Original Article

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Radiology Section

Precision in Practice: A Cross-sectional Study Involving MRI T2 Dixon and Conventional Sequence in Detecting Focal Multiple Myeloma Lesions

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ABSTRACT

Introduction: Multiple Myeloma (MM) represents a malignant proliferation of plasma cells derived from a single clone. Imaging of the skeleton beyond symptomatic areas is useful for myeloma staging and subsequent follow-up for treatment response and disease relapse. Despite research comparing the Dixon sequence to conventional sequences in a variety of musculoskeletal disorders, there is a lack of studies regarding the Dixon sequence's application in MM.

Aim: To compare the contrast of MM focal lesions in all four T2-weighted Dixon and Conventional T1-weighted spin-echo and Short Tau Inversion Recovery (STIR) images.

Materials and Methods: This cross-sectional study was conducted in the Department of Radiology at Kovai Medical Centre and Hospitals (KMCH), Coimbatore, Tamil Nadu, India. All newly diagnosed and known cases of MM, either biopsy-proven or strongly suspected based on other diagnostic testing conforming to International Myeloma Working Group (IMWG) criteria from December 2020 to July 2022, were included in the study. A total of 43 patients with 142 focal MM lesions were included. Contrast between focal MM lesions and surrounding bone marrow was calculated on T1-weighted spin-echo, STIR, and T2-weighted Dixon (all four) images. Statistical analysis was done using repeated measures of Analysis of Variance (ANOVA) with Bonferroni correction to control the type I error on multiple comparisons to find the significant difference between multivariate analyses. A probability value of 0.05 was considered a significant level for all statistical tools.

Results: The study population consisted of 21 men and 22 women with a mean age of 65.3±8.6 years {Mean±Standard Deviation (SD)}. Contrast values in all four T2 Dixon images, STIR, and T1-weighted images were as follows: T2 Dixon Fat-only (FO) images (0.86.±0.09) (SD); range: (0.46-0.99), T2-weighted Dixon Water-only (WO) images (0.54±0.14) (SD); range: (0.14-0.82), T2 Dixon In-phase (IP) images (0.20±0.13) (SD); range: (0.02-0.41), T2-weighted Dixon Out-phase (OP) images (0.53±0.19) (SD); range: (0.12-0.87), STIR images (0.47±0.12) (SD); range: (0.12-0.73), and T1 images (0.23±0.12) (SD); range: (0.01-0.55). The mean contrast was highest on T2 Dixon fat-only images ($p<0.0005$) compared to T1 images, with the lowest contrast seen in IP images and intermediate values in OP images.

Conclusion: In conclusion, fat-only images of the T2 multipoint Dixon sequence provide significant contrast compared to conventional T1-weighted imaging. Dixon water-only images provide fat suppression that is not inferior to STIR images. While Dixon techniques in the diagnosis of MM did not significantly differ from the conventional sequence, Dixon stands out from conventional sequences when considering the study duration and contrast between the lesion and normal bone marrow.

Keywords: Contrast, Fat suppression, Magnetic resonance imaging, Red marrow

INTRODUCTION

Multiple Myeloma (MM) represents a malignant proliferation of plasma cells derived from a single clone. The tumour, its products, and the host response to the tumour result in several organ dysfunctions and symptoms [1]. Premalignant diseases like Monoclonal Gammopathy of Undetermined Significance (MGUS) and Smoldering MM (SMM) precede MM, serving as a starting point for the highly heterogeneous disease [2]. Myeloma becomes more prevalent with age, with a median diagnosis age of 70 years, and males are more commonly affected than females [3].

According to an Indian Council of Medical Research (ICMR) consensus document published in 2017, the global 5-year prevalence of MM is 4.3/100,000, with India having a 1.4/100,000 population [4]. MM accounts for 1% of all cancer-related deaths, claiming approximately 5,900 lives in India annually and representing 15% of all haematological malignancies. Osteolytic lesions in the bone marrow are present in 80% of newly diagnosed cases, with 10% developing over time [5]. The International Myeloma Working Group (IMWG) [6] revised the criteria for MM diagnosis in 2014, incorporating imaging modalities such as Computed Tomography (CT), Positron Emission Tomography-CT (PET-CT) and Magnetic Resonance Imaging (MRI) alongside biochemical markers.

The fatty component of vertebral bone marrow increases gradually with age [7]. Chemical shift imaging can reveal intravoxel fat that is not visible with conventional T1-weighted sequences. Dixon techniques, including single-point Dixon, two-point Dixon, or multi-point Dixon, allow for the measurement of fat and water-specific signals in-phase (IP) and out-of-phase (OP) [8]. Traditionally used for identifying and characterising pathologies in the liver, kidney, and adrenal lesions, the Dixon-based approach has been beneficial [9].

Patients with MM having negative radiographs or limited radiographic disease should undergo an MRI of the axial skeleton. Follow-up examinations every 3-6 months are strongly advised for patients with diffuse infiltration, a single focal lesion, or equivocal findings [10]. MRI exhibits higher sensitivity and reproducibility than PET-CT, enhancing the detection of diffuse marrow involvement and small foci of myeloma involvement in bone marrow [11].

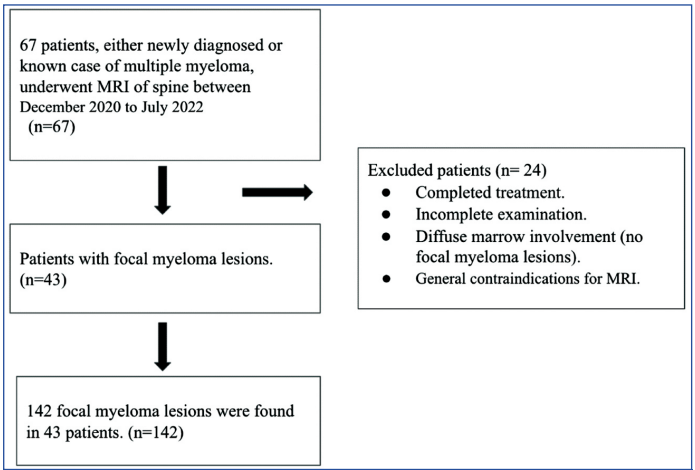
Regarding fat suppression, Multi-point Dixon minimises variations in image quality across patients [12]. While studies comparing the Dixon sequence to conventional sequences in various musculoskeletal diseases exist, there is a lack of data on its use in MM [13-18]. No comparative study in India has demonstrated the imaging quality and diagnostic accuracy of identifying focal MM lesions in T2 Dixon sequences on MRI in MM patients. Additionally, literature scarcity persists on whether the T2 Dixon sequence can substitute the conventional T1 sequence in detecting focal myeloma lesions. The present study aimed to explore the potential of T2 Dixon as a standalone sequence in MM.

MATERIALS AND METHODS

The present cross-sectional study was conducted in the Department of Radiology at Kovai Medical Centre and Hospital, Coimbatore, Tamil Nadu, India, from December 2020 to July 2022, following approval from the hospital's Ethics and Scientific Committee (EC/AP/840/12/2020) Each participant provided written informed consent before undergoing an MRI.

Sample size calculation: The sample size was estimated based on an article [19], considering standard deviations of 0.21, 0.19, and 0.20 in T2 Dixon, T1-weighted, and STIR sequences, respectively. Sample size calculation was performed using N Master 2.0 software.

Inclusion and exclusion criteria: The study included all newly diagnosed and known cases of multiple myeloma (MM), either biopsy-proven or strongly suspected based on other diagnostic tests conforming to IMWG criteria. Patients with diffuse infiltrative patterns, those who completed treatment, and those with an incomplete MRI protocol were excluded from the study. Out of the 67 MM patients who underwent an MRI examination of the spine during the study period, 43 patients with evidence of focal MM lesions in conventional MRI sequences were further evaluated [Table/Fig-1].



[Table/Fig-1]: Flowchart showing patient inclusion and exclusion in the study.

Study Procedure

MRI technique: MRI was performed using either a Siemens MAGNETOM Skyra 3T MRI with dedicated coils. 43 patients underwent scans, with acquired sequences in the conventional protocol including turbo spin-echo T1-weighted, T2-weighted, and STIR sequences in sagittal planes. A T2-weighted multipoint Dixon sequence in the sagittal plane with four images (water-only, in-phase, opposed-phase, and fat-only) was added to the protocol. The imaging parameters for the 3T system are detailed in [Table/Fig-2].

Image analysis: Qualitative Analysis: All MRIs included in the study were assessed for:

1. The type (focal or diffuse) of lesion

MRI protocol	T1-weighted	T2-weighted Dixon	STIR
Repitition Time (TR)	580	2000	4050
Time to Echo (TE)	10	82	53
Time duration	1 min 48 secs	2 mins 22 secs	3 mins 13 secs
Slice thickness	3.0 mm	4.0 mm	3.0 mm
FOV	300 mm	260 mm	320 mm

[Table/Fig-2]: MRI parameters in 3T scanner systems.

2. Exact location of the lesion

Focal myeloma lesions were visualised on T1-weighted images and T2 Dixon images, using STIR images as a reference. Regions of Interest (ROIs) were measured by two radiologists-one with 15 years of experience in radiology and musculoskeletal imaging, and the other with 5 years of experience in radiology. Before conducting ROI measurements, both radiologists underwent a training session where methods were discussed. ROIs were placed by both radiologists in the same area on MRI images. The radiology observers repeated their measurements after one week to determine intraobserver variability.

Quantitative analysis: The signal intensity of focal MM lesions and surrounding bone marrow of the same vertebral body (without focal lesions) was calculated by placing round operator-determined ROIs measuring 5 mm to 15 mm in diameter. The ROIs had a mean surface of 76.7 mm^2±78.01 (SD) (20.6 mm^2–186.6 mm^2). Reference ROIs were placed on focal lesions and adjacent normal bone marrow. In the absence of normal marrow, ROIs were placed at the centre of adjacent vertebral bodies. The contrast between focal myeloma lesions and bone marrow was calculated using the formula [Table/Fig-3] [19].

$$\text{Contrast} = \frac{(\text{Lesion signal within ROI} - \text{Normal BM signal within ROI})}{(\text{Lesion signal within ROI} + \text{Normal BM signal within ROI})}$$

[Table/Fig-3]: Formula used to calculate contrast between focal myeloma lesions and bone marrow [19].
ROI: Regions Of Interest; BM: Bone marrow

STATISTICAL ANALYSIS

The data collected was analysed using International Business Machines (IBM) Statistical Package for Social Sciences (SPSS) Statistics for Windows, version 23.0 (Armonk, NY: IBM Corp.). Descriptive statistics, frequency analysis, and percentage analysis were used to characterise categorical variables, while mean and Standard Deviation (SD) were applied for continuous variables. To determine significant differences between multivariate analyses, repeated measures ANOVA was employed along with the Bonferroni correction to control the type I error in multiple comparisons. A probability value of 0.05 was considered the significant level for all the statistical tools mentioned above.

RESULTS

Among the 43 patients with MM, the age ranged from 52 to 85 years, with a mean age of 65.3±8.6 years. The study population comprised 21 males and 22 females. A total of 142 focal myeloma lesions were analysed, with 8 (5%) in the cervical spine, 92 (61%) in the dorsal spine, 32 (22%) in the lumbar spine, and 10 (7%) in the sacral spine. Both qualitative and quantitative analyses were conducted on the image sets to assess signal characteristics and contrast. Signal intensity and contrast were calculated by measuring the Signal Intensity (SI) of healthy surrounding bone marrow and focal myeloma lesions. Four sets of images from the T2-weighted Dixon sequence and T1-weighted images were compared for contrast. The mean and standard deviations of contrast for various lesions in each patient's sequences were computed to compare the overall averages of variables.

In the evaluation of 142 focal myeloma lesions in 43 patients, the mean signal intensity of the lesion on different images was as follows:

- T2-weighted Dixon fat-only images: 12.82±8.83
- T2-weighted Dixon water-only images: 275.24±99.94
- T2-weighted Dixon in-phase images: 284.87±106.68
- T2-weighted Dixon out-phase images: 319.08±123.97
- STIR images: 300.00±175.75
- T1-weighted images: 226.1±90.51 [Table/Fig-4].

Variables	Mean signal intensity	SD
STIR	300.00	175.75
T1W	226.1	90.51
Dixon Fat-only	12.82	8.83
Dixon Water-only	275.24	99.94
Dixon in-phase	284.87	106.68
Dixon Out-phase	319.08	123.97

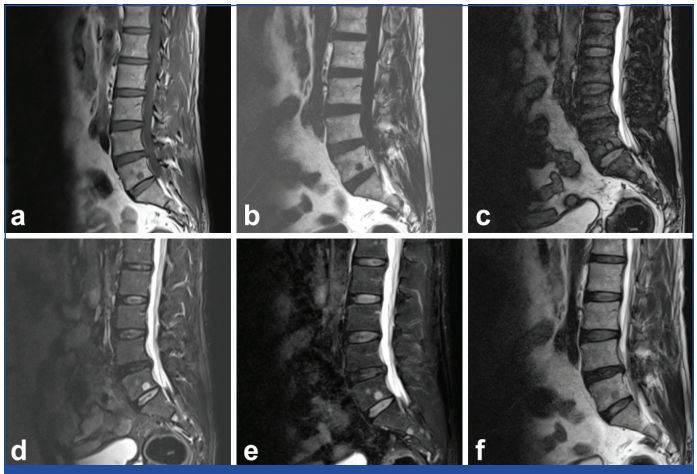
[Table/Fig-4]: Mean signal intensity and standard deviation of STIR, T1W and all four images of T2 Dixon sequence.

The mean signal intensities of all four Dixon images and T1 weighted images showed a significant drop in signal in Dixon fat-only images compared to conventional T1-weighted images.

The contrast results for all four T2 Dixon images, STIR, and T1-weighted images were as follows:

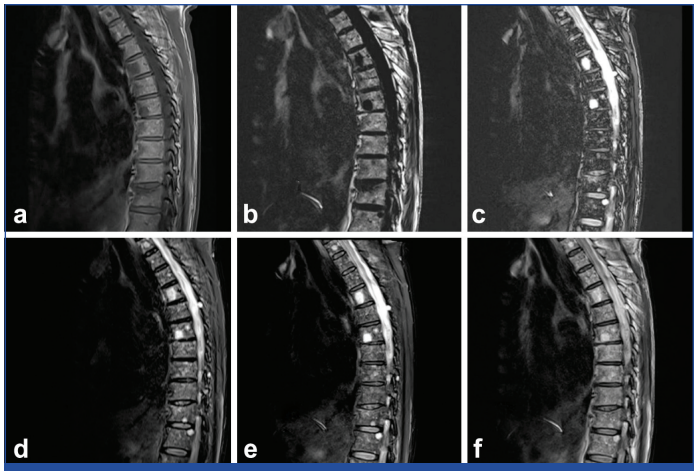
- T2-weighted Dixon fat-only images: 0.86±0.09
- T2-weighted Dixon water-only images: 0.54±0.14
- T2-weighted Dixon in-phase images: 0.20±0.13
- T2-weighted Dixon out-phase images: 0.53±0.19
- STIR images: 0.47±0.12
- T1-weighted images: 0.23±0.12

The MRI images of focal MM lesions are depicted in [Table/Fig-5,6]. comparisons using the Bonferroni test revealed a statistically significant difference between three images (fat-only, water-only, and out-phase) of T1-weighted images (p-value <0.001) [Table/Fig-7].



[Table/Fig-5]: Sagittal sections of the lumbosacral spine show multiple well-defined low signal intensity focal myeloma lesions in T1W (A) and Fat-only (b) images. These well-defined focal myeloma lesions show high signal intensity on out-phase (c), STIR (d), Water alone (e), and In-phase (f) images.

The mean contrast was highest on T2-weighted Dixon fat-only images, lower on T1-weighted images. Contrast in water-only images (fat-suppressed images) was comparable to STIR images, with the lowest contrast seen on in-phase images and intermediate values in out-phase images [Table/Fig-8].



[Table/Fig-6]: Sagittal sections of the dorsal spine show multiple well-defined low signal intensity focal myeloma lesions in T1W (a) and Fat-only (b) images. These well-defined focal myeloma lesions show high signal intensity on Out-phase (c), STIR (d), Water alone (e), and In-phase (f) images.

(I) Lesion		Mean difference	Std. Error	p-value	95% CI for difference	
					Lower bound	Upper bound
STIR	Fat	0.387	0.012	0.0005	0.423	0.352
	Water	0.065	0.012	0.0005	0.100	0.030
	In	0.269	0.016	0.0005	0.221	0.317
	Out	0.061	0.018	0.0150	0.115	0.007
T1W	Fat	0.625	0.012	0.0005	0.660	0.590
	Water	0.302	0.015	0.0005	0.349	0.256
	In	0.031	0.013	0.2260	0.007	0.069
	Out	0.298	0.022	0.0005	0.364	0.233

[Table/Fig-7]: Pairwise comparisons between T1, STIR and all four Dixon images using the Bonferroni test.

Variables	Mean contrast	SD
STIR	0.47	0.12
T1W	0.23	0.11
Dixon Fat-only	0.86	0.09
Dixon Water-only	0.54	0.14
Dixon In-phase	0.20	0.13
Dixon Out-phase	0.53	0.19

[Table/Fig-8]: Contrast in STIR, T1W and all four images from the T2 Dixon sequence.

DISCUSSION

In multiple myeloma (MM), the second most common haematological malignancy after Non-Hodgkin's Lymphoma (NHL), bone lesions develop in 90% of patients during the course of the illness [6]. Therefore, imaging for diagnosis and follow-up is essential. With the introduction of new diagnostic criteria for MM by the International Myeloma Working Group (IMWG) in 2014 [6], MRI is gaining importance, particularly in early phases, disease activity assessment, and treatment response monitoring [20]. The bone marrow, consisting of 60% haemotopoietic cells and 40% fat cells, is primarily composed of fat present in yellow and red marrow [21]. A key diagnostic criterion to differentiate neoplastic tissue from normal marrow in neoplastic lesions is the replacement of normal bone marrow by proliferating cells, resulting in fat signal loss in the marrow [22,23]. This loss of signal intensity should be interpreted relative to the skeletal muscle signal to distinguish neoplastic lesions from red bone marrow with varying cellularity levels [24]. Dixon T2-weighted fat-only images are quicker to interpret as they are specific to fat signal only. With the elimination of fat, bone marrow replacement

lesions show no intralesional signal compared to adjacent bone marrow, eliminating the need to compare signal intensity to adjacent muscle [17].

The Dixon sequence has undergone several advancements, including phase-correction algorithms in acquisition and postprocessing fields, improving image quality. Focal and diffuse bone marrow lesions play a role in disease progression [25], emphasising the need for the best imaging technique for identifying and characterising localised bone marrow lesions. Focal MM lesions were well visualised in T1-weighted, STIR, and T2 Dixon sequence images in this study. There was a significant signal drop in fat-only sequences compared to conventional T1 images, with significantly higher contrast in fat-only images. The other image sets also showed significant differences in contrast compared to T1-weighted images. Water-only images were not inferior to STIR images quantitatively for detecting focal myeloma lesions, suggesting the potential incorporation of Dixon in vertebral lesion detection and post-treatment monitoring.

Compared to traditional STIR methods, Dixon sequences have been shown to offer superior fat suppression and image quality in various clinical settings. Most high-signal bone marrow changes on MRI were observed on both STIR and water-only T2W Dixon images, emphasising the importance of studying bone marrow signal changes using the same imaging techniques [26]. Therefore, the Dixon sequence is expected to be equal or superior to conventional imaging for MM evaluation. Few studies have evaluated the role of Dixon in focal myeloma lesion assessment, with some studies showing higher contrast and lesion detection rates with Dixon images compared to conventional imaging [27].

In conclusion, Dixon sequences offer advantages such as improved contrast-to-noise ratio, reduced acquisition time, and superior fat suppression, making them valuable in various imaging applications [28]. The use of Dixon for skeletal screening and bone metastasis detection has shown promising results, potentially replacing multiple sequences in conventional imaging protocols [18]. Further research and clinical studies are warranted to explore the full potential of Dixon sequences in oncology imaging protocols.

Limitation(s)

The study did not evaluate the sensitivity of the T2-weighted Dixon sequence compared to T1 or STIR sequences in detecting MM lesions, nor did it assess the impact of the patient's treatments on the contrast.

CONCLUSION(S)

In conclusion, fat-only images from the T2 multipoint Dixon sequence offer significant contrast compared to conventional T1-weighted imaging. With recent advances in imaging technology, Dixon could be integrated as a single sequence for imaging focal myeloma lesions, potentially reducing acquisition time and enhancing diagnostic confidence compared to using multiple morphologic sequences for detection. The analysis of a large number of patients represents one of the strengths of the present study.

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