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ORIGINAL ARTICLE

^{18}F-FDG PET/MRI fusion in characterizing pancreatic tumors: comparison to PET/CT

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Abstract
Objective To demonstrate that positron emission tomography (PET)/magnetic resonance imaging (MRI) fusion was feasible in characterizing pancreatic tumors (PTs), comparing MRI and computed tomography (CT) as mapping images for fusion with PET as well as fused PET/MRI and PET/CT.
Methods We retrospectively reviewed 47 sets of ^{18}F-fluorodeoxyglucose (^{18}F -FDG) PET/CT and MRI examinations to evaluate suspected or known pancreatic cancer. To assess the ability of mapping images for fusion with PET, CT (of PET/CT), T1- and T2-weighted (w) MR images (all non-contrast) were graded regarding the visibility of PT (5-point confidence scale). Fused PET/CT, PET/T1-w or T2-w MR images of the upper abdomen were evaluated to determine whether mapping images provided additional diagnostic information to PET alone (3-point scale). The overall quality of PET/CT or PET/MRI sets in diagnosis was also assessed (3-point scale). These PET/MRI-related scores were compared to PET/CT-related scores and the accuracy in characterizing PTs was compared.
Results Forty-three PTs were visualized on CT or MRI, including 30 with abnormal FDG uptake and 13 without. The confidence score for the visibility of PT was significantly higher on T1-w MRI than CT. The scores for additional diagnostic information to PET and overall quality of each image set in diagnosis were significantly higher on the PET/T1-w MRI set than the PET/CT set. The diagnostic accuracy was higher on PET/T1-w or PET/T2-w MRI (93.0 and 90.7%, respectively) than PET/CT (88.4%), but statistical significance was not obtained.
Conclusion PET/MRI fusion, especially PET with T1-w MRI, was demonstrated to be superior to PET/CT in characterizing PTs, offering better mapping and fusion image quality.

Keywords ^{18}F-FDG · PET/MRI · PET/CT · Pancreatic tumor

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Introduction

FDG PET/CT, a combination of positron emission tomography with the glucose analog 2-deoxy-2-(^{18}F)fluoro-D-glucose ([^{18}F-FDG PET) and computed tomography (CT), is now accepted as a powerful imaging modality in evaluating various kinds of malignancies [1, 2]. PET/CT has been reported to be more useful than PET alone, with helpful anatomical and morphological information from its CT portion. Although several studies demonstrated that "diagnostic" contrast-enhanced (CE) CT was superior to non-CE CT for the CT portion of PET/CT in accurate lesion evaluation [3–8], most PET/CT examinations are still being performed with non-CE CT using low current in many institutions and hospitals. Reasons for this include the consideration of side effects of iodine contrast media or

the avoidance of longer examination time, higher radiation dose, and harder interpretation load. However, PET/CT with "non-diagnostic" CT often causes inconclusive interpretation when CT only functions to localize the site of FDG uptake.

Integrated PET/magnetic resonance imaging (MRI) has been developed recently, as a next generation modality following PET/CT. Our group developed a completely integrated PET/MRI scanner for small animals [9]. Prototype PET/MRI scanners for humans have also begun to be used in the pre-clinical phase [10, 11]. Higher diagnostic performance of PET/MRI over PET/CT is expected in the head and neck and pelvic regions, where MRI provides better image quality than CT owing to its better contrast resolution.

MRI has also been frequently used recently to evaluate upper abdominal malignancies including pancreatic cancer [12–15]. Pancreatic cancer is likely to be an appropriate target for PET/MRI, as the lesions are often poorly visualized or not visualized on non-CE CT in PET/CT examinations, even those showing abnormal FDG uptake. Although we do not consider PET/MRI or PET/CT to be a single perfect imaging modality for evaluating pancreatic cancer, information on FDG uptake in pancreatic lesions substantially affects patient management in clinical situations. Thus, we sought to determine whether PET/MRI fusion was feasible in characterizing pancreatic tumors, comparing MRI and CT as mapping images for fusion with PET as well as fused PET/MRI and PET/CT. As an initial study, main pancreatic lesions were evaluated in this study. Although fused PET/MR images in the present study were generated from PET and MR images obtained from different scanners, we believed it possible to demonstrate the expected advantages of PET/MRI over PET/CT in characterizing pancreatic tumors before integrated PET/MRI scanners are available in clinical situations.

Materials and methods

This retrospective study included 47 sets of ^{18}F-FDG PET/CT and MRI examinations performed within a month of each other to evaluate suspected or known pancreatic cancer. All examinations were performed before initial treatment. Patients were aged from 32 to 90 years (mean 68); 28 were males and 19 females.

^{18}F-FDG PET/CT

PET/CT imaging was performed with an integrated scanner (Gemini GXL, Philips). Whole-body images, generally from the top of the skull to mid-thigh, were acquired about 60 min after intravenous injection of ^{18}F-FDG at a dose of 0.10 mCi/kg body weight. The PET portion was acquired using the following parameters: 3D emission scan, 2 min scan/bed position × 11 positions, OSEM reconstruction, 4.0 mm slice thickness/interval. Acquisition parameters for the CT portion (16-slice CT) were as follows: breath-hold during normal expiration from the level of apex of lungs to the lower pole of kidneys, without intravenous nor oral contrast media, 120 kVp and 50 effective mAs, 5.0 mm slice thickness/4.0 mm interval.

Abnormal FDG uptake was defined as visually increased FDG uptake as compared to surrounding normal pancreatic tissue, and abnormal FDG uptake corresponding to malignant lesions (suspected) was selected to evaluate accuracy. The standardized uptake value (SUV), which is the decay-corrected tissue activity divided by the injected dose per patient body weight, was calculated at the tumor. The maximum pixel value of SUV within each tumor (SUV_{max}) was used to express tumor activity semiquantitatively, although it did not affect the interpretation regarding malignant or not in this study.

Abdominal MRI

MRI was performed with a 3.0T scanner (Signa Excite HD 3.0T, GE Healthcare). As the CT portion of PET/CT was performed without contrast media, non-CE transaxial T1- and T2-weighted (w) images were used for comparison and for fusion with PET in this study. T1-w MR images were acquired with a 3D spoiled gradient echo sequence (LAVA) with fat-suppression technique. The imaging parameters were as follows: TR 4.7 ms, TE 2.3 ms, flip angle 12°, 3.0 mm slice thickness (no gap). T2-w MR images were obtained with a single-shot fast spin echo sequence using the following parameters: TR 1200 ms, TE 90 ms, 5.0 mm slice thickness/0.5 mm interslice gap. T1-w and T2-w images covering pancreatic lesions were fused with PET semiautomatically using bilateral renal shapes as landscape with a dedicated software (Syntegra, Philips). Morphological information including the size and internal structure (cystic or solid) was recorded.

Image analysis

To assess the suitability of mapping images for fusion with PET, CT (of PET/CT), T1-w and T2-w MR images were graded regarding the visibility of pancreatic tumors with a 5-point confidence scale (1, definitely absent; 2, probably absent; 3, equivocal; 4, probably present; and 5, definitely present). Fused PET/CT, PET/T1-w or T2-w MR images were evaluated to determine whether additional diagnostic information to PET alone due to mapping images, such as lesion characterization or localization, was achieved, using a 3-point scale (1, no; 2, slightly added; and 3, significantly

added). The overall quality of each image set, i.e. the set comprising PET images, mapping images (CT, T1-w or T2-w MRI), and the fusion of them as regards diagnosis was assessed with a 3-point scale (1, poor; 2, acceptable; and 3, excellent).

Mapping images for pancreatic lesions were interpreted without PET information separately by two board-certificated nuclear medicine physicians/radiologists (both having double board-certifications), who were only aware that patients had PET/CT or MRI examinations for known or suspected pancreatic cancer. After that, evaluation of additional diagnostic information over PET alone or overall quality of each image set was performed using PET images, mapping images (CT, T1-w or T2-w MRI), and the fusion of them by the same nuclear medicine physicians/radiologists. Discrepancies in interpretation were recorded and then resolved by consensus. These results did not affect patient management.

Diagnostic accuracy was also evaluated regarding malignancy of pancreatic tumors using the image sets of PET/CT, PET/T1-w and PET/T2-w MRI.

Statistical analysis

The agreement on scores between 2 readers for visibility of pancreatic tumor, additional diagnostic information over PET alone, or overall quality of each image set for diagnosis was evaluated with kappa analysis.

After discrepancies were resolved by consensus, scores for visibility of pancreatic tumor were compared between CT and T1-w or T2-w MRI using a Wilcoxon signed rank test. The proportion of score 5 (definitely present) was also compared between CT and T1-w or T2-w MRI with a McNemar test. Scores regarding additional diagnostic information over PET alone and overall quality of each image set for diagnosis were also compared between the image sets of PET/CT and PET/T1-w or T2-w MRI with a Wilcoxon signed rank test. The proportions of score 3, "significantly added" for additional diagnostic information over PET alone and "excellent" for overall quality of each image set for diagnosis, were evaluated with a McNemar test. Diagnostic accuracy was also evaluated with a McNemar test. A P value less than 0.05 was considered statistically significant.

These analyses were also performed for the subgroups of tumors with [$SUV_{max} \geq 3$] and [$SUV_{max} < 3$], and [size $\geq$ 3 cm] and [size $<$ 3 cm].

Results

Forty-three pancreatic tumors were visualized on CT or MRI in 47 sets of FDG PET/CT and MRI examinations to evaluate suspected or known pancreatic cancer. Tumor sizes for these 43 ranged from 1.3 to 10 cm (mean 3.3 $\pm$ 1.6). The 43 tumors included 27 adenocarcinomas, 2 neuroendocrine tumors, 1 inflammatory lesion, and 13 benign cystic lesions. Abnormal FDG uptake was observed in 30 of the 43 tumors on PET, in all of the 27 adenocarcinomas, 2 neuroendocrine tumors, and 1 inflammatory lesion. SUV_{max} ranged from 1.4 to 16 (mean 5.1 $\pm$ 3.5) for these tumors. All of the 13 tumors without abnormal FDG uptake were benign cystic lesions. Although negative examinations may have certain meanings in clinical situations, 4 sets of negative PET/CT and MRI examinations (no abnormal findings) were excluded from the analyses in this study.

The results of agreement on interpretation between the two readers are summarized in Table 1. The frequency of agreement was high, ranging from 86 to 93%, in all evaluations. Kappa analyses revealed that the agreements in these evaluations were all statistically significant ($P < 0.01$ for all), with kappa values ranging from 0.66 to 0.91.

Representative image sets of FDG PET and CT, T1-w, or T2-w MRI, and the fusion of them are shown in Fig. 1a, b. Fused PET/T1-w or T2-w MR images were successfully generated in all cases.

The confidence score regarding visibility of pancreatic tumor was 4.4 $\pm$ 0.73 on CT, 4.8 $\pm$ 0.37 on T1-w, and 4.5 $\pm$ 1.1 on T2-w MR images for the 43 tumors after consensus (Fig. 2). T1-w MR images provided significantly higher scores than CT ($P < 0.01$), but T2-w MRI did not. The proportion of score 5 (definitely present) was significantly higher on both T1-w (84%) and T2-w MRI (77%) than on CT (53%, both $P < 0.01$) (Table 2). Comparison of scores between CT and T1-w or T2-w MRI is

Table 1 Agreement of interpretation between two readers

	Frequency of agreement (%)	Kappa value
Visibility of pancreatic tumor		
CT	88	0.85*
T1-w MRI	93	0.69*
T2-w MRI	88	0.73*
Additional diagnostic information over PET alone		
PET/CT	93	0.88*
PET/T1-w MRI	86	0.73*
PET/T2-w MRI	86	0.77*
Overall quality of each image set in diagnosis		
PET/CT set	88	0.66*
PET/T1-w MRI set	93	0.91*
PET/T2-w MRI set	86	0.75*

* $P < 0.01$

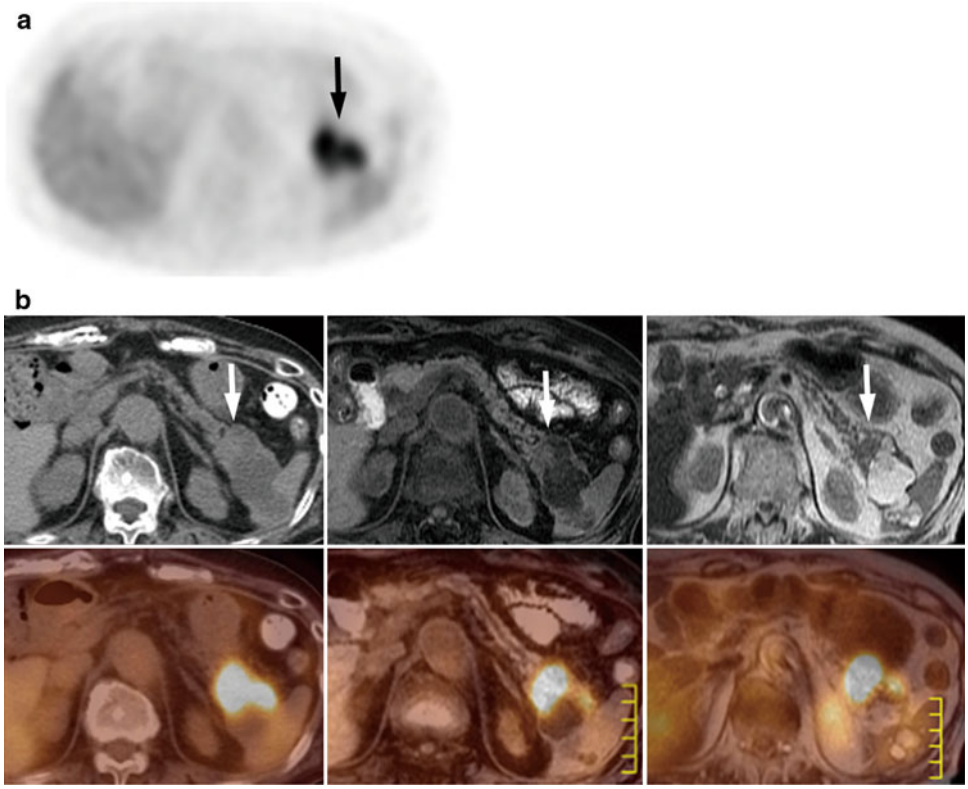

Fig. 1 Eighty-two-year-old female with pancreatic cancer (tail). Size: 4.0 cm, SUV_{max}: 11.3. A pancreatic tumor was equally well visualized either on CT, T1-w- or T2-w MR images (*white arrows*), with main pancreatic duct dilatation in the tail. Intense FDG uptake was clearly observed on PET (*black arrow*). Additional diagnostic information over PET alone or overall image quality of fusion was also considered to be equivalent among image sets of PET/CT, PET/T1-w MR, and PET/T2-w MR images. **a** FDG PET, **b** *upper left* CT, *upper middle* T1-w MRI, *upper right* T2-w MRI, *lower left* PET/CT, *lower middle* PET/T1-w MRI, and *lower right* PET/T2-w MRI

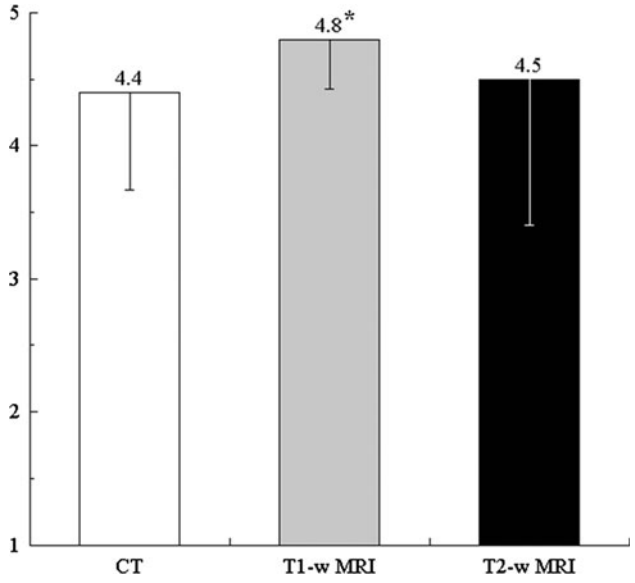

Fig. 2 Mean confidence score regarding visibility of pancreatic tumor on mapping images ($n = 43$). The score on T1-w MR images was significantly higher than that on CT, but the score on T2-w MRI was not higher than that on CT. (Scores 1, definitely absent; 2, probably absent; 3, equivocal; 4, probably present and 5, definitely present; $*P < 0.01$)

also listed in Table 2. Both T1-w and T2-w MRI exhibited scores higher or equal to those of CT in most cases.

In Fig. 3a, b, a pancreatic tumor (neuroendocrine tumor) was depicted only on T1-w MRI. A tiny focus of FDG uptake was observed, but interpretation of fused images was difficult with poor mapping images of CT and T2-w MRI.

Table 2 Confidence score regarding visibility of pancreatic tumor

Proportion of score 5 (definitely present)			
CT	53%		
T1-w MRI	84%*		
T2-w MRI	77%*		
Comparison of scores between CT and T1-w or T2-w MRI ($n = 43$)			
T1-w MRI > CT	17	T2-w MRI > CT	12
=	24	=	26
<	2	<	5

* $P < 0.01$ versus CT

The score regarding additional diagnostic information over PET alone was 2.1 ± 0.63 on PET/CT, 2.3 ± 0.74 on PET/T1-w, and 2.2 ± 0.69 on PET/T2-w MR images for the 43 tumors (Fig. 4). PET/T1-w MR images exhibited significantly higher scores than PET/CT ($P < 0.01$), but PET/T2-w MRI did not. The proportion of score 3 (significantly added) was significantly higher on PET/T1-w MRI (47%) than on PET/CT (23%, $P < 0.01$). The proportion of score 3 was 33% on PET/T2-w MR images, but it did not reach statistical significance compared to PET/CT (Table 3). Both PET/T1-w and PET/T2-w MRI exhibited scores higher or equal to those of PET/CT in most cases,

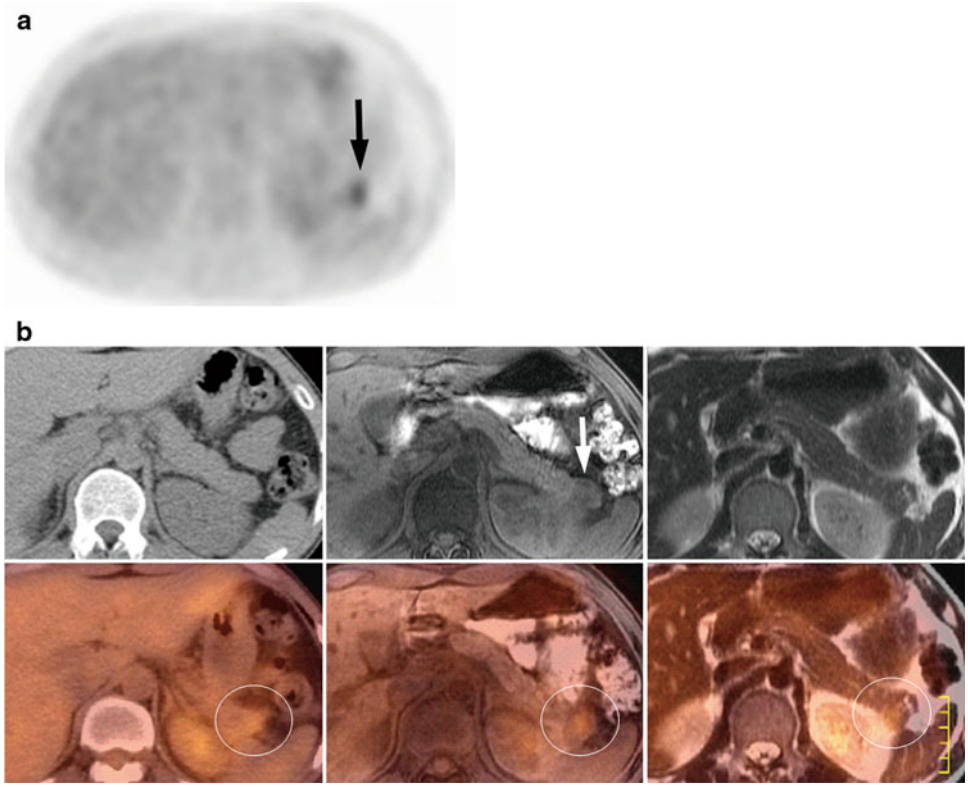

Fig. 3 Thirty-two-year-old male with neuroendocrine tumor of the pancreas (tail). Size: 2.0 cm, SUV_{max}: 3.1. Pancreatic tumor was clearly visualized solely on T1-w MRI (*white arrow*). A tiny focus of moderate FDG uptake was observed (*black arrow*), but interpretation of fused images was difficult with poor mapping images of CT and T2-w MRI (*white circle*). Slight misregistration was observed on PET/CT, but no tumor was detected on CT in slices where the lesion was supposed to be present. **a** FDG PET, **b** *upper left* CT, *upper middle* T1-w MRI, *upper right* T2-w MRI, *lower left* PET/CT, *lower middle* PET/T1-w MRI, and *lower right* PET/T2-w MRI

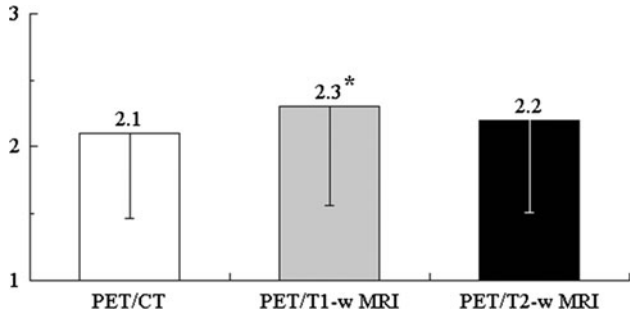

Fig. 4 Mean score for additional diagnostic information over PET alone with fusion images ($n = 43$). The score on PET/T1-w MR images was significantly higher than that on PET/CT, but the score on PET/T2-w MRI was not higher than that on CT. (Scores 1, no; 2, slightly added; and 3, significantly added; $*P < 0.01$)

although the proportion of equal scores between PET/CT and PET/T1-w or T2-w MRI was higher than that in the confidence score regarding visibility of tumor (Table 3).

The score for overall image quality in diagnosis was significantly higher in the image set of PET/T1-w MRI (2.5 ± 0.51) than in that of PET/CT (2.2 ± 0.41, $P < 0.01$). The image set of PET/T2-w MRI (score 2.4 ± 0.50) was also superior to that of PET/CT in this analysis ($P = 0.03$) (Fig. 5). The proportion of score 3 (excellent) was significantly higher in the image set of PET/T1-w MRI (53%) than in that of PET/CT (21%, $P < 0.01$). The proportion of score 3 was 40% on the image set of PET/T2-w MRI, but it was not statistically significantly higher than that of PET/CT (Table 4). Comparison of scores among 3 image sets revealed that both PET/T1-w and T2-w MRI exhibited scores higher or equal to those of PET/CT in most cases (Table 4).

Figure 6a, b shows the case in which the advantage of T1-w MRI was clearly demonstrated. The pancreatic tumor itself was clearly depicted only on the mapping image of T1-w MRI. This caused better overall image quality in diagnosis on the PET/T1-w MRI set than on the PET/CT or PET/T2-w MRI sets.

The subgroup analysis in the tumors with [$SUV_{max} \geq 3$] and [$SUV_{max} < 3$], and [size $\geq$ 3 cm] and [size $<$ 3 cm] exhibited the same results regarding the visibility of pancreatic tumors as those dealing with all tumors. T1-w MRI was superior to CT as mapping images in all of the SUV_{max} and tumor size subgroups. T2-w MRI was not superior to CT. As to scores for overall image quality in diagnosis, the image set of PET/T1-w MRI provided higher scores than the set of PET/CT both in the [SUVmax $\geq$ 3] and [SUVmax $<$ 3] subgroups. PET/T2-w MRI did not show higher scores than the set of PET/CT in either subgroup. The image sets of PET/T1-w and PET/T2-w MRI provided significantly higher scores for overall image quality in diagnosis than the set of PET/CT in the [size $\geq$ 3 cm] subgroup.

The diagnostic accuracy regarding malignancy was 88.4% on the image set of PET/CT, 93.0% on PET/T1-w MRI, and 90.7% on PET/T2-w MRI. Although the accuracy

Table 3 Additional diagnostic information over PET alone with fusion images

Proportion of score 3 (significantly added)			
PET/CT	23%		
PET/T1-w MRI	47%*		
PET/T2-w MRI	33%		
Comparison of scores between PET/CT and PET/T1-w or T2-w MRI ($n = 43$)			
PET/T1-w MRI > PET/CT	10	PET/T2-w MRI > PET/CT	5
=	33	=	37
<	0	<	1

* $P < 0.01$ versus PET/CT

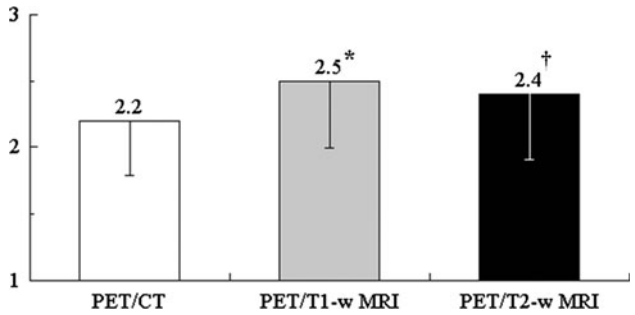

Fig. 5 Mean score for overall quality of image set in diagnosis ($n = 43$). The score on the image set of PET/T1-w MRI was significantly higher than that on PET/CT. The score on the image set of PET/T2-w MRI was also higher than that on PET/CT. (Score 1, poor; 2, acceptable; and 3, excellent; *$P < 0.01$, †$P = 0.03$)

Table 4 Overall quality of image set in diagnosis

Proportion of score 3 (excellent)			
PET/CT set	21%		
PET/T1-w MRI set	53%*		
PET/T2-w MRI set	40%		
Comparison of scores between PET/CT set and PET/T1-w or T2-w MRI set ($n = 43$)			
PET/T1-w MRI set > PET/CT set	15	PET/T2-w MRI set > PET/CT set	9
=	27	=	33
<	1	<	1

* $P < 0.01$ vs. PET/CT set

was higher on the image set of PET/T1-w or T2-w MRI than PET/CT, no significant differences were observed between them.

Discussion

Pancreatic tumors are often poorly visualized or not visualized on the CT portion of PET/CT, if the CT is performed as "non-diagnostic" using low current without contrast media. This potentially causes equivocal PET/CT diagnoses in clinical situations. In this study, only 53% of all pancreatic lesions were accompanied by the confidence score of 5 (definitely present) regarding visibility of the tumor on the CT portion of PET/CT, which was significantly lower than T1-w or T2-w MR images (84 and 77%, respectively). CT may have functioned to localize the focus of abnormal FDG uptake, but did not help to provide definite findings for PET/CT in such a situation. One may argue that the CT portion should be "diagnostic" using sufficiently higher current with contrast media, but many institutions and hospitals perform PET/CT in a manner similar to ours because of several restrictions such as a crowded examination schedule. All MR images evaluated in this study were also performed without contrast media.

In general, T1-w MR images are good at visualizing anatomical structures, while T2-w MR images detect abnormal tissues. T2-w MR images are usually superior to T1-w MRI in detecting malignant lesions. Pancreatic tumors are, however, known to be well depicted on T1-w MR images. Most of them represent low signal intensity in the normal pancreatic tissue, which shows relatively high intensity due to its abundant protein content on T1-w MR images. Gabata et al. [16] demonstrated that fat-suppressed T1-w MR images were superior to T2-w MRI in detecting pancreatic cancer. In this study as well, T1-w MR images were considered to be superior to T2-w MRI in visualizing pancreatic tumors with the higher confidence scores. While cystic components were better recognized on T2-w MRI, T1-w MR images appeared to be sufficient as mapping images for PET in detecting pancreatic tumors. However, other studies are obviously required to determine which MR sequence is better as mapping images for PET to evaluate metastatic liver or lymph node lesions.

Both of the scores for additional diagnostic information over PET alone and overall image quality of fusion in diagnosis were highest in the image set of PET/T1-w MRI. The mapping image quality was considered to affect the grade of these advantages provided by image fusion. In their article dealing with FDG PET/CE CT, Antoch et al. [4] described the superiority of CE CT as compared to non-CE CT for fusion with PET, especially when tumor FDG uptake was low. In this study, the image set of PET/T1-w MRI demonstrated superior overall image quality of fusion to PET/CT in the [SUVmax < 3] subgroup. Pancreatic cancer lesions often exhibit mild or moderate FDG uptake due to the abundant fibrous component in solid lesions or due to the tiny solid portion in cystic ones. These facts are considered to influence the advantage of PET/T1-w MRI fusion over PET/CT in characterizing pancreatic tumors as an integrated diagnostic imaging technique.

Fused PET/MR images were generated from PET and MR images obtained from different scanners in this study.

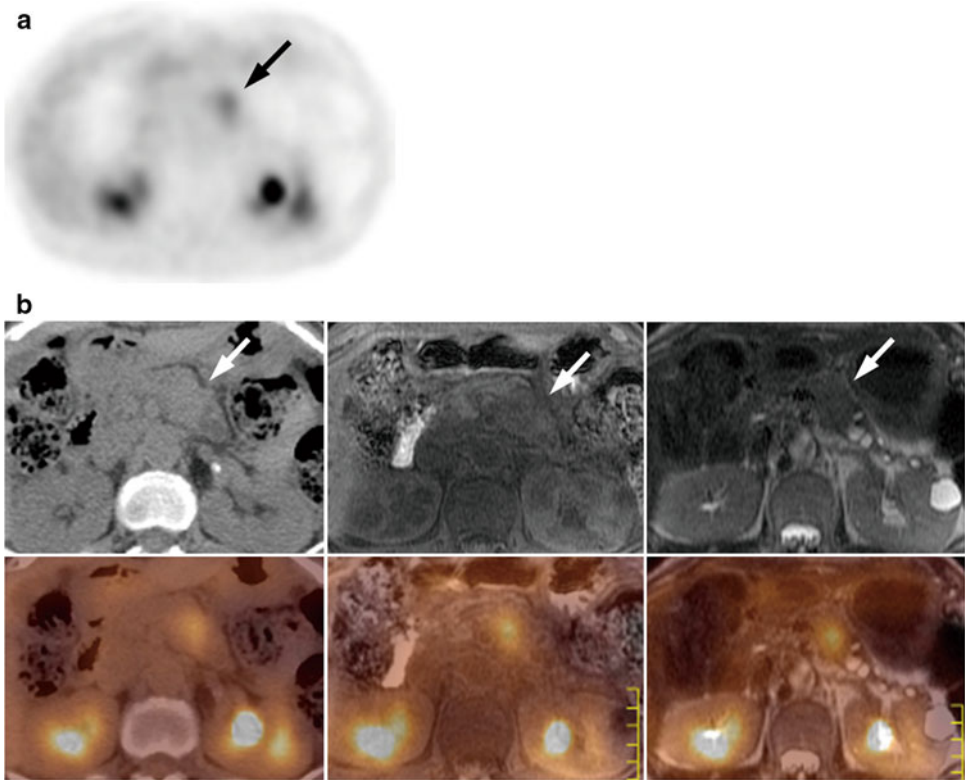

Fig. 6 Sixty-nine-year-old female with pancreatic cancer (body). Size: 2.5 cm, SUV_{max}: 3.3. Abnormal FDG uptake was observed on PET (*black arrow*). The pancreatic tumor was clearly depicted as an area of low signal intensity on the T1-w MRI (*white arrow*). The T2-w MRI exhibited slightly high signal intensity at the area, but CT failed to detect the tumor (*white arrows*). This caused better overall image quality in diagnosis on the PET/T1-w MRI set than the set of PET/CT or PET/T2-w MRI. **a** FDG PET, **b** *upper left* CT, *upper middle* T1-w MRI, *upper right* T2-w MRI, *lower left* PET/CT, *lower middle* PET/T1-w MRI, and *lower right* PET/T2-w MRI

Image quality of the fused images was much better than expected, and was considered to be feasible in characterizing pancreatic tumors. Of note is that the present study compared these image sets of PET and MRI to the set of PET and CT. Although several studies have been conducted regarding PET and MRI fusion in body tumors [17–21], the advantages of PET/MRI fusion over PET/CT were reported only in a limited number of patients. This particular study demonstrated that the image set of PET/T1-w MRI was superior to PET/CT in characterizing pancreatic tumors. This warrants further studies with integrated PET/MRI scanners in characterizing pancreatic tumors, which will be available in clinical situations in the near future.

Limitations in this study included the fact that this study focused only on pancreatic tumor lesions. Although we admit that PET/CT is used as a staging modality in various malignancies, the purpose of this study was to test if PET/MRI fusion resolved equivocal findings for pancreatic lesions, which were often observed in clinical PET/CT examinations. Evaluation of metastatic lesions with PET/MRI is necessary as a next step. MRI may be sufficient to characterize pancreatic tumors, but the purpose of this study was to determine the feasibility of PET/MRI fusion, comparing MRI and CT as mapping images for fusion with PET as well as fused PET/MRI and PET/CT. The use of "diagnostic" MR images may be another limitation, even when performed without contrast enhancement, since the CT images used in this study represented "non-diagnostic" quality obtained as the CT portion of PET/CT. However, a study using non-contrast MRI at 1.5 T performed more than 15 years ago demonstrated the superior performance of MRI over dynamic CE CT in evaluating pancreatic cancer [22]. Degraded MR images might have caused decreased detection of pancreatic tumors, but the detection was expected to be at least comparable to that on CT.

In conclusion, PET/MRI fusion, especially PET with T1-w MRI, was superior to PET/CT in characterizing pancreatic tumors, offering better mapping and fusion image quality as well as better diagnostic performance. Although the PET and MR images were obtained from different scanners, the present study demonstrated the expected advantages of PET/MRI fusion over PET/CT in characterizing pancreatic tumors and warrants future studies to investigate specific roles for integrated PET/MRI.

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Conflict of interest No authors has any conflict of interest.

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