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ORIGINAL ARTICLE

Diagnostic performance of fluorodeoxyglucose positron emission tomography/magnetic resonance imaging fusion images of gynecological malignant tumors: comparison with positron emission tomography/computed tomography

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Abstract
Purpose. We compared the diagnostic accuracy of fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) and PET/magnetic resonance imaging (MRI) fusion images for gynecological malignancies.
Materials and methods. A total of 31 patients with gynecological malignancies were enrolled. FDG-PET images were fused to CT, T1- and T2-weighted images (T1WI, T2WI). PET-MRI fusion was performed semiautomatically. We performed three types of evaluation to demonstrate the usefulness of PET/MRI fusion images in comparison with that of inline PET/CT as follows: depiction of the uterus and the ovarian lesions on CT or MRI mapping images (first evaluation); additional information for lesion localization with PET and mapping images (second evaluation); and the image quality of fusion on interpretation (third evaluation).
Results. For the first evaluation, the score for T2WI (4.68 ± 0.65) was significantly higher than that for CT (3.54 ± 1.02) or T1WI (3.71 ± 0.97) ($P < 0.01$). For the second evaluation, the scores for the localization of FDG accumulation showing that T2WI (2.74 ± 0.57) provided significantly more additional information for the identification of anatomical sites of FDG accumulation than did CT (2.06 ± 0.68) or T1WI (2.23 ± 0.61) ($P < 0.01$). For the third evaluation, the three-point rating scale for the patient group as a whole demonstrated that PET/T2WI (2.72 ± 0.54) localized the lesion significantly more convincingly than PET/CT (2.23 ± 0.50) or PET/T1WI (2.29 ± 0.53) ($P < 0.01$). Conclusion. PET/T2WI fusion images are superior for the detection and localization of gynecological malignancies.

Key words PET · MRI · Fusion image · Gynecological malignant tumors

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Introduction

Inline positron emission tomography/computed tomography (PET/CT) systems provide highly accurate fusion images of metabolic and anatomical images that are useful for detecting malignant tumors and their locations.[1,2] However, contrast resolution of CT for different tissues is limited especially in the head and neck and pelvis when low-dose exposure is employed. In contrast, magnetic resonance imaging (MRI) has several advantages over CT, such as high tissue contrast and no radiation exposure. The diagnostic ability of MRI for uterine cervical carcinoma and ovarian masses was proven to be higher than that of CT owing to the high tissue contrast of the former.[3–5] In the study presented here, we exam-

ined the usefulness of PET/MR fusion images in comparison with that of inline PET/CT for evaluating gynecological tumors. We hypothesized that PET/T2WI was superior to other fusion images, such as PET/CT, for gynecological tumors.

Materials and method

Patients

From April 2007 to May 2008, a total of 31 patients with gynecological cancer were retrospectively analyzed by means of inline PET/CT with 2-deoxy-2-[^{18}F]fluoro-D-glucose (FDG) and by MRI within a month. The clinical information is summarized in Table 1. There were 25 patients with uterine cervical cancer, 3 with endometrial cancer, and 3 with ovarian cancer. In all, 21 of the 25 patients were studied before undergoing any treatment, and the others were studied after surgical resection, radiotherapy, chemotherapy, or radiochemotherapy.

PET/CT scanning

All of the patients were fasted at least 4 h before injection of FDG at a dose of 3.7 MBq/kg. After intravenous administration, patients were asked to remain still in a dark, quiet room for 60 min. Whole-body PET imaging was started immediately after CT imaging at 60 min after injection (Gemini GXL; Philips Medical Systems, Eindhoven, The Netherlands). Acquisition parameters for the CT portion (16-slice CT) consisted of breath-holding during normal expiration, scanning from the level of the apex to the lower pole of the pelvis, no intravenous or oral contrast media, 120 kVp and 50 effective mAs, and 5.0 mm slice thickness/4.0-mm interval. The PET images were acquired with the following parameters: three-dimensional (3D) emission scan, 2 min scan/bed position × 11 positions (15 cm/position), ordered-subset expectation maximization (OSEM) reconstruction, 4.0 mm slice thickness/interval.

Table 1. Patients' characteristics

Total no. of patients	31
Median age (years)	57.6 (range 34–85)
Median tumor size (mm)	43.7 (range 10.0–166.7)
Diagnoses of gynecological malignant lesions	
Cervical cancer	25
Endometrial cancer	3
Ovarian cancer	3
History of treatment	
Cervical cancer	
None	18
CT	0
RT	2
CRT	2
Operation	1
Endometrial cancer	1
None	
CT	1
RT	1
Ovarian cancer	2
CT + operation	1

CT, chemotherapy; RT, radiotherapy; CRT, chemoradiotherapy

MRI scanning

The MRI study was performed with a 1.5 T MRI system (Signa Excite HD 1.5T; GE Medical Systems, Waukesha, WI, USA) or a 3.0 T MRI system (Signa Excite HD 3.0T; GE Medical Systems) within 1 month before or after PET/CT imaging. We used non-contrast-enhanced transaxial T1-weighted images (T1WI) and T2-weighted images (T2WI) for image fusion. The T1WI were acquired with a 3D spoiled gradient recalled echo (GRE) sequence using the fat-suppression technique. The respective imaging parameters of the 1.5 T and 3.0 T scanners were TR 5.1 and 4.7 ms, TE 2.4 and 4.2 ms; flip angle 12° and 12°; slice thickness 3.0 and 4.0 mm (no gap). The T2WI were obtained with a single-shot fast spin echo (FSE) sequence using the following parameters for both 1.5-T and 3.0-T scanners: TR 6000 ms, TE 80 ms, 5.0 mm slice thickness/1-mm interslice gap.

Image fusion

The PET and MRI image fusion was semiautomatically done using Osirix imaging software (version 3.2.1).[6] Osirix uses ITK (Insight Segmentation and Registration Toolkit) which employs leading-edge segmentation and registration algorithms in two, three, and more dimensions. First, we selected transaxial images of the CT scans of PET/CT and MRI T2WI corresponding to the femoral head in each patient by visual inspection. Second, 3D space adjustments were applied to both PET/CT and MRI T1WI and T2WI. The PET images were fused on the MRI images for image analysis.

Image analysis

Two nuclear medicine physicians inspected images having the information that the patients have gynecological cancer. They visually inspected CT, noncontrast T1WI, T2WI, PET/CT, PET/T1WI, and PET/T2WI scans of gynecological malignancies. They evaluated the depiction of lesions by CT, T1WI, and T2WI, as well as the localization of abnormal FDG uptake, by means of side-by-side inspection of PET and CT (PET+CT), PET

and T1WI (PET+T1WI), and PET and T2WI (PET+T2WI) according to the rating scale described below. The final evaluation was of how convincingly the abnormal accumulations in certain lesions were diagnosed using PET/CT, PET/T1WI, and PET/T2WI. The rate of agreement for the two physicians was also assessed for each evaluation. In case of disagreement, consensus evaluation was obtained after discussion.

First, the depiction of the primary tumor in the uterus and ovarian malignancy on CT images, T1WI, and T2WI was evaluated with the following five-point rating scale 1, definitely no lesions; 2, probably no lesions; 3, equivocal finding; 4, probably positive lesions; 5, definitely positive lesions. Second, we placed PET images side by side with CT images, T1WI, and T2WI (PET+CT, PET+T1WI, and PET+T2WI, respectively) for evaluation of how much additional information for lesion localization was provided by CT, T1WI, and T2WI. For this evaluation a three-point rating scale was used: 1, no additional information was provided regarding the site of FDG accumulation; 2, the site of the FDG accumulation was possibly localized; 3, the site of the FDG accumulation was definitely identified.

Third, we assessed the quality of diagnosis by PET/CT, PET/T1WI, and T2WI in terms of how convincingly FDG accumulation was detected in certain anatomical structures. For this assessment, the following three-point rating scale was used: 1, poor; 2, acceptable; 3, excellent. The analysis was performed for the patient group as a whole and for patient subgroups classified according to the magnitude of FDG accumulation. The FDG accumulation was evaluated in terms of maximum standardized uptake value (SUV_{max}) in the region of interest (ROI). The threshold for accumulation was set at 3.0 of SUV_{max}, and the patients were divided into two subgroups: those with $SUV_{max} \geq 3.0$ ($n = 25$) and those with $SUV_{max} < 3.0$ ($n = 6$).

Statistics

The five-point rating scale for lesion detection by CT, T1WI, and T2WI and the three-point rating scale for fusion images were statistically analyzed with the Wilcoxon matched-pair signed-rank test. The rate of agreement between the two physicians was assessed using a weighted kappa coefficient, which was statistically compared by means of Student's *t*-test.

Results

For the first evaluation—depiction of the uterus and the ovarian lesions on CT images, T1WI, and T2WI—the kappa coefficients of agreement between the two physicians were 0.70 ± 0.103 for CT, 0.70 ± 0.09 for T1WI, and 0.80 ± 0.07 for T2WI. The rate of agreement was significantly higher for T2WI than for CT ($P < 0.05$) or T1WI ($P < 0.05$). After consensus was reached about lesion detection, the scores for lesion detection by CT, T1WI, and T2WI were 3.54 ± 1.02, 3.71 ± 0.97, and 4.68 ± 0.65, respectively. The score for T2WI was significantly higher than those for CT or T1WI ($P < 0.01$).

For the second evaluation—how much additional information for lesion localization was provided by CT, T1WI, and T2WI—the rates of agreement between the two physicians were 0.62 ± 0.24 for PET+CT, 0.54 ± 0.14 for PET+T1WI, and 0.66 ± 0.11 for PET+T2WI. There was no significant difference in the rate of agreement among these methods. The scores for the localization of FDG accumulation by PET+CT, PET+T1WI, and PET+T2WI were 2.06 ± 0.68, 2.23 ± 0.61, and 2.74 ± 0.57, respectively, which indicated that T2WI provided significantly more additional information for the identification of anatomical sites of FDG accumulation than did CT ($P < 0.01$).

For the third evaluation—the quality of diagnosis by PET/CT, PET/T1WI, and T2WI—the rates of agreement between the two physicians were 0.64 ± 0.130 for PET/CT, 0.59 ± 0.129 for PET/T1WI fusion images, and 0.79 ± 0.12 for PET/T2WI fusion images. The rate of agreement was significantly higher for PET/T2WI than for PET/CT or PET/T1WI ($P < 0.05$). After consensus was reached, the three-point rating scale for the patient group as a whole demonstrated that PET/T2WI (2.72 ± 0.542) localized the lesion significantly more convincingly than PET/CT (2.23 ± 0.50) or PET/T1WI (2.29 ± 0.53) ($P < 0.01$).

In the subgroup analysis, the scores on the three-point rating scale for patients with SUV_{max} of ≥3.0 ($n = 25$) were 2.32 ± 0.476 for PET/CT, 2.40 ± 0.500 for PET/T1WI, and 2.72 ± 0.541 for PET/T2WI. The corresponding scores for patients with SUV_{max} of <3.0 ($n = 6$) were 1.83 ± 0.408, 1.83 ± 0.408, and 2.67 ± 0.516, respectively. The rating scale between the subgroups showed a significant reduction for PET/CT ($P < 0.01$) and PET/T1WI ($P < 0.01$) but not for PET/T2WI (Figs. 1, 2).

Discussion

T2WI is superior to CT in its ability to detect lesions of uterine and ovarian cancer.[1–5] T2WI, even with low-magnetic-field MRI, has proven itself superior for staging uterine carcinoma,[7,8] and it was found to be able to depict an intramural nodule and abnormal wall thickening, which indicate a malignant lesion.[3,5] The results of

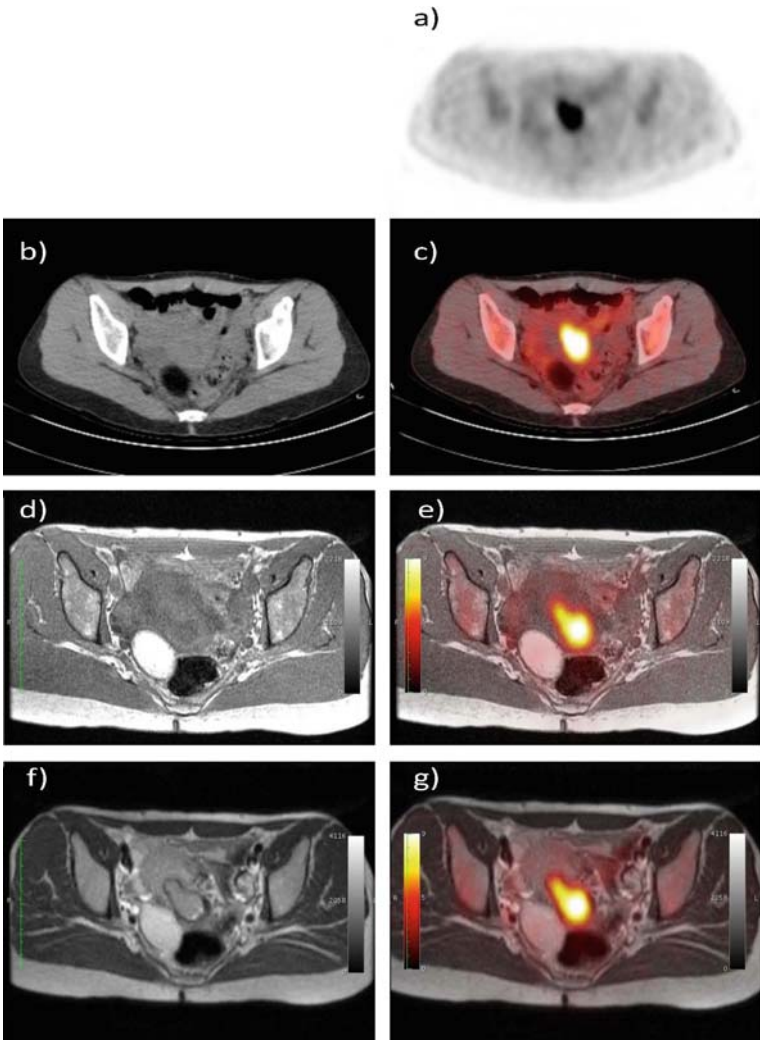

Fig. 1. Case of cervical cancer. Positron emission tomography (PET) shows abnormal accumulation of fluorodeoxyglucose (FDG) in the pelvis. The lesion is not clear on the computed tomography (CT) scan with magnetic resonance T1-weighted imaging (T1WI), whereas the uterine cervix shows a mass lesion with T2WI. With fusion imaging, the lesion seen with T2WI accords with an abnormal accumulation of FDG. **a** CT. **b** CT/PET fusion. **c** T1WI. **d** T1WI/PET fusion. **e** T2WI. **f** T2WI/PET fusion

our analyses of CT obtained with the PET/CT system and MRI were consistent with those of previous studies,[9,10] which is the result of the high tissue contrast provided by T2WI.

Localization of the site of FDG accumulation is important for FDG-PET imaging. When mass lesions depicted by CT or MRI are associated with FDG accumulation, they are diagnosed as metabolically active and with a high probability of malignancy. PET/CT and PET/MRI fusion images are therefore especially beneficial for diagnosing lymph node metastasis.[11–13]

Differentiation of physiological from abnormal FDG accumulation is also important on FDG-PET diagnosis. SUV_{max} of 3.0 has been used as a differentiation index.[14–16] In the pelvis, FDG is known to accumulate in the normal uterine endometrium, ovary, urinary tract, rectum, and colon. The magnitude of physiological FDG accumulation varies as the urinary tract may have an SUV_{max} of more than 10.0 or endometrium may have an SUV_{max} of <3.0.[15] The SUV_{max} value itself is therefore not a reliable index. Instead, when FDG accumulation is found in normal organs or tissues as confirmed by CT or MRI, a convincing diagnosis of physiological accumulation can be made.

Our study demonstrated that the site of FDG accumulation can be more accurately identified by T2WI than by CT or T1WI. It is therefore only reasonable that PET/T2WI fusion images produced a more convincing diagnosis of the anatomical site of FDG accumulation than did CT or T1WI.[3] It is noteworthy that the ability to localize low-level FDG accumulation significantly deteriorated when CT or T1WI was utilized for fusion images. In several patients, mild to moderate FDG accumulation was found in small masses depicted by T2WI but not by CT or T1WI. FDG accumulation fused on the T2WI was correctly evaluated in these patients after taking the partial volume effect into account.

Our study indicated that separately obtained but fused PET/T2WI images are superior to the PET/CT images obtained with inline PET/CT. This is partly due

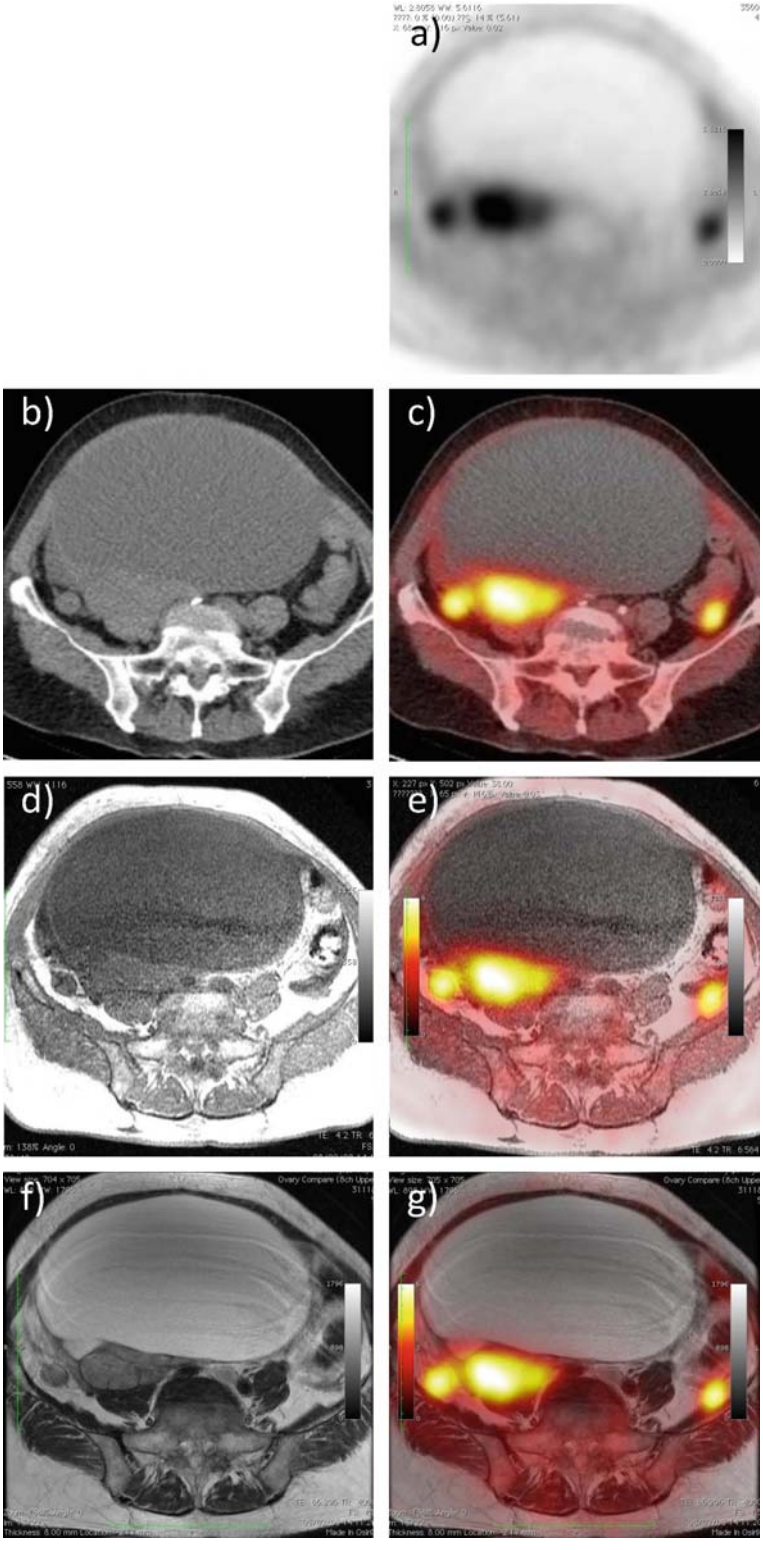

Fig. 2. Case of ovarian serous cystadenocarcinoma. PET shows abnormal accumulation in the pelvis. With CT and MRI T1WI, the border of a solid portion and the cystic ingredient is indistinct. With T2WI, the border of a solid portion and the cystic portion becomes clear. Also, with the fusion image, we confirm a solid portion and show abnormal accumulation of FDG. **a** CT. **b** CT/PET fusion. **c** T1WI. **d** T1WI/PET fusion. **e** T2WI. **f** T2WI/PET fusion

to the fact that the CT images of PET/CT were obtained with limited radiation exposure whereas the MRI images were obtained with high-quality MRI systems, so the diagnostic ability of PET/CT fusion images was partly underestimated.

Several trials have reported improved diagnostic ability of PET/CT for uterine cancer and ovarian cancer.[17–19] Kitajima et al. employed contrast-enhanced CT in addition to FDG PET/CT, and anatomical information on abnormal FDG accumulation was much

improved by fusing FDG PET images with those of the contrast-enhanced CT.[18,19]

A drawback of the PET/MRI fusion images is misregistration due to the movement of organs between the PET and MRI studies. Pelvic organs may show little respiratory movement, but urinary volume and location of gas in the intestine, colon, and rectum may affect the location of surrounding organs. Another limitation of the present study is that pelvic MR images but not whole-body MR images were used for PET/MRI fusion images. Therefore, only the primary lesions and surrounding organs in the pelvis were evaluated. For a comparative study of diagnostic ability for metastasis, whole-body MRI is needed for the fusion images. Inline PET/MRI is expected to minimize these drawbacks of the PET/MRI fusion strategy, and several groups are developing a PET/MRI technique for experimental studies and clinical use.[20,21] Another limitation is that only two readers visually evaluated the images by subjective scoring. The evaluation depends on the reader's ability and individual impression. In addition, our patients had mostly cervical cancer, with the other cancers being represented by only three cases each. Therefore, our conclusion may be limited to cervical cancer and not be applied to general gynecological malignancies.

Conclusion

The results of our study demonstrate that MRI T2WI was superior to CT and MRI T1WI in localizing FDG accumulation and in convincingly diagnosing uterine and ovarian cancer.

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