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Abstract

We compared gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA) enhanced T1-weighted images (T1-Gd) with the histopathological findings in 13 patients with bone or soft tissue sarcomas. Signal intensity of the viable tumor tissue was increased in T1-Gd in 92% of the patients. The necrotic or cystic areas in the tumor were not enhanced, rendering them distinctly. The degree of enhancement of the edematous area around the tumor was similar to or more marked than that of the tumor in 54% of the patients. Area showing inflammatory cells infiltration and edematous areas in the tumor tissue were also enhanced. Thus, the effect of preoperative chemotherapy in tumor tissues other than necrotic and cystic areas tended to be underestimated in T1-Gd. Its effect should be comprehensively evaluated based on not only T1-Gd but also T2-weighted images and findings of other imaging techniques.

KEYWORDS: gadolinium, diethylenetriaminepentaacetic acid(DTPA), magnetic resonance(MR), bone neoplasms, soft tissue neoplasms

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Gadolinium-DTPA Enhanced Magnetic Resonance Imaging of Bone and Soft Tissue Sarcomas in Comparison with Pathological Findings

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We compared gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA) enhanced T1-weighted images (T1-Gd) with the histopathological findings in 13 patients with bone or soft tissue sarcomas. Signal intensity of the viable tumor tissue was increased in T1-Gd in 92% of the patients. The necrotic or cystic areas in the tumor were not enhanced, rendering them distinctly. The degree of enhancement of the edematous area around the tumor was similar to or more marked than that of the tumor in 54% of the patients. Area showing inflammatory cells infiltration and edematous areas in the tumor tissue were also enhanced. Thus, the effect of preoperative chemotherapy in tumor tissues other than necrotic and cystic areas tended to be underestimated in T1-Gd. Its effect should be comprehensively evaluated based on not only T1-Gd but also T2-weighted images and findings of other imaging techniques.

Key words : **gadolinium, diethylenetriaminepentaacetic acid (DTPA), magnetic resonance (MR), bone neoplasms, soft tissue neoplasms**

Bone and soft tissue tumors have come to be treated surgically with an emphasis on preservation of the affected limb (1). An operation of this nature requires a precise evaluation of the anatomical location of the tumor and the extent of its invasion into the surrounding tissues (2). Magnetic resonance imaging (MRI) has high contrast resolution and provides images in various directions. In bone and soft tissue tumors, this method is useful for visualizing tumor extension into the bone marrow or outside the bone (3, 4). However, it is difficult to make a qualitative diagnosis of the tumor except in specific cases, or to differentiate the tumor from the surrounding edematous area (5). In recent years, the advantages of Gd-DTPA enhanced T1-weighted images (T1-Gd) that allow more accurate differentiation have reported (6). However, there are only a few reports on T1-Gd of bone and soft tissue tumors, and its usefulness in cases of these tumors has not been established. We analyzed T1-Gd in comparison with histopathological findings in 13 patients with bone and soft tissue sarcoma in order to address the question of the usefulness of the technique.

Materials and Methods

The subject group consisted of 13 patients (9 with bone sarcoma and 4 with soft tissue sarcoma) in whom

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Table 1 Diagnosis and chemotherapy on the 13 patients included in the study

Diagnosis	Number of patients	
	with chemotherapy	without chemotherapy
Bone tumors		
Osteosarcoma	4	0
Ewing's sarcoma	1	0
Malignant fibrous histiocytoma	2	0
Malignant giant cell tumor	1	0
Chondrosarcoma	0	1
Soft tissue tumors		
Synovial sarcoma	1	1
Liposarcoma	0	1
Recurrent osteosarcoma in muscles	1	0
Total	10	3

T1-weighted images (T1WI), T2-weighted images (T2WI), and T1-Gd could be compared with the resected specimens. Preoperative chemotherapy was administrated to 10 patients (Table 1). T1WI (TR, 600 ms; TE, 25 ms), T2WI (TR, 2,000 ms; TE, 100 ms), and T1-Gd (TR, 600 ms; TE, 25 ms; scanning starts immediately after injection of 0.1 mmol/kg of Gd-DTPA) were obtained using a 0.5 T superconducting device (RESONA: Yokogawa Medical, Japan). Enhanced degrees and structures in or around the tumor, and the effects of chemotherapy were evaluated in comparison with histopathological findings of the resected specimens.

The effects of preoperative chemotherapy were evaluated hitopathologically and determined by the necrosis rate of a longitudinally cut specimen from the largest plane of the tumor.

Results

Enhanced tissues in the tumor. Tumor cells at various stages of viability were present in the tumor especially in the patients treated with preoperative chemotherapy. We defined the area which is not thought to be completely nonviable as viable tumor area, and divided enhancement degrees of viable tumor tissues from the 13 patients into 4 grades: (−) to (＋); (−) is negative, (±) is uncertain whether enhanced or not, (+) is slightly enhanced, and (＋) is strongly enhanced (the same intensity as fat). The areas including viable tumor cells were (+) or (＋) in 12 patients (Table 2). Only in Case 4, clear enhancement effect of viable tumor cells was not found. Areas free of tumor cells that consisted of necrotic and cystic tissues were not enhanced in any patient. The enhanced tissues in the tumor other than the viable tumor cell areas corresponded to areas showing dilated blood vessels mixed with fibrous tissues and those showing inflammatory cells infiltration (Table 2).

Enhanced structures around the tumor. The degrees of enhancement of the surrounding tumor tissues were similar to or greater than that of the viable tumor area in 7 patients (Cases 2, 4, 6–8, 10, 13). These enhanced tissues consisted of edematous muscle, and inflammatory bone marrow. Such signal intensity of T2WI of the tissue surrounding the tumor was higher than that of the viable tumor in 3 patients (Cases 4, 7, 8). It was possible to differentiate the tumor from the surrounding reactive tissue in these 3 patients.

Evaluation for the effects of preoperative chemotherapy by MRI. The enhanced region is generally thought to be a viable tumor tissue area. Therefore, we evaluated the effect of chemotherapy by defining the enhanced area as the viable tumor area, and comparing the results with histopathological findings (Table 3). The effect of chemotherapy appeared to be about 60 % in T1-Gd but was demonstrated to be 95 % by histopathological examination in Case 1. The effect of chemotherapy appeared to be about 10 % by T1-Gd, but was 97 % histopathologically in Case 3. Since the areas free of viable tumor cells were also enhanced by T1-Gd, it seemed to be difficult to make accurate evaluation for the effects of treatment. However, T1-Gd were useful for evaluating the effectiveness of treatment in patients with a tumor consisting of necrotic and cystic areas after chemotherapy.

Table 2 Enhancement degrees and structures of tissues in or around the tumor

Case No.	Diagnosis	Chemotherapy with (+) without (−)	Enhancement degrees[a] and structures in the tumor			Enhancement degrees[a] and structures around the tumor	
			Viable tumor tissues (degrees)	Necrotic or cystic areas (degrees)	Other enhanced structures in the tumor (histopathological findings)	Enhancement (degrees)	Histopathological findings
Bone tumors							
1	Osteosarcoma	+	++	−	Inflammatory cells, vascular dilation	−	
2	Osteosarcoma	+	+	−	Inflammatory cells, vascular dilation	+	Muscle edema
3	Osteosarcoma	+	++	−	Inflammatory cells, vascularized fibrous tissue	−	
4	Osteosarcoma	+	±	−		++	Muscle edema[b]
5	MFH	+	++	−	Vascularized fibrous tissue	−	
6	MFH	+	++	−	Inflammatory cells, vascularized fibrous tissue	++	Muscle edema
7	Malignant GCT	+	+	−		++	Inflammatory bone marrow[b]
8	Ewing's sarcoma	+	++	−		++	Muscle edema[b]
9	Chondrosarcoma	−	+	−		−	
Soft tissue tumors							
10	Synovial sarcoma	+	++	−		++	Muscle edema
11	Synovial sarcoma	−	++	−		−	
12	Liposarcoma	−	++	−		−	Muscle edema
13	Recurrent osteosarcoma	+	++	−		++	

a: See text for division into 4 grades. *b*: On T2 weight images, the signal intensity of surrounding tumor in cases 4, 7, and 8 was higher than that of viable tumor tissue area. MFH: malignant fibrous histiocytoma, GCT: giant cell tumor

Table 3 Evaluation for effects of preoperative chemotherapy by MRI and histopathological findings

Case No.	Diagnosis	T1-Gd[a] (%)	Histopathological necrosis rate (%)
Bone tumors			
1	Osteosarcoma	60	95
2	Osteosarcoma	60	60
3	Osteosarcoma	10	97
4	Osteosarcoma	5	10
5	MFH	80	95
6	MFH	80	98
7	Malignant GCT	10	20
8	Ewing's sarcoma	50	80
Soft tissue tumors			
10	Synovial sarcoma	70	70
13	Recurrent osteosarcoma	80	80

a: Gd-DTPA enhanced T1 weighted image. MFH, GCT: See Table 2.

Case Presentations

Case 3. A 16-year-old girl with osteosarcoma of the right femur. The signal intensity of the entire tumor was low on T1WI after preoperative chemotherapy (Fig. 1a), and inhomogenous enhancement was observed on T1-Gd (Fig. 1b). The unenhanced area, corresponding to the C area in the resected specimen was necrotic (Figs. 1b, 1d, 1e, and 1g). Possibly-viable cells were observed only in the D area (Figs. 1b, 1d, 1e, and 1h). The other areas lacked viable cells, but were slightly enhanced (Figs. 1b, 1d, 1e, and 1f). The effect of preoperative chemotherapy appeared to be about 10 % on T1-Gd but was 97 % histopathologically.

Case 6. A 27-year-old man with malignant fibrous histiocytoma of the tibia. On T1-Gd, the

B area (vascuralized fibrous tissue area) was enhanced clearly (Figs. 2a, 2b, 2d, 2e, and 2f). Possibly-viable tumor cells were observed only at point C in the resected specimen (Figs. 2b, 2d, 2e, and 2g). The enhanced area was larger than the viable tumor area. The D area was a necrotic cyst caused by chemotherapy, which was not enhanced (Figs. 2b, 2d, 2e, and 2h).

Case 7. A 38-year-old woman with malignant giant cell tumor of the left femur. On T1-Gd, the B area was enhanced clearly (Figs. 3a, 3b, 3d, and 3e). However, this area showed

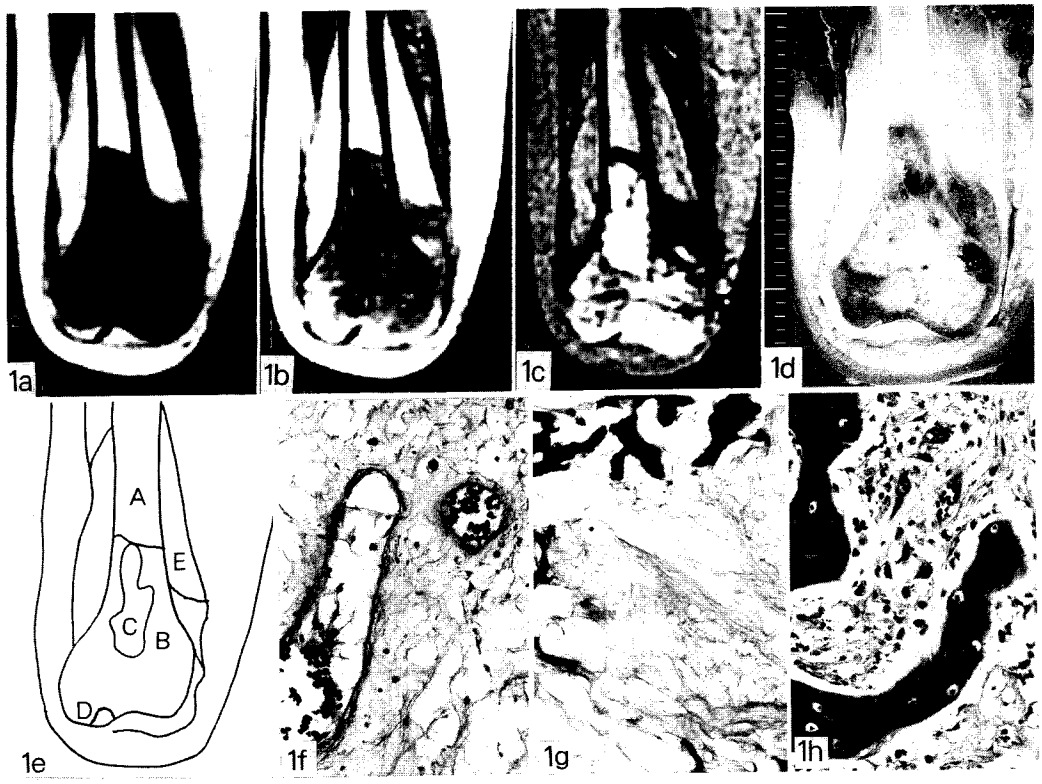
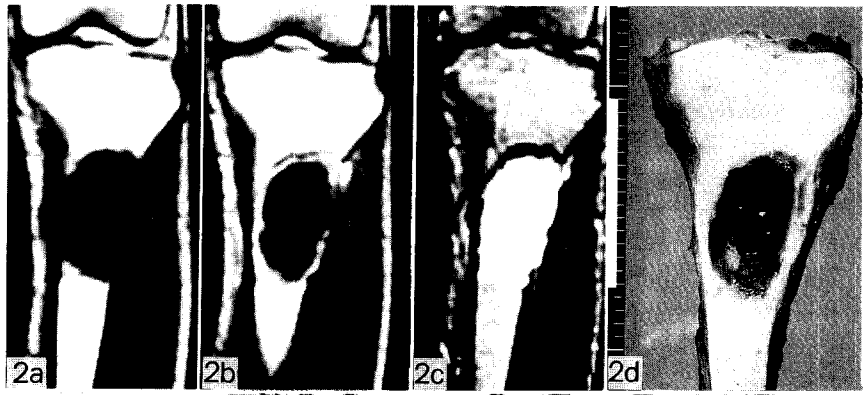


Fig. 1 Case No. 3, osteosarcoma after preoperative chemotherapy. **a**; T1WI. **b**; T1-Gd. **c**; T2WI. **d**; resected specimen. **e**; illustration scheme of the resected specimen. A: unaffected fatty bone marrow. B: vascularized fatty (fibrous) tissue area with inflammatory cell infiltration. C: necrotic area. D: viable tumor cell area. E: Area of atrophic muscle with fatty infiltration. **f**; vascularized fibrous tissue (B) (H.E. stain, × 200). **g**; necrotic tumor tissue after chemotherapy (C) (H.E. stain, × 200). **h**; possibly-viable tumor cells (D) (H.E. stain, × 200).

Fig. 2 Case No. 6, malignant fibrous histiocytoma after preoperative chemotherapy. **a**; T1WI. **b**; T1-Gd. **c**; T2WI. **d**; resected specimen. **e**; illustration schema of the resected specimen. A: unaffected fatty bone marrow. B: vascularized fibrous tissue area. C: possibly-viable tumor cells area. D: cyst formation after chemotherapy. **f**; vascularized fibrous tissue (B) (H.E. stain, × 200). **g**; possibly-viable tumor cells (C) (H.E. stain, × 200). **h**; necrosis after chemotherapy (D) (H.E. stain, × 200).

Fig. 3 Case No. 7, malignant giant cell tumor after preoperative chemotherapy. **a**; T1WI. **b**; T1-Gd image. **c**; T2WI. **d**; resected specimen. **e**; illustration schema of the resected specimen. A: unaffected fatty bone marrow. B: edematous area with inflammatory cell infiltration. C: tumor area (giant cell rich area). D: tumor area (fibrosarcomatous area). E: necrotic area. **f**; fnflammatory cell infiltration (B) (H.E. stain, × 200). **g**; giant cell rich area (C) (H.E. stain, × 200). **h**; fibrosarcomatous area (D) (H.E. stain, × 100).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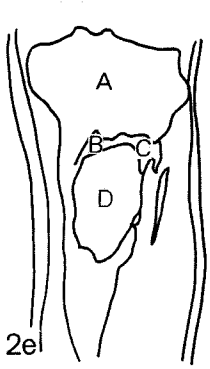
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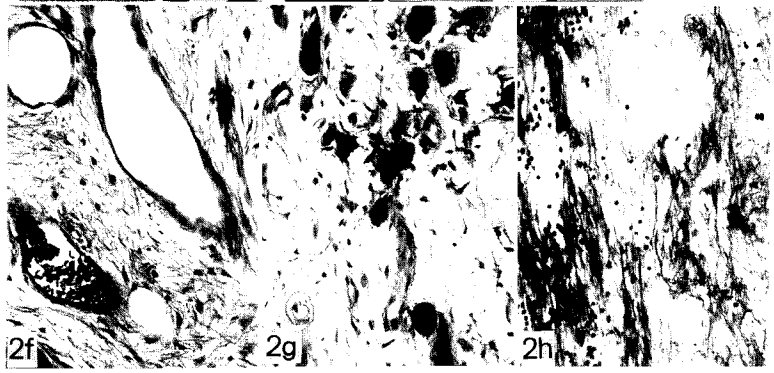
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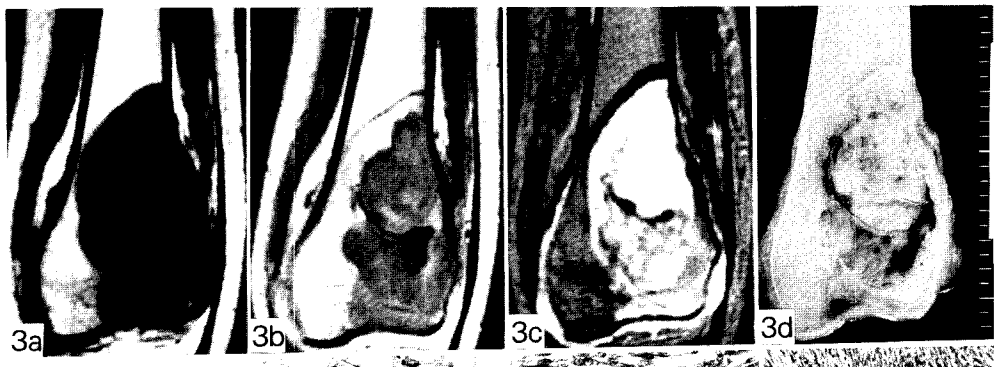
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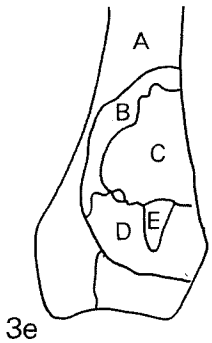
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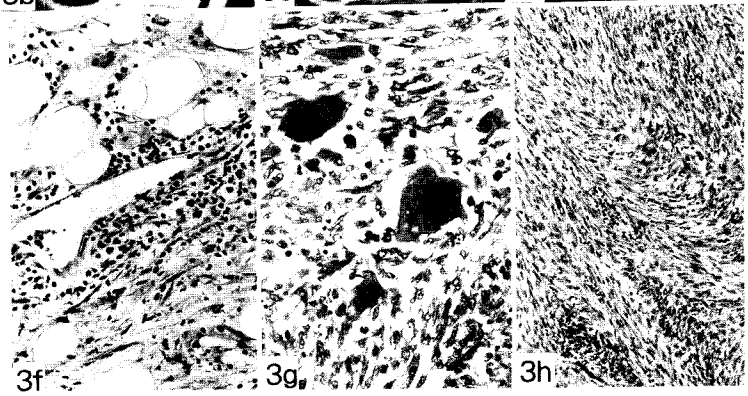
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only inflammatory cell infiltration and no viable tumor tissue (Fig. 3f). The C and D areas were enhanced slightly (Figs. 3a, 3b, 3d, and 3e). The C area was rich in giant cells (Figs. 3g), and the D area was composed of fibrosarcomatous tissue (Fig. 3h); the degrees of enhancement of areas C and D were similar (Fig.3a, 3b, and 3e). There was no relation between grades of malignancies and degrees of enhancement of viable tumor tissues.

Discussion

T1-Gd were reported to be useful for the detailed evaluation of internal properties and vascularity of the tumor since the viable solid portion of the tumor and area rich in blood vessels are enhanced but not the necrotic or cystic areas (7). Beltran *et al.* showed an increased contrast between the tumor and muscle, and clear visualization of the extent of tumor invasion using T1-Gd (8).

In this study, the degree of enhancement of viable tumor tissue was (+) or (++) in 92 % of the patients. Most of the tumor area in which blood supply was abundant was enhanced. Necrotic tissues or cysts were not enhanced in any patients, and these areas could be distinguished on T1-Gd (Figs. 1b and 2b). In the patients treated by chemotherapy, granulomatous and fibrous tissues which are rich in blood vessels but without tumor cells were variously enhanced (Figs. 1b, 1f, 2b, and 2f), and areas showing inflammatory cell infiltration were similarly enhanced (Figs. 3b and 3f). Therefore, residual viable tumor cells in chemotherapy cases were overestimated.

Erlemann *et al.* reported that following preoperative chemotherapy, all areas considered viable upon histopathologic examination, as well as the nonviable zone containing highly vascularized granulation tissue, showed high signal intensity on T1-Gd (9). In addition, the contrast between the tumor and bone marrow or subcutaneous tissue tended to be decreased (Figs. 1b, 2b, and 3b). Tumor/fat and tumor/bone marrow contrast was found to be 37-43 % lower when T1-Gd were used than when unenhanced T1WI were used (10).

Since patients with malignant tumors receive preoperative chemotherapy, differentiation between the tumor and the surrounding edematous reactive zone after chemotherapy is essential to the curative surgery (11). In malignant tumors, a high-signal area is often observed around the tumor on T2WI (8, 10). Ito *et al.* reported that the solid viable portion of the tumor was markedly enhanced while the reactive zone was slightly enhanced on T1-Gd, suggesting the usefulness of these images for differentiating the two areas (12). Another study comparing T1-Gd with resected specimens showed enhancement of richly vascularized as well as possibly edematous structures (7).

In the present study, the degree of enhancement of the edematous area around the tumor was similar to or more marked than that of the tumor in 54 % of the patients (Table 3). Therefore, the differentiation was not always clearly discernible, and there was a risk that the tumor might be estimated to be larger than the actual size. The tumor could be sometimes differentiated from the surrounding edematous area on T2WI due to high signal intensity caused by the relatively abundant water content (Figs. 3c 3d and 3e, B area).

When enhanced areas in images of the patients who had had preoperative chemotherapy were considered to be viable tumor areas, the treatment effect tended to be underestimated in comparison to the histopathological findings. However, in patients showing necrosis or cyst formation, a more accurate evaluation of the effects of preoperative chemotherapy could be obtained on T1-Gd. The effects of preoperative chemotherapy should be evaluated comprehensively based on not only T1-Gd but also T2WI and findings obtained by other imaging techniques.

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