

Role of Magnetic Resonance In-Phase and Out of Phase Sequences in Differentiating Benign from Suspicious Vertebral Marrow Lesion

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Abstract

Background: Vertebral marrow lesions are commonly seen in older age groups of patients, due to a variety of causes ranging from infections, traumatic collapse, osteoporotic collapse, and neoplastic vertebral marrow changes.

Aim of Study: The aim of this study was to evaluate the value of in and opposed phase MRI sequences in the characterization and differentiation between benign and malignant vertebral focal marrow lesions.

Subjects and Methods: This prospective study was conducted at Ain Shams University hospitals. The study included 30 patients with focal lesions in the spine. The study period ranged from 6-9 months.

Results: The sensitivity and specificity of Out of phase "Drop of signal" using contrast as a reference, the sensitivity was 95.2%, while specificity was 87.5%, AUC was 0.865 (95% CI: 0.69-0.96) with significant difference as *p*-value was (<0.05).

Conclusion: Utilizing in phase and out of phase sequences greatly assist in diagnosing suspicious marrow lesions, hence this technique is greatly reducing the need for Intravenous contrast administration.

Key Words: *Chemical shift imaging – Vertebral marrow lesion – In-Phase/opposed -phase images.*

Introduction

MEDASTATIC disease to Bone which affects the axial skeleton(vertebral body, iliac bone, the proximal femora, and humerus) is a common sequelae in many cancers as an early or late presentation of the disease [1].

Metastatic bone disease (MBD) is commonit is detected in up to 65-75% of patients with breast or prostate cancer, in over 35% of patients with lung cancer; and almost all patients with sympto-

matic multiple myeloma have focal lesions or a diffuse bone marrow infiltration. Metastatic bone disease can cause a variety of symptoms and is often associated with a poorer prognosis, with high social and health-care costs.

MRI has the highest sensitivity for detecting both diffuse and focal bone marrow involvement. In spite of its high sensitivity, MRI is of only limited specificity in the evaluation of bone marrow alterations. This limited specificity requires additional, sometimes invasive diagnostic steps to obtain accurate diagnosis [2].

In an effort to differentiate between benign and malignant disease, morphologic criteria as well as diffusion imaging has been used. Because benign vertebral fractures should contain fatty marrow and malignant processes replace normal marrow, differentiation of these 2 processes should be possible with in-phase/opposed-phase imaging [3].

In-phase/opposed-phase imaging has been used extensively in separating benign from malignant adrenal lesions as well as differentiating fatty infiltration of the liver from neoplastic disease. In-phase/opposed-phase imaging of the spine should be a sensitive and specific way to differentiate benign from malignant lesions [3].

The study aimed to evaluate the value of in and opposed phase MRI sequences in the characterization and differentiation between benign and malignant vertebral focal marrow lesions.

Subjects and Methods

The study was a prospective study carried out at Ain Shams University Hospitals on 30 patients with focal lesions in the spine. The duration of the study was 6 months, from August 2021 – March 2022.

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Inclusion criteria: Patients diagnosed with vertebral lesion or vertebral bone marrow abnormality and patients suspected to have vertebral lesion.

Exclusion criteria: Patients with the following were excluded from the study: Pacemaker, claustrophobia, metallic Foreign Body in the Eye, triggerfish" Contact Lens, gastric Reflux Device, insulin Pumps, temporary Transvenous Pacing Leads Patients with contraindications to intravenous MRI contrast will be excluded if contrast is needed, e.g.: Allergic to IV contrast, high serum creatinine, low GFR or severe renal impairment.

Ethical considerations: The study group were informed about the nature and purpose of the study and written consent was obtained before history taking.

Methods: All patients included in the study were subjected to the following:

Detailed history taking including: Personal data: Name, age, sex, occupation, address, a designed sheet was fulfilled for every patient to document his data, past history of previous interventions and family history of any disease.

Careful clinical examination: General examination in the form of vital signs (Blood pressure, Temperature, Heart rate, Respiratory rate) and signs of (Pallor, Cyanosis, Jaundice, and Lymph node enlargement).

Contrast study was needed in some cases, in these cases a cannula was inserted for contrast media injection before starting the examination

If contrast was needed: Instruction to fast at least 4hrs, laboratory: Serum creatinine assay and GFR and gadolinium injection with a dose of 0.1mmol/kg or 0.2ml/kg and follow rate of 1-2ml/sec flushed by 20ml of a saline was done.

Magnetic resonance imaging:

Study procedures: All MRI studies were performed by using a 1.5 Tesla super-conducting Magnet (Philips Systems) in the following sequences: Sagittal and axial T2, (TR, 3000, TE 100), sagittal STIR, (TR: 3500, TE, 80; TI, 165), sagittal in-phase (TR, 400; TE, 4.6; flip angle, 80 °) and opposed-phase gradient recalled-echo sequences (TR, 400; TE, 2.3; flip angle, 80 °) were acquired and post contrast axial and Sagittal Fat suppressed T1 sequence was acquired. An equal sized region of interest (ROI) cursor was placed over the same area of abnormal bone marrow on the in-phase as

well as on the opposed-phase images. A computation of the signal intensity ratio (SIR) of the marrow on the opposed phase to signal intensity measured on the in-phase images was done.

Risks and complications: As regards risks and complications of MRI contrast administration, nephrogenic systemic fibrosis was a recognized, but rare complication. It usually occurs in patients with serious kidney disease. There was a very low risk of an allergic reaction if contrast material was used. Such reactions were usually mild and controlled by medication, and may be in form of nausea, vomiting, headache and itching.

Data management and analysis: The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 23). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

Results

This study was conducted on 30 patients, 36.7% were males and 63.3% were females with mean age of the study group was 47.73 ± 11 years ranged from 22 to 70 years. Table (1).

Regarding Contrast and out of phase findings, 73.3% of patients were positive with contrast and negative with out of phase. Within contrast positive patients 77.3% were heterogeneous, 18.2% were homogenous and 4.5% were peripheral Table (2).

Regarding diagnosis of malignancy, 53.3% of patients had malignant tumors, the most common tumor was breast cancer 56.4%, prostate cancer 25% and Hodgkin lymphoma, non-Small cell Carcinoma & Rhabdomyosarcoma (6.2%). 53.3% of patients had metastasis to vertebrae Table (3).

The sensitivity and specificity of Out of phase "Drop of signal" using contrast as a reference, the sensitivity was 95.2%, while specificity was 87.5%, AUC was 0.865 (95% CI: 0.69-0.96) with significant difference as p -value was (<0.05) Table (4).

Table (1): Demographic data for the study group.

	Mean / N	SD / %	Median (IQR)	Range
Age	47.73	11.00	48 (42-52)	(22-70)
Sex:				
Male	11	36.7%		
Female	19	63.3%		

Table (2): Contrast and out of phase findings for the study group.

	N	%
Contrast:		
No	8	26.7
Yes	22	73.3
Contrast (N=22):		
Heterogeneous	17	77.3
Homogenous	4	18.2
Peripheral	1	4.5
Out of phase "Drop of signal":		
No	22	73.3
Yes	8	26.7

Table (3): Diagnosis of malignancy, its type and diffusion to vertebrae for the study group.

	N	%
Malignancy history:		
No	14	46.7
Yes	16	53.3
Type of malignancy (N=16):		
Breast Cancer	9	56.4
Prostate Cancer	4	25
Hodjkin lymphoma	1	6.2
Non-Small cell Carcinoma	1	6.2
Rhabdomyosarcoma	1	6.2
Diffuse to vertebrae:		
No	14	46.7
Yes	16	53.3

Table (4): Roc curve for to detect malignancy using contrast as a reference.

	Contrast		AUC (95% CI)	P-value	Sensitivity	Specificity	PPV	NPV
	Yes (N=22)	No (N=8)						
Out of phase "Drop of signal":								
No (N=22)	21 (95.5%)	1 (12.5%)	0.865	<0.001	95.2	87.5	95.2	87.5
Yes (N=8)	1 (4.5%)	7 (87.5%)	(0.69-0.96)					

Case (1):

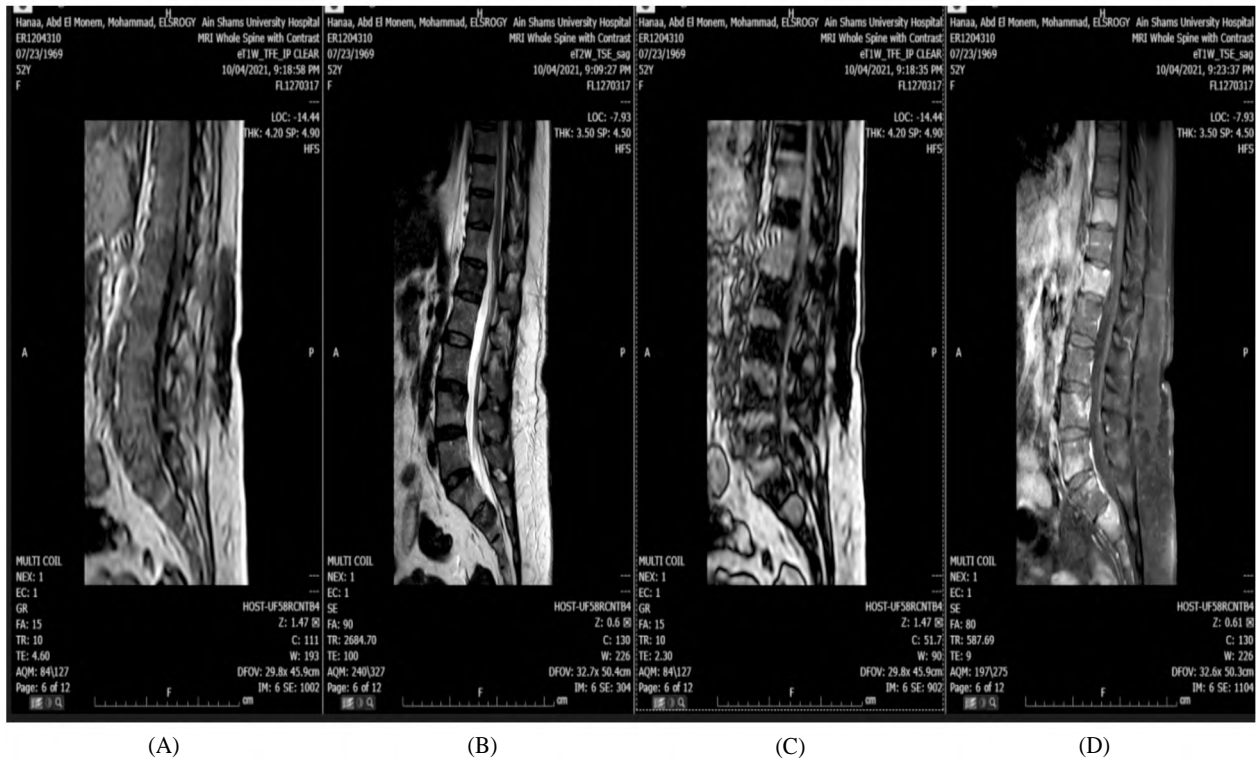
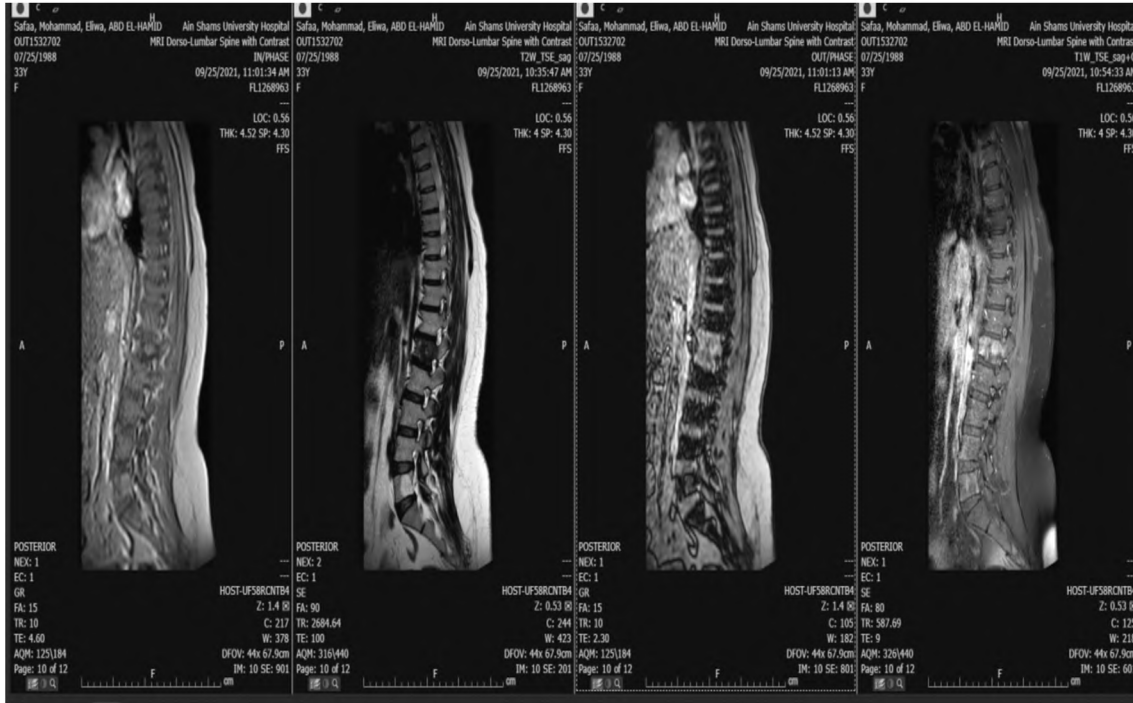


Fig. (1): (A): Female patient 55 years old (Known case of metastatic breast cancer), Picture 1: In Phase: It displays high signal Intensity at D11, L1, L4, vertebral bodies bone marrow signal at in phase sequence. (B): T2: It displays low Signal Intensity at D11, L1, L4, vertebral bodies bone marrow signal at T2 sequence. (C): Out of Phase: It shows no drop of signal at D11, L1, L4, vertebral bodies bone marrow signal at the out of Phase sequence. (D): T1 Post Contrast: It shows heterogeneous post contrast enhancement at D11, L1, L4, vertebral bodies bone marrow at post contrast study.

Patient history:

- Female patient 35 years old (Known case of metastatic breast cancer).

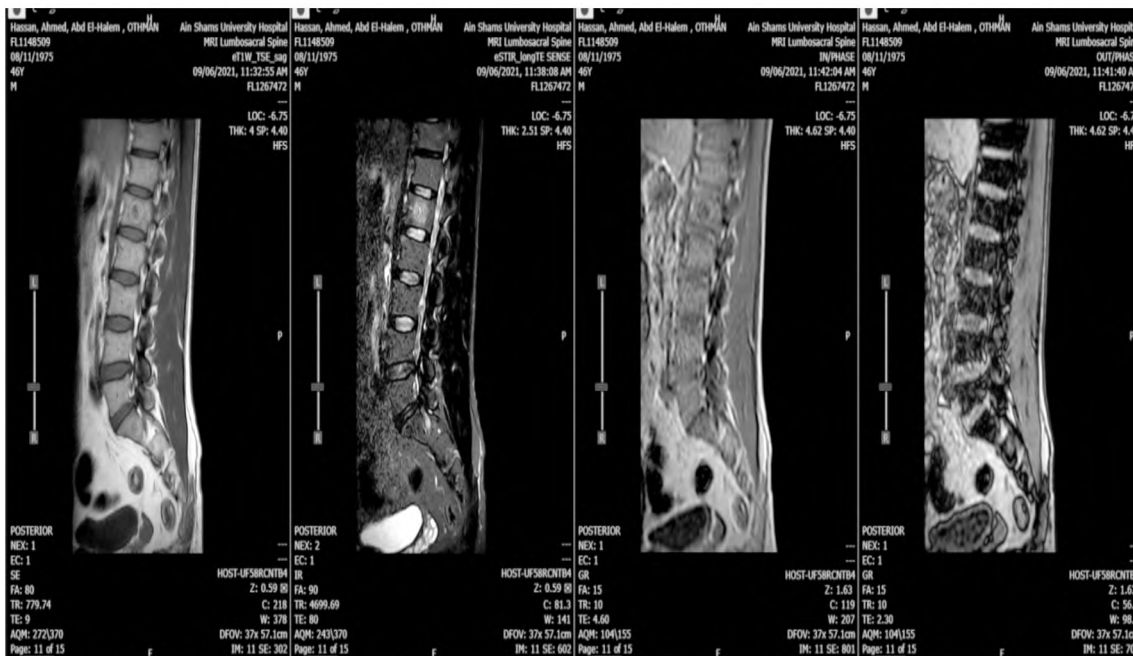


(A) (B) (C) (D)

Fig. (2): (A): Inphase: It displays high signal Intensity at L1 vertebral body bone marrow signalat in phase sequence. (B): T2: It displays low signal Intensity at L1 vertebral body bone marrow signalat T2 sequence. (C): Out of Phase: It shows no drop of signal at L1 vertebral body bone marrow signal at out of phase sequence. (D): T1 Post Contrast: It shows heterogeneous post contrast enhancement at L1 vertebral body bone marrow at post contrast study.

Patient history:

- Male Patient 48 years old complain of lower back pain, No history of malignancy (Known Case of Typical Hemangioma).



(A) (B) (C) (D)

Fig. (3): (A): T1: It displays high signal Intensity at L1 vertebral body bone marrow signal at T1 sequence. (B): STIR: It displays high signal intensity at L1 vertebral body bone marrow signal at STIR sequence. (C): In phase: It displays high Signal Intensity at L1 vertebral body bone marrow signal at in phase sequence. (D): Out of phase: It shows drop of signal at L1 vertebral body bone marrow signal at Out of Phase sequence.

Patient history:

- Female patient 28 years old complain of lower back pain.
- No history of malignancy (Known case of Atypical hemangioma).



Fig. (4): (A): In phase: It displays high signal Intensity at L2 vertebral body bone marrow signal at in phase sequence. (B): T2: It displays high signal Intensity at L2 vertebral body bone marrow signal at T2 sequence. (C): Out of phase: It shows no drop of signal at L2 vertebral body bone marrow signal at out of phase sequence due to the presence of intra cytoplasmic lipids (microscopic fat intracellular). (D): T1 post contrast: It shows no contrast enhancement of L2 vertebral body bone marrow signal at post contrast study.

Discussion

Magnetic resonance imaging (MRI) is a good non-invasive modality for evaluation of bone marrow as well as for detection of marrow lesions. It can reveal subtle changes in physiological as well as pathological marrow composition in the form of signal alteration and thus can be helpful in knowing the cause of vertebral lesions [4].

This study was conducted on 30 patients, 36.7% were males and 63.3% were females with mean age of the study group was 47.73 ± 11 years ranged from 22 to 70 years.

Our results were supported by study of El-Samie et al., [5] as they reported that a total of 50 consecutive oncology patients (31 women and 19 men), with suspicious spinal focal bone marrow lesions on conventional MRI examination were recommended for further evaluation for more characterization. The patients' ages ranged from 29 to 86 years, (mean \pm 59 years).

However, in the study of Tadros & Louka [4] the studied population included 30 patients, 18 males (60%) and 12 females (40%). The mean age was 54 ± 13 years ranging from 25 to 80 years.

Whereas Wadhawan et al., [6] revealed that the mean age of the patients was 59 ± 12 years. The mean age for malignant lesion was 57 ± 11.5 years, and that for benign lesions was 63 ± 12.5 years. There was no statistically significant difference between the age groups in differentiating benign and malignant vertebral marrow lesions ($p=0.290$). The studied population included 17 males and 13 females. There was no statistically significant difference between males and females in terms of involvement of benign and malignant vertebral lesions ($p=0.102$).

The present study showed that regarding contrast and out of phase findings, 73.3% of patients were positive with contrast and negative with out of phase. Within contrast positive patients 77.3% were heterogeneous, 18.2% were homogenous and 4.5% were peripheral.

In the study of Mohson [1] most of the suspicious lesions appearing low on T1W, high on T2W and Fatsat sequences this represents seen in 16/58 (27.5%) of those only 7 (12%) patients are really metastasis, while when adding the high out of phase/in phase ratio the percentage decrease from 27.5% to 8.5% (5/55). The out of phase/in phase ratio (OIR) greater than 1 is seen in suspicious bony lesion.

Also, Van Vucht et al., [7] demonstrated that mean % signal intensity (SI) drops on out-of-phase (OOP) for non-neoplastic (NN) lesions was 36.6%, for benign neoplastic (BN) 3.19% and for malignant neoplastic (MN) 3.24% ($p < 0.001$).

Furthermore, Wadhawan et al., [6] stated that on CSI, signal intensity ratio (SIR) of normal vertebrae was calculated in 27 vertebrae. The mean SIR of normal vertebrae was 0.306 ± 0.144 . The mean SIR on CSI of malignant vertebral lesions was 0.967 ± 0.24 and of benign vertebral lesions it was 0.76 ± 0.235 .

Vertebral marrow lesions are one of the most common pathologies seen in the elderly population. The causes include infections, traumatic collapse, osteoporotic collapse, and neoplastic vertebral marrow changes, out of which osteoporosis and metastasis are the major causes. The metastasis in spine contributes to nearly 39% of all bone metastases [8].

The initial imaging modality usually includes conventional radiography; however, many vertebral marrow lesions remain obscured on conventional radiography. CT can also be used for differentiation of this lesion. It is more dependable in revealing the calcifications and cortical outlines of bone as compared to X-ray. It can also delineate the extent of the tumour destruction more effectively. However, it is not very sensitive in the detection of, or in differentiating between, osteoporotic benign and malignant vertebral marrow lesions [9].

The current study showed that regarding diagnosis of malignancy, 53.3% of patients had malignant tumors, the most common tumor was breast cancer 56.4%, prostate cancer 25% and Hodgkin lymphoma, non-small cell carcinoma & rhabdomyosarcoma (6.2%). 53.3% of patients had metastasis to vertebrae.

In accordance with our results study of Mohson [1] as they reported that the study sample consisted of 55 females and 25 males, the breast cancer is the main primary in females and represents 30/58 patients while the prostate cancer is main cancer

in males, the later represent 7/58 patients. The MR examination in the control group is normal in 18/22 patients, the remaining four reveals typical hemangioma in two, atypical hemangioma in one and modic I endplate changes in the remaining one. While the examination of the patients with primary cancer reveals metastasis in 12/58.

In the study of Tadros & Louka [4], those with known primary malignant lesion were 23 patients (76.7%), while 7 patients (23.3%) had no known primary malignancy.

In the study in our hands, the sensitivity and specificity of Out of phase "Drop of signal" using contrast as a reference, the sensitivity was 95.2%, while specificity was 87.5%, AUC was 0.865 (95% CI: 0.69-0.96) with significant difference as p -value was (< 0.05).

In accordance with our results study of Wadhawan et al., [6] as they reported that when the CSI value was used in differentiating osteoporotic benign and malignant vertebral lesion, the area under the curve came was 0.758 and the p -value was 0.006 which was statistically significant. If the cut-off value of SIR on CSI was taken as 0.96, then the sensitivity and specificity for differentiating benign osteoporotic and malignant lesions was 83.3% and 58.70%, respectively, and the PPV was 34.48%. The NPV was 93.10%, and on biopsy it was proven to be CA lung-metastasis.

The CSI value in our study is in agreement with the CSI value reported by Tadros & Louka [4], i.e. 0.94, but less than the cut off value reported by Ogura et al., [10], i.e. 1, and Zampa et al., [11], i.e. 1.2.

In a study done by Zidan et al., [12] in 32 patients, the SIR value on CSI was 0.91, which had a sensitivity of 93% and specificity of 82% to differentiate benign from malignant vertebral lesions.

Martel et al., [13] demonstrated that lesion in a vertebral body that shows hypointensity in T1WI, hyperintensity on STIR and T2WI, and a signal intensity ratio > 0.8 has a sensitivity of 97.2%, specificity of 90% and accuracy of 91.2% with respect to the diagnosis of a malignant lesion. However, Filippo et al., [14] used opposed phase gradient techniques and a signal intensity ratio cut-off of 1.2 to differentiate between benign and malignant vertebral lesions.

Also, Mohson [1] revealed that most of the suspicious lesions appearing low on T1W, high on

T2W and Fatsat sequences this represents seen in (27.5%) of those only (12%) patients are really metastasis, while when adding the high out of phase/in phase ratio, the percentage decrease from 27.5% to 8.5%, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) and overall accuracy of out of phase/in phase ratio in detecting metastasis within the vertebral marrow are 66.6%, 90.7%, 61.4%, 92.4%, and 86% respectively.

Furthermore, El-Samie et al., [5] revealed that SIR values were ranged between 1.1 and 2.6 in malignant lesions while it ranged from 0.47 to 0.9 in benign lesions; when a SIR of 1 as a cutoff was chosen, it showed high sensitivity and specificity (96.8% and 93.65% respectively).

Conclusion:

Utilizing in phase and out of phase sequences greatly assist in diagnosing suspicious marrow lesions, hence this technique is greatly reducing the need for Intravenous contrast administration.

Declaration:

- No Funds.
- All participants in the research agree to publish.

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دور تسلسل التصوير بالرنين المغناطيسي فى الطور المتقابل فى التفريق بين أورام النخاع البؤرى الفقرى الحميدة والخبيثة

الخلفية: تلاحظ آفات نخاع العمود الفقرى بشكل شائع فى الفئات العمرية الأكبر من المرضى، وذلك بسبب مجموعة متنوعة من الأسباب تتراوح من العدوى، والانهيار الرضحي، وانهيار هشاشة العظام، وتغيرات نخاع العمود الفقرى الورمى. على الرغم من أن هشاشة العظام هى أحد الأسباب الأكثر شيوعاً لانهيار العمود الفقرى، إلا أن ورم خبيث فى العمود الفقرى يُلاحظ أيضاً بشكل متكرر جداً، ويشكل حوالى ٣٩٪ من جميع النقائل العظمية.

الهدف والأهداف: كان الهدف من هذه الدراسة هو تقييم قيمة متواليات التصوير بالرنين المغناطيسي فى الطور المتعارض والمتعارض فى التوصيف والتمييز بين آفات النخاع البؤرى الفقرى الحميدة والخبيثة.

المواضيع والطرق: أُجريت هذه الدراسة المستقبلية فى مستشفيات جامعة عين شمس. شملت الدراسة ٣٠ مريضاً يعانون من آفات بؤرية فى العمود الفقرى. تراوحت فترة الدراسة ما بين ٦ أشهر.

النتائج: أُجريت هذه الدراسة على ٣٠ مريضاً، ٣٦.٧٪ منهم ذكور و ٦٣.٣٪ إناث مع متوسط عمر مجموعة الدراسة كان ٤٧.٧٣ ± ١١ سنة تراوحت من ٢٢ إلى ٧٠ سنة، فيما يتعلق بنتائج التباين وخارج المرحلة، كان ٧٣.٣٪ من المرضى إيجابيين مع تباين وسليبيين مع خارج المرحلة. فى المقابل، كان ٧٧.٣٪ من المرضى الموجبين غير متجانسين، و ١٨.٢٪ كانوا متجانسين و ٤.٥٪ محيطيين، وفيما يتعلق بتشخيص الأورام الخبيثة، فإن ٥٣.٣٪ من المرضى يعانون من أورام خبيثة، وكان أكثر الأورام شيوعاً سرطان الثدي ٦.٤٪ وسرطان البروستاتا ٢٥٪ وسرطان الغدد الليمفاوية هودجكين وسرطان الخلايا غير الصغيرة وساركومة العضلات المخططة (٦.٢٪). ٥٣.٣٪ من المرضى يعانون من ورم خبيث فى الفقرات وحساسية وخصوصية (إسقاط الإشارة) خارج الطور باستخدام التباين كمرجع، كانت الحساسية ٩٥.٢٪، بينما كانت النوعية ٨٧.٥٪، كانت منطقة تحت المنحنى ٠.٨٦٥ مع اختلاف كبير كقيمة p كان (>٠.٠٥).

بناءً على النتائج التى توصلنا إليها: نوصى بإجراء مزيد من الدراسات حول حجم العينة الأكبر وعلى نطاق جغرافى كبير للتأكد على استنتاجنا.