Received:
6 July 2015

Revised:
31 August 2015

Accepted:
3 September 2015

doi: 10.1259/bjr.20150552

Cite this article as:

Nakajo M, Nakajo M, Jinguji M, Fukukura Y, Nakabeppu Y, Tani A, et al. The value of intratumoral heterogeneity of ^{18}F -FDG uptake to differentiate between primary benign and malignant musculoskeletal tumours on PET/CT. *Br J Radiol* 2015; **88**: 20150552.

FULL PAPER

The value of intratumoral heterogeneity of ^{18}F -FDG uptake to differentiate between primary benign and malignant musculoskeletal tumours on PET/CT

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Objective: The cumulative standardized uptake value (SUV)-volume histogram (CSH) was reported to be a novel way to characterize heterogeneity in intratumoral tracer uptake. This study investigated the value of fluorine-18 fludeoxyglucose (^{18}F -FDG) intratumoral heterogeneity in comparison with SUV to discriminate between primary benign and malignant musculoskeletal (MS) tumours.

Methods: The subjects comprised 85 pathologically proven MS tumours. The area under the curve of CSH (AUC-CSH) was used as a heterogeneity index, with lower values corresponding with increased heterogeneity. As 22 tumours were indiscernible on ^{18}F -FDG positron emission tomography, maximum standardized uptake value (SUV_{max}), mean standardized uptake value (SUV_{mean}) and AUC-CSH were obtained in 63 positive tumours. The Mann-Whitney U test and receiver operating characteristic (ROC) analysis were used for analyses.

Results: The difference between benign ($n = 35$) and malignant tumours ($n = 28$) was significant in AUC-CSH

($p = 0.004$), but not in SUV_{max} ($p = 0.168$) and SUV_{mean} ($p = 0.879$). The sensitivity, specificity and accuracy for diagnosing malignancy were 61%, 66% and 64% for SUV_{max} (optical threshold value, >6.9), 54%, 60% and 57% for SUV_{mean} (optical threshold value, >3) and 61%, 86% and 75% for AUC-CSH (optical threshold value, ≤ 0.42), respectively. The area under the ROC curve was significantly higher in AUC-CSH (0.71) than SUV_{max} (0.60) ($p = 0.018$) and SUV_{mean} (0.51) ($p = 0.005$).

Conclusion: The heterogeneity index, AUC-CSH, has a higher diagnostic accuracy than SUV analysis in differentiating between primary benign and malignant MS tumours, although it is not sufficiently high enough to obviate histological analysis.

Advances in knowledge: AUC-CSH can assess the heterogeneity of ^{18}F -FDG uptake in primary benign and malignant MS tumours, with significantly greater heterogeneity associated with malignant MS tumours. AUC-CSH is more diagnostically accurate than SUV analysis in differentiating between benign and malignant MS tumours.

INTRODUCTION

Morphological diagnosis of musculoskeletal (MS) tumours has been improved with the advent and development of ultrasonography, CT and MRI. However, the ability to characterize them and to differentiate malignant from benign lesions appears still limited by these morphological imaging modalities.^{1,2}

Glucose analogue fluorine-18 fludeoxyglucose (^{18}F -FDG) represents the lesion glycolytic activity and has been widely used as a tracer of positron emission tomography (PET)³ and PET/CT in oncology.⁴ There is increasing evidence in the literature^{5,6} to support the incremental benefit of ^{18}F -FDG PET/CT in the evaluation of MS tumours along with conventional anatomical imaging. ^{18}F -FDG uptake in

a lesion has been evaluated using a visual scoring system and maximum or mean standardized uptake value (SUV) for characterization of MS tumours. However, there is controversy over the degree of ^{18}F -FDG uptake to differentiate between benign and malignant MS tumours because of a certain amount of overlap in ^{18}F -FDG uptake between them.⁶⁻⁹ In general, ^{18}F -FDG uptake in tumours is not homogeneous, and this heterogeneity might be attributed to necrosis,¹⁰ cellular proliferation,¹¹ blood flow,¹² microvessel density¹³ and hypoxia.¹⁴⁻¹⁶ Thus, the evaluation of the intratumoral heterogeneity of ^{18}F -FDG uptake may provide us with the additional information about the tumour characteristics. Recently, the cumulative SUV-volume histogram (CSH) was reported to be a method to characterize heterogeneity in intratumoral ^{18}F -FDG uptake, and the area

under curve of the cumulative SUV-volume histograms (AUC-CSHs) was used as a heterogeneity index. A lower AUC-CSH was assumed to correspond to a more heterogeneous distribution.^{17,18}

The aim of this study was to examine the value of ¹⁸F-FDG intratumoral heterogeneity in comparison with SUV to discriminate between primary benign and malignant MS tumours.

METHODS AND MATERIALS

Patients

The study group comprised consecutive patients referred to ¹⁸F-FDG PET/CT evaluation of primary MS tumours. Patients were eligible for the study if they underwent surgical resection or biopsy of the tumours. Since the pathological diagnoses were the standards of reference, the lesions without histological confirmation were excluded, even if they underwent ¹⁸F-FDG PET/CT studies.

From January 2011 to December 2012, 100 patients were candidates for this study. 15 patients were excluded because the pathological diagnosis was not made. Finally, 85 patients (46 females and 39 males; mean age 51 ± 19 years; age range 14–83 years) were enrolled.

Imaging protocols

Fluorine-18 fludeoxyglucose positron emission tomography/CT protocols

All PET/CT examinations were performed using a PET/CT system (DiscoveryTM PET/CT 600; GE Medical Systems, Milwaukee, WI). All patients were instructed to fast for at least 5 h before scanning. Image acquisition started 1 h after intravenous injection of ¹⁸F-FDG of 140–210 MBq. At ¹⁸F-FDG injection, their mean plasma glucose level was 98 mg dl^{-1} (range: 83–131 mg dl^{-1}).

A CT acquisition from skull vertex to feet was performed with a 16-slice CT scanner [GE Medical Systems, Milwaukee, WI; 3.75 mm slice thickness, a pitch of 1.75, 120 keV and auto milliamperage (mA) (35–100 mA depending on the patient's total body mass)]. This was followed by the PET acquisition, mirroring the area covered by CT. Acquisition time was 2.5 min per bed position with 14–15 bed positions. Emission data were reconstructed with a three-dimensional ordered-subset expectation maximization algorithm (VuePoint Plus; GE Healthcare, 16 subsets, 2 iterations) to 192×192 matrices using the CT data for attenuation correction. The reconstructed transaxial spatial resolution for PET was 5.1 mm full width at half maximum in-plane.

Image analyses

Visual analyses

All PET/CT images were displayed at the workstation (Advantage Windows Workstation; GE Healthcare). Two nuclear medicine radiologists (MJ and YN with 4 and 2 years' experience in PET/CT interpretation, respectively), who knew the purpose of PET/CT studies but were blinded to pathological results, interpreted PET/CT images. A lesion was scored as 0: no visible uptake; 1: uptake weaker than normal surrounding organs such as muscle or was considered as non-tumoural uptake; 2: mild uptake between 1 and 3; 3: ¹⁸F-FDG uptake similar to liver uptake; and 4: ¹⁸F-FDG uptake higher than liver uptake.¹⁹ In cases of disagreement, consensus was made by the two readers

and another nuclear medicine radiologist (AT with 11 years' experience in PET/CT interpretation). For the determination of diagnostic performance, Scores 0 and 1 were considered negative and Scores 2–4 were considered positive.

Quantitative analysis for fluorine-18 fludeoxyglucose positron emission tomography/CT-positive lesions

Maximum standardized uptake value (SUV_{max}), mean standardized uptake value (SUV_{mean}) and CSH of MS tumours were assessed by another nuclear medicine radiologist (MTN with 9 years' experience in PET/CT interpretation) according to the interpreted results. However, as negative lesions were indiscernible on PET, SUV_{max} , SUV_{mean} and CSH were obtained in positive lesions only. To calculate the SUV_{max} and SUV_{mean} , the volume of interest (VOI) was determined by a SUV threshold contour which accurately delineated tumoural uptake from uptake in the surrounding normal tissues, using dedicated software (Advantage Windows Workstation; GE Healthcare). SUV_{max} was defined as the maximum tissue concentration of ¹⁸F-FDG (in kBq ml^{-1}) in the structure delineated by the VOI divided by the activity injected per gram body weight (in kBq g^{-1}). SUV_{mean} was defined as the average SUV within the delineated VOI.

CSH was reported to be a method to characterize heterogeneity in intratumoural tracer uptake.^{17,18} The following calculation method of CSH was reported by Watabe et al¹⁸ to differentiate between gastrointestinal stromal tumours and abdominal malignant lymphomas. CSH was obtained by plotting the percent volume of a tumour with a SUV above a certain threshold against that threshold, which was varied from 0% to 100% of the SUV_{max} . The area under curve of this plot (AUC-CSH) was used as a heterogeneity index, with lower values corresponding with increased heterogeneity. The available software was not able to automatically calculate the percentage volume of a tumour with threshold SUVs from 0% to 100% continuously at our institution (Kagoshima University); the AUC-CSH was calculated by setting SUV_{max} (%) at 0%, percentages increased every 10% and 100%.

Statistical analyses

Pathological findings were the standards of reference. The PET interpreted results and pathological results were correlated by two nuclear medicine radiologists (MTN and MYN with 11 years' experience in PET/CT interpretation) in consensus. Tumour size was expressed as the maximum diameter of the resected tumour. They also measured lesion size on CT, when the size was not available by surgical resection. The differences in the tumour size, SUV_{max} , SUV_{mean} and AUC-CSH between benign and malignant tumours were examined using the Mann–Whitney *U* test. To examine the applicability of SUV_{max} , SUV_{mean} and AUC-CSH for discrimination between benign and malignant tumours, receiver operating characteristic (ROC) analyses were conducted. Sensitivity, specificity, accuracy, positive-predictive value (PPV) and negative-predictive value (NPV) were calculated for diagnosing malignant MS tumours on visual analysis, SUV_{max} , SUV_{mean} and AUC-CSH. The optimal cut-off points for SUV_{max} , SUV_{mean} and AUC-CSH that maximized the value of the Youden index by the formula: sensitivity + specificity – 1.²⁰ To evaluate interobserver agreement on image interpretation, κ -statistics were used.²¹

Table 1. Subtypes of musculoskeletal tumour and results of visual analysis on fluorine-18 fludeoxyglucose positron emission tomography (PET)/CT

Benign tumours	Number		Malignant tumours	Number	
	Total	PET positive		Total	PET positive
Schwannoma	10	8	Liposarcoma	13	4
Giant-cell tumour	5	5	MFH	11	11
Lipoma	5	0	Myxofibrosarcoma	4	4
Neurofibroma	4	4	Chondrosarcoma	2	1
Desmoid-type fibromatosis	3	3	Osteosarcoma	2	2
Fibrous dysplasia	3	3	Synovial sarcoma	2	2
Osteochondroma	3	3	Dermatofibrosarcoma	1	1
Ganglion	2	0	Epithelioid sarcoma	1	1
PVNS	2	2	Hemangiopericytoma	1	1
Angiolipoma	1	1	Pleomorphic sarcoma	1	1
Chondroblastoma	1	1			
Elastofibroma	1	1			
Fibroma	1	1			
Nodular fasciitis	1	1			
Non-ossifying fibroma	1	1			
Periosteal chondroma	1	1			
Enchondroma	1	0			
Haemangioma	1	0			
Organizing haematoma	1	0			
Total	47	35		38	28

MFH, malignant fibrous histiocytoma; PVNS, pigmented villonodular synovitis.

Mean values were expressed as mean $\pm$ standard deviation. A value of $p < 0.05$ was considered to be statistically significant, and all p -values presented were two-sided. The statistical analysis was performed using the MedCalc Statistical Software (MedCalc Software, Mariakerke, Belgium).

RESULTS

There were 47 benign and 38 malignant tumours. 39 benign and 31 malignant tumours were proven by histological examinations of surgical specimens. The other 15 tumours were proven by histological examinations of biopsied specimens. The tumour size was 54 ± 27 mm (range: 15–110 mm) in 47 benign tumours and 67 ± 39 mm (range: 18–170 mm) in 38 malignant tumours ($p = 0.170$).

Visual analysis

On visual analysis, the interobserver agreement between the two radiologists was substantial agreement ($\kappa = 0.75$, seven disagreed findings). There were 35 positive (Scores 2–4) and 12 negative (Scores 0–1) benign tumours and 28 positive and 10 negative malignant tumours (Table 1). When we defined a positive lesion as a malignant tumour, there were 28 true-positive, 10 false-negative, 35 false-positive and 12 true-negative tumours. Thus, the sensitivity, specificity, PPV, NPV and accuracy for diagnosing malignant MS tumours were 74%, 26%, 44%, 55% and 47%, respectively, on visual analysis (Table 2). The visually negative lesions excluded from the quantitative analysis were 12 benign tumours (5 lipomas, 2 each of schwannoma and ganglion and 1 each of enchondroma,

Table 2. Visual diagnostic performance for diagnosing malignant musculoskeletal tumours on fluorine-18 fludeoxyglucose positron emission tomography/CT

Sensitivity	Specificity	Accuracy	PPV	NPV
73.7% [28/38] (56.9–86.6)	25.5% [12/47] (13.9–40.3)	47.1% [40/85] (36.1–58.2)	44.4% [28/63] (31.9–57.5)	54.5% [12/22] (32.2–75.6)

NPV, negative-predictive value; PPV, positive-predictive value.

Numbers in parentheses are 95% confidence intervals and numbers in brackets are the number of lesions.

Table 3. Quantitative data of fluorine-18 fludeoxyglucose positron emission tomography/CT-positive musculoskeletal tumours

Index	Benign tumours (<i>n</i> = 35)	Malignant tumours (<i>n</i> = 28)	<i>p</i> -value
SUV _{max}	6.9 ± 4.4 (1.9–19.7)	9.2 ± 6.0 (2.0–22.0)	0.168
SUV _{mean}	3.3 ± 1.7 (1.2–8.5)	3.3 ± 1.6 (1.2–8.6)	0.879
AUC-CSH	0.52 ± 0.10 (0.34–0.75)	0.43 ± 0.14 (0.25–0.70)	0.004

AUC-CSH, area under curve of cumulative standardized uptake value–volume histograms; SUV_{max}, maximum standardized uptake value; SUV_{mean}, mean standardized uptake value.

Range values are shown in parentheses.

haemangioma, organizing haematoma) and 10 malignant tumours (9 liposarcomas and 1 chondrosarcoma).

Quantitative analysis for fluorine-18 fludeoxyglucose positron emission tomography/CT-positive lesions

There was no significant difference between 35 benign and 28 malignant positive tumours in the SUV_{max} and SUV_{mean} (benign vs malignant: SUV_{max}, 6.9 ± 4.4 vs 9.2 ± 6.0, *p* = 0.168; SUV_{mean}, 3.3 ± 1.7 vs 3.3 ± 1.6, *p* = 0.879). The AUC-CSH was significantly lower in malignant tumours than in benign tumours (benign vs malignant: 0.52 ± 0.10 vs 0.43 ± 0.14, *p* = 0.004) with malignant tumours exhibiting more heterogeneous uptake than benign tumours (Table 3). There was no significant difference in size (50 ± 25 mm vs 60 ± 32 mm, *p* = 0.23).

The optimal threshold value was >6.9 for SUV_{max}, >3 for SUV_{mean} and ≤0.42 for AUC-CSH to diagnose malignant tumours, respectively. The sensitivity, specificity, accuracy and area under the ROC curve (AUC-ROC) were 61%, 66%, 63% and 0.60 for SUV_{max}, 54%, 60%, 57% and 0.51 for SUV_{mean} and 61%, 86%, 75% and 0.71 for AUC-CSH, respectively (Table 4). The PPV and NPV were 59% (17/29) and 68% (23/34) for SUV_{max}, 52% (15/29) and 62% (21/34) for SUV_{mean} and 77% (17/22) and 73% (30/41) for AUC-CSH, respectively. Although the SUV_{max} was superior to SUV_{mean} in the AUC-ROC (SUV_{max} vs SUV_{mean}, *p* = 0.001), the AUC-CSH was superior to SUV_{mean} and to SUV_{max} in the AUC-ROC (AUC-CSH vs SUV_{mean}, *p* = 0.005; AUC-CSH vs SUV_{max}, *p* = 0.017).

SUV_{max}, SUV_{mean} and AUC-CSH of 14 benign and 10 malignant MS tumour subtypes are shown in Figure 1a–c, respectively.

SUV_{max} yielded 12 false-positive benign lesions [1 each of chondroblastoma, fibroma, non-ossifying fibroma, pigmented villonodular synovitis (PVNS) and schwannoma, 2 fibrous dysplasia and 5 giant-cell tumours] and 11 false-negative malignant lesions [1 dermatofibrosarcoma, 3 each of liposarcoma and malignant fibrous histiocytoma (MFH) and 4 myxofibrosarcomas]. SUV_{mean} yielded 14 false-positive benign lesions (1 each of chondroblastoma, fibroma, neurofibroma, non-ossifying fibroma and schwannoma, 2 each of PVNS and fibrous dysplasia and 5 giant-cell tumours) and 13 false-negative malignant lesions (1 dermatofibrosarcoma, 4 each of liposarcoma, MFH and myxofibrosarcoma). AUC-CSH yielded 5 false-positive benign lesions (1 each of neurofibroma, PVNS and schwannoma, and 2 giant-cell tumours) and 11 false-negative malignant lesions (1 synovial sarcoma, 3 each of liposarcoma and MFH and 4 myxofibrosarcomas). Thus, false-positive benign lesions in AUC-CSH decreased considerably when compared with that observed in SUV_{max} and SUV_{mean}. Representative images of benign and malignant MS tumours are shown in Figures 2 and 3, respectively.

DISCUSSION

Diagnostic imaging plays a major role in the evaluation of patients with MS tumours. However, the differentiation between malignant and benign MS tumours remains a major challenge in diagnostic imaging. ¹⁸F-FDG PET is uniquely suited for evaluating metabolic activity in human tumours for diagnostic imaging purpose. The initial studies^{7,22–24} suggested the high diagnostic performance of ¹⁸F-FDG PET in differentiating between benign and malignant MS tumours. For example, Feldman et al⁷ reported 91% sensitivity, 100% specificity and 91.7%

Table 4. Diagnostic performance of three indices for diagnosing malignant musculoskeletal tumours

Index	Threshold value criterion	Sensitivity	Specificity	Accuracy	AUC-ROC
SUV _{max}	>6.9	60.7% (17/28)	65.7% (23/35)	63.5% (40/63)	0.60
		40.6–78.5 ^a	47.8–80.9 ^a	50.4–75.3 ^a	0.47–0.72 ^a
SUV _{mean}	>3.0	53.6% (15/28)	60% (21/35)	57.1% (36/63)	0.51
		33.9–72.5 ^a	42.1–76.1 ^a	44.0–69.5 ^a	0.38–0.64 ^a
AUC-CSH	≤0.42	60.7% (17/28)	85.7% (30/35)	74.6% (47/63)	0.71
		40.6–78.5 ^a	69.7–95.2 ^a	62.1–84.7 ^a	0.59–0.82 ^a

AUC-CSH, area under curve of cumulative standardized uptake value–volume histograms; AUC-ROC, area under the receiver operating characteristic curve; SUV_{max}, maximum standardized uptake value; SUV_{mean}, mean standardized uptake value.

Numbers in parentheses are the number of lesions.

^a95% confidence interval.

Figure 1. Graph shows SUV_{max} (a), SUV_{mean} (b) and AUC-CSH (c) of musculoskeletal tumour subtypes. Open circles indicate benign tumours, and filled circles indicate malignant tumours. The horizontal lines indicate the optimal threshold values for diagnosing malignant tumours [6.9 for SUV_{max} (a), 3 for SUV_{mean} (b) and 0.42 for AUC-CSH (c)]. AG, angiolioma; AUC-CSH, area under curve of cumulative standardized uptake value-volume histograms; CB, chondroblastoma; CS, chondrosarcoma; DF, desmoid-type fibromatosis; DS, dermatofibrosarcoma; EF, elastofibroma; ES, epithelioid sarcoma; FB, fibroma; FD, fibrous dysplasia; GCT, giant-cell tumour; HP, haemangiopericytoma; LP, liposarcoma; MF, myxofibrosarcoma; MFH, malignant fibrous histiocytoma; NF, nodular fasciitis; NFB, neurofibroma; NOF, non-ossifying fibroma; OC, osteochondroma; OS, osteosarcoma; PC, periosteal chondroma; PS, pleomorphic sarcoma; PVNS, pigmented villonodular synovitis; SS, synovial sarcoma; SUV_{max} , maximum standardized uptake value; SUV_{mean} , mean standardized uptake value; SW, schwannoma.

Figure 2. A 66-year-old female presented with schwannoma in the right buttocks. The threshold tumour area (green stripes) shows over 30% (a), 50% (b) and 70% (c) of the maximum standardized uptake value (SUV_{max} ; percent volume = 100%, 82.5% and 39.5%, respectively). The SUV_{max} and area under curve of cumulative SUV-volume histograms (d) were 4.0 and 0.65, respectively. The axial, coronal and sagittal images are shown in the left, middle and right columns, respectively. The areas surrounded by red, including the green stripes, are those of positive uptake in the whole tumour.

accuracy for diagnosing malignancy in 35 benign and malignant MS tumours. However, the diagnostic performance of ^{18}F -FDG PET to differentiate them has been controversial because of the considerable number of false-positive and false-negative lesions.^{8,9} Reported false-positive lesions are PVNS, neurofibroma, schwannoma, desmoid-type fibromatosis, giant-cell tumour, chondroblastoma, enchondroma,

non-ossifying fibroma and fibrous dysplasia, infection and other benign lesions, and false-negative lesions are liposarcoma and chondrosarcoma.^{6-9,25-29}

In our study, when a positive lesion was defined as a malignant lesion on visual analysis, the specificity was very low owing to many false-positive benign MS tumours [74% (35/47)]. Indeed,

Figure 3. A 52-year-old female presented with malignant fibrous histiocytoma in the left popliteal lesion. The threshold tumour area (green stripes) shows over 30% (a), 50% (b) and 70% (c) of the maximum standardized uptake value (SUV_{max} ; percent volume = 57.9%, 22.9% and 10.6%, respectively). The SUV_{max} and area under curve of cumulative SUV-volume histograms (d) were 10.3 and 0.34, respectively. The axial, coronal and sagittal images are shown in the left, middle and right columns, respectively. The areas surrounded by red, including the green stripes, are those of positive uptake in the whole tumour.

almost all of our false-positive benign MS tumours were included in the above reported false-positive benign MS tumours. Thus, our results confirm the findings of previously published studies^{27,30} that many benign MS tumours can have moderate to high ^{18}F -FDG uptake. There were also 10 false-negative malignant tumours which were 9 liposarcomas and 1 chondrosarcoma. They are typical false-negative malignant tumours.^{8,9,24,28}

In our study, there was no significant difference in the SUV_{max} or SUV_{mean} of ^{18}F -FDG-positive benign and malignant tumours. Although a previous meta-analysis³¹ has reported that the difference in the SUV_{mean} between malignant and benign soft-tissue tumours was statistically significant, our data showed no significant difference in the SUV_{mean} between them. Yamamoto et al³² examined the ^{18}F -FDG PET findings of 40 soft-tissue tumours (33 malignant and 7 benign tumours), and the SUV was higher in malignant

lesions than in benign lesions, but this difference was not statistically significant like our study (benign vs malignant: SUV_{max} 3.71 ± 1.20 vs 7.85 ± 6.92 , $p = 0.26$). Shin et al³³ reported that the sensitivity, specificity and diagnostic accuracy of ^{18}F -FDG PET/CT for diagnosing malignant MS tumours were 80%, 65.2% and 73% with a cut-off SUV_{max} of 3.8, and they mentioned that their results were not as good as other reported results using average cut-off SUV_{max} values from 2.0 to 2.5. Similarly, our data showed the difficulty to define a reliable cut-off value for differentiation between benign and malignant ^{18}F -FDG PET-positive MS tumours because of wide overlap of SUV_{max} between them.

Although, in our study, there was no significant difference in the SUV_{max} or SUV_{mean} between benign and malignant ^{18}F -FDG-positive MS tumours, the AUC-CSH was significantly lower in malignant tumours than in benign ones. The SUV_{max} reflected only a single voxel with the maximum uptake, and a few PET studies^{17,18,34} have focused on the intratumoral distribution of ^{18}F -FDG. The CSH method was recently reported for parameterizing heterogeneous intratumoral ^{18}F -FDG uptake in non-small-cell lung cancer.¹⁷ Watabe et al¹⁸ evaluated ^{18}F -FDG intratumoral heterogeneity of 9 gastrointestinal stromal tumours and 12 malignant lymphomas by the AUC-CSH which was significantly lower in the former than in the latter (0.41 ± 0.14 vs 0.64 ± 0.008 , $p = 0.001$), suggesting that ^{18}F -FDG uptake is more heterogeneous in the former than in the latter. Therefore, they considered that the evaluation of the intratumoral metabolic heterogeneity on ^{18}F -FDG PET images might help discriminate between these tumours. In our study, the SUV_{max} and AUC-CSH showed the same sensitivity, however, the specificity was higher in the AUC-CSH than in the SUV_{max} . These findings indicate that the evaluation of the intratumoral metabolic heterogeneity of ^{18}F -FDG PET-positive MS tumours may be more useful for

reducing the rate of false-positive MS tumours than increasing the rate of true-positive MS tumours.

Our study had the following limitations. First, our study was a retrospective study with a limited number of patients and a possible selection bias. Therefore, the usefulness of the AUC-CSH for discrimination between benign and malignant MS tumours should be examined by a prospective study with larger patients by the same study protocol. Second, quantitative evaluation was not performed in the 22 PET-negative lesions because negative lesions were indiscernible on PET. Even if there was grade 1 uptake (uptake weaker than normal surrounding organs such as muscle) in the tumour, the AUC-CSH was also not able to be calculated, because the delineated VOI which delimited the pathological lesion uptake from the normal uptake in surrounding normal tissues was not able to be made. To calculate the correct SUV_{mean} , the delineated VOI was also needed. If there was grade 1 uptake in the tumour, the SUV_{max} might have been to be calculated by using the CT guidance. However, the purpose of this study is to investigate the value of AUC-CSH in comparison with SUV_{max} and SUV_{mean} to discriminate between primary benign and malignant MS tumours, and calculation of all three parameters was needed in each tumour.

CONCLUSION

The heterogeneity index AUC-CSH shows that ^{18}F -FDG uptake is significantly more heterogeneous in primary malignant MS tumours. AUC-CSH has a higher diagnostic accuracy than SUV analysis for the differentiation of benign from malignant MS tumours, through improved specificity. However, it remains of insufficient diagnostic accuracy to permit avoidance of histological sampling, which remains necessary in all cases.

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