Whole-body positron emission tomography with 18F-fluorodeoxyglucose is an effective method to detect extra-pelvic recurrence in uterine sarcomas

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Summary

Purpose of investigation: To assess the clinical use of F-18-fluorodeoxyglucose positron emission tomography (FDG-PET) in the post-therapy surveillance of uterine sarcoma. *Methods:* Eight whole-body FDG-PET studies were performed in seven women with previously treated uterine sarcoma. Conventional image studies (computed tomography) and physical examinations were performed for follow-up. All FDG-PET studies were indicated to localize suspected recurrences noted by conventional methods. *Results:* The per case sensitivity of the FDG-PET studies and CT scans was 85.7% (6/7) and 100% (7/7), respectively (p = 0.174). FDG-PET was able to detect seven extrapelvic metastastic sites below the diaphragm (7/7, sensitivity: 100%), including the liver, spleen, paraaortic lymph node, spine and paracolic gutter, as well as pulmonary lesions in five patients, while the CT scan detected only three lesions (3/7, sensitivity: 42.9%; p = 0.070). FDG-PET detected only four recurrent pelvic lesions (4/6) and CT scan detected six (6/6) recurrent pelvic lesions (66.7% vs 100%, p = 0.455). *Conclusions:* The FDG-PET showed a better detection rate than the abdominal CT scan for extrapelvic metastatic lesions and a similar detection rate as well as abdominal CT scan. FDG-PET can serve as a useful detection tool for patients with uterine sarcomas because nearly 80% of recurrence involve an extrapelvic site.

Key words: FDG-PET; Recurrent uterine sarcoma; Post-treatment surveillance.

Introduction

Uterine corpus sarcomas are generally classified as leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), and carcinosarcoma (MMMT) [1]. These sarcomas are rare gynecological cancers, and represent only about 3-5% of all uterine tumors. The initial choice of treatment for these tumors is surgery. Adjuvant treatment, such as radiotherapy or chemotherapy, has shown little improvement in the survival rate or in decreasing the rate of recurrence [3-9]. The recurrence rate of uterine sarcoma is 30% to 60%, depending on the kind of sarcoma [10]. After staging and treatment, there is no standard program for post-therapy surveillance of these patients with uterine sarcoma. All follow-up modalities are performed mainly for the detection of recurrences, so that early treatment can be started. Uterine sarcoma may recur locally and/or at distant sites. Nearly 80% of all recurrences will involve an extrapelvic site [4, 5], and these cancers usually recur with a median time to recurrence of eight to 16 months [3-5]. Although the options for patients who experience a recurrence are still limited, the site of recurrence (local or distant) as well as the time of detection (early or late) may determine the options for follow-up treatment. The accuracy of conventional morphological imaging, such as computed tomography (CT) or magnetic resonance imaging (MRI) and ultrasound (US) in detecting recurrence may be decreased by post-surgical and post-radiation change [11-16]. Tumor markers could serve as a reflection of active tumor, but they have been unable to localize the site of recurrence, so the value of tumor markers for uterine sarcoma is still questionable [17].

Fluorine-18 fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) (FDG-PET) is a metabolic image, and has been useful in the detection, staging, and treatment monitoring of many kinds of cancers. Its application in uterine sarcoma has seldom been reported [18-21], and few reports have mentioned its utility in the post-treatment detection of recurrence [19-21]. In the present study, we retrospectively assessed the contribution of FDG-PET in the post-therapy surveillance of seven Asian women with uterine sarcoma.

Materials and Methods

Between July 1998 and September 2003, seven patients with uterine sarcoma were eligible for enrollment. All seven (mean age: 53.7 ± 10.5 years) had undergone staging surgery and adjuvant treatment, and received eight FDG-PET studies. One patient had undergone two FDG-PET studies. After the initial standard treatment, all patients received routine follow-up, which comprised regular outpatient visits every month, pelvic examinations, including vaginal Papanicolaou smears and image studies (X-ray, ultrasound, CT for pelvic, abdominal or

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Table 1. — *Patient profile.*

Patient No.	Age	Histology	Tumor stage	Final diagnosis	FDG-PET	CT scan	Locations detected by PET	Tumor marker CA-125	Following procedure	Treatment and status after PET
1	66	MMMT	III	Rec	TP	TP	Distant (retroperitoneal cavity, spleen)	Unknown	Operation	Lost F/U
2	52	MMMT	II	Rec	TP	TP	Local+distant (Paracolic gutter and pelvic lesions)	Normal	Operation	C/T and no rec within 1 year
3	49	MMMT	IC	Rec	TP	TP	Distant (Paraarotic, pelvic LAP and spine)	Unknown	Biopsy were performed to confirm paraaortic lymph node and spie metastasis	Expired 3 months later
4-1	39	ESS	IB	Rec*	TP	TP	Distant (paratracheal and lung)	Elevation	No operation	Hormone tx and rec within one year
4-2				Rec	TP	TP	Local + distant (ovarian metastasis)	Elevation	Operation	C/T, then no pelvic rec
5	48	LMS	I	Rec	FN	TP	Negative	Normal	Biopsy	C/T then expired within 1 year
6	53	Uterine sarcoma	I	Rec	TP	TP	Distant (lung and spine)	Unknown	Biopsy	C/T and no rec within 1 year
7	69	LMS	I	No rec	TN	FP	Negative	Normal	Biopsy	F/U and no rec within one year

MMMT: Malignant Mixed mullerian tumor; ESS: Endometriral stromal sarcoma; LMS:leiomyosarcoma; LN: lymph node; Meta: metastases; TP: true positive; TN: true negative; FP: false positive; FN: False negative; C/T: Chemotherapy; R/T: Radiotherapy; F/U: Follow-up; US: ultrasound; LAP: lymphadenopathy; Distant: Out of pelvic region; Local: in pelvic region; Rec: recurrence with pathologic proof; Rec*: recurrence without pathologic proof but clinically proven.

chest), and some patients had serum tests for CA-125. Uterine sarcomas were initially classified from Stage I to III, based on the international Federation of Gynecology and Obstetrics (FIGO) staging systems.

In this study, all FDG-PET studies were indicated for post-treatment patients with uterine sarcoma. All of the patients were prepared with overnight fasting to reduce serum glucose and insulin levels to near basal concentration before ^{18}F-FDG injections. FDG-PET was performed with a Scanditronix 15WB whole body PET Scanner (Scanditronix, Sweden) for all patients. The FDG-PET scan was started 50 minutes after an intravenous injection of 10-15 mCi of ^{18}F-FDG. To avoid bladder and urethral artifacts, an intravenous injection of diuretics (Lasix) was prescribed and a Foley catheter was implaced to empty the bladder. Images were obtained and reconstructed on the transaxial, sagittal, and coronal planes, and also in rotating fashion. The PET images were interpreted by two nuclear physicians, who were blinded to the CT imaging. Any focal uptake of ^{18}F-FDG, which is not considered to be physiologic on FDG-PET images, was recorded.

The CT scans were obtained from Siemens Somatom Plus 4 Power; the CT images were interpreted by two radiologists, who were blinded to the PET findings. CT and FDG-PET imaging results were reported according to the sites and sizes of all detected lesions. The final diagnosis of recurrence in this study was established by local biopsy, surgery, or clinical follow-up.

Results

Eight whole body FDG-PET imaging studies were performed in seven patients with uterine sarcomas. All (8/8) of the FDG-PET studies were indicated due to a suspected recurrence in a conventional image study and/or a symptomatic presentation.

Overall sensitivity and specificity in the imaging study

The characteristics of all patients are listed in Table 1. (Figure 1-3). Six out of seven patients were confirmed to have recurrence or metastasis. The per case sensitivity of the FDG-PET studies and CT scans was 85.7% (6/7) and 100% (7/7), respectively (p = 0.174) (Tables 1 and 2), and

Table 2. — *Sensitivity and specificity of PET and CT scan.*

	PET	CT scan	p value
Per case			
Sensitivity	85% (6/7)	100% (7/7)	0.174
Specificity	100% (1/1)	0% (0/1)	1.000
Per lesion			
Sensitivity	87.5% (14/16)	75%(12/16)	0.654
Specificity	100% (1/1)	0% (0/1)	1.000

Table 3. — *Location of recurrent or metastastic tumor detected by image studies.*

Location below diaphragm	PET	CT scan
Extrapelvic lesions		
Intraperitoneal tumor	1	0
Bone (spine)	2	0
Paraaortic lymph node	1	0
Peritoneal carcinomatosis	1	1
Liver	1	1
Spleen	1	1
Intrapelvic lesions		
Pelvic tumor	3	5
Pelvic lymph node	1	1
Above diaphragm		
Lung	2	2
Paratracheal region	1	1

(a) (b, c)

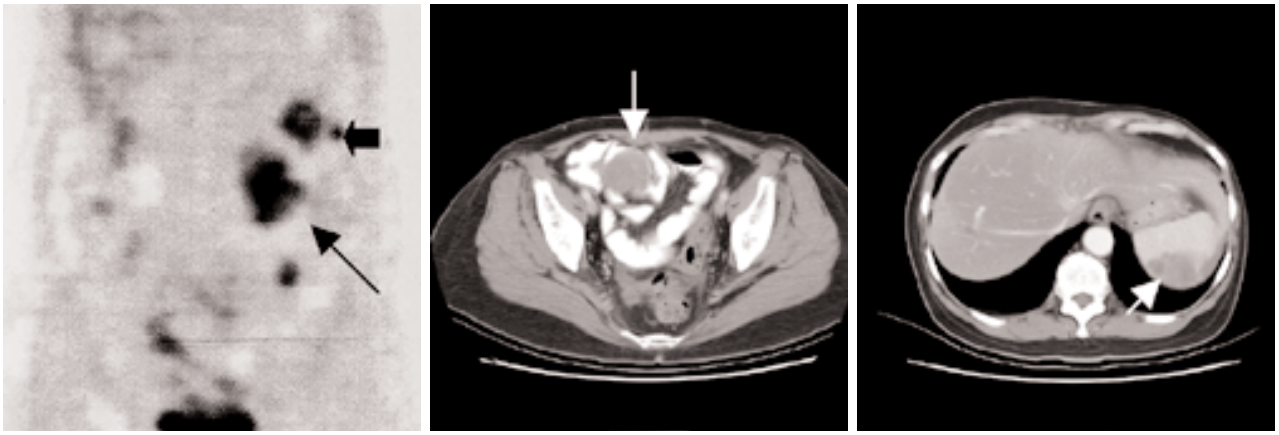

Figure 1. — Patient 1 (a case of MMMT): (a) whole body FDG-PET detected peritoneal carcinomatosis and spleen metastasis (black arrows, coronal view) (b, c) abdominal CT showed carcinomatosis and spleen tumor (white arrows, transaxial view).

(a) (b) (c)

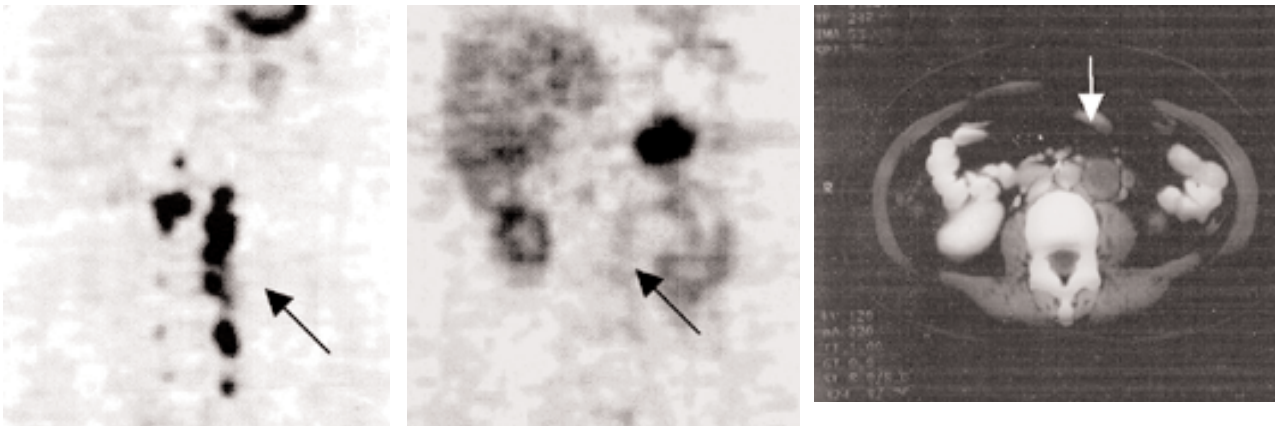

Figure 2. — Patient 3 (a case of MMMT with disseminated metastasis): (a) whole body FDG-PET showed paraaortic lymph node metastasis (black arrows, coronal view) (b) not seen in 11C-acetate PET (coronal view) (c) abdominal CT did not show this metastasis (white arrows, transaxial view).

(a) (b)

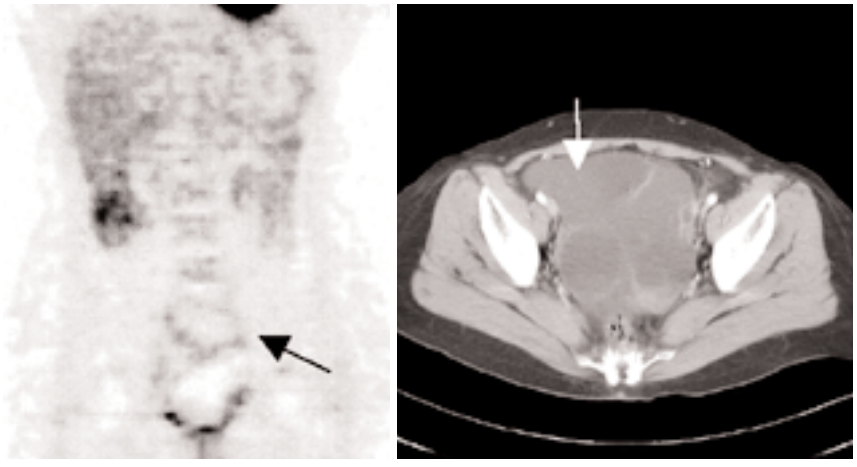

Figure 3. — Patient 4 (a case of low grade ESS): (a) whole body FDG-PET detected recurrence of pelvic cystic lesions which had increased intensity of ^{18}FDG uptake in peripheral area (black arrow, coronal view) (b) abdominal CT revealed clearly recurrent cystic tumors (white arrow, transaxial view).

the per case specificity of the same two studies was 100% (1/1) and 0% (0/1), respectively (p = 1.000). The per lesion sensitivity of the FDG-PET studies and CT scans was 87.5% (14/16) and 75% (12/16), respectively (p = 0.654) (Tables 1 and 2), and the per lesion specificity of the same two studies was 100% (1/1) and 0% (0/1), respectively (p = 1.000).

Table 4. — *Sensitivity according to lesion locations*.

Sensitivity according to lesion location	PET	CT scan	p value
Below diaphragm	84.6%(11/13)	69.2%(9/13)	0.645
Extrapelvic lesions	100% (7/7)	42.9% (3/7)	0.070
Intrapelvic lesions	66.7%(4/6)	100% (6/6)	0.455
Above diaphragm	100% (3/3)	100% (3/3)	

Extrapelvic lesions below the diaphragm

In the present study, FDG-PET was able to detect seven extrapelvic metastastic sites below the diaphragm (7/7, sensitivity: 100%), including the liver, spleen, paraaortic lymph node, spine and paracolic gutter, as well as pulmonary lesions in five patients (Tables 3 and 4), while the CT scan detected only three lesions (3/7, sensitivity: 42.9%; p = 0.070). The FDG-PET study detected extrapelvic metastatic lesions in the spine in two patients, an abdominal lesion in one patient, and paraaortic lymphadenopathy in one patient, all of which CT or US missed. The FDG-PET also added more information for tumor extension in three of six patients, especially paraaortic lymph node and spinal metastases.

Intrapelvic lesions below the diaphragm

FDG-PET detected only four recurrent pelvic lesions (4/6, sensitivity: 66.7%), including pelvic tumors and pelvic lymph nodes, which were also noted in the conventional imaging studies of these patients, and CT scan detected six (6/6,100%; p = 0.455) recurrent pelvic lesions (Tables 3 and 4). Pathology confirmed the recurrence in the six patients.

Lesion above the diaphragm

The capability of the FDG-PET study to detect lesions (3/3, 100%) above the diaphragm, including lung and paratracheal lesions, was equal to that of the chest CT scan (3/3, 100%) (Tables 3 and 4).

The follow-up FDG-PET imaging study played a role in deciding the follow-up treatment. Confirmation of the recurrent pelvic lesions or operative extrapelvic lesions by the conventional imaging study, and then by the FDG-PET study, compelled the oncologist to perform surgery (Table 1). Other metastases or recurrent lesions had been treated by adjuvant chemotherapy (Table 1). Due to the disseminated diseases noted in both the FDG-PET study and CT scan in patient 3, palliative support treatment was given. The only case with a suspected lesion seen in the conventional study and a false-negative result in the FDG-PET study was conservatively followed-up. The patient expired within one year, even though she received adjuvant chemotherapy after the symptoms appeared. Patient 7, with a true negative FDG-PET image study, underwent a local biopsy for lesions seen in the CT scan, and no recurrence of the suspected lesion was confirmed. The patient had no recurrence during a one-year follow-up.

Discussion

The prognosis of uterine sarcoma has been considered to be poor, and the recurrence rate has been high, even in early stages [1-10,17, 22, 23]. In this study of seven patients with uterine sarcoma, the clinical staging was I in five, II in one, and III in one. However, six of seven (85%) patients with uterine sarcoma had recurrence (4 in Stage I, 1 in Stage II and 1 in Stage III). This was comparable with previous reports.

PET is now widely used in the field of gynecological oncology, including breast, cervical, and ovarian cancer [24-29]. It is a particularly useful tool because it evaluates the whole body in a single examination. Conventional image studies cannot survey the whole body at one time in one study. The more imaging studies that are performed, the more anxiety and medical costs the patients must endure.

Studies of FDG-PET applied in the post-surveillance of uterine sarcoma are limited. Umesaki *et al*. reported three studies on the utility of a preoperative diagnosis of uterine sarcoma. They reported PET had 100% positive findings for five sarcomas (including one recurrent case of leiomyosarcoma) for preoperation diagnosis, compared with 80% by MR imaging study, and 40% with US [18, 19]. Jadvar *et al*. reported a patient with metastastic leiomyosarcoma, who had received a total abdominal hysterectomy, bilateral oophorectomy, and omentectomy six months earlier, and presented with a lower abdominal wall soft tissue mass [20]. Murakami *et al*. recently reported on eight patients with sarcoma after primary treatment of uterine sarcoma, who underwent FDG-PET for the detection of recurrence. Final diagnoses of recurrence were established in five cases. The recurrence sites revealed by PET were in the intraperitonum, liver, lung, bone and retroperitoneal lymph nodes. The overall sensitivity of FDG-PET, CT and US was 100%, 60% and 60%, respectively [21]. In the present study, the rate of detection of recurrence by FDG-PET and conventional imaging studies was 87.5% (14/16) and 75% (12/16), respectively.

In extrapelvic metastastic sites below the diaphragm, FDG-PET showed a better detection rate than abdominal CT scans (7/7, 100% vs 3/7, 42.9%, respectively). The FDG-PET studies detected extrapelvic lesions of the spine in two patients and paraarotic lymphadenopathy in one patient, which were metastatic locations that the abdominal studies had missed. The diagnosis of lymph node abnormalities with CT largely depends on size. However, normally-sized lymph nodes may be diseased, and in contrast, enlarged lymph nodes may show an

inflammatory response and be free of disease. In the cases of ovarian cancer, Murakami *et al*. reported PET findings could detect normally-sized metastases of lymph nodes in 50% of cases of retroperitoneal metastases, which could not be detected by CT [21]. PET has a better detection rate in bone metastases patients than the CT scan. These are the reasons why PET had a better detection rate in extrapelvic lesions. The capability of the FDG-PET studies to detect these lesions (3/3, 100%) above the diaphragm, including lung and paratracheal lesions, was almost equal to that of the chest CT scan (3/3, 100%). Thus, PET is a good method to detect extrapelvic lesions, including in the lymph nodes, bone, upper abdomen, and chest.

However, FDG-PET did not show a good detection rate in pelvic recurrent lesions (4/6, 66.7%) in this study, compared with abdominal CT scans (6/6, 100%). Many papers in oncology have reported that PET is of limited use in the detection of malignant tumors less then 1 cm in size. The minimum size of tumors detected by PET depended on the sites of recurrence [21]. It is hard to detect a small pelvic tumor near the bladder due to the accumulation of FDG in the urinary tract. These regions usually cannot be precisely identified in FDG-PET imaging due to bowel or urethral tracer accumulation. Combined PET/CT could efficiently contribute to distinguishing a physiological tracer uptake from tumor lesions in the abdomino-pelvic region. PET/CT allows for the accurate localization of foci or radiotracer, and provides precise anatomic landmarks for recurrent disease, especially in the abdomino-pelvic area [30]. PET/CT can also be used with uterine sarcoma in the future.

There were no false positive results in our FDG-PET studies, and visual evaluation of the FDG-PET study results was performed by an experienced radiologist. Acute edema or inflammation may induce the uptake of ^{18}FDG with a high intensity [31]. To overcome this limitation, quantitative assessment with standard uptake values (SUVs) and the percentage of residual activity (% RA) in the FDG-PET study may improve the distinguishing of false-positive findings [32]. Further study for the quantitative assessment of post-treatment recurrence should be done.

In extrapelvic metastastic sites, FDG-PET showed a better detection rate in this study than abdominal CT scanning, although FDG-PET did not have a good detection rate for pelvic recurrent lesions, compared to the abdominal CT scan. Nonetheless nearly 80% of all recurrences in uterine sarcoma will involve an extrapelvic site, so whole-body FDG-PET imaging studies can be a useful tool in the detection of recurrence and metastases in extrapelvic sites in patients with uterine sarcoma. Therefore, larger studies are needed to evaluate the complementary role of FDG-PET and conventional imaging studies in the detection of distant metastasis.

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