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Diagnostic value of whole -body diffusion weighted imaging added to bone scan in early diagnosis of bone metastases in breast cancer patients

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Abstract

Background Metastases to the bones are a frequent location of metastasis in advanced breast cancer and are responsible for substantial morbidity and healthcare expenses. Imaging has been crucial in directing patient therapy for decades, contributing to the staging and response evaluation of the skeleton. This research aimed to assess the diagnostic value of whole-body magnetic resonance imaging with diffusion-weighted imaging added to radionuclide bone scans for early diagnosis of bone metastases in breast cancer patients.

Results The study was a prospective observational cohort study performed on 20 patients with breast cancer and suspected bone metastases. The patients were evaluated first by obtaining a detailed personal history. Laboratory tests, including CBC, liver, and kidney function tests were assessed. All patients were examined by diffusion-weighted whole-body MRI (DWIBS; diffusion-weighted imaging with background body signal suppression) images and bone scintigraphy after intravenous injection of 20 mci of technetium-99m (^{99m}Tc) methylene diphosphonate using a dual head gamma camera. The total number of lesions detected by bone scan was 74, and 75 lesions were seen by DWIBS. Twenty-four lesions were missed by bone scan and detected by DWIBS. Fourteen lesions were detected by bone scan and found free by DWIBS examination in the spine and pelvic bones.

Conclusions Whole body DWIBS seems to be a promising method of imaging in detecting bone metastases from breast cancer that could be used complementary to the traditional bone scan for more accurate diagnosis and staging of the tumor, helping to determine the most appropriate protocol of management.

Keywords Breast cancer, Bone scan, MRI, Scintigraphy, Metastasis, DWIBS

Background

Breast cancer is by far the most prevalent solid tumor in women globally, accounting for 15 percent of all cancer-related deaths in women each year. Once the diagnosis has been established, the prognosis of the illness primarily relies on the disease's stage of progression and the selection of the appropriate treatment [1].

Patients diagnosed with advanced breast cancer are most affected by skeletal metastases. Several studies reported variable incidences of the development of breast

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Abd elsalam *et al. Egypt J Radiol Nucl Med*   (2023) 54:102

Page 2 of 13

cancer. According to the research of Tahara et al., roughly 70% of patients with advanced breast cancer would develop bone metastases. It has been found that between 17 and 37% of women with metastatic illness have bone-only metastases. According to Jiang et al., the percentage of advanced malignant tumors that have spread to the bones is between 30 and 75%. Bone metastases are a frequent cancer consequence, with a frequency of 65–75% in breast cancer, as reported by D'Oronzo et al. [2–4].

In this regard, the sternum, pelvis, and thoracic spine are most prone to metastases. However, the involvement of other bones, such as the skull and femur, by metastases is also conceivable. It should be noted that bone metastases frequently result in skeleton-related events such as spinal cord compression, bone fractures, pain, and hypercalcemia. In this aspect, metastases most often occur in the pelvis, thoracic spine, and sternum. On the other hand, participation [5].

Standard imaging methods have significant limitations in identifying metastatic bone disease and evaluating therapy response. Recently, there has been a resurgence of interest in using whole-body MRI with diffusion-weighted sequence to evaluate malignant bone disease [6].

Whole-body magnetic resonance imaging (WB-MRI) is superior to other methods for identifying bone metastases. The whole body may be assessed with only one scan, saving time and money. In addition, it may be used to assess the patient as a whole and track improvement as therapy progresses. For instance, diffusion-weighted imaging (DWI) for whole-body scanning is currently part of the standard protocol for whole-body magnetic resonance imaging (WB-MRI) [7].

This study aimed to assess the diagnostic value of whole-body magnetic resonance imaging with diffusion-weighted imaging added to radionuclide bone scans for early diagnosis of bone metastases in breast cancer patients.

Methods

The prospective observational cohort study included 20 patients pathologically proven to have breast cancer with suspected bone metastases. The study was performed at the University Hospital from August 2021 to January 2022. Exclusion criteria included patients with contraindications to MRI, like those with a pacemaker or metallic foreign body, severe claustrophobia, or patients with a history of another malignancy.

The patients were evaluated by obtaining a detailed personal history, then laboratory tests, including CBC, liver, and kidney function tests. All patients were examined by diffusion-weighted whole-body MRI and bone scintigraphy. Interpretation of diffusion-weighted whole-body MRI was made by two experienced radiologists (25 and 20 years of experience) in consensus. Bone scintigraphy was achieved by a nuclear medicine consultant with 15 years of experience.

Bone scan (skeletal scintigraphy)

Three hours after the intravenous administration of 20 mci of technetium-99m (99mTc) methylene diphosphonate, imaging was done using a dual-head gamma camera. Only planned imaging in the anterior and posterior planes of the whole body was obtained. The identification and evaluation of hot spots were made.

Whole body MRI diffusion

MRI examinations were performed using a 1.5-Tesla General Electric Health Care System. The SENSE parallel imaging approach was used in the axial image with 4 stacks utilizing a Q body coil. Lesions were evaluated qualitatively with DWI. No intravenous paramagnetic contrast agent was administered.

Imaging protocol

Whole body diffusion-weighted imaging (WB-DWI) parameters

Axial DWI was done from the skull vault to the midthigh using b-values of 0 s/mm^2 and 1000 s/mm^2 with a slice thickness of 5 mm. Typically, the axial DWI acquisition consisted of four consecutive stations, each taking approximately 6 min to acquire. The high b-value images were then reconstructed in orthogonal planes as thin multiplanar reconstructions (5 mm) and thick 3D maximum intensity projections (MIPs), usually displayed using an inverted grey scale. DWIBS (diffusion-weighted imaging with background body signal suppression) qualitative analysis was performed directly from the reformatted view on three planes. Signals from normal tissue such as blood vessels, fat, muscle, and bowel were suppressed. However, other normal structures, such as the spleen, ovaries, endometrium, and the spinal cord, remained visible.

Other pulse sequences parameters

The MRI of the whole body also included Tl and STIR pulse sequences with the following parameters:(Table 1).

Image interpretation

- The MRI results were evaluated by two experienced radiologists (25 and 20 years of experience) in consensus.
- DWIBS (diffusion-weighted imaging with background body signal suppression) pictures were applied to 2D MIP coronal images in inverted gray-

Abd elsalam *et al. Egypt J Radiol Nucl Med*   (2023) 54:102

Page 3 of 13

Table 1 Whole body MRI Tl and STIR pulse sequences parameters

Parameter	T1	T2	STIR
TR	466	1221	6800
TE	18	80	70
FOV	48 cm	48 cm	48 cm
Slice thickness	8 mm	8 mm	8 mm
Gap	1 mm	1 mm	1 mm

scale. Physiological signals from organs, including the heart, intestines, and arteries, were muted.

- Focal lesions in the bone marrow were defined by altered signal intensity as low signal on T1WI and high signal on T2WI, STIR, and restricted diffusion at DWIBS.
- The number and localization of the lesions were assessed among the different sequences.

In DWIBS qualitative analysis

The lesions were only categorized according to the subjectively rated signal pattern, signal intensity, and morphology without taking into account the apparent diffusion coefficients (ADC) (Figs. 1 ,2, 3, 4, and 5), which were not quantified due to the difficulty in calculating ADC value with only b 0 and b 1000 s/mm^2. Malignant lesions were assumed to exhibit considerably greater signal intensities and variability on their profile than benign ones. In addition to the diffusion-weighted sequence, T1- weighted and STIR images were also evaluated for anatomical correlation to accurately detect pathology and rule out artifacts from the diffusion-weighted sequence series (Figs. 1, 2, 3, 4, and 5).

Data and statistical analysis

Statistical Package for Social Sciences (SPSS) was used for data administration and analysis, version 25. Using means and standard deviations, numerical data were summarized. Numbers and percentages served as a summary of categorical data. The Kappa agreement was used to detect the agreement between MRI diffusion and
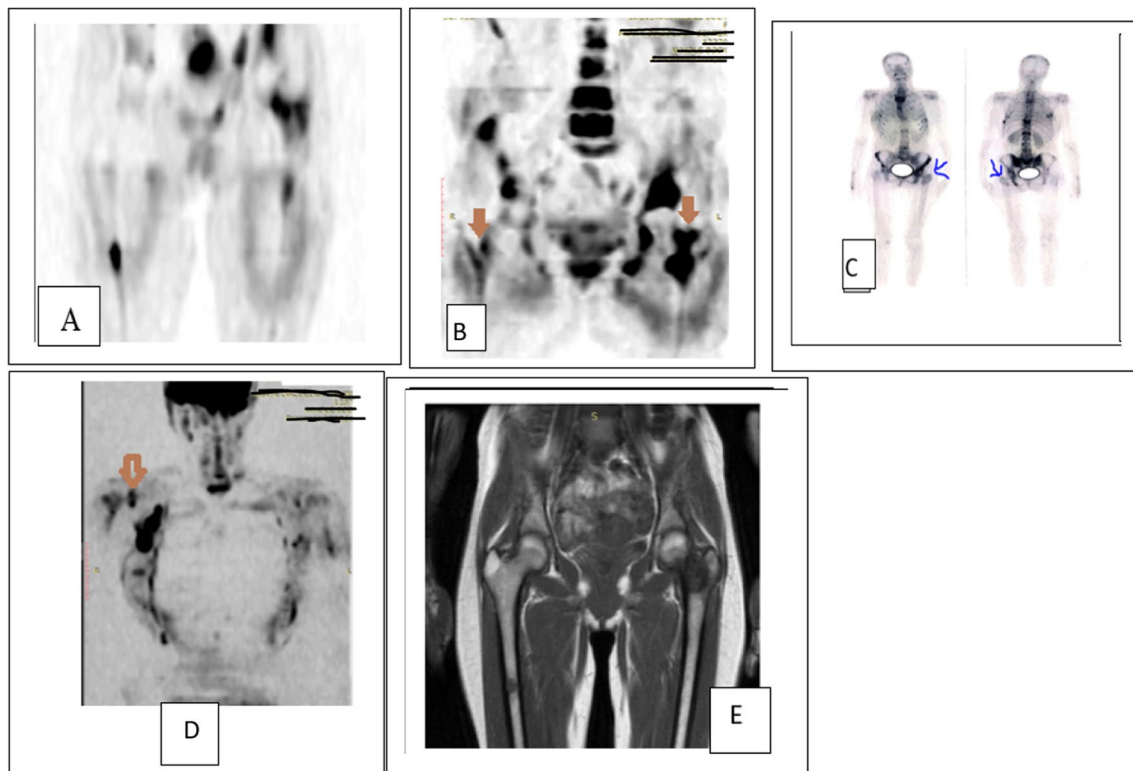
Fig. 1 Thirty-year-old female with Rt. Breast invasive duct carcinoma GII. DWIBS showed bilateral femoral shaft areas of restricted diffusion (**A, B**), appearing of low T1 signal (**E**), while in bone scan (**C**), only left trochanteric metastatic lesion. The right humeral head area of restricted diffusion (orange arrow) at (**D**) image while not seen in bone scan image (**C**). Both studies show multiple bony metastatic lesions at dorsal, lumbar vertebra, iliac bones, and ribs. The patient was managed based on the results of the MRI study; by palliative radiotherapy on weight-bearing area (bilateral femur) and lumbar spine, followed by chemotherapy. No role of surgery in patients with multiple bony metastases

Abd elsalam *et al. Egypt J Radiol Nucl Med*   (2023) 54:102

Page 4 of 13
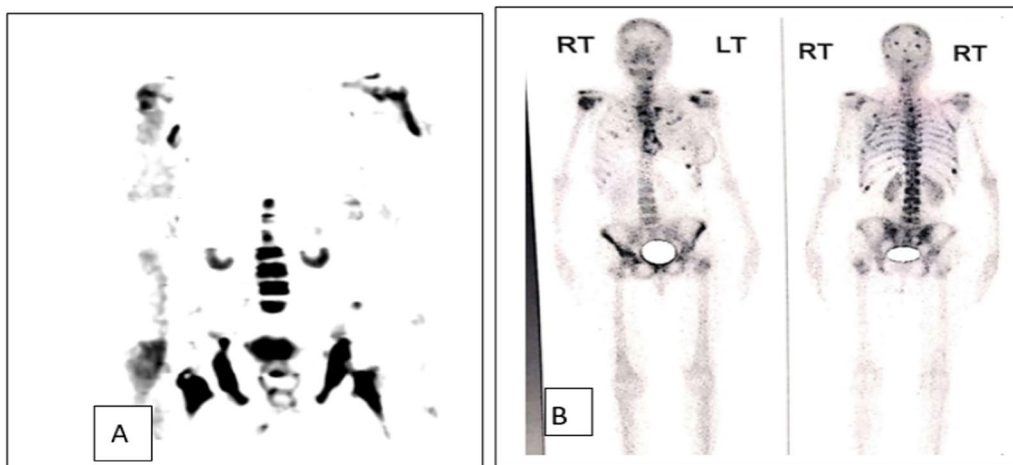
Fig. 2 Sixty-three-year-old female with bilateral breast cancer. DWIBS **A** shows right femoral shaft area of restricted diffusion, **B** shows bilateral femoral necks and upper shaft areas of restricted diffusion at most of the spine, ribs, pelvic bones, upper femora, and humeri. Bone scans couldn't detect femoral metastatic lesions. The patient was managed based on the results of the MRI study; palliative radiotherapy on both upper femora followed by chemotherapy. No role of surgery in patients with multiple bony metastases
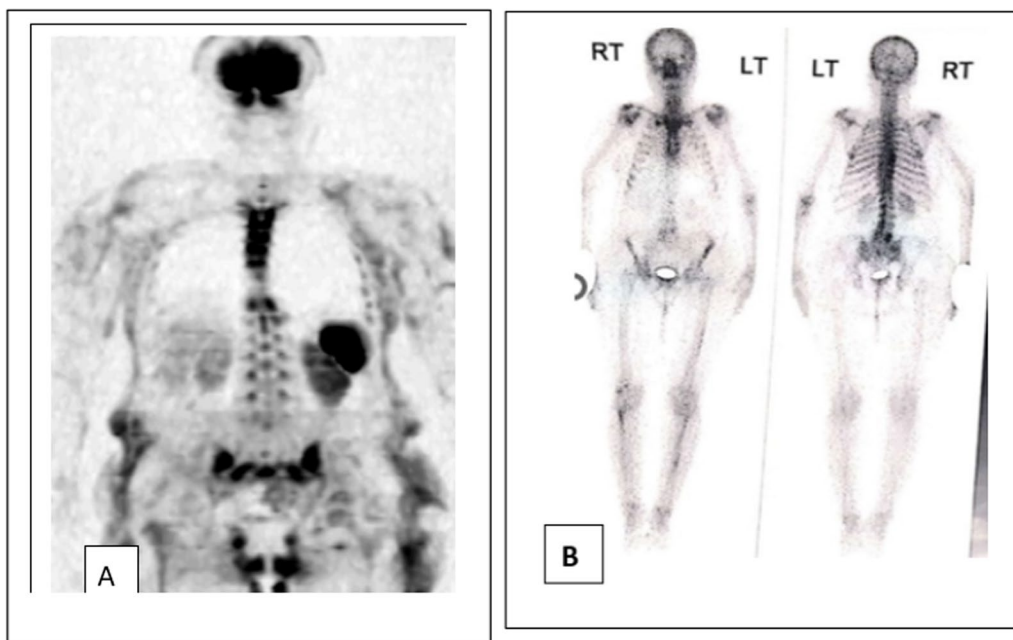
Fig. 3 Sixty-three years old female was diagnosed with left breast invasive duct carcinoma GII. DWIBS (**A**) showed no abnormal marrow signal at all examined bones, while bone scan (**B**) revealed bony lesions at the lower dorsal and L5 vertebra. The patient's management was based on the results of the MRI study. Surgical treatment (MRM) was done, followed by chemo and radiotherapy

Bone scan regarding the suspected lesion for metastases. All tests were two-sided. P values < 0.05 was considered significant.

### Ethical considerations
The study was approved by the local research and ethical committee number (FMBSUREC/06072021). Written informed consent was obtained from each patient before enrollment.

Results
Twenty female Patients, ages ranged from 30 to 76 years (mean 49 ± 12), were pathologically proven to have breast cancer with suspected bone metastases and no history of
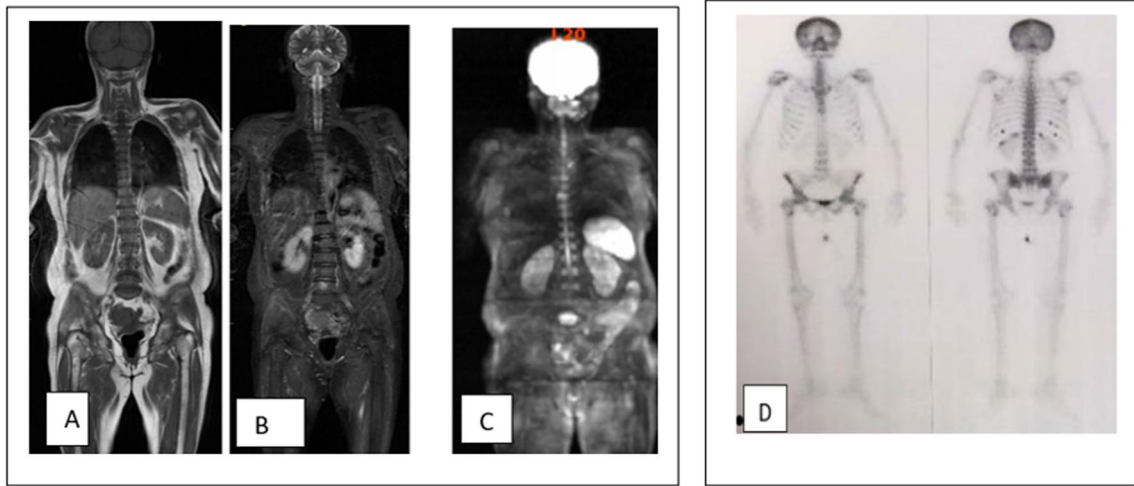
Fig. 4 Fifty-year-old female patient with Right invasive breast duct carcinoma grade II. No bony lesions were detected at T1, STIR, or DWIBS (**A, B, C**). Bone scan (**D**) showed abnormal increase in trace uptake at the skull, multiple ribs, right sacroiliac joint, and both femures. Palliative treatment was used
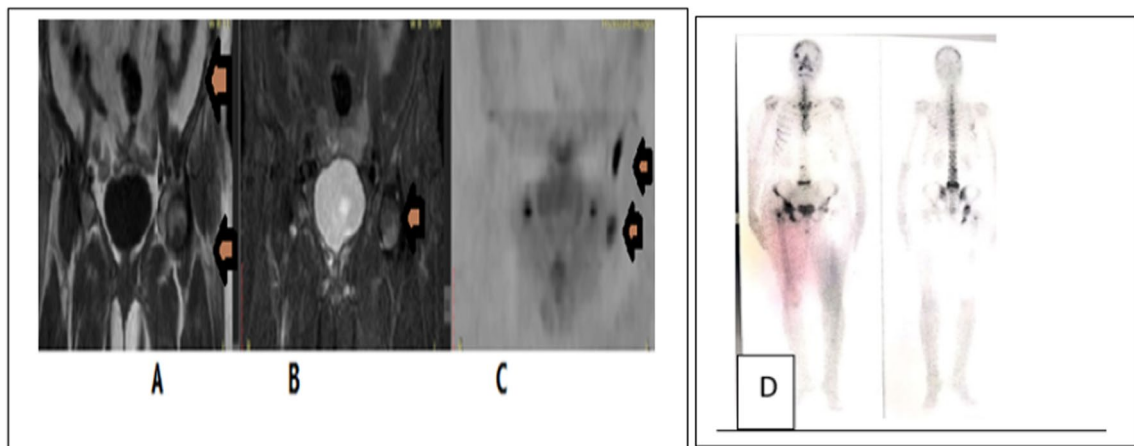
Fig. 5 Left pelvic bony metastasis seen at bone scan (**D**), hypointense at coronal T1WI (**A**), hyperintense at coronal STIR (**B**), and restricted diffusion at DWIBS (**C**)

another malignancy. About half of the patients had RT breast cancer, and only one patient with bilateral breast cancer. Most patients had invasive duct carcinoma (IDC) grade 2 (90%).

The bony lesion in the chest wall (Table 2)
This table showed that among the 20 females, the Bone scan (BS) was able to detect 3 lesions in 4 (20%) females, two lesions in 5 (25%) females, one lesion in 1 (5%) female, and the remaining 10 (50%) females were negative by BS. Different MRI sequences showed variable detection results; T1 could detect only 1 (5%) female to have 4 lesions, 2 (10%) females to have 2 lesions and

the same for 1 lesion. STIR could detect 4 lesions in 1 (5%) female, 2 lesions in 3 (15%) females, and 1 lesion in 1 (5%) female. DWIBS was able to detect 4 lesions in 2 (10%) females, 3 lesions in 2 (10%) females, 2 lesions in 2 (10%) females, and 1 lesion in 1 (5%) female.

There was a significant agreement between Bone scan (BS) and DWIBS in the detection of lesions of chest bone metastases in female patients with breast cancer. The highest number of lesions in the chest bones were found by BS. The superiority of MRI sequences was only in the detection of 2 lesions, while BS detected them as one lesion. The agreement between BS and T1 & STIR was not significant. The agreement of detection

Abd elsalam *et al. Egypt J Radiol Nucl Med*   (2023) 54:102

Page 6 of 13

Table 2 Bony lesion in the chest wall

MRI sequences	Number of lesions	bony metastases in the chest in bone scan (BS)				Total in each modality	Kappa	P- value
		negative	1 lesion	2 lesions	3 lesions			
T1	**Negative**	10(5%)	0(0%)	4(20%)	1(5%)	**15(75%)**	0.160	0.159
	1 lesion	0(0%)	0(0%)	1(5%)	1(5%)	**2(10%)**		
	2 lesions	0(0%)	1(5%)	0(0%)	1(5%)	**2(10%)**		
	4 lesions	0(0%)	0(0%)	0(0%)	1(5%)	**1(5%)**		
STIR	**Negative**	10(50%)	0(0%)	4(20%)	1(5%)	**15(75%)**	0.145	0.237
	1 lesion	0(0%)	0(0%)	1(5%)	0(0%)	**1(5%)**		
	2 lesions	0(0%)	1(5%)	0(0%)	2(10%)	**3(15%)**		
	4 lesions	0(0%)	0(0%)	0(0%)	1(5%)	**1(5%)**		
DWIBS	**Negative**	10(50%)	0(0%)	3(15%)	0(0%)	**13(65%)**	0.283	0.023*
	1 lesion	0(0%)	0(0%)	1(5%)	0(0%)	**1(5%)**		
	2 lesions	0(0%)	1(5%)	0(0%)	1(5%)	**2(10%)**		
	3 lesions	0(0%)	0(0%)	1(5%)	1(5%)	**2(10%)**		
	4 lesions	0(0%)	0(0%)	0(0%)	2(10%)	**2(10%)**		
Total lesions in BS		**10(50%)**	**1(5%)**	**5(25%)**	**4(20%)**	**20(100%)**		

- *The blue color indicates the additive value of BS modality*
- *The pink color indicates the additive value of MRI sequences*

of chest bone lesions was significant between all MRI sequences.

In female patients with breast cancer metastatic to chest bone, twenty-three lesions (in ten patients) were detected by bone scan, and nineteen lesions (in seven patients) were detected by DWIBS. The agreement between bone scan and DWIBS in fifty lesions (seven patients).

The other three patients found to have lesions in the bone scans were free from metastases by DWIBS examination and had no other bony lesions leading to converting their treatment from palliative to curative treatment.

Bony lesions in pelvic bones (Table 3)

This table showed that among the 20 females, BS could detect 3 lesions in 2 (10%) females, 2 lesions in 2 (10%) females, and 1 lesion in 5 (25%) females. Different MRI sequences showed that T1 could only detect 2 lesions in 2 (10%) and 1 lesion in 4 (20%) females. STIR images could detect 2 lesions in 3 (15%) females and 1 lesion in 4 (20%) females. DWIBS could detect 3 lesions in 1 (5%) female, 2 lesions in 2 (10%) females, and 1 lesion in 3 (15%) females. There was an insignificant agreement between BS and T1 & STIR, and DWIBS in the detection of lesions of pelvic bone metastases in female patients with breast cancer.

Table 3 Bony lesions in Pelvic bones

MRI sequences		bony metastases in pelvic bones in **bone scan (BS)**				Total	Kappa	P- value
		Negative	**1 lesion**	**2 lesions**	**3 lesions**			
T1	**Negative**	8(40%)	5(25%)	1(5%)	0(0%)	**14(70%)**	-0.081	0.587
	1 lesion	3(15%)	0(0%)	1(5%)	0(0%)	**4(20%)**		
	2 lesions	0(0%)	0(0%)	0(0%)	2(10%)	**2(10%)**		
STIR	**Negative**	8(40%)	5(25%)	0(0%)	0(0%)	**13(65%)**	0.048	0.747
	1 lesion	3(15%)	0(0%)	1(5%)	0(0%)	**4(20%)**		
	2 lesions	0(0%)	0(0%)	1(5%)	2(10%)	**3(15%)**		
DWIBS	**Negative**	7(35%)	5(25%)	0(0%)	0(0%)	**12(60%)**	0.177	0.207
	1 lesion	3(15%)	0(0%)	0(0%)	0(0%)	**3(15%)**		
	2 lesions	1(5%)	0(0%)	0(0%)	1(5%)	**2(10%)**		
	3 lesions	0(0%)	0(0%)	0(0%)	1(5%)	**20(100%)**		
	Total	**11(55%)**	**5(25%)**	**2(10%)**	**2(10%)**	**20(100%)**		

- *The blue color indicates the additive value of BS modality*
- *The pink color indicates the additive value of MRI sequences*

According to this table, female patients with breast cancer metastatic to pelvic bones; had fifteen lesions (in nine patients) detected by bone scan, and fourteen lesions (in eight patients) were seen by DWIBS. The agreement between bone scan and DWIBS in nine lesions (in four patients). The other five patients (five lesions) who had lesions in the bone scan were free from lesions by DWIBS, which were not detected by DWIBS.

According to this table, three patients with four lesions were missed by bone scan but detected by DWIBS, which led to a change in the management of patients into palliative radiotherapy due to weight bearing area.

Bony lesions in the spine (Table 4)

This table showed that among 20 females, BS could detect 3 lesions in only 1 (5%) female, 2 lesions in 4 (20%) females, and 1 lesion in 8 (40%) females. Different MRI sequences showed that T1 could detect 3 lesions in 2(10%), 2 lesions in 3 (15%) females, and 1 lesion in 1 (5%) female. STIR could detect 3 lesions in

2(10%), 2 lesions in 3 (15%) females, and 1 lesion in 3 (15%) females. DWIBS could detect 4 lesions in 1 (5%) female, 2 lesions in 2 (10%) females, and 3 lesions in 3 (15%) females.

There was a significant agreement between BS and all MRI sequences in the detection of lesions of spines metastases in female patients with breast cancer. Despite missed lesions by MRI sequences, they still had additive values in the number of lesions in cases with a lesser number of lesions detected by BS.

According to this table, female patients with breast cancer metastatic to the spine; we had nineteen lesions (in thirteen patients) were detected by bone scan, and nineteen lesions (in nine patients) were detected by DWIBS. The agreement between bone scan and DWIBS in twelve lesions (in nine patients). DWIBS saw more lesions in the whole spine in the same patients.

Other four patients (seven lesions) found to have lesions in the bone scan were free DWIBS examination.

We had seven lesions missed by bone scan and detected by DWIBS, three at one patient,

Table 4 Bony lesions in the spine

MRI sequences		Bony metastases in the spine in bone scan (BS)				Total	Kappa	P- value
		Negative	1 lesion	2 lesions	3 lesions			
T1	Negative	6(30.0%)	5(25.0%)	2(10%)	1(5%)	14(70%)	0.214	0.046*
	1 lesion	0(0%)	1(5%)	0(0%)	0(0%)	1(5%)		
	2 lesions	0(0%)	1(5%)	2(10%)	0(0%)	3(15%)		
	3 lesions	1(5%)	1(5%)	0(0%)	0(0%)	2(10%)		
STIR	Negative	6(30%)	3(15%)	2(10%)	1(5%)	12(60%)	0.353	0.005*
	1 lesion	0(0%)	3(15%)	0(0%)	0(0%)	3(15%)		
	2 lesions	0(0%)	1(5%)	2(10%)	0(0%)	3(15%)		
	3 lesions	1(5%)	1(5%)	0(0%)	0(0%)	2(10%)		
DWIBS	Negative	6(30%)	3(15%)	2(10%)	0(0%)	11(55%)	0.373	0.002*
	1 lesion	0(0%)	3(15%)	0(0%)	0(0%)	3(15%)		
	2 lesions	0(0%)	1(5%)	1(5%)	0(0%)	2(10%)		
	3 lesions	1(5%)	1(5%)	1(5%)	1(5%)	4(20%)		
Total		7(35%)	8(40%)	4(20%)	1(5%)	20(100%)		

- *The blue color indicates the additive value of BS modality*
- *The pink color indicates the additive value of MRI sequences*

Bony lesions in femur and tibia (Table 5)

This table showed that among the 20 females, BS could detect 2 lesions in 3 (15%) females and 1 lesion in 3 (15%) females. Different MRI sequences showed that T1 could detect 2 lesions in 5 (25%) females, and 1 lesion in 1 (5%) female. STIR could detect 3 lesions in 1 (5%) female, 2 lesions in 4 (20%) females, and 1 lesion in 1 (5%) female. DWIBS could detect 3 lesions in 1 (5%) female, 2 lesions in 5 (25%) females, and 1 lesion in 1 (5%) female.

There was a significant agreement between BS and all other MRI sequences in the detection of lesions of femur and tibia metastases in female patients with breast cancer. DWIBS showed additive values in assessing the number of lesions in cases with fewer lesions detected by BS.

According to this table, in female patients with breast cancer metastatic to femur and/or tibia bones; we had nine lesions (in six patients) detected by bone scan, and fourteen lesions (in seven patients) detected by DWIBS. The agreement between bone scan and DWIBS in seven lesions (in five patients). One patient with a positive bone scan showed negative bony lesions by DWIBS. The other two patients (three lesions) were missed by bone scan and detected by DWIBS.

Bony lesions in the arm (Table 6)

This table showed that among the 20 females, BS could detect 2 lesions in 1 (5%) female and 1 lesion in 1 (5%) female. Different MRI sequences showed that T1 could

Table 5 Bony lesions in Femur and Tibia

MRI sequences		Bony metastases in femur and tibia in bone scan (BS)			Total	Kappa	P-value
		Negative	1 lesion	2 lesions			
T1	Negative	13(65%)	0(0%)	1(5%)	14(70%)	0.462	0.005*
	1 lesion	1(5%)	0(0%)	0(0%)	1(5%)		
	2 lesions	0(0%)	3(15%)	2(10%)	5(25%)		
STIR	Negative	13(65%)	0(0%)	1(5%)	14(70%)	0.471	0.002*
	1 lesion	1(5%)	0(0%)	0(0%)	1(5%)		
	2 lesions	0(0%)	2(10%)	2(10%)	4(20%)		
	3 lesions	0(0%)	1(5%)	0(0%)	1(5%)		
DWIBS	Negative	12(60%)	0(0%)	1(5%)	13(65%)	0.400	0.010*
	1 lesion	1(5%)	0(0%)	0(0%)	1(5%)		
	2 lesions	1(5%)	2(10%)	2(10%)	5(25%)		
	3 lesions	0(0%)	1(5%)	0(0%)	1(5%)		
	Total	14(70%)	3(15%)	3(15%)	20(100%)		

- *The blue color indicates the additive value of BS modality*
- *The pink color indicates the additive value of MRI sequences*

only detect 2 lesions in 1 (5%) female and 1 lesion in 3 (15%) females. STIR could detect 2 lesions in 1 (5%) female and 1 lesion in 3 (15%) females. DWIBS could detect 2 lesions in 3 (15%) females and 1 lesion in 3 (15%) females.

There was a significant agreement between BS and DWIBS in the detection of lesions of arm bone metastases in female patients with breast cancer. The superiority of MRI sequences was in the detection of lesions that were negative with BS. The agreement between BS and T1 & STIR was not significant. This meant that MRI and BS were complementary to each other when possible.

Abd elsalam *et al. Egypt J Radiol Nucl Med*   (2023) 54:102

Page 10 of 13

Table 6 Bony lesions in The Arm

Modalities		Bony metastases in arm in bone scan (BS)			Total	Kappa	P- value
		Negative	**1 lesion**	**2 lesions**			
T1	Negative	15(75%)	0(0%)	1(5%)	16(80%)	0.259	0.104
	1 lesion	2(10%)	1(5%)	0(0%)	3(15%)		
	2 lesions	1(5%)	0(0%)	0(0%)	1(5%)		
STIR	Negative	15(75%)	0(0%)	1(5%)	16(80%)	0.259	0.104
	1 lesion	2(10%)	1(5%)	0(0%)	3(15%)		
	2 lesions	1(5%)	0(0%)	0(0%)	1(5%)		
DWIBS	Negative	14(70%)	0(0%)	0(0%)	14(70%)	0.296	0.036*
	1 lesion	3(15%)	0(0%)	0(0%)	3(15%)		
	2 lesions	1(5%)	1(5%)	1(5%)	3(15%)		
Total		18(90%)	1(5%)	1(5%)	20(100%)		

- *The blue color indicates the additive value of BS modality*
- *The pink color indicates the additive value of MRI sequences*

According to this table, female patients with breast cancer metastatic to arm bones; we had three lesions (in two patients) detected by bone scan, and nine lesions (in six patients) detected by DWIBS. The agreement between bone scan and DWIBS in three lesions (in two patients). The other four patients (five lesions) were missed by bone scan and detected by DWIBS.

Bony lesions in the skull
There 30% (six lesions in six patients) had positive skull metastases detected by BS only.

Total number of lesions
There was a significant difference between the total number of metastases detected by BS and MRI T1, T1 and DWIBS and STIR and DWIBS.

The total number of lesions detected by bone scan was seventy-four lesions. Seventy-five lesions were detected by DWIBS. Although the total number of lesions was nearly similar, the distribution of individualized lesions in each region was differently detected by the two modalities. Twenty-four lesions were missed by bone scan and seen by DWIBS. Fourteen lesions were detected by bone scan and found free by

Abd elsalam *et al. Egypt J Radiol Nucl Med*　(2023) 54:102

Page 11 of 13

DWIBS examination, especially spine and pelvic bones, which led to a change in the management plan of most patients.

Management of patients

According to the results of DWIBS, patients were divided into two groups:

- Patients proved to have bony metastases (9 patients) started palliative radiotherapy and chemotherapy.
- For patient with no evidence of bony metastases (11 patients) management plan had been changed to curative treatment.

Discussion

Despite bone being the most prevalent location for metastases from breast cancer, there are major gaps in the ability to detect metastatic bone disease and evaluate therapeutic efficacy using current imaging techniques [6].

Bone scans (BS) are the gold standard for diagnosing bone metastases. BS is a low-cost, very sensitive imaging technology that lacks specificity [8]. Whole-body MR imaging using diffusion-weighted sequences has recently gained attention as a potential diagnostic tool for evaluating skeletal malignancies. Direct evaluation of bone and soft-tissue disorders is possible with whole-body MRI without the need for injected contrast agents or ionizing radiation [9].

This study was conducted at University Hospital to compare the efficacy and diagnostic value of non-contrast whole body Magnetic Resonance with diffusion-weighted imaging against Radionuclide bone scans in the early detection of bone metastases in patients with breast cancer.

The current study found a significant difference between the number of metastasis detected by BS and MRI T1, between T1 and DWIBS, and between STIR and DWIBS. The total number of lesions detected by bone scan was 74. The number of lesions detected by DWIBS was 75. Although the total number of lesions was nearly similar, the two modalities detected the distribution of individualized lesions in each region differently. Twenty-four lesions were missed by bone scan and detected by DWIBS. Fourteen lesions were detected by bone scan and found free by DWIBS examination, especially spine and pelvic bones.

Metastasis to the skull was detected in 30% of patients by bone scan, while no skull lesions were detected by DWIBS. Causes of missed lesions at diffusion images included low tumor infiltration of the skull vault and skull base metastases due to adjacent high signal intensity of the brain [10]. Regarding the current study, difficulty in

assessing skull and rib lesions also referred to the absence of dedicated MRI coils (we used only body coil) with the signals passing through air-bone-soft tissue resulting in in unclear images. Some anatomic regions are difficult to analyze, particularly the ribs and skull. However, this limitation may be overcome by breath-hold acquisition [11].

Although scintigraphy was better than WB-MRI for identifying skull bony metastases, no case was detected as an isolated skull metastasis. However, in all previously reported cases, the skull metastasis was either clinically evident or associated with other metastases. Therefore, the possibility of isolated occult skull vault metastasis being missed on WB-MRI would be extremely unlikely [12].

To our knowledge, no previous study assessed the complementary role of both techniques based on the individual lesion analysis. However, the present study found that whole-body MRI with its different imaging sequences was superior to bone scan in the detection of some lesions that couldn't be identified by the BS. On the other hand, some lesions couldn't be detected by MRI and were detected by BS.

Whole-body MRI has been studied in several diagnostic trials. Like ours, they have shown high sensitivity for detecting breast cancer metastatic lesions. Whole-body MRI was reported to be more effective than BS in detecting bone metastases in research comparing MRI, CT, and BS for identifying bone metastases in primary breast cancer [1]. However, they did note that MRI successfully identified bone metastases in all seven patients. No false-positive cases were described subsequently in a sensitivity equal to 100% and a specificity equal to 100%. Two of the seven patients with bone metastases were found by bone scintigraphy. In contrast, a false-positive result was found in a patient who did not have bone metastases, resulting in a sensitivity of 28.6% and a specificity of 99.4% [1].

Compared to BS, WB-MRI is more accurate in detecting bone metastases, according to research by [13]. When comparing WB-MRI with BS for bone metastases identification, the former had a sensitivity of 98%. In comparison, the latter had just 82%, and the specificity was nearly equal (93 and 91 percent) for both, respectively. Jambor et al., in their region-based analysis, found that the WB-MRI protocol, including T1W, STIR, and DWI sequences, has a sensitivity of 91%, a specificity of 99%, and an accuracy of 97%. They also reported that DWI associated with STIR and T1W images can reduce false positive lesions [14]. The study of Minamimoto et al. compared 99mTc-MDP scintigraphy, whole-body MRI, and combined 18F-NaF and 18F-FDG PET/CT in patients with prostate and breast cancer. In total ninety-eight lesions were identified by 18F2/ 18F-FDG PET/CT

Abd elsalam *et al. Egypt J Radiol Nucl Med*   (2023) 54:102

Page 12 of 13

in 30 subjects, 79 lesions were detected by MRI of whole-body in 28 subjects, 53 lesions were detected by bone scintigraphy in 30 subjects, 85 lesions were identified by a combination of whole-body MRI and bone scintigraphy in 28 subjects [15]. Based on their meta-analysis, Liu et al. conclude that WB-MRI is superior to FDG-PET and BS for the identification of skeletal metastases in breast cancer [16]. In their study comparing bone scans and whole-body MRI for the detection of bone metastasis**,** Sohaib et al. found that 13 of the 15 patients with bone metastases were correctly identified as true-positive by whole-body MRI. In comparison, 11 of these 15 patients were correctly identified by bone scintigraphy. When comparing the two methods on a patient-by-patient basis, MRI demonstrated a non-significantly greater sensitivity (87%) for detecting bone metastases than bone scintigraphy (73%) [17].

There were several possible explanations for the varying degrees of success between the various imaging techniques. Bone scintigraphy, unlike whole-body MRI, evaluates the bone matrix reaction to cancer cells rather than metastatic foci themselves, making them indirect reporters of malignant bone marrow pathologic characteristics. Bone scintigraphy can identify metastatic progression only when the surrounding bone structure has changed. In bone scintigraphy, bone metastases are detected by enhanced osteoblast activity, which causes differential tracer accumulation at mineral deposition sites [18] while**,** changes in water diffusivity indicate cellularity changes inside lesions and marrow fat displacement provides early signals of disease development, all of which may be seen on a whole body MRI scan [9].

The ability to see metastatic tissue in the bone marrow using MRI is a huge benefit. Thus, osteolytic metastases were detectable before the breakdown of cortical bone had started, which was often the case with CT. The absence of ionizing radiation and the increased soft tissue contrast provided by MRI may be especially useful in diagnosing non-osseous lesions [19].

Successful treatment of metastatic breast cancer is related to a recovery of normal bone marrow fat after the malignant cells have been eliminated by displacement and replacement of normal bone marrow fat cells. Bone metastases may be detected using MRI because of their ability to distinguish between normal and diseased bone marrow. The structural and functional characteristics of bone marrow may be assessed using magnetic resonance imaging (MRI) sequences such as T1WI, DWI, and Dixon quantitative chemical shift imaging (which calculates water and fat percentage) [20].

The present study also found that the accuracy of detection of breast cancer metastases to the bone using the T1 sequence of MRI was lower to STIR and DWIBS.

The combination of all MRI sequences T1, STIR, and DWIBS showed the best diagnostic accuracy.

Larbi et al. compared the diagnostic accuracy of T1, STIR, and high b-values DWI sequences when used in conjunction with whole-body MRI to evaluate bone involvement in prostate cancer and multiple myeloma. Similar to our findings, they found that using a combination of sequences was more effective than using any one sequence alone for diagnosing bone involvement, with T1 having the lowest diagnostic value. The performance of T1-STIR and STIR-DWI combinations was significantly worse than that of T1-STIR-DWI combinations [21].

Additionally, Goda et al. found that evaluating bone lesions by DWI, STIR, or T2-WI alone yields high false results of non-tumor lesions, recommending the combination of the three techniques for higher accuracy in detecting skeletal lesions in their study on the role of whole-body diffusion-weighted MRI in the detection of metastasis and lymphoma [22].

Because DWI allows MRI to evaluate functional tissue properties without the need for a contrast agent, it performs well in detecting both osteolytic and osteoblastic lesions, which may account for DWI's higher accuracy in the detection of metastases. Combining substantial diffusion-weighting with background signal suppression of organs, blood arteries, and bodily fluids, DWI displays tumoral lesions with great signal contrast compared to the surrounding tissue [23].

Conclusions

Whole-body MRI seemed to be a promising method of imaging in the detection of metastases from breast cancer that could be used complementary to the traditional bone scan for more accurate diagnosis and staging of the tumor, helping to determine the most appropriate management protocol.

Recommendation

We recommended that breast cancer patients with suspected bony metastases and negative bone scans should be referred to whole-body MRI with diffusion. Even patients with positive bone scans benefit from doing whole body MRI with diffusion, as it can detect more lesions or lesions in weight-bearing areas not seen by a bone scans that may require palliative radiotherapy.

Abbreviations
DWIBS   Diffusion-weighted imaging with background body signal suppression
WB-MRI   Whole-body magnetic resonance imaging
BS   Bone scan
DWI   Diffusion-weighted imaging

Abd elsalam *et al. Egypt J Radiol Nucl Med*   (2023) 54:102

Page 13 of 13

Availability of data and materials
All data are available at the corresponding author who has the authority to respond if there is any query.

Declarations

Ethics approval and consent to participate
The study was approved from the ethical committee of Faculty of Medicine Beni-suef University. Data were collected after obtaining informed written consent of all cases.

Consent for publication
All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests
The authors declare that they have no competing interests.

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