

Whole-Body Diffusion-Weighted Imaging with Background Suppression Magnetic Resonance Imaging in Patients with Multiple Myeloma

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ABSTRACT

Background:

Multiple myeloma (MM) is a monoclonal plasma cell proliferative disease characterized by primary bone marrow infiltration and excessive production of abnormal monoclonal immunoglobulin. The aim of the present study is to assess the detection of bony lesions in patients with MM using whole-body diffusion-weighted imaging with background body signal suppression (WB-DWIBS).

Patients and methods: A prospective study was conducted on 28 consecutive patients (18 males, 10 females); mean age 55 (SD 9) years with pathologically proven MM, who underwent WB-DWIBS on a 1.5-T MR scanner. Image analysis was performed and numbers of bony lesion were recorded according to affection of each anatomical site. For this study, we compared the number of lesions detected by T1, STIR and DWIBS.

Results: Our results showed that DWIBS was able to detect a large number of lesions compared to T1 and STIR, but yet did not reach statistical significance (P value >0.05).

Conclusion: that WB-MRI using morphological sequences and the DWIBS technique is a reliable imaging modality for detection of MM lesions, whether focal, diffuse or combined. DWIBS was able to detect larger number of lesions than morphological sequences yet did not reach statistical significance.

Keywords: Multiple myeloma, Whole-body MRI, DWIBS.

INTRODUCTION

Multiple myeloma (MM) is a monoclonal plasma cell proliferative disease characterized by primary bone marrow infiltration and excessive production of abnormal monoclonal immunoglobulin ^[1]. Up to 90% of MM patients experience bone lesions during the course of their illness, highlighting the value of imaging tests both at the time of diagnosis and during follow-up, especially in light of the fact that the number and size of focal bone lesions have been shown to be indicators of prognosis ^[2,3].

Despite the fact that whole-body MRI (WB-MRI) with T1- and T2-weighted contrast-enhanced images has been shown to have advantages over traditional skeletal survey in clinical routine, conventional radiography is still used in the staging procedure for newly diagnosed and relapsed MM patients. It offers crucial further information since, for instance, osteoporosis can be a symptom of tumour infiltration but is hard to distinguish from senile osteoporosis on traditional radiography. Additionally, an additional medullary tumour expansion may be undetected on x-ray imaging but is easily detected by MRI ^[4,5].

WB- MRI is thus advised in all patients with an apparent single plasmocytoma of the bone and at least in MM patients with normal conventional radiography. It is important to note that a restricted MR examination that only examines the spinal and pelvic bone marrow maybe inferior to radiographic skeletal scan , but whole body MRI has been demonstrated to be superior to skeletal survey and also to computed tomography ^[6].

There is some evidence to suggest that MRI can even measure the disease load in MM patients. In patients with MM at the time of initial diagnosis, the

degree of bone marrow involvement as measured by WB-MRI corresponds with other conventional disease indicators and may independently predict survival. With MRI, Turbo Spin-Echo (TSE) short TI Inversion Recovery (STIR) sequences are the most effective at identifying focal bone marrow involvement. In the event of diffuse infiltration, unenhanced T1-weighted SE pictures are preferable, and signal intensity measures following contrast delivery can improve sensitivity for detecting diffuse infiltration. Due to reduced renal function, contrast media, however, pose a danger to patients with multiple myeloma. Contrast studies may be replaced by diffusion-weighted imaging with background body signal suppression (DWIBS) is suggested ^[7].

Takahara et al. provided the initial description of DWIBS in 2004. Since then ,Numerous authors have emphasized the technique's significant promise for oncological imaging. The inherent contrast of DWIBS, which is based on enhanced signal intensity in tissue with constrained water diffusivity, is used to diagnose malignant tumour illness. By observing the microscopic movement of water molecules, the method enables non-invasive detection of tissue with increased cellularity. Different solid tumour entities have been staged using diffusion-weighted WB- MRI ^[7,8].

The main aim of this study is to assess role of whole-body diffusion magnetic resonance imaging with background body signal suppression [DWIBS] in the evaluation of MM patients.

PATIENTS AND METHODS

This study was conducted in the Radiology Department of Mansoura University Hospitals during the period from 2019 to 2021. MRI was done for 28 patients pathologically confirmed MM. There were 18 males and 10 females. Their ages ranged from 55 years to 72

years. All patients were examined with whole body MRI with diffusion and background suppression (DWIBS).

Patients' selection:

Patients of this study underwent whole body MRI before chemotherapy and radiotherapy regimens. We excluded patients who had contraindications to MRI as metal implants and claustrophobia, patients refused to complete the examination due to long time and patients were highly irritable with severe excessive motion. The value of the study was explained to the patients. They agreed to participate in the study, and consents were taken from them, and the medical research ethics committee of Mansoura University approved the current study.

Technique and methods:

Whole-body MRI was performed using a 1.5-Tesla (T) machine whole-body scanner (Philips, Ingenia), using a table moving technique. Images are acquired using the integrated body coils and acquired in the coronal plane. By the combination of the moving tabletop, table extender and image-melding software the scan can time is about 25–35 min and total exam time is about 45 min, including patient positioning and survey acquisition. All patients were prepared by 1- Asking patients for presence or absence of cardiac pacemakers, any neurosurgical clips, embedded metal fragments, dental prostheses, piercings and missed period. 2- Asking patients to change clothes if having any metallic objects including breast holders, belts, or jewels. 3- Informing patients about the knocking sound that is heard during the examination, the relatively longer time of MR examination and instructed to be motion less. Patients were examined in the supine foot first position on the rolling table plate. Positioning of the upper extremities is dictated by patient habit. In cachectic patients, the arms are easily placed over the thorax and abdomen. In larger patients, the arms are placed above the head, requiring an additional coronal acquisition and an additional 4 min scan time.

Image acquisition:

At first three-plane localizer scout view were performed for the region of interest. Pulse sequences used in image acquisition are:

I- T1 FSE sequence:

Whole-body coronal non-fat saturated TIWI for seven separate sites: 1- Head, neck, chest apex, proximal upper limb, and cervical spine. 2- Chest, upper

abdomen, upper limb, dorsal and upper lumbar spine. 3- Lower abdomen and upper pelvis. 4- Lower pelvis and thighs. 5- Distal femori, knee joint and proximal both tibiae. 6- Tibia and fibula. 7- Distal tibia, distal fibula, and foot. These images were obtained by FSE with the following imaging parameters: TR= 400 ms; TE =4 ms; slice thickness, 6= mm; FOV=, 300-360 mm and matrix= 256x256.

II-Whole-body MRI using short tau inversion recovery (STIR):

Coronal STIR images were obtained for the whole body in seven separate sites with the following parameters: TR=3000-5000 ms; TE=70 ms ; TI=165 ms ; slice thickness= 6mm ; FOV = 300-360 mm and the matrix = 256x256.

III-Diffusion-weighted whole-body imaging:

It is performed using the STIR EPI diffusion-weighted technique with a high b value for background suppression. Signals from normal tissue such as blood vessels, fat, muscle, and bowel are suppressed. However, other normal structures such as the spleen, prostate, testes, ovaries, endometrium, and spinal cord remain visible. Areas showing restricted diffusion, for example, highly cellular lymph node or areas of marrow infiltration are strikingly depicted.

Whole-body DWI with background body signal suppression (DWIBS):

The free-breathing approach allows thin slices (Slice thickness; 3mm), it is done with the following parameters: B-value=800, TR=7410 ms, TE=60 ms, TI=165ms, matrix =256x256, and FOV=250 mm.

Post- imaging processing:

Post processing and interpretation Images of each sequence of body regions are then realigned to produce whole-body images using the dedicated software to facilitate instant review at the workstations. Interpretation is done by scrolling through the images at the workstation. Images are well analyzed searching for any soft tissue or bone marrow pathological changes.

Image analysis:

Visual analysis of the three types of MRI images was performed. Each site of abnormal signal intensity not from normal anatomical structure was considered as MM lesion.

Ethical consent:

An approval of the study was obtained from Mansoura University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The statistical analysis of data was done using the Statistical Package for Social Science, version 22 (SPSS Inc., Chicago, IL, USA). Qualitative data were described as numbers and percentages. Monte Carlo and Kruskal-Wallis tests were used for comparison between groups, as appropriate. P value ≤ 0.05 was considered to be statistically significant.

RESULTS

Table 1 demonstrates sociodemographic and laboratory characteristics of the study group. The percentage of male to female ratio was (64.3/35.7) and the mean age was 55. Most of the studied cases had ISS grade III (60%), followed by grade I (33.3%) and lastly grade II which was reported in only one case. The majority of the studied cases had positive CD56 (83.3%), while positive CD138 was recorded in all cases. The mean value of b2m, Albumin, Haemoglobin, Calcium, Creatinine, LDH and BMA were 6.8, 3.2, 10, 9.1, 0.9, 229 and 60 respectively.

Table (1): Sociodemographic and laboratory characteristics of the study group.

Patients	N=28
Gender	No. (%)
Male	18 (64.3)
Female	10 (35.7)
Age	55.4 ± 9.8
ISS (N=15)	No. (%)
I	5 (33.3)
II	1 (6.7)
III	9 (60.0)
CD56	No. (%)
Positive	15 (83.3)
Negative	3 (16.7)
CD138	No. (%)
Positive	21 (100.0)
b2m	6.8 (2.4-12.5)
Albumin	3.2±0.8
Haemoglobin	10±2
Calcium	9.1±1.5
Creatinine	0.9 ±0.12
LDH	229 ±55.1
BMA %	60 ±13.1

Age, albumin, hemoglobin, and calcium are expressed as mean (SD) while b2m, creatinine, LDH, and BMA% are expressed as median (range)

Table 2 shows distribution of lesions in skeleton by MRI techniques (T1,STIR, DWIBS), combined distribution (**Figure 1**) was the most common the percentage value 57.1%, 53.6%, 50%, respectively, followed by focal distribution (**Figures 2 and 3**) with percentage value 28%, 32.1%, and 32.1%, respectively, and the last was diffuse distribution with percentage value 14.3%, 14.3%, and 17.9%, respectively.

Table (2): Distribution of lesions in the skeleton by T1, STIR, and DWIBS MRI techniques.

Distribution	Technique			Test of significance
	T1 N=28	STIR N=28	DWIBS N=28	
	No. (%)	No. (%)	No. (%)	
Combined	16 (57.1)	15 (53.6)	14 (50.0)	Monte Carlo test P=0.98
Focal	8 (28.6)	9 (32.1)	9 (32.1)	
Diffuse	4 (14.3)	4 (14.3)	5 (17.9)	

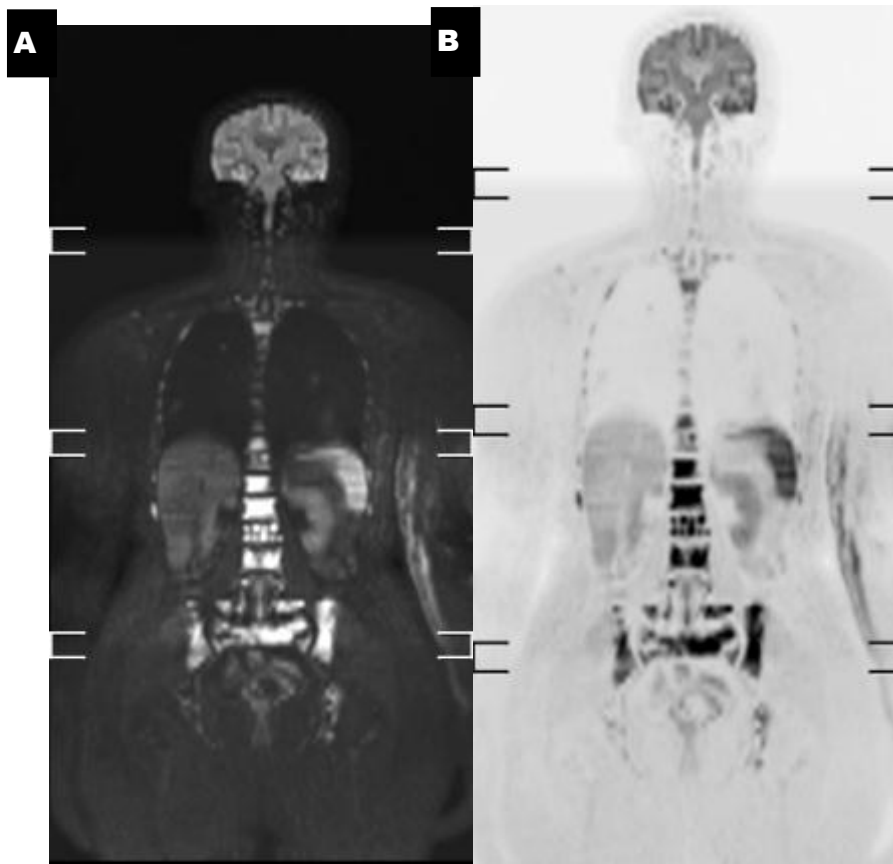


Figure (1): WB- MRI of 63ys old female patient with pathologically proven MM.(A) Coronal STIR whole body image shows multiple hyper-intense areas in both iliac bones and multiple level vertebrae. (B)Coronal inverted DWIBS shows restricted diffusion of these areas (combined pattern).

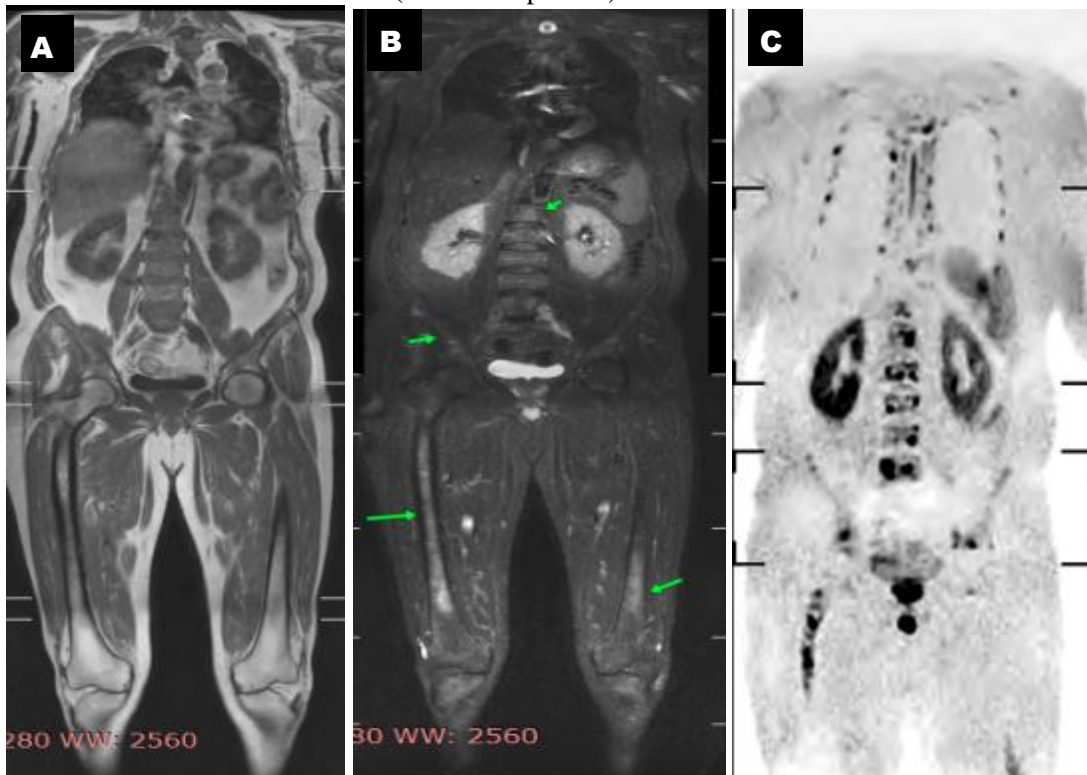


Figure (2): WB-MRI of 51 years old male patient pathologically proven MM. (A) coronal T1 WB-MRI shows multiple focal lesions of hypo-intense signal seen in pelvic bone, both femurs, ribs and multiple level vertebrae. (B) Coronal STIR image shows hyper-intense signal of these lesions.(C) Coronal inverted DWIBS shows restricted diffusion of these lesions .(note better detection and characterization of lesion in DWIBS) (multifocal pattern).

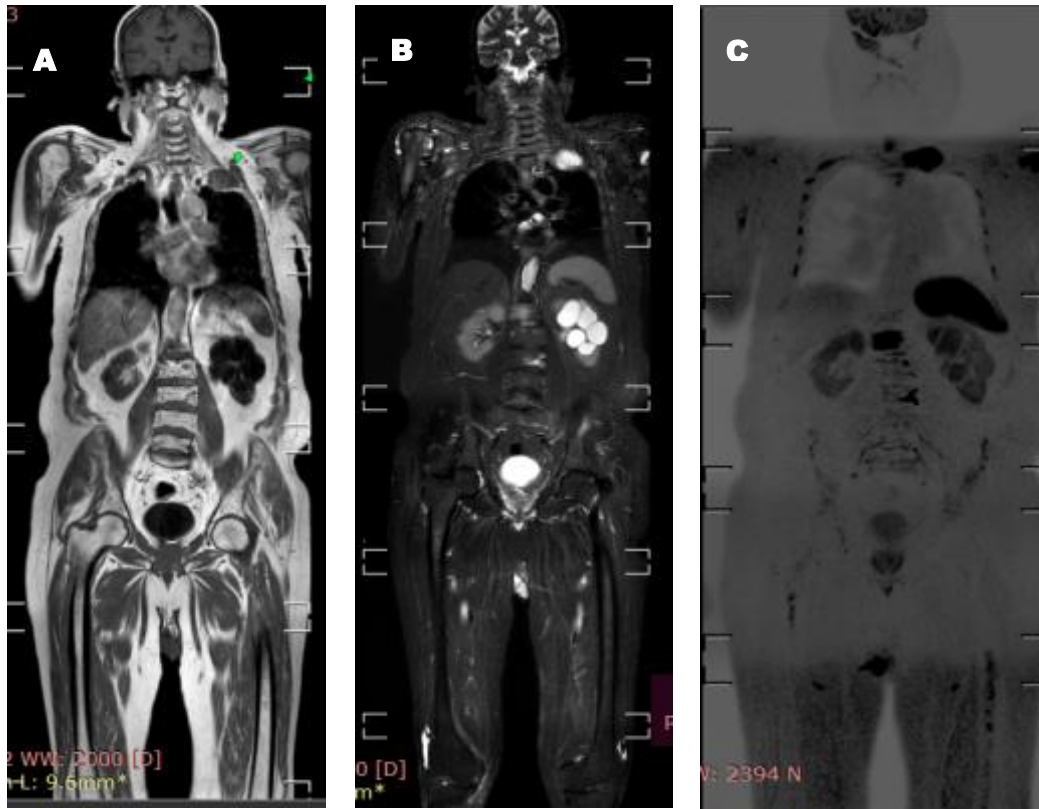


Figure (3): WB-MRI of 65 years old male patient pathologically proven MM .(A) coronal T1 WB-MRI shows multiple focal lesions of hypo- intense signal seen in scanned bones (spine ribs ,both humeri, pelvis and both femurs). (B) coronal STIR image shows hyper- intense signal of these lesions. (C) Coronal inverted DWIBS shows restricted diffusion of these lesions .Also abnormal soft tissue seen at 1st left rib with the same abnormal signal.

Table 3 demonstrates total number of lesions according to anatomical sites by MRI techniques. The number of lesions in Sternum and ribs, Spine, Upper limb, Pelvis and pro-femur and Lower limb were (26, 18 and 24), (137, 146 and 184), (83, 73 and 84), (343, 333 and 439) and (12, 12 and 13) as recorded by T1, STIR and DWIBS, respectively.

Table (3): Total number of lesions according to anatomical sites by MRI techniques.

Anatomical site	T1	STIR	DWIBS
Sternum and ribs	26	18	24
Spine	137	146	184
Upper limb	83	73	84
Pelvis and pro-femur	343	333	439
Lower limb	12	12	13

Table 4 reveals comparison of the number of lesions in different anatomical regions by MRI techniques. There were no statistically significant differences between MRI techniques as regards the localization of lesions number in different anatomical regions (Sternum and ribs, Spine, Upper limb, Pelvis, Lower limb and Skeleton) (P>0.05).

Table (4): Comparison of the number of lesions in different anatomical regions by MRI techniques.

No. of lesions Median (min-max)	T1	STIR	DWIBS	Test of significance*
Sternum and ribs	3 (1-6)	2.5 (1-6)	1.5 (1-20)	0.83
Spine	5 (1-15)	5.5 (1-16)	7 (1-25)	0.85
Upper limb	5 (2-18)	6 (2-20)	7 (2-22)	0.92
Pelvis	14 (5-40)	17 (4-36)	19.5 (2-41)	0.17
Lower limb	3 (1-5)	3 (1-5)	6.5 (6-7)	0.08
Skeleton	25 (1-65)	23.5 (1-65)	29 (1-83)	0.32

*Kruskal-Wallis test.

DISCUSSION

WB-MRI is becoming increasingly relevant for the assessment of patients with MM due to full body coverage, excellent sensitivity for detecting bone marrow involvement before or without bone destruction (i.e., in the case of a diffuse pattern), and the accessibility of advanced techniques as DWI^[9,10].

The European Society for Medical Oncology guidelines regard WBMRI as a viable option for bone marrow imaging, and in the UK, it is advised as first-line imaging for all patients with a suspected new diagnosis of myeloma^[11].

Furthermore, the European Myeloma Network guidelines advise WBMRI for asymptomatic SMM patients with no visible lytic disease on CT at initial diagnosis and then on an annual basis after that^[12,13].

In current study, WB-MRI with T1, STIR and DWIBS sequences could detect myeloma bony lesions, either spinal or appendicular, also soft tissue component and vertebral compression. It could evaluate spread of the disease in different regions of the body using a single examination.

The WB- DWI has been improved by the introduction of DWIBS, a diffusion weighted pulse sequence paired with a STIR sequence. This sequence allowed greater homogeneous suppression of the background signal as well as acquisition during free breathing, thus permitting more time for the acquisition, a higher number of signal averages, a better SNR, and acquisition of thinner slices. The better fat suppression at the edges of the FOV provided by the STIR sequence and the acquisition of thinner slices also allows for better MPR and MIP of whole-body images. The enhancement characteristics of different lesions on WB- DWI are different, which may depend on tissue compositions, blood flow perfusion, and T2 effect of every site. Due to the dense cellularity, diminished intercellular space and high karyoplasmic ratio of malignant lesions, the diffusion activities of intra-and extracellular water are restricted, so malignant lesions show high signal on DWI. For primary and metastatic tumors have similar cellularity, both appear high signal intensity on DWI, so whole body DWI can not only be used to screen metastases of whole body, but also to search primary tumors, compared with other imaging modalities.

In our study, WB-MRI was used to analyze the skeletal and bone marrow involvement in 28 patients with a diagnosis of MM, We compared the number of lesions found on T1- weighted and STIR images and DWIBS located in the spine, sternum and ribs, upper limbs, pelvis and femur. The combined distribution pattern was the most common, with a percentage value of 57.1%,53.6%,50.0%respectively followed by the focal distribution pattern with percentage value of 28%,32.1%, 32.1%, respectively, and the last was the diffuse distribution pattern with percentage value of 14.3%,14.3%,17.9% in the MRI sequences (T1,STIR, and DWIBS) respectively.

While, **Ippolito et al.**^[14] study showed a total of 15/64 patients (23.4%) had no lesions in all anatomic regions. Between patients with bone involvement (n= 49/64, 76.6%), the majority exhibit a focal pattern (n= 29/64, 59.2%), followed by combined (n = 16/64, 32.7%), and diffuse pattern (n = 4/64, 8.1%).

Most patients showed skeletal involvement by bone lytic lesions with both focal and combined patterns in the spine, pelvis and pro-femur. The number of lesions in these sites was (137, 146, and 184) and (343, 333, and 439) as recorded by T1, STIR and DWIBS respectively. The number of lesions in the lower limbs (from the distal part of the femurs to the feet), and the upper limbs were (12, 12 and 13) and (83, 73 and 84), as recorded by T1, STIR, and DWIBS respectively.so these sites are considered to be less frequently affected.

These findings are consistent with a research in which 64 patients were examined. According to the distribution of lesions by anatomical district and number, the spine, pelvis, sternum, and ribs were the most frequently affected anatomical districts. the spine (n= 40, 81.6%) was followed by the pelvis (n= 33, 67.4%), sternum and ribs (n= 23, 46.9%), upper limbs (n= 12,24.5%), skull (n= 6, 12.3%), and lower limbs (n= 6, 12.3%)^[14].

For this study, we compared the number of lesions detected by T1, STIR and DWIBS. It shows that DWIBS was able to detect many lesions compared to T1and STIR yet did not reach statistical significance (P value >0.05).

According to a study comparing DWIBS and conventional radiography, the latter detects more lesions, leading to an elevation in the Durie-Salmon Plus stage in over one-third of patients. This method appears to be especially useful in anatomical zones that traditional radiography finds challenging to explore (ribs, pelvis and spine)^[15].

Another study discovered that WB-DWI MRI provided improved lesion conspicuity compared to standard T1 and contrast-enhanced MRI sequences because it provided excellent image contrast between healthy and diseased marrow^[16,17].

Using the individual sequences showed significantly lower diagnostic performance than the combination of sequences in detecting bone involvement, with T1 showing the lowest diagnostic value. T1-STIR and STIR-DWI combinations showed significantly lower performance than the combination of T1-STIR-DWI. T1-STIR-DWI achieved the best diagnostic value but was not significantly superior to the combination of T1-DWI^[18].

The fact that signal strength relies on both water diffusion and T2 relaxation time is one drawback of visual evaluation of DW images. As a result, a region with a lengthy T2 relaxation time could continue to be extremely intense on DW pictures and might be misinterpreted for a region with restricted diffusion (T2 shine through effect), which can be differentiated

by using the ADC map. Another drawback is that many typical anatomical tissues, including the spinal cord, ovaries, testicles, bone marrow, endometrial lining, intestinal wall, peripheral nerves, and brain ganglia, exhibit various degrees of hindered water diffusion at DWI, resulting in false-negative results^[19, 20]. Another issue is susceptibility artefacts, which can hide lesions and decrease image quality, producing false negative results^[21]. There are a few limitations to this study. First, this study was conducted on a relatively small number of patients. The second is the large amount of data to be postprocessed and interpreted.

In conclusion, WB-MRI using morphological sequences and the DWIBS technique is a reliable imaging modality for detection of MM lesions, whether focal, diffuse or combined. DWIBS was able to detect larger number of lesions than morphological sequences yet did not reach statistical significance.

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Author contribution: Authors contributed equally in the study.

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