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# Diagnosis of spinal metastasis: are MR images without contrast medium application sufficient?

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ABSTRACT

*Objective:* To determine the usefulness of adding contrast-enhanced (CE) magnetic resonance imaging (MRI) to conventional MRI for evaluation of spinal metastases.

*Materials and methods:* One-hundred-and-two whole spine MR examinations, obtained for metastasis work-up within a 2-month period, from 65 men and 37 women (mean age, 64 years) with extra-spinal tumor, who also underwent CE-MRI, were retrospectively evaluated by three radiologists. The number of spine segments with bone marrow involvement was interpreted using a 3-point confidence scale (probable metastasis, equivocal, probably benign) during session 1 (conventional imaging) and session 2 (addition of CE-MRI to conventional imaging). The patients were assigned to 14 categories based on the changes in confidence rating between sessions 1 and 2; these were aggregated to four groups indicating the degree of usefulness of CE-MRI: definitely useful, equivocal, not useful, and presumed non-metastatic groups. Clinical information, metastatic bone type, the number of probably metastatic segments, and anatomical level and position were compared among the former three groups.

*Results:* The readers assigned 39–53% of cases to the definitely useful group. The number of probably metastatic segments differed significantly among the three groups for all readers ($p \leq 0.046$). Age, sex, primary cancer, metastatic bone type, and anatomical level and position were similar.

*Conclusion:* Adding CE-MRI to conventional MRI was useful for objectively detecting and characterizing spinal segments with metastases in 39–53% of cases. However, there were no clinical or radiological factors that could predict the usefulness of CE-MRI in evaluating spinal metastases, except for the number of metastatic segments.

## 1. Introduction

The spine is the most common osseous metastatic site and the third most common metastatic site overall, after the lung and the liver [1,2]. Approximately 30–70% of the patients who die due to cancer have spinal metastases at postmortem examination and about 14% of the patients with spinal metastases will develop symptomatic lesions during their illness [3]. The major clinical presentations of spinal metastasis are local or radicular pain, with or without motor weakness, sensory loss, and loss of sphincter control. If a cancer patient presents with pain or neurological symptoms, a radiological evaluation should be made to determine the presence, number, and extent of spinal metastatic lesions in order to start the most appropriate treatment.

Magnetic resonance (MR) imaging is a widely available modality for evaluating suspected spinal metastasis, as it offers unparalleled visualization of the spinal column and cord. It provides superior imaging of bone marrow infiltration, allows characterization of the levels of involvement, and can delineate the associated cord compression and extraosseous soft tissue component of a neoplasm [4,5]. It also facilitates diagnosis of spinal metastases at an earlier stage than other modalities [6–8].

There is a lack of consensus about the routine MR sequences that are necessary for clinical assessment of spinal metastasis. The American College of Radiology has recommended MR imaging without contrast

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for evaluation of patients with known malignancy who present with back pain [9,10]. However, they also state that contrast is useful for patients suspected of having epidural or intra-spinal disease. In routine clinical practice, although additional contrast-enhanced (CE) MR imaging is performed to increase the sensitivity and the specificity of the MR examination, it also has the disadvantage of invasiveness, time constraints, and cost. Furthermore, there have been inconsistent reports about the value of adding CE-MR imaging to conventional MR imaging to evaluate spinal metastases [11–16]. Several studies have shown that CE-MR imaging is useful in spinal metastasis including delineation of spinal bone metastases, delineation and characterization of extradural and pial metastases [14–16]. These were papers published in the 1990s that used low magnetic field MRI and gadopentetic acid contrast agents and they did not describe the extent to which CE-MR imaging is useful for spinal metastasis. Recently Johnson el al. [11] reported that unenhanced T1-weighted images may be sufficient for evaluation of possible cord compression in patients with spinal metastases. However, that study was a comparison of radiation treatment plans by MR sequences for known patients with spinal metastasis. Although CE-MR imaging is widely used in spinal imaging, there are no reports indicating the usefulness of CE-MR imaging for detecting and characterizing spinal metastases or in which cases this approach is more useful as compared to conventional MR imaging.

Therefore, the purpose of this study was to determine the degree of usefulness of adding CE-MR imaging to conventional MR imaging for the evaluation of spinal metastases, and whether there are factors than can predict the usefulness of CE-MR imaging in such cases.

## 2. Materials and methods

### 2.1. Study population

This retrospective study was approved by our institutional review board, and the need to obtain informed consent from patients was waived due to the retrospective nature of the study.

A total of 124 consecutive whole spine MR examinations for metastasis work-up were performed at our institution, from May to June 2017. The inclusion criteria consisted of adult patients with extra-spinal tumor who underwent CE-MR imaging. The patients' electronic medical records were reviewed. Patients with a primary tumor or tumor-like lesion in the spine (*n* = 7), patients without a primary tumor (*n* = 6), patients under the age of 18 (*n* = 3), and patients who underwent MR imaging without CE-MR imaging (n = 6) were excluded (Fig. 1).

Finally, a total of 102 MR examinations were included (mean patient age, 64.2 years; age range, 18–91 years), comprising 65 men (mean age, 64.4 years; age range, 20–91 years) and 37 women (mean age, 63.9 years; age range, 18–83 years). Pain was the most common cause of spine MR examinations for metastasis work-up (*n* = 41), including spinal pain (*n* = 35) and non-spinal pain (*n* = 6). Other reasons for performing spine MR examinations were follow-up for previous metastasis (*n* = 28), suspected metastasis on another imaging modality (*n* = 26), and pretreatment screening (*n* = 7). The primary tumors were as follows: prostate adenocarcinoma (n = 28), lung cancer (*n* = 23 [adenocarcinoma, 15; squamous cell carcinoma, 5; small cell carcinoma, 3]), gastrointestinal cancer (*n* = 16 [colorectal adenocarcinoma, 11; gastric adenocarcinoma, 4; appendiceal adenocarcinoma, 1]), breast ductal carcinoma (*n* = 7), liver cancer (*n* = 4 [hepatocellular carcinoma, 3; cholangiocarcinoma, 1]), intracranial tumor (n = 4 [glioblastoma multiforme, 1; choroid plexus carcinoma, 1; germinoma, 1; adenoid cystic carcinoma, 1]), renal cell carcinoma (*n* = 3), lymphoma (n = 3 [diffuse large B cell = 2, Burkitt, 1]), multiple myeloma (n = 3), acute lymphoblastic leukemia (*n* = 2), thymic carcinoma (n = 2), bladder transitional carcinoma (*n* = 1), thyroid cancer (n = 1), malignant melanoma (n = 1), malignant pheochromocytoma (n = 1), gallbladder cancer (n = 1), endometrial cancer (n = 1), and retroperitoneal neuroendocrine carcinoma (n = 1). Previous treatment histories were as follows: no treatment (*n* = 33), chemotherapy (*n* = 24), concurrent chemoradiation therapy (*n* = 22), hormone therapy (*n* = 8), radiation therapy excluding the spine (*n* = 4), chemotherapy with hormone therapy (n = 4), radiation with hormone therapy (n = 3), concurrent chemoradiation therapy with hormone therapy (n = 2), and unknown history (n = 2). Eighteen patients had a history of prior radiation therapy to the spine. Neurological symptoms were present in 29 patients, and included motor (*n* = 8), sensory (*n* = 12), motor and sensory (n = 8), and motor, sensory, and sphincter (n = 1) symptoms. The mean time interval between tumor confirmation and MR examination was 29.87 months (range, 0–390 months).

### 2.2. Image acquisition

MR images were acquired using a 3-T MR unit (Ingenia; Philips Healthcare, Best, the Netherlands) in 100 patients and a 1.5-T MR unit (Intera; Philips Healthcare) in two patients with a spine-array surface coil. The conventional protocol for whole-spine MR imaging for metastasis work-up using the 3-T MR unit consisted of sagittal and axial T1 and T2 weighted images. The parameters for each sequence are presented in Table 1. For contrast-enhanced T1-weighted imaging, we intravenously administered a bolus of gadobutrol (Gadovist; Schering, Berlin, Germany) (0.1 mmol/kg/body weight), immediately followed by a 20-mL saline flush at the same injection rate.

### 2.3. Image analysis

Three radiologists (reader 1, a professor-level radiologist with

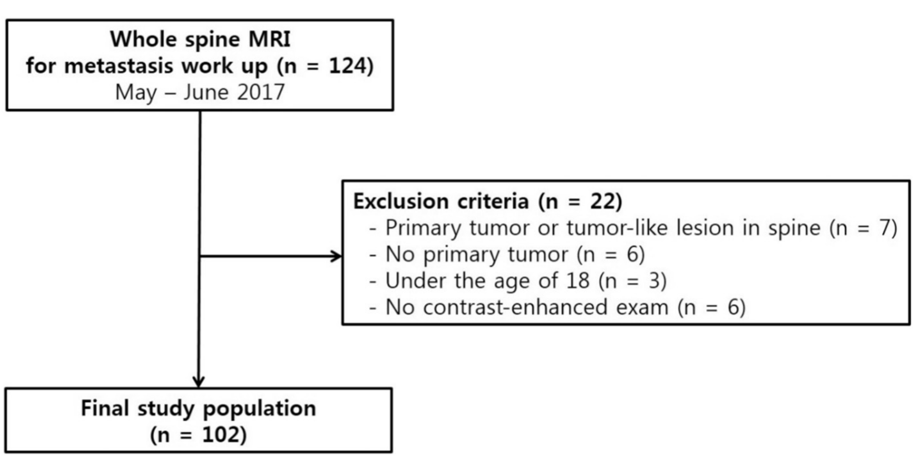


**Fig. 1.** Flow chart for patient selection.

**Table 1**
MR imaging parameters

| | T1-weighted TSE | | T2-weighted TSE | | Contrast-enhanced T1-weigthed multi-echo Dixon TSE | |
|---|---|---|---|---|---|---|
| | Sagittal | Axial | Sagittal | Axial | Sagittal | Axial |
| Repetition time (ms) | 400–650 | 400–650 | 2000–2900 | 3400–4400 | 450–650 | 400–650 |
| Echo time (ms) | 10 | 10 | 120 | 120 | 15 | 15 |
| Field-of-view (cm) | 25–40 | 25–40 | 25–40 | 25–40 | 25–40 | 15 |
| Matrix | 440 × 429 | 440 × 429 | 304 × 225 | 440 × 429 | 352 × 391 | 304 × 260 |
| Slice thickness/gap (mm) | 4.0/0.4 | 8.0/2.0 | 4.0/0.4 | 8.0/2.0 | 4.0/0.4 | 8.0/2.0 |
| Mean acquisition time | | | | | 6 min 47 s | 6 min 54 s |

**Table 2**
Category according to the usefulness of contrast-enhanced MR imaging

| | Presumed metastatic lesion | | | | | | | | | | | | | Presumed non-metastatic lesion |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Definitely useful | | | | | | | Equivocal | | | | | Not useful | |
| | Useful in characterization[b] | | | | | Useful in detection[c] | Useful in both | | | | | | | |
| Category[a] | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| Probable metastasis | ↓ | ↓ | – | ↑ | ↑ | ↑ | ↑ | ↓ | ↓ | ↓ | – | ↑ | – | |
| Equivocal | – | ↓ | ↓ | ↓ | ↓ | – | ↓ | ↑ | ↑ | ↑ | ↑ | ↑ | – | |
| Probably benign | ↑ | ↑ | ↑ | – | ↑ | ↓ | ↓ | – | ↑ | ↓ | ↓ | ↓ | – | |

[a] The patients were divided into 14 categories according to the total number of changes made in the confidence rating (probable metastasis, equivocal, probably benign) between session 1 (conventional imaging, T1- and T2WI) and session 2 (addition of CE-MR imaging to conventional imaging) as follows: Category 1, decreased number of probably metastatic segments, no change of equivocal segments, increased number of probably benign segments; Category 2, decreased number of probably metastatic segments, decreased number of equivocal segments, increased number of probably benign segments; Category 3, no change of probably metastatic segments, decreased number of equivocal segments, increased number of probably benign segments; Category 4, increased number of probably metastatic segments, decreased number of equivocal segments, no change of probably benign segments; Category 5, increased number of probably metastatic segments, decreased number of equivocal segments, increased number of probably benign segments; Category 6, increased number of probably metastatic segments, no change of equivocal segments, decreased number of probably benign segments; Category 7, increased number of probably metastatic segments, decreased number of equivocal segments, decreased number of probably benign segments; Category 8, decreased number of probably metastatic segments, increased number of equivocal segments, no change of probably benign segments; Category 9, decreased number of probably metastatic segments, increased number of equivocal segments, increased number of probably benign segments; Category 10, decreased number of probably metastatic segments, increased number of equivocal segments, decreased number of probably benign segments; Category 11, no change of probably metastatic segments, increased number of equivocal segments, decreased number of probably benign segments; Category 12, increased number of probably metastatic segments, increased number of equivocal segments, decreased number of probably benign segments; Category 13, no change of probably metastatic segments, no change of equivocal segments, no change of probably benign segments; Category 14, all segments are probably benign in both session 1 and session 2. Category 1, 2, 3, 4, 5, 6, and 7 were classified as definitely useful group of CE-MR imaging. Category 8, 9, 10, 11, and 12 were classified as equivocal of CE-MR imaging. The Category 13 was classified as not useful group of CE-MR imaging. The Category 14 was classified as presumed non-metastatic lesion group.

[b] Useful in characterization means that CE-MR imaging was useful to distinguish whether the detected lesion was metastatic or benign.

[c] Useful in detection means that CE-MR imaging was useful to detect new metastases that were not detected in the evaluation via conventional imaging alone.

**Table 3**
Usefulness of contrast-enhanced MR imaging

| | Presumed metastatic lesion | | | | | Presumed non-metastatic lesion |
|---|---|---|---|---|---|---|
| | Definitely useful | | | Equivocal | Not useful | |
| | Useful in characterization | Useful in detection | Useful in both | | | |
| Reader 1 | | | | | | |
| Number of patients | 14 | 12 | 15 | 14 | 13 | 34 |
| Total | | 41 (40) | | 14 (14) | 13 (13) | 34 (33) |
| Reader 2 | | | | | | |
| Number of patients | 20 | 17 | 17 | 12 | 10 | 26 |
| Total | | 54 (53) | | 12 (12) | 10 (10) | 26 (26) |
| Reader 3 | | | | | | |
| Number of patients | 21 | 6 | 13 | 22 | 17 | 23 |
| Total | | 40 (39) | | 22 (22) | 17 (17) | 23 (23) |

Note − Data represent number of subjects (%).

17 years of experience in spine imaging; reader 2, a fellowship-training radiologist with 7 years of experience in spine imaging; reader 3, a resident-training radiologist with 9 months of experience in spine imaging) retrospectively reviewed MR images. Each radiologist interpreted the MR images independently and knew only that the patients underwent MR imaging for evaluation of metastasis.

Each patient's spine MR imaging was interpreted twice by each radiologist. The two interpretations reflected two different MR imaging protocols presented at distinct readout sessions: 1) conventional MR imaging (T1- and T2-weighted images); 2) addition of CE-MR imaging

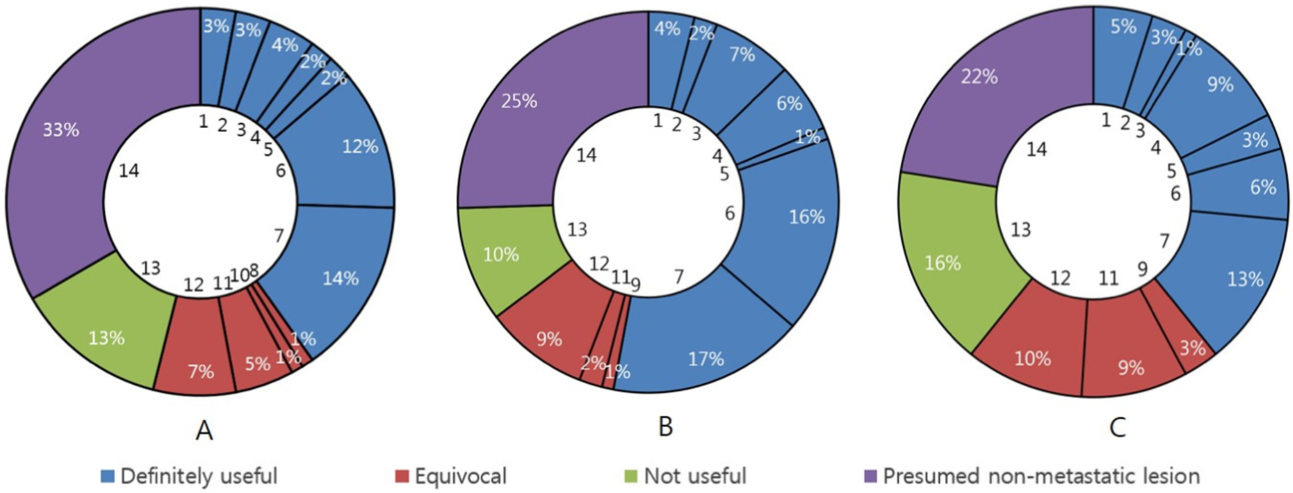


**Fig. 2.** Graphs of usefulness of contrast-enhanced MR imaging for each reader. A. reader 1, B. reader 2, C. reader 3. Numbers inside donut circle refer to the categories.

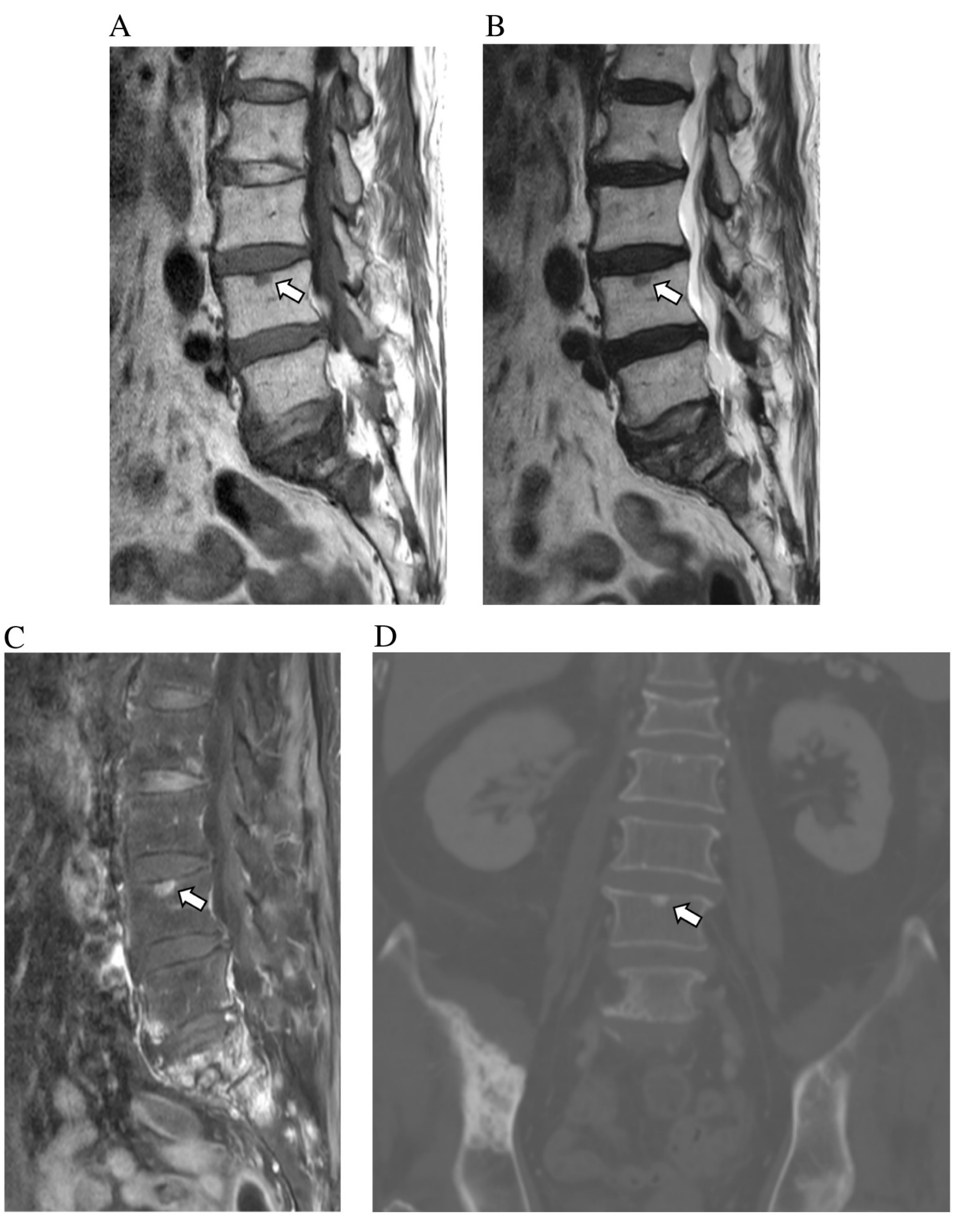


**Fig. 3.** MR images in an 80-year-old man with lung cancer. A, B. Sagittal T1-weighted (A) and sagittal T2-weighted (B) turbo spin-echo MR images show a hypointense lesion at the upper endplate of the L4 vertebral body (arrow) and upper sacrum. C. Sagittal fat-suppressed contrast-enhanced T1-weighted image shows enhancement of the L4 (arrow) and upper sacral lesions. D. Coronal computed tomography reformatted image shows a sclerotic lesion at the L4 vertebral body (arrow) and right pelvic bone. The masses were concluded to be osteoblastic metastases. All three readers interpreted the L4 lesion as equivocal metastasis during session 1 (reading of T1- and T2-weighted images) and as probable metastasis during session 2 (reading of contrast-enhanced images in addition to conventional images). The reading category was classified as category 4 (increased number of probably metastatic segments, decreased number of equivocal segments, no change of probably benign segments during session 2, with reference to session 1; useful in characterization of metastasis) and the degree of usefulness of contrast-enhanced imaging was determined as definitely helpful. All three readers recorded the subjective overall usefulness as 2, the highest score.


**Fig. 4.** MR images in a 77-year-old man with colon cancer. A, B. Sagittal T1-weighted (A) and sagittal T2-weighted (B) turbo spin-echo MR images show no definite spinal metastasis. C. Sagittal fat-suppressed contrast-enhanced T1-weighted image shows a suspected metastatic mass with rim enhancement (arrow). Computed tomography-guided biopsy was performed, and the mass was confirmed as metastasis. None of the three readers could detect the metastasis during session 1 (reading of T1- and T2-weighted images), but all detected the metastasis during session 2 (reading contrast-enhanced images in addition to the conventional images). Reading category was classified as 6 (increased number of probably metastatic segments, no change of equivocal segments, and decreased number of probably benign segments during session 2, with reference to session 1; useful in detection of metastasis) and the degree of usefulness of the contrast-enhanced imaging was determined as definitely helpful. All three readers recorded the subjective overall usefulness as 2, the highest score.

to conventional MR imaging. The reading sessions for the same patient were separated by at least 2 weeks to decrease recall bias. Reports from previous readout sessions were not consulted, reviewed, or altered at subsequent sessions.

The number of spine segments showing bone marrow involvement was recorded according to a confidence rating on a 3-point scale (probable metastasis, equivocal, probably benign). The spine segments were divided into the cervical vertebral body, cervical posterior element, thoracic vertebral body, thoracic posterior element, lumbar vertebral body, lumbar posterior element, and sacral vertebral body. The sacrum was evaluated only at the vertebral body position, because it was difficult to count the involved segments in the posterior element. To summarize, the number of spine metastases in each of the seven segments was counted according to the confidence rating. For example, if the metastases were in the whole spine, the number of probable metastases would be 7 cervical vertebral bodies, 7 cervical posterior elements, 12 thoracic vertebral bodies, 12 thoracic posterior elements, 5 lumbar vertebral bodies, 5 lumbar posterior elements, and 5 sacral vertebral bodies. Spinal canal metastases, including epidural extension, leptomeningeal metastasis, and intramedullary metastasis, were also

**Table 4**
Usefulness of contrast-enhanced MR imaging depending on clinical information and number of involved segments on conventional MR imaging

| | Presumed metastatic lesion | | | $p$ | Presumed non-metastatic lesion |
|---|---|---|---|---|---|
| | Definitely useful | Equivocal | Not useful | | |
| Reader 1 | | | | | |
| Age[a] | 67.3 ± 11.3 (40–88) | 67 ± 14.2 (38–87) | 62.3 ± 12.2 (41–80) | 0.434 | |
| Sex | | | | 0.128 | |
| Male | 28 | 10 | 5 | | |
| Female | 13 | 4 | 8 | | |
| Primary cancer | | | | 0.727 | |
| Lung | 12 | 4 | 2 | | |
| Prostate | 10 | 4 | 4 | | |
| Gastrointestinal | 5 | 1 | 3 | | |
| Miscellaneous[b] | 14 | 5 | 4 | | |
| Type | | | | 0.39 | |
| Pure lytic | 11 | 4 | 1 | | |
| Blastic and mixed | 27 | 6 | 9 | | |
| Unknown[c] | 3 | 4 | 3 | | |
| Number of segment on session 1[a] | 10.1 ± 13.3 (0–47) | 6.7 ± 13.6 (0–52) | 21.5 ± 25.2 (0–52) | 0.046 | |
| Total | 41 | 14 | 13 | | 34 |
| Reader 2 | | | | | |
| Age[a] | 67.4 ± 14.5 (18–91) | 62.8 ± 12.8 (38–78) | 60.7 ± 11.7 (45–80) | 0.28 | |
| Sex | | | | 0.279 | |
| Male | 30 | 5 | 3 | | |
| Female | 24 | 7 | 7 | | |
| Primary cancer | | | | 0.027 | |
| Lung | 11 | 5 | 3 | | |
| Prostate | 20 | 0 | 1 | | |
| Gastrointestinal | 7 | 2 | 2 | | |
| Miscellaneous[b] | 16 | 5 | 4 | | |
| Type | | | | 0.431 | |
| Pure lytic | 11 | 4 | 1 | | |
| Blastic and mixed | 32 | 6 | 7 | | |
| Unknown[c] | 11 | 2 | 2 | | |
| Number of segment on session 1[a] | 9.3 ± 12.7 (0–53) | 7.4 ± 14.7 (0–53) | 22.7 ± 26.1 (0–53) | 0.033 | |
| Total | 54 | 12 | 10 | | 26 |
| Reader 3 | | | | | |
| Age[a] | 68.6 ± 11.2 (38–88) | 64.5 ± 17.1 (18–86) | 60.5 ± 12.1 (41–85) | 0.104 | |
| Sex | | | | 0.827 | |
| Male | 25 | 12 | 11 | | |
| Female | 15 | 10 | 6 | | |
| Primary cancer | | | | 0.619 | |
| Lung | 13 | 5 | 2 | | |
| Prostate | 10 | 6 | 6 | | |
| Gastrointestinal | 6 | 4 | 3 | | |
| Miscellaneous[b] | 11 | 7 | 6 | | |
| Type | | | | 0.92 | |
| Pure lytic | 9 | 2 | 5 | | |
| Blastic and mixed | 26 | 7 | 11 | | |
| Unknown[c] | 5 | 13 | 1 | | |
| Number of segment on session 1[a] | 9.2 ± 13.6 (0–53) | 6.0 ± 15.3 (0–53) | 35.1 ± 25.1 (0–53) | < 0.001 | |
| Total | 40 | 22 | 17 | | 23 |

Note − Data represent number of subjects (%), except where noted otherwise.
[a] Data are indicated as mean ± standard deviation with ranges in parentheses.
[b] Primary cancer < 5 are classified as miscellaneous, and the miscellaneous cases are excluded from the statistical analysis.
[c] Cases without radiograph or computed tomography images within 6 months from MR examination to evaluate the metastatic type are classified as unknown, and the unknown cases are excluded from the statistical analysis.

evaluated. Epidural extension was graded into 6 (0, 1a, 1b, 1c, 2, 3) grades according to the epidural spinal cord compression scale grading [17]. The involvement of leptomeningeal and intramedullary metastases was recorded as presence or absence. In session 2, the subjective overall usefulness of CE-MR imaging (0 = no, 1 = slightly, 2 = much), which was a subjective opinion as to whether CE-MR imaging helped to determine whether metastases were present, was additionally recorded. Each radiologist also recorded the time required for reading MR images at each session.

One radiologist (reader 2) evaluated metastatic bone type using radiography and computed tomography images obtained within 6 months of the MR imaging. The metastatic bone type was divided into lytic, mixed, and blastic [18].

### *2.4. Statistical analysis*

We consulted a statistician (professor of medical statistics with 8 years of experience in statistics) about analysis of our data. All statistical analyses were performed with the R software package (version 3.4.1;R Foundation for Statistical Computing, Vienna, Austria) and SPSS 19.0 (IBM Corp., Armonk, NY, USA).

For analysis, the patients were divided into 14 categories according to the total number of changes made in the confidence rating (probable metastasis, equivocal, probably benign) between session 1 (conventional imaging, T1- and T2-weighted imaging) and session 2 (addition of CE-MR imaging to conventional imaging) (see Table 2). For example, Category 4 involved an increased number of probably metastatic segments, a decreased number of equivocal segments, and no change in the

**Table 5**
Usefulness of contrast-enhanced MR imaging depending on anatomical level and position

| | Presumed metastatic lesion | | | $p$ | Presumed non-metastatic lesion |
|---|---|---|---|---|---|
| | Definitely useful | Equivocal | Not useful | | |
| Reader 1 | | | | | |
| Level | | | | 0.892 | |
| Cervical | 24 | 4 | 11 | | 63 |
| Thoracic | 34 | 10 | 17 | | 41 |
| Lumbar | 27 | 5 | 17 | | 53 |
| Sacrum[a] | 22 | 3 | 9 | | 68 |
| Position | | | | 0.226 | |
| Vertebral body | 34 | 14 | 18 | | 36 |
| Posterior element[a] | 32 | 6 | 9 | | 55 |
| Reader 2 | | | | | |
| Level | | | | 0.507 | |
| Cervical | 28 | 4 | 9 | | 61 |
| Thoracic | 40 | 11 | 15 | | 36 |
| Lumbar | 32 | 7 | 18 | | 45 |
| Sacrum[a] | 21 | 2 | 13 | | 66 |
| Position | | | | 0.965 | |
| Vertebral body | 49 | 12 | 14 | | 27 |
| Posterior element[a] | 36 | 9 | 9 | | 48 |
| Reader 3 | | | | | |
| Level | | | | 0.019 | |
| Cervical | 21 | 10 | 13 | | 58 |
| Thoracic | 29 | 20 | 16 | | 37 |
| Lumbar | 35 | 9 | 22 | | 36 |
| Sacrum[a] | 20 | 1 | 15 | | 66 |
| Position | | | | 0.148 | |
| Vertebral body | 39 | 22 | 18 | | 23 |
| Posterior element[a] | 32 | 8 | 17 | | 45 |

Note − data represent number of subjects.

[a] The sacrum was evaluated only at the vertebral body because it is difficult to count the involved segments of the posterior element.

number of probably benign segments (Fig. 3); Category 6 involved an increased number of probably metastatic segments, no change in the number of equivocal segments, and a decreased number of probably benign segments (Fig. 4). We aggregated the categories into four groups according to the degree of usefulness of CE-MR imaging: (1) definitely useful group, Categories 1, 2, 3, 4, and 5 as useful in characterization of metastasis, Category 6 as useful in detection of metastasis, and Category 7 as useful in both characterization and detection of metastasis (useful in characterization means that CE-MR imaging was useful to distinguish whether the detected lesion was metastatic or benign; useful in detection means that CE-MR imaging was useful to detect new metastases that were not detected in the evaluation via conventional imaging alone); (2) equivocal group, Categories 8, 9, 10, 11, and 12; (3) not useful group, Category 13; and (4) presumed non metastatic group, Category 14. The clinical information (age, sex, and primary cancer) and metastatic bone type were analyzed with Fisher's exact test and the number of probably metastatic segments in session 1 was compared among the definitely useful, equivocal, and not useful groups using the Kruskal-Wallis test.

Grouping according to the degree of usefulness of CE-MR imaging at each anatomical level (cervical, thoracic, lumbar, sacrum) and anatomical position (vertebral body, posterior element) was performed in the same way and compared among the three groups with Fisher's exact test.

Epidural extensions between session 1 and session 2 were assessed using Wilcoxon's signed-rank tests. Inter-reader reliability for the categories of three readers was assessed using the intraclass correlation coefficient (ICC). The degree of agreement based on the ICC value was interpreted using the following criteria: 0–0.20, poor; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good; and 0.81–1.00, excellent [19]. For all tests, $p < 0.05$ was considered indicative of a statistically significant difference.

## 3. Results

The readers assigned 39–53% of cases to the definitely useful group, 12–22% of cases to the equivocal group, 10–17% of cases to the not useful group, and 23–33% of cases to the presumed non-metastatic lesion group. In the definitely useful group, the number of cases assigned to the "useful in characterization of metastasis," "useful in detection of metastasis," and "useful in both characterization and detection of metastasis" groups were 14, 12, and 15 cases for reader 1, respectively; 20, 17, and 17 cases for reader 2, respectively, and 21, 6, and 13 cases for reader 3, respectively (Table 3, Figs. 3 and 4). Results of each category are summarized in Fig. 2.

The number of probably metastatic segments in session 1 was significantly different between the definitely useful, equivocal, and not useful groups for all readers ($p = 0.046$ for reader 1, $p = 0.033$ for reader 2, and $p < 0.001$ for reader 3). In contrast, age, sex, primary cancer, metastatic bone type, anatomical level, and anatomical position were not significantly different among the three groups for all readers, excepting primary cancer for reader 2 and anatomical level for reader 3 ($p \geq 0.128$) (Tables 4 and 5).

Epidural extension was not significantly different between session 1 and session 2 for all readers ($p \geq 0.30$ for all). Leptomeningeal and intramedullary metastasis could not be calculated because of the small sample size ($n < 2$). Inter-reader reliability for the categories assigned by the three readers was good (ICC = 0.742, $p < 0.001$).

The subjective overall usefulness score of CE-MR imaging was 1.00 ± 0.84 for reader 1, 1.31 ± 0.72 for reader 2, and 1.57 ± 0.50 for reader 3. The time taken for reading images in session 1 was 4 h (26 studies/h) for reader 1, 5 h for reader 2 (20 studies/h), and 6 h (17 studies/h) for reader 3, while that for reading images in session 2 was 5 h (20 studies/h) for reader 1, 6 h and 30 min for reader 2 (16 studies/h), and 8 h (13 studies/h) for reader 3.

## 4. Discussion

Our study showed that the addition of CE-MR imaging was useful for objectively detecting and characterizing spinal segments with metastases in 39–53% of cases. It was also useful subjectively. However, there were no clinical or radiological factors that could predict the usefulness of CE-MR imaging in evaluating spinal metastases, except for the number of metastatic segments.

MR imaging is the only imaging technique that allows direct visualization of bone marrow and its components with high spatial resolution. The combination of unenhanced T1-weighted- and fat suppression-sequences have shown to be most useful for the detection of bone marrow abnormalities, and are able to discriminate benign from malignant bone marrow changes [20]. However, on conventional images, spinal metastases may mimic or obscure normal red marrow or other benign lesions, such as hemangioma, discogenic endplate changes, and discitis-osteomyelitis, particularly in patients with primary tumor. In our study, after adding CE-MR imaging, the number of spine segments with an equivocal rating decreased, or segments rated as probable metastasis were changed to a rating of probably benign in 13–21%, suggesting that CE-MR imaging can help characterize the spinal metastases. The increase in the number of spine segments with probable metastases after adding CE-MR imaging was 6–17%, which represents cases where CE-MR imaging is helpful in detecting spinal metastases. In addition, 13–17% of cases were helpful in both detection and characterization of spinal metastases. In summary, the addition of CE-MR imaging was useful for the objective detection and characterization of spinal segments with metastases in 39–53% of cases. It was also found to be subjectively useful by all readers, and particularly by the less-experienced radiologist.

We had expected that detection of spinal metastasis in the posterior element and metastases that have relatively less enhancement, such as osteoblastic metastases, might differ significantly between conventional MR imaging evaluation and evaluation with addition of CE-MR imaging to conventional imaging, but found that they were not significantly different. This may be due to the many overlapping imaging features of spinal metastasis [20]. The only factor that was significantly different among the three groups in all readers was the number of probably metastatic segments in session 1. CE-MR imaging may not be particularly useful in disseminated or diffuse spinal metastases, because T1-weighted imaging is sufficient for diagnosis. The epidural extension was also not significantly different between sessions 1 and 2. In our experience, evaluation of epidural extension in T2-weighted images was better in CE-MR imaging.

The primary goals of treatment are to relieve pain and preserve or restore function when managing patients affected by spinal metastasis [21]. Back pain, the most common presenting symptom in patients with tumor metastasized to the bone or epidural space, often precedes the development of other neurological symptoms by weeks or months, and functional outcome depends on the neurological condition at the time of presentation [22]. Therefore, it is important to evaluate the cause of spinal symptoms in patients with primary cancer; moreover, accurate evaluation of the extent and location of spinal metastasis is also important for planning radiotherapy and surgical treatment [23]. Advances in imaging have improved the sensitivity of detecting spinal metastases and the specificity of differentiating these from other processes that involve the spine; these advances include diffusion-weighted imaging, dynamic contrast imaging, and dual-energy computed tomography [13,24–27]. CE-MR imaging is a widely used, well-established protocol and it is easier to use than the advanced imaging methods mentioned above. The overall additional time required for a whole-spine axial and sagittal CE-MR examination was only about 14 min. Furthermore, the interpretation and helpfulness of adding CE-MR imaging to conventional MR imaging did not differ according to the reader's level of experience, although there was some difference in reading time.

Unlike previous reports [12,28–31] that compared the diagnostic accuracy for spinal metastasis between these radiological modalities, we assigned patients to 14 possible categories, according to the changes in the confidence rating occurring between session 1 and session 2, and then combined these categories into four groups according to the degree of usefulness of CE-MR imaging. It may be inappropriate to define the added CE-MR imaging as a standard reference, because the purpose of the study was to evaluate the usefulness of CE-MR imaging, and the reported value of adding CE-MR imaging to conventional MR imaging for evaluating spinal metastasis is controversial [11–16]. Furthermore, in clinical practice, biopsy is not performed on all spinal metastases, and MR imaging is often used to judge spinal metastases.

There were several limitations to our study. First, we did not compare the radiological findings with a reference standard such as pathological confirmation or with available follow-up imaging to verify the suspicion of a metastatic lesion. Second, there was a possibility of compensatory changes in the number of confidence ratings between sessions 1 and 2 because we used the change in the overall number of confidence ratings for analysis. Third, we did not compare changes in patients' management such as biopsy sites and field of view of radiation therapy between evaluation of conventional imaging and addition of CE-MR imaging. Fourth, the study population was relatively small. The number of individuals in the definitely useful group, but not those in the equivocal and not useful groups, could be subjected to parametric analysis.

## 5. Conclusion

Adding CE-MR imaging to conventional MR imaging was useful for objectively detecting and characterizing spinal segments with metastases in 39–53% of cases. However, there were no clinical or radiological factors that could predict the usefulness of CE-MR imaging in evaluating spinal metastases, except for the number of metastatic segments.

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