

Dixon Chemical Shift Magnetic Resonance Imaging for Differentiating Benign, Malignant, and Non-Neoplastic Bone Marrow Lesions

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ABSTRACT

Background: On magnetic resonance imaging (MRI), bone marrow (BM) lesions cause a localized or widespread change in signal strength or a heterogeneous signal pattern, which results in a steady water signal. Finding out how well Dixon chemical shift imaging distinguishes between benign neoplastic, malignant, and non-neoplastic BM lesions was the goal of this study.

Methods: For this prospective investigation, 40 individuals of both sexes with suspicious

bone tumors or indeterminate marrow lesions or altered BM signal intensity on T1 and T2 WI. The control group consisted of twenty participants. Every participant in the study underwent an MRI, including the Dixon method. The spine was the most often affected area by bone marrow lesions.

Results: The signal dropout % value in benign BM lesions was significantly higher ($P < 0.05$) than in the malignant and control groups. The signal intensity ratio (SIR) of the benign group was significantly lower than that of the malignant and control groups. While signal dropout % sensitivity, specificity, PPV, and NPV were 91.67%, 60.0%, 73.3%, and 80.0%, respectively, SIR's sensitivity, specificity, PPV, and NPV were 91.67%, 75.0%, 84.6%, and 85.7% instead. The receiver operator characteristic for signal drop out percentage yielded an AUC of 0.977, while SIR's gave an AUC of 0.951.

Diagnosis accuracy of Dixon MRI in the studied patients was with sensitivity, specificity, PPV, NPV, and accuracy 87.50%, 75%, 84.0%, 80% and 82.50%, respectively.

Conclusions: With its quantitative indicators, Dixon MRI is a useful and quick tool for addressing problems. It has a great capacity to distinguish between benign and malignant BM lesions with high diagnostic accuracy, sensitivity, and specificity

Keywords: Bone Marrow, Benign, Malignant, Non-Neoplastic, Dixon Chemical Shift, Magnetic Resonance Imaging.

1. INTRODUCTION

Human blood cells are produced in the bone marrow (BM). After bone, muscle, and fat, it is the fourth biggest organ in the body in terms of weight. Normal BM consists of water, fat, and cellular components [1].

The only imaging technique that allows for direct visualisation of the BM and the detection of BM lesions is magnetic resonance imaging (MRI). It can uncover subtle alterations in both physiological and pathological marrow composition indicated by signal changes [2, 3].

Standard magnetic resonance (MR) protocols for bone marrow (BM) assessment comprise T1 weighted (T1W), T2 weighted (T2W), and short tau inversion recovery (STIR) sequences. Red bone marrow (RBM) has an intermediate low signal intensity on T1W and a high signal intensity on T2W because of its high water content. Yellow bone marrow (YBM) exhibits a high

signal intensity in T1W and T2W due to its high-fat content [4].

BM lesions produce a relatively uniform water signal on MRI, resulting in hypointense lesions on T1W sequences and hyperintense lesions on T2W sequences. Red bone marrow (RBM) and abnormal bone marrow (BM) in the T1W sequence show diffusely equal or lesser intensity than the nearby muscle or disc. STIR and T2W fat-suppressed images show a high signal intensity in RBM reversion and malignancies. Because of this, using only standard MRI techniques to distinguish hyperplastic red marrow from other bone marrow replacement disorders is almost difficult [1, 5]. Thus, innovative techniques such as chemical shift imaging (CSI) have demonstrated encouraging outcomes in distinguishing between malignant and benign bone marrow lesion [3].

Alterations in chemistry, MRI employs the various oscillation frequencies of protons in water and fat. The out-of-phase BM signal intensity is decreased because normal BM comprises water and fat. There is no signal loss when the BM becomes malignantly invaded because the fat components of the BM is replaced by tumoral infiltration [6]. Named for its inventor, the Dixon approach was first created in 1984. This technique is well known in abdominal radiology for detecting liver steatosis and distinguishing benign adrenal adenomas from other adrenal tumours [7, 8]. The Dixon approach isolates fat and water proton signals into two separate pictures by separating them based on their different resonance frequencies or chemical shifts. The two complicated pictures from in-phase (IP) and opposed-phase imaging are added and subtracted to get selective images of fat and water. Consequently, the Dixon approach functions as a water-fat separation method rather than an actual fat-suppression procedure [9].

The purpose of this study was to evaluate Dixon CSI's ability to differentiate between benign neoplastic, malignant, and non-neoplastic BM lesions

Patients and Procedures:

This prospective investigation comprised 40 patients of both sexes who had altered BM signal intensity on T1 and T2 WI, indeterminate marrow lesions, or suspected bone tumours. The study was carried out at Tanta University Hospitals in Tanta, Egypt, between June 2022 and June 2024 with permission from the Ethical Committee. The patient or their family members gave their informed written permission.

Exclusion criteria were patients with contraindications to MRI examination like those with any metallic prosthesis, artificial pacemakers, or claustrophobic and refused to participate in the research.

All patients underwent thorough history taking, clinical examination, and MR examination [the study utilized a 1.5 T MRI General Electric (GE) machine (closed magnet) and a Siemens area 1.5 T MRI machine (closed magnet). Prior to entering the examination room, the subjects who had studied were told to take off all ferromagnetic items such as metal objects. They were educated on the significance of remaining still and calm during the examination. There is no particular preparation required for the patient prior to the MRI.

The selection of coil and patient position was refined for each examination based on the suspected level of BM abnormalities and generally remained consistent across the different pulse sequences.

In certain instances, a 0.1 mmol/kg body weight intravenous injection of Gd-DTPA contrast media was administered, and then 20 ml of sterile saline solution was administered in an antecubital vein done followed by the acquisition of T1WI and Dixon sequences: acquisition of T2FSE Dixon sequence was done in all patients and control cases with the following imaging parameters: TR/TE 3000/81 m.sec, slice thickness: 3.7 mm; FOV 34x34; matrix 288x224. Acquisition time :3 minutes. Dixon sequence is named Dixon in Siemens machines and IDEAL in GE machines.

All images were sent to the PACS workstation. The Dixon images included in-phase (IP), opposed-phase (OP), water-only (WO = IP + OP), and fat-only (FO = IP - OP) images. Initially, regions exhibiting atypical signal intensity on conventional T1- or T2-weighted images were analyzed in conjunction with T2 Dixon chemical shift images. Subsequently, the signal intensity of the bone marrow (BM) lesions was evaluated on both IP and OP images by employing a region of interest (ROI) cursor to measure the fat content within the abnormal area. The average signal intensity measurements were obtained using the PACS software. In cases where multiple lesions were identified, the largest lesion was chosen for analysis. The percentage of signal dropout and the signal intensity ratio (SIR) were calculated using the following formulas: SIR = out-of-phase signal intensity value / in-phase signal intensity value and signal dropout % = [(SI IP – SI OP) / SI IP] x 100.

Statistical analysis

Statistical analysis was conducted utilizing SPSS version 26 (IBM Inc., Chicago, IL, USA). The normality of the data distribution was evaluated through the Shapiro-Wilks test and histograms. Quantitative parametric variables were presented as means with standard deviations (SD) and compared between the two groups using an unpaired Student's t-test. For quantitative non-parametric data, results were expressed as medians with interquartile ranges (IQR) and analyzed using the Mann-Whitney test. Qualitative variables were reported in terms of frequency and percentage (%) and were examined using either the Chi-square test or Fisher's exact test, as appropriate. A two-tailed P value of less than 0.05 was considered statistically significant. The ROC curve was employed to evaluate diagnostic performance, including sensitivity, specificity,

positive predictive value (PPV), and negative predictive value (NPV).

2. RESULTS

Demographic data and sites of examination in MRI were insignificantly different between both groups. **Table 1**

Table 1: Distribution of the studied cases according to demographic data and sites examined in MRI

		Patients (n=40)	Control (n=20)	Test of Sig.	P
Age (years)		46.33±12.52	44.95±12.34	t= 0.403	0.688
Sex	Male	15(37.5%)	10(50.0%)	$\chi^2=0.857$	0.355
	Female	25(62.5%)	10(50.0%)		
Sites examined in MRI	LSS	16(40.0%)	6(30.0%)	FET=3.132	0.936
	Dorsal spine	6(15.0%)	3(15.0%)		
	Cervical spine	5(12.5%)	2(10.0%)		
	Knee	2(5.0%)	3(15.0%)		
	Hip	6(15.0%)	3(15.0%)		
	Tibia	2(5.0%)	1(5.0%)		
	Humerus	2(5.0%)	1(5.0%)		
	Foot	1(2.5%)	1(5.0%)		

Data are presented as mean \pm SD or frequency (%). MRI: Magnetic resonance imaging, LSS: Lumbar spinal stenosis. FET: Exact Fisher test, χ^2 : Chi square test, t: Student t-test

Distribution of the patients according to clinical presentation, medical history, previous imaging modalities, final diagnosis of BM lesions and number of lesions were enumerated in this table. **Table 2**

Table 2: Distribution of the patients according to clinical presentation, medical history, previous imaging modalities, final diagnosis of BM lesions and number of lesions

			N=40
Clinical presentation	Routine workup (Asymptomatic)		17(42.5%)
	Regional Pain		23(57.5%)
	Pathological fracture		8(20.0%)
Medical history	History of malignancy		26(65.0%)
	Hemoglobinopathy (Anemia)		7(17.5%)
	Free medical history		11(27.5%)
Previous imaging modalities	X-ray		15(37.0%)
	CT		4(10.0%)
	PET-CT		11(27.5%)
	Bone scan		10(25.0%)
Final diagnosis of BM lesions	Non- neoplastic	Red marrow reconversion	3(7.5%)
		Focal marrow hyperplasia	2(5.0%)
		Osteomyelitis	2(5.0%)

		Spondylodiscitis	1(2.5%)
		Bone infarction	1(2.5%)
		Reactive marrow edema	2(5.0%)
		Benign vertebral collapse	3(7.5%)
	Benign neoplastic	Hemangioma	2(5.0%)
		myelofibrosis	1(2.5%)
	Malignant neoplastic	Metastasis	13(32.5%)
		Lymphoma	1(2.5%)
		Multiple myeloma	4(10.0%)
		Malignant nerve sheath tumor	1(2.5%)
		Ewing sarcoma	1(2.5%)
		Chordoma	1(2.5%)
		Malignant vertebral collapse	5(12.5%)
	Pathology	Benign	15(37.5%)
		Malignant	25(62.5%)
Number of lesions	Single		20(50.0%)
	Multiple		14(35.0%)
	Diffuse		6(15.0%)

Data are presented as frequency (%). CT: Computed tomography, PET: Positron emission tomography.

Signal drop out % value in benign BM lesions was significantly higher than malignant BM lesions ($P<0.05$). SIR value in benign BM lesions was significantly lower than malignant BM lesions ($P<0.05$).

Table 3: Comparison between studied groups according to conventional MRI findings and fat suppression quality

			Patients (n=40)	Control (n=20)	Test of Sig.	P
MRI findings	T1WI signal pattern	Diffuse hyperintense	5(12.5%)	20(100.0%)	$\chi^2=42.0$	<0.001*
		Diffuse hypointense	3(7.5%)	0(0.0%)	$\chi^2=1.579$	0.544 [#]
		Focal hypointense	31(77.5%)	0(0.0%)	$\chi^2=32.069$	<0.001*[#]
		Focal hyperintense	2(5.0%)	0(0.0%)	$\chi^2=32.069$	<0.001*[#]
		Variegated	1(2.5%)	0(0.0%)	$\chi^2=32.069$	<0.001*[#]
		Signal void	3(7.5%)	0(0.0%)	$\chi^2=1.579$	0.544 [#]
	T2WI signal	Homogenous	18(45.0%)	20(100.0%)	$\chi^2=17.368$	<0.001*
		Heterogenous	22(55.0%)	0(0.0%)		
	STIR signal	Hyperintense signal	32(80.0%)	0(0.0%)	$\chi^2=36.667$	<0.001*[#]
		Hypointense signal	8(20.0%)	20(100.0%)	$\chi^2=34.286$	<0.001*[#]
	Contrast		12(30.0%)	0(0.0%)	7.50	0.005*

Fat suppression quality	Dixon MRI	Good	40(100.0%)	20(100.0%)	-	-
		Poor	0(0.0%)	0(0.0%)		
	STIR	Good	38(95.0%)	20(100.0%)	-	0.548
		Poor	2(5.0%)	0(0.0%)		

Data are presented as frequency (%). * Significant P value < 0.05. # P value for Fisher Exact test for comparing between the two studied groups due to small sample. MRI: magnetic resonance imaging, STIR: Short tau inversion recovery, χ^2 : Chi square test

Signal drop out % value in benign BM lesions was significantly higher than malignant and control groups ($P < 0.05$). SIR value was significantly lower in benign group than malignant and control groups ($P < 0.05$). Dixon Fat suppression quality was good in all patient and control cases, while STIR sequence fat suppression quality was good in 38 patients and all control cases. **Table 4**

Table 4: Comparison of Dixon MRI parameters signal drop out % & signal intensity ratio between patients and control group

	Benign (n=15)	Malignant (n=25)	Control (n=20)	Test of Sig.	p
Signal dropout %	40.31±13.02	10.69±6.88	44.40±17.19	F=45.604*	<0.001*
SIR	0.58±0.14	0.89±0.13	0.54±0.17	F=34.106*	<0.001*

Data are presented as mean \pm SD or frequency (%). * Significant P value < 0.05. SIR: Signal intensity ratio, F: for one way ANOVA test.

ROC for signal drop out % gave AUC 0.977 while SIR gave AUC 0.951 with sensitivity, specificity, PPV and NPV of signal drop out % 91.67 %, 75.0%, 84.6%, and 85.7%, respectively while, sensitivity, specificity, PPV and NPV of SIR 91.67 %, 60.0 %, 73.3% and 80.0 %, respectively. **Figure 1**

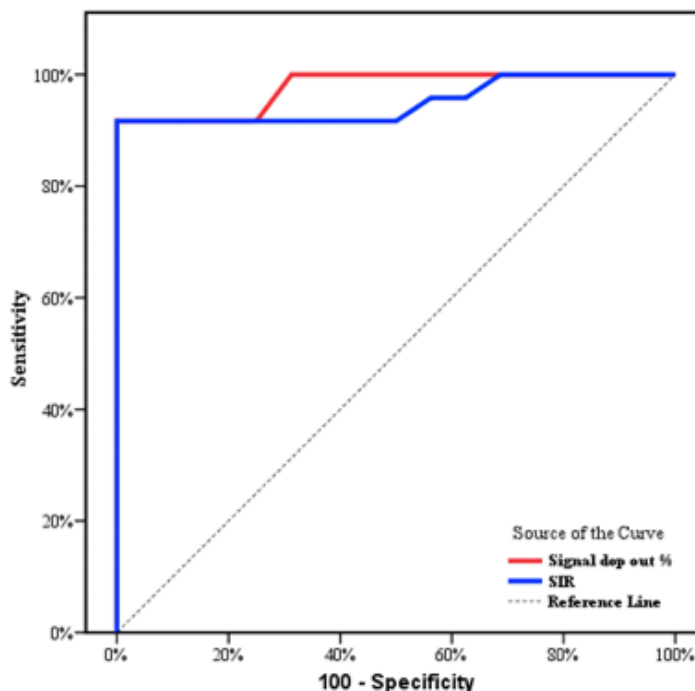


Figure 1: ROC curve between benign and malignant bone marrow lesions according to signal drop out % and SIR

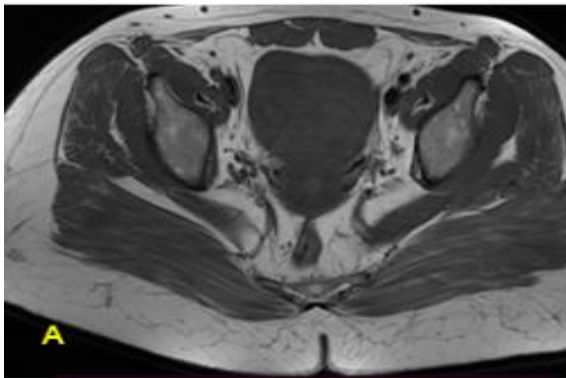
Diagnosis accuracy of Dixon MRI in the studied patients was with sensitivity, specificity, PPV, NPV, and accuracy 87.50 %, 75%, 84.0%, 80% and 82.50 %, respectively. **Table 5**

Table 5: Diagnosis accuracy of Dixon MRI in the studied patients

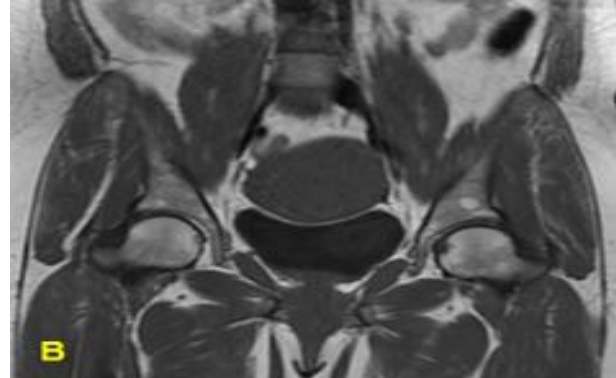
	Benign (n=15)	Malignant (n=25)	Sensitivity	specificity	PPV	NPV	Accuracy
Benign	12(80.0%)	4(16.0%)	87.50	75.0	84.0	80.0	82.50
Malignant	3(20.0%)	21(84.0%)					

Data are presented as frequency (%). PPV: Positive predictive value, NPV: Negative predictive value.

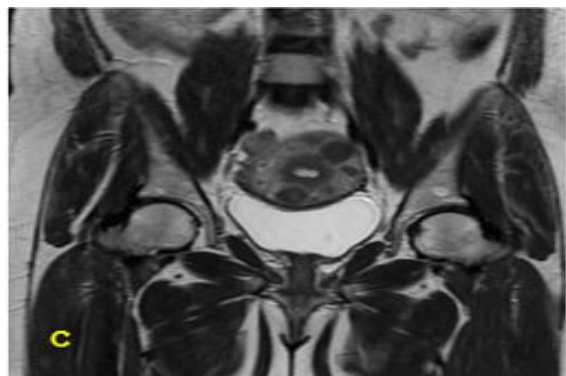
Case 1: a 50-year-old female patient presented with hip pain. Conventional MRI revealed hypointense signal of BM of both iliac bones in T1WI, isointense signal in T2WI and hyperintense in STIR sequence, no bony destruction or extra-osseous soft tissue components. With a signal drop out percentage of 61% and a SIR of 0.38, indicating a non-neoplastic lesion, Dixon MRI showed a significant decrease in marrow signal intensity in an out-of-phase sequence. Red marrow reconversion was diagnosed by imaging. With a signal drop out percentage of 61% and a SIR of 0.38, indicating a non-neoplastic lesion, Dixon MRI showed a significant decrease in marrow signal intensity in an out-of-phase sequence. Red marrow reconversion was diagnosed by imaging. **Figure 2**



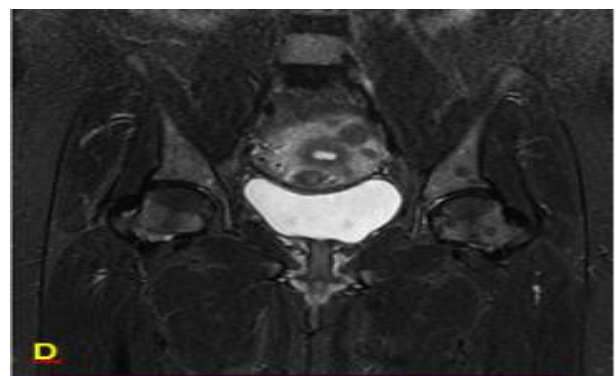
(A)



(B)



(C)



(D)

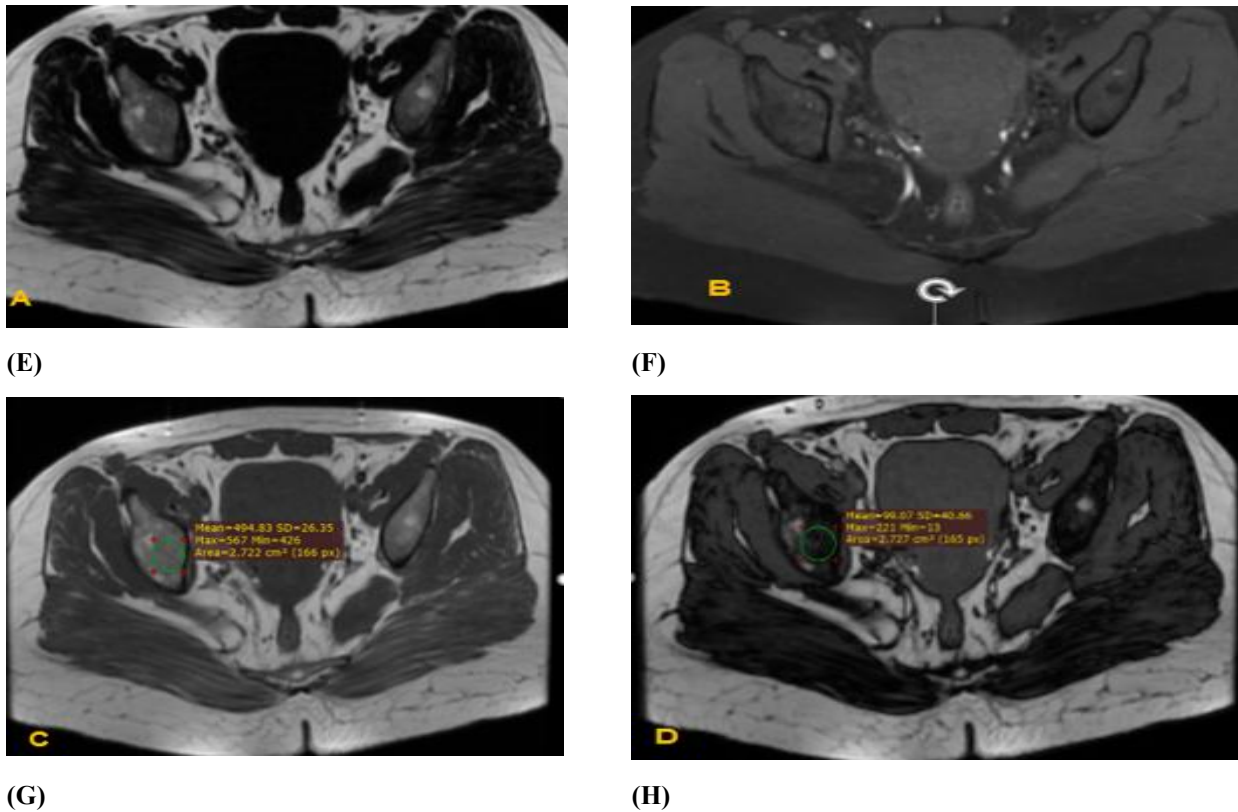
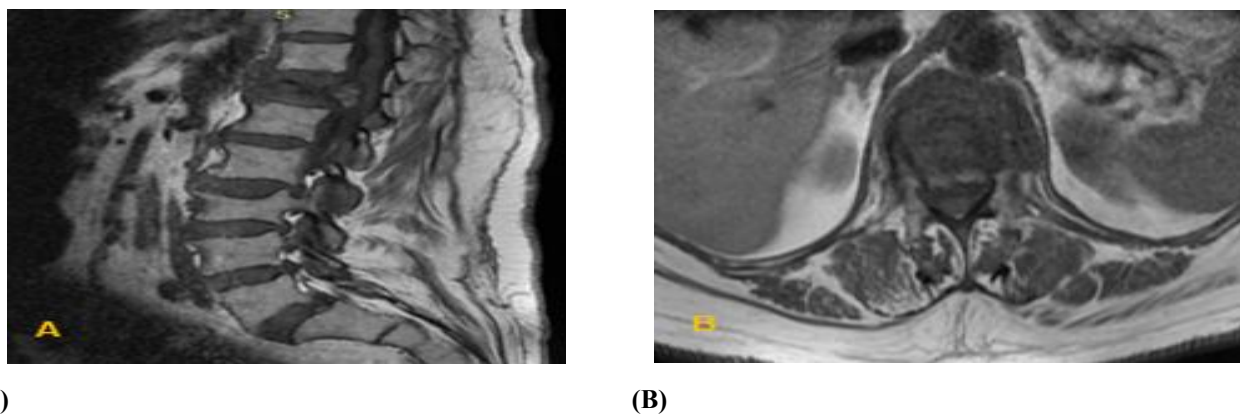


Figure 2: Conventional MRI (A) Axial T1WI, Coronal (B) T1WI, (C) T2WI, (D) Short tau inversion recovery image of both hip joints, Dixon MRI (E) Axial fat only, (F) axial water only, (G) in phase and (H) Out-of-phase image

Case 2: A 57-year-old male patient with bronchogenic carcinoma presented with back pain. Conventional MRI revealed decreased height of D12 vertebra with alerted BM signal intensity displaying hypointense signal in T1WI, T2WI & hyperintense signal in STIR image as well as convex posterior border and retro pulsed bony fragment compressing the cord. With a signal drop out percentage of 8% and a SIR of 0.92, indicating an underlying neoplastic lesion, Dixon MRI showed no decline in the signal intensity of the marrow lesion in the out-of-phase sequence. Malignant vertebral collapse was diagnosed by imaging. **Figure 3**



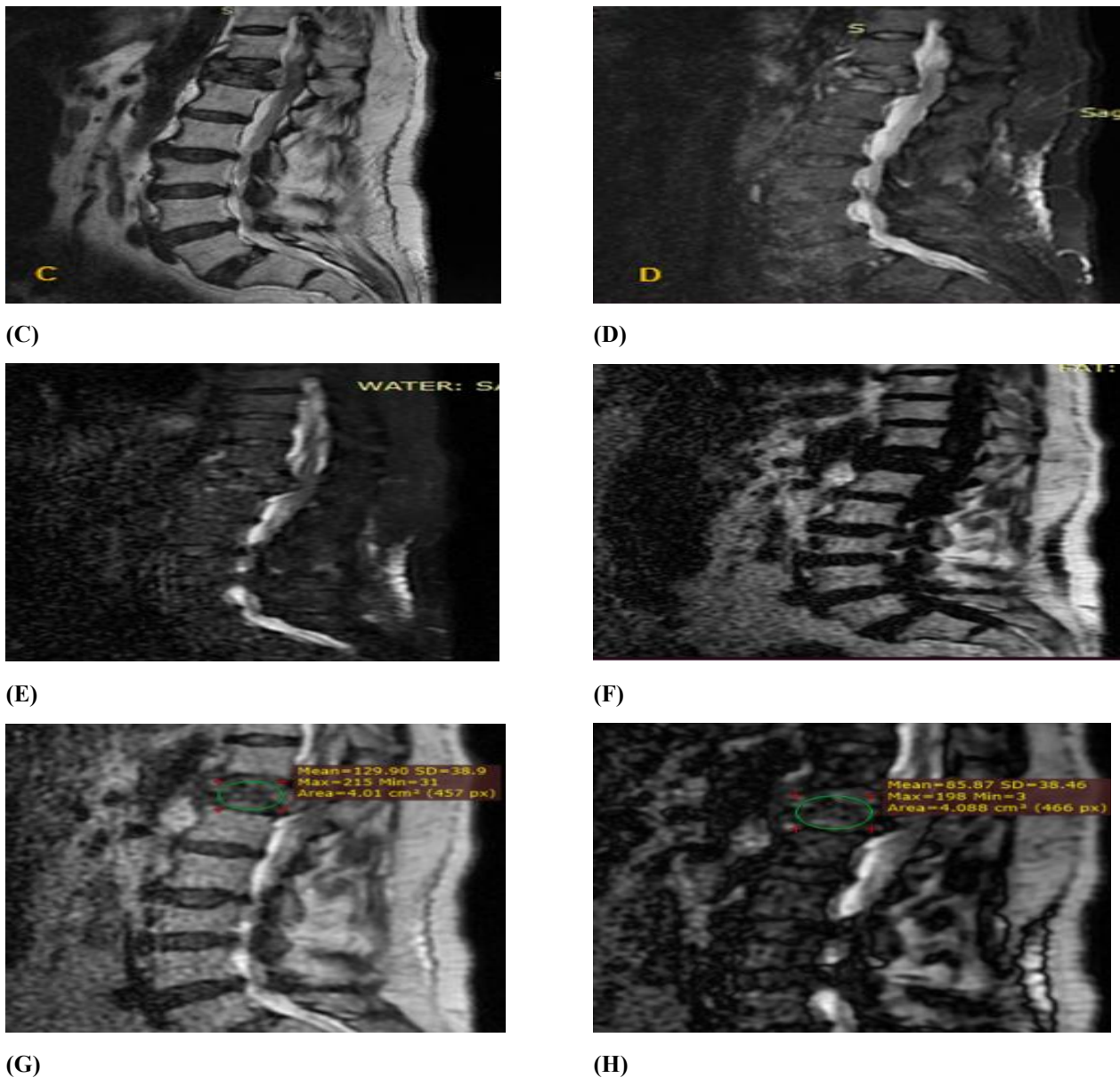


Figure 3: Conventional MRI (A) Sagittal T1WI, (B) Axial T1WI, (C) Sagittal T2WI, (D) Short tau inversion recovery image of the lumbosacral spine, Dixon MRI MRI of the lumbosacral spine (E) Water only, (F) Fat only, (G) in-phase image and (H) Out-of-phase image

3. DISCUSSION

Human blood cell generation is carried out by the BM, the biggest haematopoietic organ in the body. Normal BM contains water, fat, and cellular elements [1].

In our study, 67% the BM lesions were in the axial skeleton. Oki Nozomi et al. [10] shown that the most frequent location for BM lesions was the spine, namely the lumbar region. Twenty-six malignant neoplastic lesions, two benign neoplastic lesions, and fourteen non-neoplastic lesions were found.

In our study BM lesions present with 6 patterns on T1W images as the following: diffuse hyperintense (12.5%), diffuse hypointense (7.5%), focal hypointense (77.5%), focal hyperintense (5%), variegated (2.5%) and signal void (7.5%). Diffuse hypointense pattern could be detected in both red marrow reversion and haematological malignancy. Burcu Akman et al. [4] stated in that both red marrow reversion and hematological malignancy are difficult to diagnose by conventional MRI, hence other techniques like CSI are needed to differentiate them.

In our study, the mean values of signal drop out % of the benign lesions were 40.31 ± 13.02 , and of malignant lesions were 10.69 ± 6.88 . By Roc curve analysis, cut-off value ≤ 22 , AUC 0.977(95 % CI 0.939 – 1.0%) with sensitivity, specificity,

PPV, and NPV of 91.67 %, 75.0%, 84.6%, and 85.7% respectively. H.Douis et al. ^[11] discovered that benign lesions had larger mean values of signal intensity loss than malignant lesions. With a cut-off value of 16.9%, they were 36.3% (SD 26.6%) for benign lesions and 5.7% (SD 18.6%) for malignant lesions. This yielded the highest accuracy, with an AUC of 0.839 (95 % CI 71.9–95.9%), sensitivity of 91.7%, specificity of 72.7%, negative predictive value of 97.1%, and positive predictive value of 47.8%. However, a cut-off value of 35% with 95% specificity, 100% sensitivity, 100% positive predictive value, and 95.2% negative predictive value was reported by Yasser Ragab et al. ^[12].

The mean values of SIR of the benign lesions were 0.58 ± 0.14 , and of malignant lesions were 0.89 ± 0.13 . By Roc curve analysis, cut off value was 0.82, AUC 0.951 (95 % CI 0.881 – 1.0) with sensitivity, specificity, PPV, and NPV of 91.67 %, 60.0 %, 73.3%, and 80.0 % respectively

This is similar to the results of the study of Burcu Akman et al. ^[4] found that the mean values of SIR were higher in malignant lesions (0.97 ± 0.16 for malignant lesions and 0.69 ± 0.31 for benign lesions) with cut-off value 0.82 ($P < 0.001$), AUC: 0.828 , sensitivity 83.3%, specificity was 87%. While Brahmdeep S. Wadhawan et al. ^[3] said that the cut-off value was 0.96, with a sensitivity of 83.3%, specificity of 58.70%, PPV of 34.8, NPV of 93.10%, and AUC of 0.758. Regarding the overall diagnostic accuracy of the Dixon technique for distinguishing between neoplastic and non-neoplastic lesions, our study found that there were 12 true negative cases (diagnosed as benign or non-neoplastic) and 21 true positive (TP) cases (diagnosed as malignant) that were confirmed by biopsy, positron emission tomography (PET)/computed tomography (CT), or follow-up.

In our study, the Dixon technique showed sensitivity, specificity, PPV, and NPV 87.50 %, 75%, 84.0%, and 80% with an accuracy of 82.50 %. This agrees with Asif Saifuddin et al. ^[13] found that the T2 Dixon approach had a high diagnosis accuracy of 77.8%, 86.6%, 59.1%, 93.4%, and 83.5% for separating benign from malignant BM lesions, with sensitivity, specificity, positive predictive value, and negative predictive value.

Dixon images showed excellent fat suppression in 100% of cases compared to the STIR sequence which showed good suppression in 95% of cases. Also Ophelye Chiabai et al. ^[14] reported in their study high image quality and good fat suppression of water only images of the Dixon technique in comparison to STIR sequences.

Limitations of the study included that the sample size was relatively small besides the unavailability of fat fraction maps software which allows automated, multiple, accurate, and more anatomical signal intensity measurements to become more valuable in small-sized lesions or lesions near the vertebral end plates to decrease the rate of false negative results. A definitive histological diagnosis was only available in 15 of the cases owing to the invasive nature of the technique and the difficulty of obtaining a biopsy from several lesions either owing to their small size lesions or the site of the lesions. So, in cases where biopsy was inaccessible, we depend on PET/CT and follow up after 6 months by MRI with the same sequences and parameters to assess the nature of the lesion guided by assessment of changes in its size (if size significantly increases, it denotes malignant nature), nature of the lesion (being more destructive denotes malignant nature), signal intensity changes and changes in Dixon MRI parameters (increased signal intensity loss in out of phase images detected by reduces signal drop out % and increased signal intensity ratio).

4. CONCLUSIONS

With its excellent sensitivity, specificity, and diagnostic accuracy, Dixon MRI's quantitative indicators make it a useful and quick technique for separating benign from malignant BM lesions. In order to distinguish between benign and malignant BM lesions, we advise employing Dixon MRI as a regular examination in addition to MRI.

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There is no conflict of interest.

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