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PET evaluation of fatty tumors in the extremity: Possibility of using the standardized uptake value (SUV) to differentiate benign tumors from liposarcoma

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Objective: The relative utility of various preoperative diagnostic imaging modalities, including PET (utilizing FDG and FMT), CT, and MR imaging, for evaluation of lipoma and liposarcoma, especially well-differentiated liposarcoma, was investigated. ***Methods:*** Imaging findings in 32 patients with histopathologically documented lipoma, including one with fibrolipoma and one with angiolipoma, and 25 patients with liposarcomas whose subtypes included 10 well-differentiated, 10 myxoid, and 5 other types were reviewed retrospectively. Pre-operative imaging included FDG-PET (n = 44), FMT-PET (n = 21), CT (n = 25), and MR imaging (n = 53). ***Results:*** Statistically significant imaging features of MR images favoring a diagnosis of liposarcoma involved lesions containing less than 75% fat ($p < 0.001$) as well as the presence of septa ($p < 0.001$). As compared with well-differentiated liposarcoma, benign lesions were differentiated significantly only by the presence of septa ($p < 0.001$), which also provided significant differentiation on CT ($p < 0.05$). The mean SUVs for malignant tumors were significantly higher than those for benign lesions in both FDG- and FMT-PET analyses ($p < 0.0001$, $p = 0.0011$, respectively). By using a cut-off value for FDG- and FMT-PET set at 0.81 and 1.0 respectively, which provided the highest accuracy, benign lesions were differentiated significantly from liposarcomas ($p < 0.001$, and $p < 0.02$). Furthermore, benign tumors and the three subtypes of liposarcoma were divided significantly into four biological grades by FDG- and FMT-accumulation rates ($rho = 0.793$, $p < 0.0001$; and $rho = 0.745$, $p = 0.0009$, respectively). A cut-off value of 0.81 for FDG-PET provided significant differentiation between benign lesions and well-differentiated liposarcoma ($p < 0.01$). ***Conclusions:*** The presence of septa on MR images differentiated lipomas from liposarcoma, even well-differentiated type. PET analysis, especially FDG-PET, quantitatively provided not only the differentiation but also the metabolic separation among subtypes of liposarcoma. Interpretation of the visual diagnostic modalities requires extensive experience and carries a risk of ignoring a critical portion of malignancy. PET metabolic imaging may be an objective and useful modality for evaluating adipose tissue tumors preoperatively.

Key words: lipoma, liposarcoma, subtype, FDG-PET, FMT-PET

INTRODUCTION

BENIGN LIPOMATOUS TUMORS represent a common group of tumors that cause few complaints or complications, and consist of a great variety of benign lesions of adipose tissue. A representative one, lipoma is the most common benign tumor of the soft tissues,[1] and the lesion closely

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Table 1 Patient characteristics

Patient no.	Age	Sex[a]	Histology	Location[b]	Size (cm)	MRI			CT			PET SUVs	
						Fat>75%	Nodules	Septa	Fat>75%	Nodules	Septa	FDG	FMT
Benign tumors													
1	27	M	Lipoma	IM	7 × 14 × 17	+	+	–	ND[c]	ND	ND	0.1	
2	77	M	Lipoma	IM	8 × 10 × 12	+	–	–	ND	ND	ND	0.24	0.31
3	40	M	Lipoma	IM	5 × 8 × 12	+	–	–	ND	ND	ND	0.36	
4	49	M	Lipoma	IntraM	3 × 12 × 13	+	–	–	ND	ND	ND	0.39	0.28
5	59	M	Lipoma	IM	8 × 14 × 17	ND	ND	ND	+	–	+	0.37	
6	52	F	Lipoma	IM	2 × 5 × 6	+	–	–	ND	ND	ND	0.4	
7	51	F	Lipoma	IM	4 × 8 × 13	+	–	–	ND	ND	ND	0.4	0.21
8	73	M	Lipoma	IntraM	5 × 10 × 20	+	–	+	ND	ND	ND	0.4	0.61
9	75	F	Lipoma	IntraM	6 × 6 × 11	+	–	–	+	–	–	0.42	0.22
10	67	M	Lipoma	IntraM	5 × 10 × 10	+	–	–	ND	ND	ND	0.6	1.2
11	67	F	Lipoma	IM	17 × 18 × 33	+	–	–	ND	ND	ND	0.6	
12	55	F	Lipoma	IM	7 × 10 × 12	+	–	+	ND	ND	ND	0.62	
13	63	F	Lipoma	SC	3 × 4 × 7	+	+	–	ND	ND	ND	0.66	
14	49	M	Lipoma	IM	3 × 8 × 13	+	–	–	+	–	–	0.68	0.26
15	70	F	Lipoma	IM	4 × 6 × 6	+	–	–	+	–	–	0.68	0.39
16	46	M	Lipoma	IntraM	10 × 12 × 17	+	–	+	+	–	+	0.7	
17	66	F	Lipoma	SC	1 × 2 × 2	+	–	–	ND	ND	ND	0.7	
18	44	M	Lipoma	IntraM	13 × 15 × 27	+	–	–	+	–	–	0.8	
19	42	M	Lipoma	IM	3 × 3 × 3	–	–	–	–	–	–	0.8	
20	76	M	Lipoma	IM	12 × 16 × 23	+	–	–	ND	ND	ND	0.8	0.17
21	58	F	Lipoma	SC	5 × 9 × 10	+	–	–	+	–	–	0.9	0.83
22	66	M	Fibrolipoma	IM	3 × 4 × 6	+	–	–	ND	ND	ND	0.9	0.8
23	50	M	Lipoma	IM	2 × 4 × 12	ND	ND	ND	+	–	–	0.97	0.4
24	77	F	Lipoma	IM	4 × 5 × 5	+	–	–	ND	ND	ND	1.5	
25	73	F	Lipoma	IM	5 × 7 × 7	+	–	–	ND	ND	ND		
26	55	M	Lipoma	IM	4 × 4 × 9	+	–	–	ND	ND	ND		
27	71	F	Lipoma	IM	3 × 4 × 4	+	–	–	ND	ND	ND		
28	43	F	Lipoma	IM	3 × 4 × 5	+	–	–	ND	ND	ND		
29	53	F	Lipoma	IM	5 × 10 × 19	+	–	–	ND	ND	ND		
30	44	M	Lipoma	SC	3 × 4 × 6	+	–	–	ND	ND	ND		
31	58	F	Lipoma	SC	6 × 9 × 9	+	–	–	+	–	–		
32	39	M	Angiolipoma	IM	1 × 1 × 2	–	–	–	ND	ND	ND		
Maligant tumors (Liposarcoma)													
33	51	F	Well-differentiated type	IM	3 × 4 × 10	+	–	+	ND	ND	ND	0.5	
34	65	F	Well-differentiated type	IM	3 × 9 × 12	+	–	+	+	–	+	0.82	
35	77	M	Well-differentiated type	IM	9 × 11 × 16	+	–	+	ND	ND	ND	0.83	0.61
36	62	M	Well-differentiated type	IM	3 × 6 × 7	ND	ND	ND	ND	ND	ND	0.87	0.76
37	44	F	Well-differentiated type	IM	2 × 3 × 5	+	–	+	ND	ND	ND	1.58	1.2
38	58	F	Well-differentiated type	IntraM	1 × 1 × 2	–	–	–	ND	ND	ND	1.92	
39	47	M	Well-differentiated type	IntraM	7 × 9 × 12	+	–	+	+	–	+		
40	70	F	Well-differentiated type	IM	5 × 7 × 15	+	–	+	ND	ND	ND		
41	50	F	Well-differentiated type	IM	10 × 15 × 20	ND	ND	ND	+	–	+		
42	66	M	Well-differentiated type	IM	10 × 20 × 25	+	+	+	+	+	+		
43	48	F	Myxoid type	IntraM	2 × 3 × 3	–	–	–	–	–	–	0.79	0.43
44	36	M	Myxoid type	SC	3 × 4 × 6	–	–	–	–	–	–	1.29	
45	39	F	Myxoid type	IM	7 × 8 × 15	–	–	–	–	–	–	1.9	
46	36	M	Myxoid type	SC	6 × 8 × 9	–	–	–	–	–	–	2.4	
47	42	M	Myxoid type	IM	18 × 20 × 22	–	–	–	–	+	–	2.4	1.21
48	42	M	Myxoid type	IM	13 × 14 × 16	–	+	–	–	+	–	2.4	
49	79	F	Myxoid type	IM	10 × 17 × 25	+	+	+	+	+	+	2.5	1.9
50	59	F	Myxoid type	IntraM	8 × 13 × 17	–	–	+	–	–	+	2.57	
51	78	F	Myxoid type	SC	5 × 7 × 8	–	–	–	ND	ND	ND	3.1	
52	46	M	Myxoid type	IntraM	3 × 3 × 10	–	–	–	ND	ND	ND		
53	68	F	Dedifferentiated type	SC	3 × 6 × 10	–	–	+	–	–	+	2.31	
54	66	M	Pleomorphic type	IntraM	8 × 10 × 20	–	–	–	ND	ND	ND	2.4	
55	87	M	Dedifferentiated type	IntraM	9 × 13 × 25	–	+	+	ND	ND	ND	2.4	2.4
56	77	F	Dedifferentiated type	IntraM	12 × 17 × 23	+	+	+	+	+	+	3.48	1.4
57	83	M	Dedifferentiated type	IntraM	31 × 35 × 45	+	+	+	+	+	+	6	2.1

[a]M, Male; F, Female, [b]IM, intermuscular; IntraM, intramuscular; SC, subcutaneous, [c]ND, not done.

resembles normal fat. The resemblance is too great for the fat within a lipoma to be differentiated histologically from normal fat, although biochemical and electron-microscopic differences exist.[2] On the other hand, there is a great variety in the coincidence of mesenchymal tissue within lipomatous tumors. These tumors are divided into several subtypes showing characteristic microscopic picture and specific clinical setting.[1] Despite a wide variety of histological appearances, these tumors do not metastasize and malignant change is extremely rare.[1]

Liposarcoma, a malignant lipomatous lesion, is one of the most common malignant neoplasms of soft tissue.[3] These tumors occur at all ages, but are most commonly found in individuals between 40 and 60 years of age. There is a wide variety of histological features ranging from well-differentiated lipoma-like liposarcoma to extremely cellular or pleomorphic neoplasms, and the clinical behavior of liposarcoma closely reflects its variable microscopic appearance. Two basic histological aspects of sarcoma exist: one being the stage in the development of lipoblasts, and the other being the overall degree of cellularity and cellular pleomorphism. Determination of the histological subtype and degree of differentiation is of utmost importance for prognosis and selection of the proper therapy.[3] It is also noted that differentiation between lipoma and well-differentiated liposarcoma should be done because dedifferentiation occurs in well-differentiated type that has recurred,[4] although simple excision is applied for the well-differentiated type, as it is for lipoma.[3]

The computed tomography (CT) and magnetic resonance (MR) images of fatty masses are characteristically sufficient to suggest their lipomatous nature and allow specific diagnoses. However, although CT and MRI are excellent tools for visualizing fat tissue, they are not sufficiently reliable at distinguishing well-differentiated liposarcoma from lipoma, or at evaluating biologically neoplastic activity in malignant fatty lesions.[5]

Recently, the glucose analogue fluorine-18 fluoro-2-deoxy-D-gulcose (FDG) has been widely used for positron emission tomography (PET) evaluation of musculoskeletal lesions, demonstrating a relationship between FDG uptake and histopathological grade.[6–8] The standardized uptake value (SUV), a quantitative index of tissue uptake of FDG, may provide useful information for differentiating malignant tumors from benign lesions in the musculoskeletal system.[9] In addition to these quantitative analyses, FDG-PET accurately helped to predict the eccentric or peripheral locations of malignant tissue elements in cases with necrotic tissue, fibrosis, or benign-appearing tumor elements, thus providing important guidance at biopsy.[9] However, some benign tumors such as schwannomas and giant cell tumors show high uptake in FDG-PET,[10] resulting in a limited ability to differentiate benign tumors from malignant tumors.[11] To overcome the problems in FDG-PET, we have utilized fluorine-18 alpha-methyltyrosine (FMT) as a tumor-detecting amino acid tracer for PET imaging, and demonstrated that FMT is superior to FDG in the differentiation of malignant tumors from benign musculoskeletal lesions.[12] This advantage of FMT-PET has been demonstrated especially for schwannomas.[13] On the other hand, there are some malignant tumors showing low FDG-SUV, including liposarcoma.[14]

In the present study, 57 patients with histologically diagnosed fatty tissue tumors were evaluated by multimodalities including FDG- and/or FMT-PET. Evaluations using PET analyses in the subtypes of both benign and malignant conditions and the utility in these lesions in combination with other modalities will be discussed from the histological or clinical points of view.

PATIENTS AND METHODS

Patients

Between September 1997 and December 2003, fifty-seven patients (29 males and 28 females), aged 27–87 years with a mean of 58.1 years, who were operated on in our institute, had histopathologically proven fatty tissue tumors, including benign adipose tissue tumors and liposarcoma diagnosed according to Enzinger and Weiss.[1,3] Benign lesions included 30 lipomas, one angiolipoma, and one neural fibrolipoma. Other types of benign adipose tissue tumors were not encountered in this period. We used the term *atypical lipoma* only for subcutaneous lesions, in accordance with the suggestion of the World Health Organization, as suggested by Kransdorf et al.,[5] and such cases were not included in this study. In the present study liposarcoma was classified according to Enzinger and Weiss,[3] and divided into 3 groups that exhibit distinct malignant behavior: well-differentiated (n = 10), myxoid (n = 10), and other types (n = 5). The patients' characteristics including age, sex, depth localization, and size of tumor, the latter of which was evaluated as described previously,[12,13,15] are listed in Table 1. Patients were studied in a prospective manner for the value of various preoperative diagnostic modalities that included CT scan (n = 25; 10 benign, 15 malignant lesions), MR images (n = 53; 30 benign, 23 malignant lesions), FDG-PET (n = 44; 24 benign, 20 malignant lesions), and FMT-PET (n = 21; 12 benign, 9 malignant lesions).

The local Ethics Committee (Gunma University) approved the study, and each individual participating in the study gave his or her informed consent.

Evaluation of CT and MR images

A lesion was considered completely composed of adipose tissue if it demonstrated a signal intensity and character identical to that of the subcutaneous adipose tissue in both CT and MR images. Based on the percentage of fat, the lesions were divided into 2 groups according to Einarsdottir

et al.[16]: higher than 75% or not. Additionally, the presence of nonadipose components of lesions, which according to Kransdorf et al.[5] were categorized into 2 characteristic features, thick septa and nodules, was evaluated. In the current investigation the septa distribution was evaluated by the presence of thick septa only, i.e. those thicker than 2 mm or those that had focal thickening.[5]

Table 2 Patient demographics and lesion location

Demographic	benign tumors (n = 32)	liposarcoma (n = 25)	p value[a]
Sex			
M	17	12	
F	15	13	0.701
Age (y)			
Mean	57.3	59	
Median	56.5	59	
Range	27–77	36–87	0.66
Lesion location			
Subcutaneous	5	4	
Deeper than fascia	27	21	0.7433
Size (cm^3)			
Mean	1056.4	3530.8	
Median	406	756	
Range	2–10098	2–48825	0.1631

[a]Sex and lesion location were compared using the χ^2 test. Age and Size were compared using the unpaired Welch's t-test.

PET studies

PET studies were performed as described before.[10] FDG was synthesized as described previously. FMT was produced in our cyclotron facility using the method described previously.[12] Prior to the PET study, patients fasted for at least 4 hours, at which time normal levels were confirmed by clinical laboratory tests. PET studies were performed using a whole body PET-scanner, SET2400W (Shimizu Coop, Tokyo, Japan) with a 59.5 cm transaxial field of view and a 20 cm axial field of view, which produced 63 image; planes spaced 3.125 mm apart. Transaxial resolution at the center of the field was 4.2 mm. A static, using a simultaneous emission-transmission method with a rotating external source (370 MBq $^{68}Ge/^{68}Ga$ at installation), was initiated 40 min after the injection of 185–350 MBq FDG or FMT. The software was set to provide an 8-min acquisition per bed position and 1–2 bed positions. Attenuation-corrected transaxial images with FDG and FMT were produced by an ordered subset expectation maximization (OS-EM) iterative algorithm (an ordered subset of 16 with 1 iteration). Images were reconstructed into 128 × 128 matrices with pixel dimensions of 4.0 mm in-plane and 3.125 mm axially. Using transaxial images, coronal images with 9.8-mm slice thickness were produced for visual interpretation.

Table 3 MR and CT findings of the fatty tissue tumors

Feature	Benign tumors	Liposarcoma							
		Total		Subtypes					
				Well-differentiated		myxoid		others	
		number	p value[a]	number	p value[a]	number	p value[a]	number	p value[a]
MR images	n = 30	n = 23		n = 8		n = 10		n = 5	
Percentage fat									
≥ 75%	28	10		7		1		2	
< 75%	2	13	**< 0.001**	1	0.846	9	**< 0.001**	3	**0.013**
Septa									
Positive	3	13		7		2		4	
Negative	27	10	**< 0.001**	1	**< 0.001**	8	0.783	1	**< 0.003**
Nodules									
Positive	2	6		1		2		3	
Negative	28	17	0.1164	7	0.3	8	0.543	2	**< 0.02**
CT	n = 10	n = 15		n = 4		n = 8		n = 3	
Percentage fat									
≥ 75%	9	7		4		1		2	
< 75%	1	8	0.0741	0	0.6225	7	**< 0.005**	1	0.944
Septa									
Positive	2	9		4		2		3	
Negative	8	6	0.1181	0	**< 0.05**	6	0.751	0	0.505
Nodules									
Positive	0	6		1		3		2	
Negative	10	9	0.0693	3	0.9755	5	0.138	1	0.058

[a]Imaging findings were compared using the χ^2 test with Yates correction.

PET data analysis

All PET images were prospectively interpreted in routine hard-copy consensus visual review by two experienced doctors, a radiologist and an orthopedic surgeon, and were compared to CT and MR images. For the semiquantitative analysis, functional images of standardized uptake value (SUV) were produced using attenuation-corrected transaxial images, injected dose of FDG and FMT, patient's body weight, and the cross calibration factor between PET and dose calibration. SUV was defined as follows:

$$\text{SUV} = \frac{\text{Radioactive concentration in the tumor (MBq/g)}}{\text{Injected dose (MBq)/patient's body weight (g)}}$$

Regions of interest (ROIs) 1 cm in diameter were drawn on the SUV images over the area corresponding to the tumor, which included the site of maximal FDG or FMT uptake. ROI analysis was conducted by a nuclear radiologist with the aid of corresponding CT scans and MR images. The average SUV in the ROI was defined as the tumor uptake of FDG and FMT.

Statistical analysis

Patient demographics and lesion locations were compared using the χ^2 test for categorized variables. Differences in age and size as well as mean SUV for both FDG and FMT between malignant and benign tumors were evaluated for statistical significance using the unpaired Welch's t-test, and differences among subtypes were evaluated with Bonferroni/Dunn's method as analyses of post hoc test. Spearman's rho rank-order correlation coefficient, corrected for ties, was conducted to study the strength of the relationship between subtypes and the FDG-SUV. To compare the utility of FDG- and FMT-PET for differentiating malignant from benign adipose tumors and to decide the appropriate cut-off value, we used receiver operating characteristic (ROC) curve analysis.[17] The ROC curve is depicted by plotting the true positive rates against false positive rates using all possible cut off values, and the area under the curve (AUC) calculated with an EXCEL program for calculating and graphing the ROC (Watkins, M. W. [2000] [computer software]) provides an index of image quality. The AUC of FDG- and FMT-PET were compared based on Hanley's method.[18] McNemar's test was used for comparison of sensitivities and specificities between FDG- and FMT-PET. A p value less than 0.05 was considered significant.

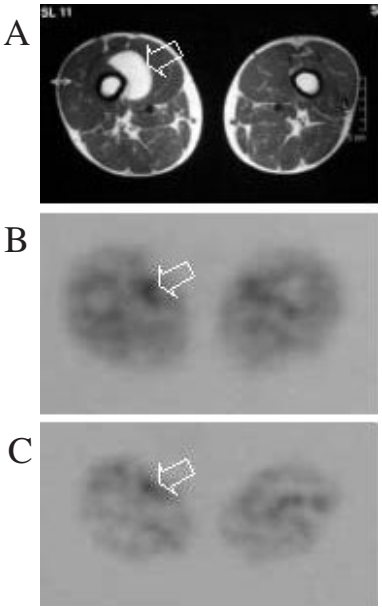

Fig. 1 A 67-year-old male (patient number, 10) with an intramuscular lipoma of the right thigh. T1-weighted MR images (A) demonstrate homogeneous fat signals without nodular or septa structures. PET scan through approximately the same level shows mildly increased FDG (B) and FMT (C) accumulation with SUV of 0.6 and 1.2 respectively.

RESULTS

The demographics and lesion locations are shown in Table 2. Differences in sex and age distributions of patients with benign adipose tissue tumors versus patients

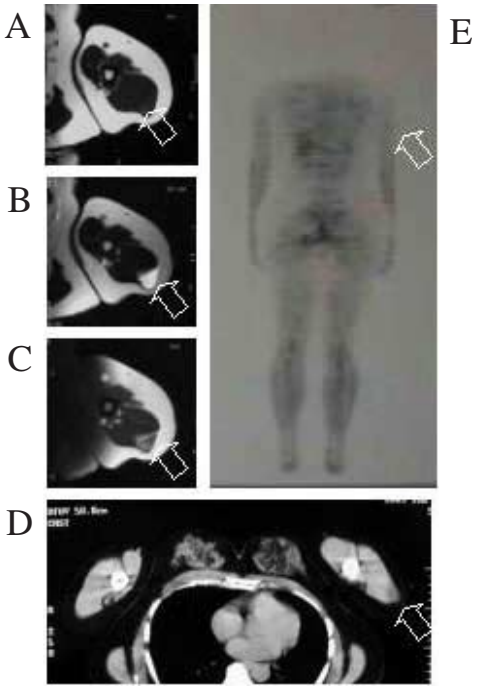

Fig. 2 An intramuscular myxoid type of liposarcoma that developed in the left arm in a 48-year-old female (patient number, 43). T1-weighted images (A) show an intramuscular low-signal lesion with fine gadolinium enhancement (C). T2-weighted images reveal a homogeneous lesion with high signals (B). CT demonstrates a homogeneous lesion with mild density (D). Neither septa nor nodular features were found in either MR images or CT scan. Whole body scan of FDG-PET reveals a mildly increased uptake with SUV of 0.79 localized in left arm.

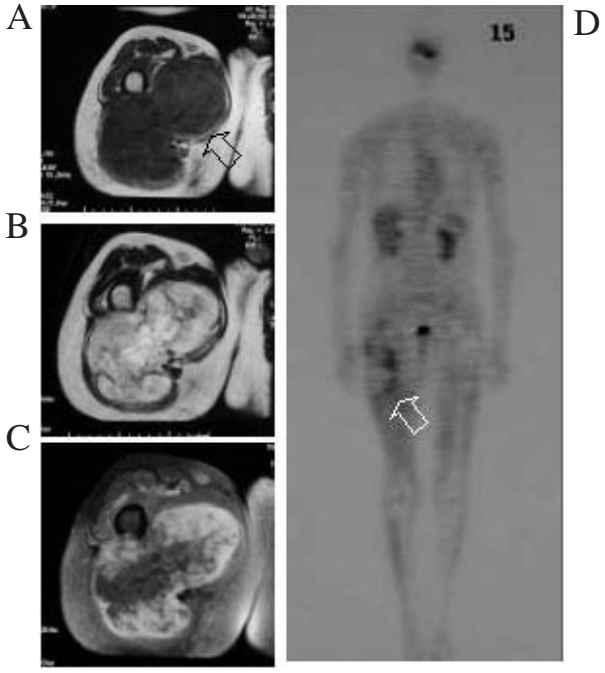

Fig. 3 An intramuscular pleomorphic type of liposarcoma that developed in the right thigh in a 66-year-old male (patient number, 54). T1-weighted images (A) show a heterogeneous low-signal lesion with fine gadolinium enhancement (C). T2-weighted images reveal a heterogeneously high signal lesion (B). Whole body scan of FDG-PET reveals heterogeneously increased uptake spots with SUV of 2.4 localized at the margin of the lesion.

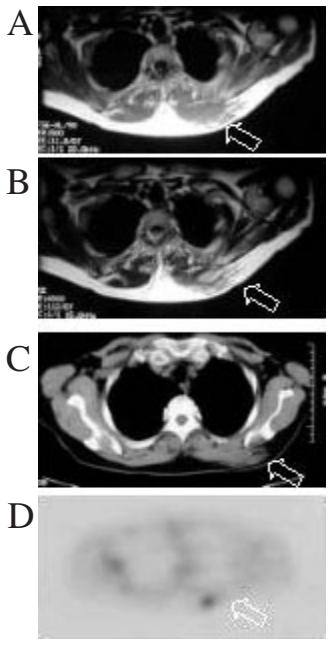

Fig. 4 A subcutaneous dedifferentiated type of liposarcoma that developed in the left back in a 68-year-old female (patient number, 53). Both T1- (A) and T2-weighted (B) images show a heterogeneous structure with mixture of high- and low-signals with nodular structures. CT scan also demonstrates nodular findings in the lesion (C). FDG PET images (D) show a mild uptake lesion with SUV of 2.31.

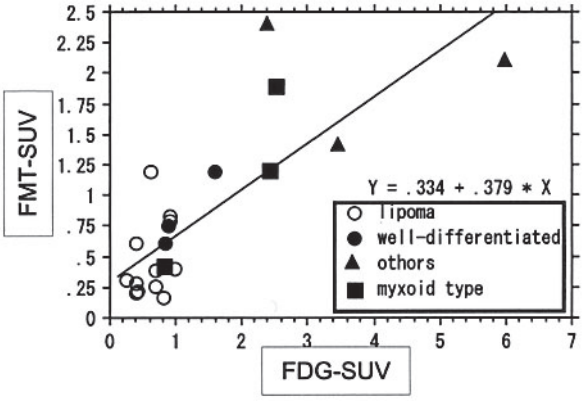

Fig. 5 Correlation between FDG- and FMT-SUVs. A significant correlation was noted ($r = 0.788$, $p < 0.0001$; $n = 21$).

with liposarcoma were not statistically significant, with p values of 0.701 and 0.660, respectively. The sizes of suspicious lesions ranged from 1 × 1 × 2 to 31 × 35 × 45 cm, which were determined by plain radiography, CT, and MRI images, and/or by gross sections of obtained specimens. There were no significant differences between benign and malignant tumors with regard to either depth localization or the size, with p values of 0.7433 and 0.1631, respectively (Table 2).

Imaging features of CT and MR images are provided in Table 3 and were determined at analysis as indicated in the footnote. Most cases (28/30) with benign tumors were composed of tissue that was identical to subcutaneous adipose tissue with more than 75% of fatty tissue MR signals (Fig. 1). This fat percentage was significantly different from that of liposarcomas ($p > 0.001$). However, the fat percentage did not differentiate lipoma from well-differentiated liposarcoma, as expected (Table 3), although most of the other type liposarcomas showed a lower fat percentage (Figs. 2, 3, 4). Significantly, compared with lipomas, septa were seen frequently in liposarcomas. Furthermore, the presence of septa was observed in 7 of 8 (87.5%) patients with well-differentiated liposarcoma, which is a significantly higher percentage than that of benign tumors ($p > 0.001$). In contrast, nodules were not encountered frequently in either lipoma or liposarcomas in the present study, and there were no statistically significant differences between lipoma and liposarcomas ($p = 0.1164$) or well-differentiated liposarcoma ($p = 0.300$) (Table 3). In the CT evaluation, the presence of septa differentiated significantly lipoma from well-differentiated liposarcoma ($p > 0.05$), but not between lipomas and whole cases of liposarcoma. Presumably most cases with myxoid type (Fig. 2) showed absence of septa, although all other liposarcomas exhibited septa in the lesions.

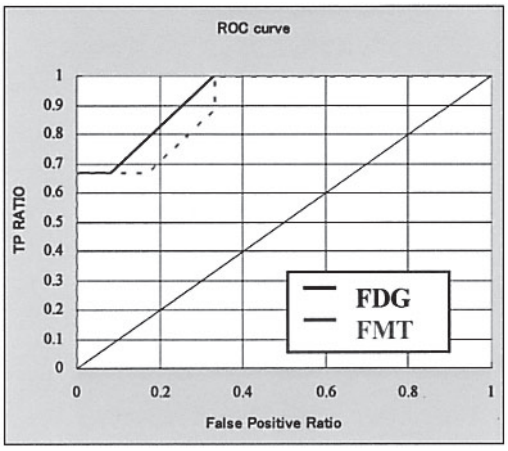

Fig. 6 ROC curves of FDG- (*solid line*) and FMT- (*broken line*) PET. Mean AUC value of each curve was 0.9306 ± 0.052 and 0.9074 ± 0.06, respectively, indicating no significant difference.

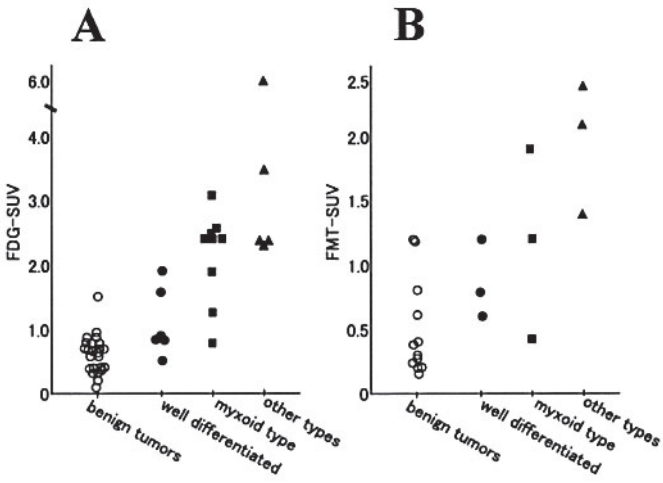

Fig. 7 Plot of tumor SUV versus subtypes for all liposarcomas in FDG- (A) and FMT-PET (B) analyses.

Table 4 Subtype distribution

Feature	Lipoma mean	Liposarcoma					
		Well-differentiated		myxoid type		others	
		mean	p value[a]	mean	p value[a]	mean	p value[a]
Demographic distribution							
Age (y)	57.3	59	0.7296	50.5	0.1568	76.2	**< 0.005**
Size (cm^3)	1056.4	1146.7	0.9674	1858.2	0.7168	11644.4	**< 0.001**
PET distribution							
FDG-SUV	0.625	1.087	0.1325	2.15	**< 0.0001**	3.318	**< 0.0001**
FMT-SUV	0.473	0.957	0.1703	1.18	**< 0.02**	1.967	**< 0.0001**

[a] Differences in age and size as well as mean SUV for both FDG and FMT between malignant subtypes and benign tumors were evaluated for statistical significance using Bonferroni/Dunn's method as analysis of post hoc test.

Tumor SUV of FDG and FMT ranged from 0.10 to 6.00 with a mean value of 1.31 ± 1.14 (n = 44), and from 0.17 to 2.40 with a mean value of 0.84 ± 0.66 (n = 21), respectively. A significant correlation (r = 0.788, p < 0.0001) between FDG and FMT SUVs was found (n = 21) (Fig. 5). The mean SUVs for malignant tumors were significantly higher than those for benign lesions in both FDG- and FMT-PET analyses (2.12 ± 1.53 vs. 0.63 ± 0.09, p < 0.0001, 1.33 ± 0.47 vs. 0.47 ± 0.10, p = 0.0011, respectively).

To differentiate benign tumors from liposarcoma, a cut-off value for FDG- and FMT-PET was set as 0.81 and 1.0, providing the highest accuracy based on the ROC curve analysis, respectively (Fig. 6). Eighteen of 20 malignant lesions and 20 of 24 benign lesions were characterized correctly by FDG-PET. The sensitivity of FDG-PET for correctly diagnosing malignancy was 90.0% with a specificity of 83.3%, resulting in an accuracy of 86.4%. The cut-off value of FDG-PET significantly differentiated malignant and benign lesions according to chi-square test with Yates correction (p < 0.001). On the other hand, with use of a cut-off value of 1.0 for SUV in FMT-PET, six of 9 malignant lesions and ten of 12 benign lesions were characterized correctly. The sensitivity of FMT-PET for correctly diagnosing malignancy was 66.7% with a specificity of 91.7% resulting in an accuracy of 81.0%, providing significant differentiation between benign and malignant lesions (p < 0.02). There was no significant difference in either sensitivity or specificity between the two PET tracers by McNemar's test (p = 0.500 or 0.625, respectively). Also the ROC curves of the two analyses showed no difference in the mean AUC values between FDG-PET (0.9306 ± 0.052) and FMT-PET (0.9074 ± 0.063), indicating the similarity of both PETs with respect to differentiation ability (Fig. 6).

Differences in age and size as well as mean SUV for both FDG and FMT among subtypes were evaluated statistically and shown in Table 4. Age and tumor size of patients with liposarcoma other than well-differentiated or myxoid types were significantly higher than those of the two types of liposarcoma as well as those of benign lesions (p < 0.005). As shown in Figure 7, benign tumors

and the three subtypes of liposarcoma were divided significantly into four biological grades by FDG- and FMT-accumulation rates using Spearman's rho rank-order correlation coefficient (rho = 0.793, $p < 0.0001$; and rho = 0.745, $p = 0.0009$, respectively), while with Bonferroni/Dunn's method as analysis of post hoc test PET values using both tracers of well-differentiated type liposarcoma were not differentiated significantly from those of benign lesions (Table 4). However, when a cut-off value FDG-PET was set as 0.81 for malignancy, 5 of 6 well differentiated-type liposarcomas were characterized correctly. Then the cut-off value provided significant differentiation between benign lesions and well-differentiated liposarcoma according to the chi-square test with Yates correction ($p < 0.01$), indicating the usefulness of FDG-PET in the differentiation of malignancy even in tumors with a fat tissue content of more than 75%.

DISCUSSION

In the current review, we identified several statistically significant features in MR and CT images to help distinguish lipoma from liposarcoma in most cases. One of the most important of these features is an MR image showing the total amount of nonadipose tissue comprising more than 25% of the lesion. Einarsdottir et al. suggested that all lesions with more fat than 75% of tumor volume were histologically diagnosed as lipomas by CT and MRI.[16] Kransdorf et al. also demonstrated that the presence of fat components less than 75% is a significant imaging feature favoring a diagnosis of liposarcoma.[5] However, among subtypes of liposarcoma well-differentiated type was predominantly composed of fat and confidently differentiated from other subtypes of liposarcoma.[19] In the present study, the presence of fat tissue components could not differentiate lipomas from well-differentiated liposarcoma. Thus the total amount of adipose tissue comprising more than 75% of the lesion may not help distinguish benign adipose tissue tumors from well-differentiated liposarcoma.

In the current study, the most striking imaging features were the ones showing the presence of thick septa. This MR imaging feature distinguished significantly benign lipomatous tumors not only from total liposarcomas, but also from well-differentiated liposarcoma. In contrast to the adipose tissue-occupying rate, the presence of septa was predominantly obvious in well-differentiated liposarcoma, as also shown in CT examination. Probably this is due to the finding that septa were not found frequently in myxoid type-liposarcoma (only 2 out of 10). Arkun et al. suggested that well-differentiated liposarcoma was composed mainly of fat with septations on MRI.[20] Jelinek et al. suggested that well-differentiated liposarcoma was predominantly composed of fat, typically with thick septation on MRI and CT.[19] Histologically, the cells characteristic of liposarcoma are often situated along or within variably sized fibrous septa or trabeculae.[3] As suggested by several radiologists,[5,21,22] thick septa may be the most important marker differentiating benign adipose tissue tumors and liposarcoma containing adipose tissue components in MR and CT images.

Previously, we demonstrated that the mean SUVs of malignant musculoskeletal tumors of various histological types were significantly higher than those of musculoskeletal benign lesions in FDG-PET.[10,12,14] Dehdashti et al. demonstrated that with the use of a cutoff value of 2.0, the sensitivity and specificity of FDG PET for differentiation of benign from malignant intraosseous lesions were 93% and 80%, respectively. We have also shown that the cutoff value of 1.9 provides excellent accuracy.[10] However, we reported that some liposarcomas showed low accumulation of FDG and ^{11}C-choline.[14] Also, by using FDG and FMT, three false negative cases were shown to be two liposarcomas and one chondrosarcoma.[12] Actually the SUV value of 1.3 was suggested as a borderline between benign and malignant cartilaginous tumors.[24] Our present data showed that the mean FDG-SUVs for liposarcoma were significantly higher than those for benign tumors, and ROC curve analysis revealed that a cut-off value of 0.81 for FDG-PET was the highest value of accuracy to differentiate significantly between benign tumors and liposarcoma. Thus the SUV value of 0.81 may be a useful borderline differentiating malignant from benign adipose tissue tumors.

Determination of the histological subtype and degree of differentiation is of utmost importance for prognosis and selection of the proper therapy.[3] Simple excision is applied for the well-differentiated type, as performed for lipoma.[3] Addition of radiation to marginal resection is recommended for myxoid-type liposarcoma.[25] Both well-differentiated and myxoid liposarcomas, which are the most common types and account for almost half of all liposarcomas, have a more favorable clinical behavior than the other histological types. MR imaging has been used for the differentiation modality.[26] In the present study, we demonstrated that the mean FDG SUVs of the myxoid type and other types of liposarcoma were significantly higher than that of well-differentiated liposarcoma by two- and three-fold, respectively. These accumulation rates corresponded significantly well to their biological malignant grades. Histological factors relating to these high accumulation rates are not known at present, but, may include higher cellularity in these subtypes than well-differentiated type. Although to elucidate the details further careful histological examination will be necessary, FDG-PET may be a useful modality for non-invasive malignant grading and for the differentiation among subtypes of liposarcoma.

Differentiation between lipoma and well-differentiated liposarcoma is also important because dedifferentiation was reported to occur in a well-differentiated type that had recurred.[4] The mean FDG-SUV of well-differen-

tiated liposarcoma was 1.5-fold higher than that of lipoma, but the difference was not significant by comparing the two groups with Bonferroni/Dunn's method as analysis of post hoc test. Fortunately, however, using a cut-off value of 0.81, provided from the above analysis with whole liposarcomas, well-differentiated liposarcoma was significantly differentiated from lipomas. It should be noted that a well-differentiated liposarcoma without septa on MR images (case 38) showed relatively high uptake of FDG, and not all lipomas with septa revealed relatively high uptake of FDG. This may indicate that FDG accumulation mechanisms in adipose tissue tumors are not related to the formation of thick septa. Visual assessments confirmed the notion since FDG accumulation is diffuse in tumor lesion, but not compatible to the septa location. Thus the lipoma cell-like tumor cells in histological examination may have possible biological metabolisms owing to liposarcoma. Although malignant possibility should be kept in mind in lesions with SUV around 0.8, the quantitative differentiation by using PET may be superior to qualitative evaluation for liposarcoma since the former requires less experience and makes total mass evaluation possible.

A significant correlation between FDG and FMT SUVs was obtained in the current study. There was no significant difference in either sensitivity or specificity between the two PET tracers from McNemar's test. Also the ROC curves of two analyses showed no difference in mean AUC values between the two PET studies. The ability of FMT-PET to differentiate the biological grades of the subtypes was similar to that of FDG-PET. These findings indicate the similarity of both PETs in the differentiation ability with regard to adipose tissue tumors. This is in contrast to our previous findings revealing the superiority of FMT-PET to FDG-PET in the differentiation between benign and malignant musculoskeletal tumors.[12] The reason for the discrepancy is uncertain at present, but, is probably attributable to the fact that benign adipose tissue tumors showed low accumulation in both FDG- and FMT-PET analyses. Thus, once adipose tissue is suspected, FMT-PET may be unnecessary from the time- and cost-consuming points of view.

CONCLUSIONS

The present study demonstrated that the presence of septa on MR images differentiated lipomas from liposarcoma, even well-differentiated type. FDG-PET analysis provided not only the differentiation, but also the quantitatively metabolic separation among subtypes of liposarcoma. Interpretation of the visual diagnostic modalities, including MR and CT images, may require an extensive experience. Also the visual images are only two dimensional, and always carry the risk of ignoring critical portions. In contrast, PET metabolic imaging may represent the potential malignant metabolisms of the whole tumor lesion. FDG-PET may be a useful modality for evaluating adipose tissue tumors preoperatively.

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