### Whole-body MRI for Detecting Metastatic Bone Tumor: Diagnostic Value of Diffusion-weighted Images

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Purpose: We assessed the diagnostic value of whole body magnetic resonance (MR) imaging (WB-MRI) using diffusion-weighted images (DWI) for detecting bone metastasis and compared it with that of skeletal scintigraphy (SS).

Materials and Methods: Thirty patients with malignancies (breast cancer, 17 patients; prostate cancer, 9; and one patient each, thyroid cancer, liposarcoma, leiomyosarcoma, and extraskeletal Ewing sarcoma) underwent both WB-MRI and SS to detect bone metastasis. All patients were followed more than 6 months by MR imaging, SS, or computed tomographic (CT) examination. For WB-MRI, patients were placed in feet-first supine position with table-top extender and quadrature body coil.

We acquired DWI (axial plane from lower neck to proximal femur) (single shot short TI inversion-recovery [STIR]: repetition time [TR] 6243/echo time [TE] 59/inversion time [TI] 180 ms; b value: 600 s/mm²; 5-mm slice thickness; 112 × 112 matrix), T1-weighted fast spin echo (T1WI), and STIR (sagittal plane of total spine images and coronal plane of whole body images) images.

Four blinded readers independently and separately interpreted images of combined MR sequences of T1WI + STIR (session 1) and T1WI + STIR + DWI (session 2).

Results: In 10 of 30 patients, we detected a total of 52 metastatic bone lesions; in the other 20, follow-up examinations confirmed no metastatic bone lesions.

For these 52 lesions, for session 2, the mean sensitivity was 96% and the positive predictive value (PPV) was 98%. Those values were superior to those of session 1 (sensitivity: 88%; PPV: 95%) and those of SS (sensitivity: 96%; PPV: 94%).

Conclusion: WB-MRI that included DWI was useful for detecting bone metastasis.

Keywords: bone metastasis, diffusion-weighted images, whole-body MRI

### Introduction

Cellular bone marrow is the initial site of metastasis seeding to bone. Skeletal scintigraphy (SS) has long been the standard instrument for detecting skeletal metastases, especially osteoblastic metastases, such as breast cancer and prostate cancer. However, the recently developed whole-body magnetic resonance imaging (WB-MRI) has proven better than SS in detecting tumors and characterizing skeletal metastases because MR imaging can detect metastatic lesions at an early stage, before the changes in bone metabolism that make lesions detectable on SS.

Diffusion-weighted imaging (DWI) is now widely used in imaging the central nervous system, especially in cases of acute stroke, although its use in...
the body has been restricted because of the limitations of slice thickness and unreliable fat suppression. However, recent advances in MR gradient technology allow DWI acquisition with high b-factors, even in the body. Moreover, Takahara and colleagues developed 3-dimensional diffusion-weighted whole-body imaging with background signal suppression (DWIBS), which produces images similar to those acquired using 2-[fluorine-18]-fluoro-2-deoxy-D-glucose (18 FDG)-positron emission tomography (PET).

However, to our knowledge, reports are limited of WB-MRI with DWI for detecting metastatic bone tumor.

We assessed the diagnostic value of DWI for detecting whole-body bony metastasis by comparing DWI images with those acquired using conventional WB-MRI and SS.

Materials and Methods

Patients
From June to October 2005, 30 patients (19 men, 11 women; aged 31 to 78 years, mean 62 years) underwent both WB-MRI and SS to detect bone metastasis (17 patients, breast carcinoma; 9, prostate carcinoma; one each, thyroid carcinoma, leiomyosarcoma, liposarcoma, and angiosarcoma). SS was performed within 3 weeks after WB-MRI. All patients were followed for more than 6 months by MR imaging, SS, or computed tomography (CT). There was no selection bias, but routine examination of skeletal screening in the 30 patients.

The study was approved by our institutional review board, and all patients gave informed consent.

MR images
All MR studies were performed on a 1.5T whole-body scanner (Master Philips Medical System, Best, The Netherlands). Patients were placed in feet-first position using a table-top extender (prototype, Philips Medical System) and quadrature body coil that allowed extension of the longitudinal field of view (FOV) to 200 cm and thereby the scanning of most of the body of adult patients from head to toe. For all patients, we performed 3 sequences as follows.

**DWI sequences**

Single shot short $T_1$ inversion recovery-echo planar imaging (STIR-EPI) sequences (repetition time [TR]: 6243/echo time [TE]: 59/inversion time [TI]: 180 ms.) were used for DWI, with b-value of 0 and 600 s/mm$^2$. We obtained 5-mm slices with 1-mm overlap of axial view during free breathing. Axial slices were acquired from the lower neck to the bottom of the pelvis using a 2-station approach. The FOV of each station was 450 mm, and the matrix was $112 \times 112$. The imaging time of the each station was 5 min, 25 s.

The radial directions of maximal intensity projection (MIP) images of each station were reconstructed and displayed as anteroposterior and left lateral views. Original axial images and MIP images were then transmitted to an equipped workstation (ViewForum, Philips) that allowed display of original and MIP images of DWI by usual images and by inverted images for background suppression.

**$T_1$-weighted fast spin echo (SE) sequences**

Sagittal images of the total spine

We acquired 5-slice sections of $T_1$-weighted fast SE images ($T_1$-WI; TR/TE: 400/13 ms; echo train length [ETL]: 4) of the total spine on the sagittal plane using a 3-station approach with slice thickness of 7 mm. The FOV of each station was 300 mm, and matrix was $352 \times 264$. Imaging time was 4 min, 33 s.

**Coronal images of the whole body**

We acquired fast field-echo (FFE) $T_1$WI (100/4.6; ETL: 128) of the whole body on the coronal plane using a 6-station approach. The FOV of each station was 300 mm. We obtained a total of 32 whole-body coronal images of this sequence anteroposterior with slice thickness of 7 mm. The matrix was 240$\times$185. Imaging time was 6 min, 24 s.

**STIR sequences**

Sagittal images of the total spine

We acquired 5 sections of STIR images (TR/TE/TI: 2500/70/170; ETL: 15) of the total spine on the sagittal plane using a 3-station approach with slice thickness of 7 mm. The FOV of each station was 300 mm. The matrix was $288 \times 316$. Imaging time was 6 min, 15 s.

**Coronal images of the whole body**

We acquired STIR images (TR/TE/TI: 1350/40/165; ETL: 65) of the whole body on the coronal plane using a 6-station approach. The FOV of each station was 300 mm. A total of 32 whole-body coronal images of this sequence were acquired anteroposterior with slice thickness of 7 mm. The matrix was $320 \times 185$. Total imaging time was 6 min, 24 s.

Imaging data of both $T_1$WI and STIR were immediately transmitted to an equipped workstation (ViewForm, Philips), where images were realigned within minutes. To create true whole-body images, images at the same slice level from each station were aligned cranial to caudal.

Total examination time, including patient positioning, was within 50 min.
Skeletal scintigraphy

Standard skeletal radionuclide scintigraphy was performed within a month before and after WB-MRI using a planar one-phase technique. The examination was performed 3 hours after injection of 550 Mbq of 99m Tc-labeled dicarboxypropane diphosphonate. Images were collected using a dual-head whole-body scanner1,9 with a high-resolution, low-energy collimator. No single photon emission computed tomography (SPECT) was used in this analysis.

Imaging assessment

Images from the 2 sessions of combined MR sequences were interpreted independently and separately by 4 blinded readers (HO, NM, SN, MK), each of whom had 6 to 15 years’ experience primarily as musculoskeletal and abdominal radiologists and had interpreted MR images of the bone and joint as part of their daily clinical and research practice. The first of the 2 sessions combined T1WI and STIR sequences, and the second session combined T1WI, STIR, and DWI. Each reader recorded the presence and location of bony lesions and assigned each a confidence rating on a 5-point scale (1 = benign, 2 = probably benign, 3 = equivocal, 4 = probably malignant, 5 = malignant).

On MR imaging, a lesion was considered malignant (score 4 or 5) when there was a focal or diffuse hypointensity on the T1-weighted scan, corresponding intermediate to high signal intensity on STIR images, and high signal intensity on DWI. A lesion was considered equivocal (score 3) in origin when the differentiation between a metastatic and benign process, such as osteoporotic fracture or bone marrow reconversion, was not possible.9 A lesion was regarded as benign (score 1 or 2) when focal tracer accumulation occurred adjacent to joint surfaces. Well-circumscribed linear tracer uptake involving the thoracic or lumbar spine or symmetrical tracer uptake of adjacent ribs was considered benign and caused by osteoporotic or traumatic fracture.9

To determine the diagnostic potential of both modalities for different anatomic lesions, MR images and bone scans were evaluated separately for the following 19 anatomical areas: skull; cervical spine; thoracic spine; lumbar spine including the sacrum; sternum; both sides of the shoulder girdle (scapula and clavicle); humerus; forearm; ribs; pelvic bone (ilium, pubis, and ischium); femur; and lower legs.9 More than 2 abnormal lesions detected within one anatomical area were counted as a single lesion. Additionally, each reader recorded the presence of extraskeletal lesions such as hepatic, pulmonary, and lymph nodal lesions.

The 2 reviewing sessions took place at an interval of more than 2 weeks.

Gold standard

To confirm and rule out initial findings and classify findings as benign or malignant, one staff radiologist evaluated follow-up MR imaging, SS, CT, and radiography studies performed over a period of at least 6 months. A lesion was considered metastatic when it showed progression on the same imaging modality on follow-up examination or fulfilled typical criteria for malignancy on follow-up examination with another imaging modality.9

Statistical analysis

The sensitivity and positive predictive value (PPV) of bone metastasis for each reader and each session were calculated with a score greater than 4 considered malignant.

Results

Metastatic bone lesions were detected in 10 of 30 patients; in the other 20, no malignant lesions were detected. In three of the 10, multiple metastatic lesions were detected (Fig. 1); a total 52 lesions were confirmed as bone metastases by follow-up examination.

Table 1 shows the number of true-positive lesions and the sensitivity for detection of bone metastasis by each reader of each session for WB-MRI. SS showed equivocal findings of 2 solitary lesions in 2 patients (score 3), which were detected by all 4 readers in session 2 as more than score 4 and more than 3 readers in session 1 (Fig. 2). On the other hand, on WB-MRI, one lesion on the lower leg, which was detected by SS, was not detected by 3
Fig. 1. A 54-year-old man with breast carcinoma. A: Multiple areas of high intensity detected in the rib, ilium, vertebral body, and other areas in a maximal intensity projection (MIP) image of diffusion-weighted imaging (DWI) by inverted image were diagnosed as multiple bone metastases. B: Multiple areas of high intensity were detected in the pelvic bone and vertebra (white arrows) in the coronal slice of STIR. In this image, the lesions of the rib were unclear. C: Multiple lesions of high uptake were found on the anteroposterior view of skeletal scintigraphy, and these findings correlated well with the MIP image of DWI.

Table 1. Sensitivity for revealing metastatic bone tumor (10 patients, 52 lesions)

<table>
<thead>
<tr>
<th></th>
<th>Reader 1</th>
<th>Reader 2</th>
<th>Reader 3</th>
<th>Reader 4</th>
<th>Mean</th>
<th>Skeletal scintigraphy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Session 1 (T1 + STIR)</td>
<td>0.94 (49)</td>
<td>0.94 (49)</td>
<td>0.75 (39)</td>
<td>0.87 (45)</td>
<td>0.88</td>
<td>0.96 (50)</td>
</tr>
<tr>
<td>Session 2 (T1 + STIR + DWI)</td>
<td>0.96 (50)</td>
<td>0.98 (51)</td>
<td>0.90 (48)</td>
<td>0.98 (51)</td>
<td>0.96</td>
<td></td>
</tr>
</tbody>
</table>

Numbers of tumors detected shown in parentheses.
DWI: diffusion-weighted imaging; STIR: Single shot short TI inversion-recovery

Readers in session 2 (Fig. 3). The mean sensitivity for the 4 readers in session 2 (DWI + T1WI + STIR) was equal to that for SS, and all readers rated higher sensitivity in session 2 than in session 1 (T1WI + STIR).

Table 2 shows the number of false-positive lesions (Fig. 4), and the PPV by reader and session. Three of 4 readers rated the PPV of session 2 higher than that of SS and three of 4 readers rated the PPV of session 2 higher than that of session 1.

**Extraskeletal lesions**

Metastatic lymph nodes were detected in 4 patients (Fig. 5).

Table 3 shows the number of true-positive lesions and the sensitivity for detection of metastatic lymph nodes by each reader of each session for WB-MRI. No significant difference occurred between the 2 sessions.

Table 4 shows the number of false-positive lesions and the PPV of metastatic lymph nodes by reader and session; all readers rated PPV in session 2 lower than that in session 1.

All readers in both sessions detected multiple hepatic metastases in 2 patients. All readers in session 2 detected pulmonary metastases in one patient.

**Discussion**

The concept of WB-MRI is not new. Several reports demonstrate its high sensitivity in detecting bone marrow metastasis and its advantages over SS. We previously reported that WB-MRI with conventional T1-weighted and STIR sequences was superior to SS for detecting metastatic lesions of the vertebral body but inferior for detecting rib le-
Fig. 2. A 68-year-old man with prostate carcinoma. 

A: An area of low intensity was detected (white arrow) in the right anterior ilium on the T1-weighted image.

B: A na r e ao fh i g hi n t e n s i t y w a s also detected in the right ilium in the axial diffusion image (white arrow).

C: Obvious high intensity recognized in the right ilium (arrow) in the maximal intensity projection image of diffusion-weighted imaging by inverted image was diagnosed as bone metastasis. All readers in session 2 scored the lesion as 5.

D: On skeletal scintigraphy, this lesion might be shown as an area of slightly high uptake (arrow) and scored 3.

Table 2. Positive predictive values for revealing metastatic bone tumor

<table>
<thead>
<tr>
<th></th>
<th>Reader 1</th>
<th>Reader 2</th>
<th>Reader 3</th>
<th>Reader 4</th>
<th>Mean</th>
<th>Skeletal scintigraphy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Session 1 (T₁ + STIR)</td>
<td>0.89 (6)</td>
<td>0.94 (3)</td>
<td>1 (0)</td>
<td>0.98 (1)</td>
<td>0.95</td>
<td>0.94 (3)</td>
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<tr>
<td>Session 2 (T₁ + STIR + DWI)</td>
<td>0.93 (4)</td>
<td>0.98 (1)</td>
<td>1 (0)</td>
<td>1 (0)</td>
<td>0.98</td>
<td></td>
</tr>
</tbody>
</table>

Numbers of false positive lesions are shown in parentheses.

DWI: diffusion-weighted imaging; STIR: Single shot short TI inversion-recovery
Fig. 3. A 65-year-old man with angiosarcoma. 

A: On whole-body coronal image of T1-weighted imaging, an area of low intensity was recognized in the right proximal tibia (white arrow).

B: Close-up view of A shows this lesion clearly (white arrow). Three readers overlooked this lesion in session 2.

C: High uptake was recognized in the right proximal tibia (arrow) and diagnosed as metastasis.

Table 3. Sensitivity for revealing metastatic lymph nodes

<table>
<thead>
<tr>
<th></th>
<th>Reader 1</th>
<th>Reader 2</th>
<th>Reader 3</th>
<th>Reader 4</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Session 1 (T1 + STIR)</td>
<td>0.5 (2)</td>
<td>0.5 (2)</td>
<td>0.5 (1)</td>
<td>0.5 (2)</td>
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<tr>
<td>Session 2 (T1 + STIR + DWI)</td>
<td>0.75 (3)</td>
<td>0.25 (1)</td>
<td>0.75 (3)</td>
<td>0.5 (2)</td>
<td>0.46</td>
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</tbody>
</table>

Numbers of tumors detected are shown in parentheses.

DWI: diffusion-weighted imaging; STIR: Single shot short TI inversion-recovery

Table 4. Positive predictive values for revealing metastatic lymph nodes

<table>
<thead>
<tr>
<th></th>
<th>Reader 1</th>
<th>Reader 2</th>
<th>Reader 3</th>
<th>Reader 4</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Session 1 (T1 + STIR)</td>
<td>0.67 (1)</td>
<td>1.0 (0)</td>
<td>1.0 (0)</td>
<td>0.22 (7)</td>
<td>0.73</td>
</tr>
<tr>
<td>Session 2 (T1 + STIR + DWI)</td>
<td>0.38 (5)</td>
<td>0.12 (7)</td>
<td>0.6 (2)</td>
<td>0.11 (17)</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Numbers of false positive lesions are shown in parentheses.

DWI: diffusion-weighted imaging; STIR: Single shot short TI inversion-recovery

associates\(^2\) introduced diffusion-weighted whole-body imaging with background suppression (DWIBS) by using free breathing, STIR, and high resolution 3D display. We introduced their methods for whole-body bone screening.

In this study, the sensitivity of session 2 (T1WI, STIR, and DWI) was equal to that of SS for detecting metastatic bone tumor. However, the decisive difference between them was that SS was equivocal for detecting 2 solitary lesions in the anterior ilium in 2 patients. Both lesions were detected by all 4 readers in session 2 and more than 3 readers in session 1. The thick structure in the anteroposterior direction makes it difficult to detect the area of the anterior ilium by only the AP-PA view of SS, so the coronal and axial slices of MR imaging and DWI-
MIP were advantageous for detecting lesions in this area.

The sensitivity of session 2 was superior to that of session 1 (without DWI) for all 4 readers, which was demonstrated primarily in the 3 cases with multiple bone lesions. The lesions of the rib and shoulder girdle were detected by adding the axial and MIP images of DWI. However, using only the coronal slice of T1WI and STIR, it was possible to overlook lesions that were present. On the other hand, three of 4 readers in session 2 did not detect the metastatic lesion in the lower leg, though it was clearly revealed and detected by SS (Fig. 3). Three of 4 readers in session 1 detected this lesion. In our present protocol, DWI ranged only from the lower neck to the bottom of the pelvis and did not cover the lower leg. Therefore, the lower leg was only analyzed by conventional coronal T1WI and STIR. Some readers may have lost concentration for inspecting the lower leg by whole-body coronal image of T1WI and STIR. If DWI had covered this area, this result would have improved.

The PPV of session 2 was slightly superior to that of session 1 and of SS, although this difference was also not statistically significant. These facts suggested that WB-MRI with DWI is superior to SS in classifying bony lesions as benign and malignant.

For extraskeletal lesions, the number of false-positive lesions was higher in session 2 than session 1 for lesions of the lymph nodes (Table 4). Although inter-observer variation was large because of the small patient population, this fact proved that DWI tended to overdiagnose the lymph nodal lesions.

In DWI pulse sequences, a B value of 1000, widely used in the brain, is more common. However, we selected 600 s/mm² because high B values, such as 1000, allow detection of only solid lesions, but not cystic ones. In our experience, the subchondral degenerative change in the acetabullum (Fig. 2) could
Fig. 5. A 55-year-old woman with breast carcinoma. A: Multiple areas of high intensity were detected in the supraclavicular, para-aortic, and intrahepatic lesions in a maximal intensity projection image on diffusion-weighted imaging by inverted image and were suspected of lymph nodal and hepatic metastases (arrows). B: The left axillary (white arrow) node was confirmed. C: The para-aortic lymph nodes (arrowhead) and ring-enhanced mass (arrow) in the liver were confirmed on computed tomography.

be detected with a B value of 600, but not with 1000. All readers diagnosed this lesion as benign, adding the information of the T1WI and STIR.

The disadvantage of WB-MRI is that it requires radiologists to evaluate a large amount of data. To minimize these problems, a DWIBS-MIP image, which can display whole body image simply and objectively, should be used frequently.

Summary

WB-MRI with DWI proved superior to SS and WB-MRI without DWI as a noninvasive and more accurate method for detecting metastatic bone tumor and can be used to detect extraskeletal lesions. However, lesions of the lymph nodes may be overdiagnosed.

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