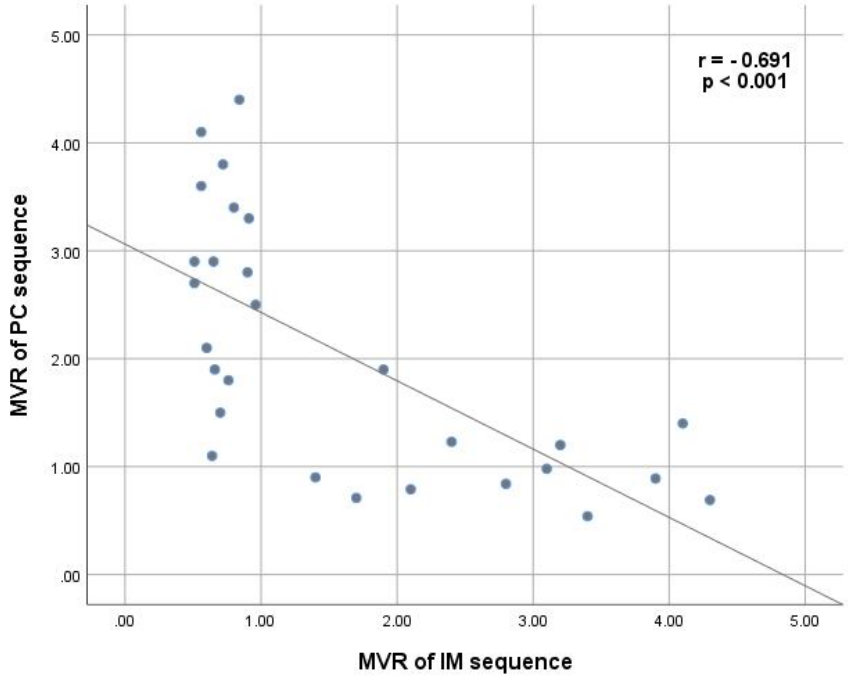

Figure (2). Correlation between MVR of IM and PC MRI sequences

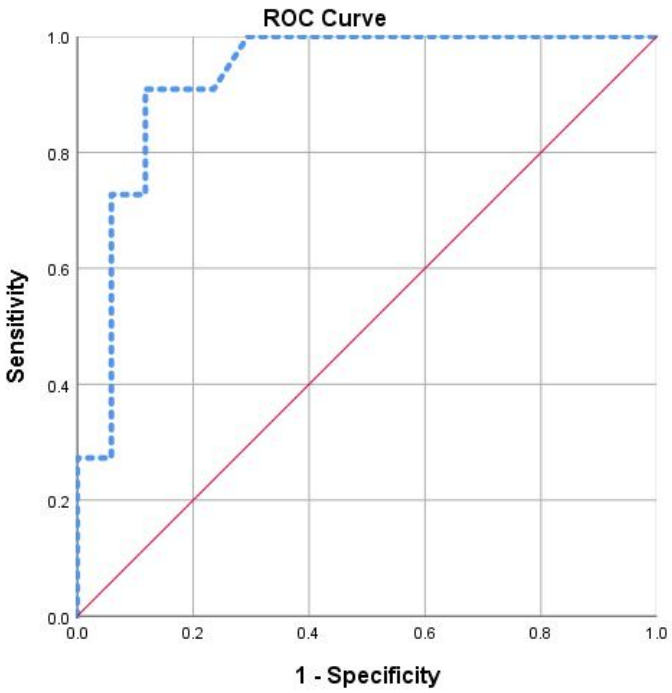

Figure (3). Receiver operator (ROC) curve for prediction of sclerotic bony lesion through MVR in PC sequence

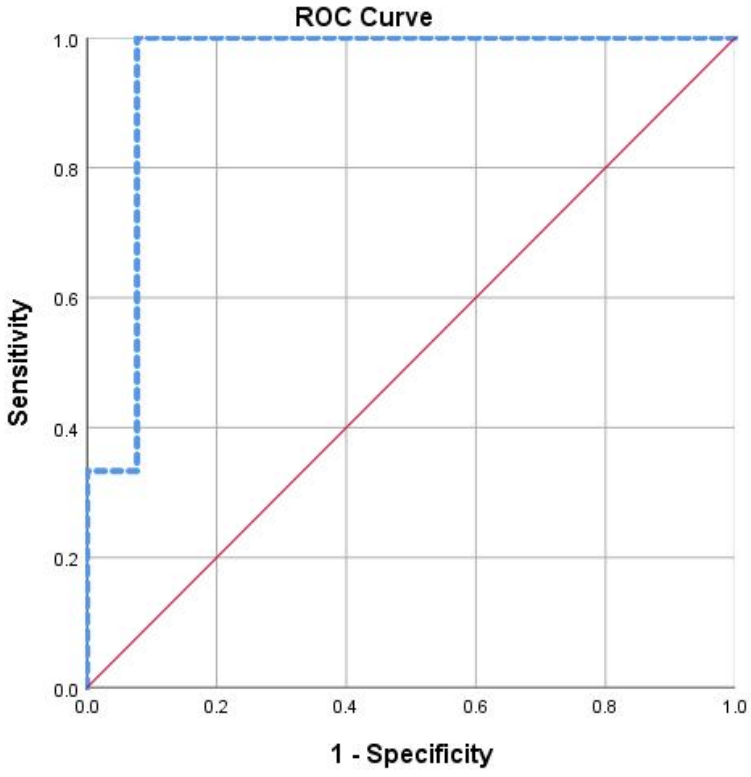

Figure (4). Receiver operator (ROC) curve for prediction of lytic bony lesion through MVR in IM sequence

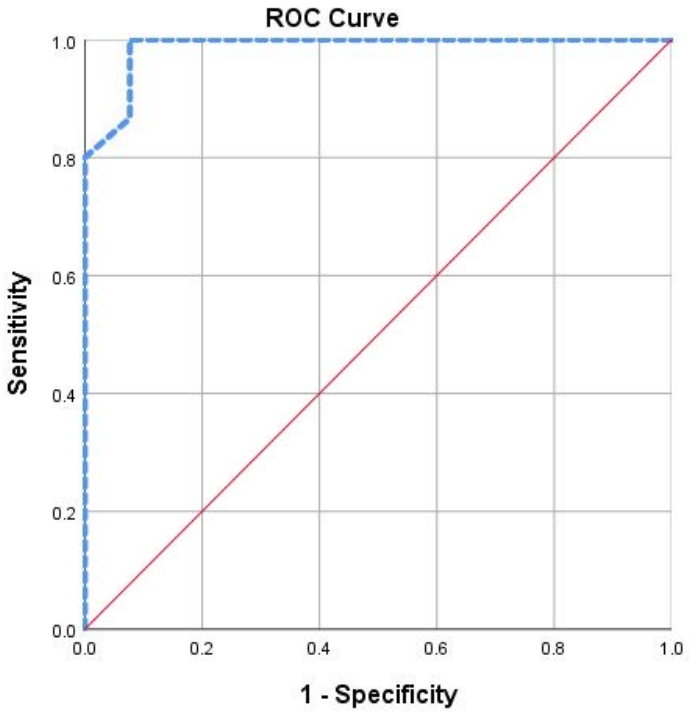

Figure (5). Receiver operator (ROC) curve for prediction of lytic bony lesion through MVR in PC sequence

Table 1. MRI-Sequence Parameter of the Imaging Protocol

	T1 TSE	T2 TSE	T2 TIRM	Susceptibility-weighted MRI
Distance factor	10%	10%	10%	20%
Phase coding direction	head to foot			
Phase-oversampling	100%	100 (80)%	100%	100%
Field-of-view	260 (280) mm2	260 (280) mm2	280 (300) mm2	240 (320) mm2
Field-of-view phase	100%			
Matrix	448	448 (384)	320	384
TR/TE	803/21 (726/813) ms	3380/106 (3300/88) ms	4000/30 (5000/37) ms	49/13.8 (49/20) ms
Flip-angle	150°	150°	150°	15
Slice-thickness	3 mm			
Phase resolution	70 (60)%	70 (75)%	75 (80)%	100%

Parameters of the imaging protocol of the lumbar spine, which differ from the cervical spine, are indicated in parenthesis. TSE = turbo spin echo, TIRM = turbo inversion recovery magnitude, MRI = magnetic resonance imaging, TR = time to repeat, TE = time to echo.

Table 2. Comparison between CT density and metastases to vertebral body signal-ratio (MVR) of the metastatic lesions

metastases to vertebral body signal-ratio (MVR)	CT morphology mean ± SD				
	Hypodense lesion (Lytic) (n=45)	Hyperdense lesion (Sclerotic) (n=33)	Mixed lesions (n=6)		
MVR-Inverted Magnitude	0.71 ± 0.15	2.69 ± 1.2 β	2.65 ± 0.78		
MVR- Phase Contrast	2.91 ± 0.86	1.02 ± 0.39 β	0.99 ± 0.29		

[a] p-values are based on Kruskal Wallis Test. Statistical significance at $P < 0.05$
Values with superscript β are different from lytic lesions

Table 3. Comparison between metastases to vertebral body signal-ratio (MVR) of the metastatic lesion and their primary source

Primary tumor, n (%)	MVR- Inverted Magnitude		MVR- Phase Contrast	
	mean ± SD	p-value	mean ± SD	
Breast cancer	1.26 ± 1.1	0.42 [a]	2.43 ± 1.11	
Prostate cancer	1.88 ± 1.37		1.69 ± 0.85	
Cancer Colon	2.57 ± 2.45		2.55 ± 2.62	
Bronchogenic carcinoma	1.4		0.9	
Multiple myeloma	1.7		0.71	
Unknown primary	2.8		0.84	
[a] p-values are based on Kruskal-Wallis Test. Statistical significance at $P < 0.05$				

Table (4). Clinical characteristics of studied patients

Variables	(n=84)
Age (years), mean ± SD	56.25 ± 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)

DISCUSSION

A prospective comparative study was conducted at our institution, aiming at calculating cut-off values for metastatic to vertebral body ratio in both inverted magnitude and phase contrast sequences, in order to ensure a more objective numerical method for differentiation between lytic and sclerotic metastatic vertebral lesions. We relied on CT as a gold standard modality of imaging to compare our results with.

Our study revealed an impressive diagnostic performance of different MRI techniques for detection of lytic and sclerotic bony lesions against the gold standard CT finding **(Tables 5 and 6 in supplementary data).** This diagnostic accuracy was in perfect agreement with Boker et al. study.

The results of our study revealed that there was a perfect inter-observer agreement between the radiologists in evaluating metastatic bony lesions using both subjective and objective assessment of conventional and susceptibility-weighted magnetic resonance imaging (SWMR) MRI sequences (exceeding 90%). This is in the same line with Boker et al. study in which there was full inter-observer agreement (100%) **[9,10].**

In agreement with our study, Böker et al. study reported that MVR measurements on susceptibility-weighted MR images and CT scans showed a significant statistical difference ($P < .001$) between predominantly osteoblastic and osteolytic metastases. MVR on T2-weighted images showed a smaller, but also significant, difference ($P = .003$), whereas no significant difference ($P > .05$) was found between predominantly osteoblastic and osteolytic metastases with T1-weighted and inverted magnitude images **[**9**].**

The moderate correlation of the MVR between susceptibility-weighted MRI and CT supports the potential of susceptibility-weighted MRI to enable reliable differentiation between metastases with a wide range of mineralization.

In our study, there were six cases with mixed metastatic bone lesions as proved by gold standard CT. These six cases were mis-interpreted by both reviewers to be sclerotic based on MRI images. The signal intensity in both T1 and T2 weighted images affected their decision despite the fact that susceptibility weighted images (IM and phase contrast) might have suggested their mixed nature when reviewed again in a retrograde assessment (after being informed with the CT findings at the end of the study). This low diagnostic performance regarding the mixed lesions cannot be fully understood putting into consideration that we only had six cases in our study. We would eventually recommend that future studies put special emphasis on the mixed lesions.

On the basis of ROC analysis, Böker et al calculated a cut-off value of 0.43 (area under the curve [AUC] = 0.87) for the inverted magnitude images and 1.47 (area under the curve AUC = 0.73) for Phase contrast images with similar diagnostic performance, compared to our study [9].The cut-off point values are accepted to be different as we use different MRI machines.

Our study had its share of limitations and challenges. The echo time is a sequence parameter that had an effect on susceptibility weighted MRI. The longer the chosen echo time, the stronger the resulting susceptibility weighting image. A longer echo time is, however, also associated with a lower overall signal-to-noise ratio and contrast-to-noise-ratio as well as stronger susceptibility artifacts. Although it may enable improved visualization of small vertebral body lesions, it is also more prone to artifacts **[11].** There were very few studies that targeted the susceptibility weighted MRI of the spine the way we did in ours, making comparison of our results to the previous similar studies limited only to some parameters and aspects of the research. Metal implants cause strong susceptibility artifacts, especially at susceptibility-weighted MRI. Therefore, vertebral bodies adjacent to implants often

cannot be reliably evaluated. We attempted yet failed to produce proper quality images in the cervical spine and upper dorsal spine lesions due to our inability to overcome the significant artifacts in the phase images which prevented proper interpretation

CONCLUSION

Based on our study results, we successfully calculated reliable cut-off values for metastatic to vertebral body signal ratio in both inverted magnitude and phase contrast sequences that would objectively enable radiologists to differentiate between predominantly osteosclerotic and osteolytic spine metastases with a better diagnostic performance and a higher accuracy. This would help immensely in the clinical practice, as we will able to predict the risk of pathological fracture for each patient and each lesion.

Finanial Disclosure:none Conflict of interest: none

REFERENCES

1. **Teodoro M, Paula M, Oscar L, Casado V, Beltrán L, Luna A.** Susceptibility Weighted Imaging for evaluation of musculoskeletal lesions. European Journal of Radiology 2021; 138: 609-11.
2. **Modir Shanechi A, Kiczek M, Khan M, Jindal G.** Spine Anatomy Imaging: An update. Clin N Am 2019; 29: 461–80.
3. **Santhosh K, Kesavadas C, Thomas B, Gupta AK, Thamburaj K**, Kapilamoorthy TR. Susceptibility weighted imaging: a new tool in magnetic resonance imaging of stroke. Clin Radiol 2009; 64: 74-83.
4. **Chen W, Zhu W, Kovanlikaya I, Kovanlikaya A, Liu T, Wang S, et al.** Intracranial calcifications and hemorrhages: characterization with quantitative susceptibility mapping. Radiology 2014; 270: 496–505.
5. **Del Grande F, Farahani SJ, Carrino JA, Chhabra A.** Bone marrow lesions: A systematic diagnostic approach. Indian Journal of Radiology and Imaging 2014; 3: 24-5.
6. **Baur A, Huber A, Ertl-Wagner B, Dürr R, Zysk S, Arbogast S, et al.** Diagnostic value of increased diffusion weighting of a steady-state free precession sequence for differentiating acute benign osteoporotic fractures from pathologic vertebral compression fractures. AJNR Am J Neuroradiol 2001; 22: 366–72.
7. **Adam WS, Fourney DR.** Evolution of treatment for metastatic spine disease. Neurosurg Clin N Am 2004; 15: 401-11.
8. **Haacke EM, Mittal S, Wu Z, Neelavalli J, Chen Y.** Susceptibility-weighted imaging: technical aspects and clinical applications, part 1. AJNR Am J Neuroradiol 2009; 30: 19–30.
9. **Böker SM, Adams LC, Bender Y, Fahlenkamp U, Wagner M, Hamm B, et al.** Differentiation of Predominantly Osteoblastic and Osteolytic Spine Metastases by Using Susceptibility-weighted MRI. Radiology 2019; 290: 146–54.
10. **Schweitzer M.** Can Susceptibility-weighted MRI Help Differentiate Osteolytic from Osteoblastic Spine Metastases? Radiology 2009; 12: 1–2.
11. **Vanel D.** MRI of bone metastases: the choice of the sequence. Cancer imaging 2004; 4: 30–5

Citation:
Ali, I., Khalil, T., Elserafy, A., Mosallam, W. Added Value of Metastasis to Vertebral body Signal Ratio in Susceptibility Weighted Magnetic Resonance Imaging in Differentiation between Lytic and Sclerotic Spine Metastatic Bone Lesions. *Zagazig University Medical Journal*, 2023; (4185-4197): -. doi: 10.21608/zumj.2023.196337.2757