

Clinical value of FDG-PET in the follow up of post-operative patients with endometrial cancer

Tsuneo SAGA,* Tatsuya HIGASHI,* Takayoshi ISHIMORI,* Marcelo MAMEDE,* Yuji NAKAMOTO,*
Takahiro MUKAI,* Toru FUJITA,* Kaori TOGASHI,* Shigeo YURA,** Toshihiro HIGUCHI,**
Masato KITA,** Shingo FUJII** and Junji KONISHI*

*Department of Nuclear Medicine and Diagnostic Imaging and **Department of Obstetrics and Gynecology,
Graduate School of Medicine, Kyoto University

Objective: The clinical usefulness of FDG-PET in the follow up of post-operative patients with endometrial cancer was retrospectively evaluated. **Methods:** Twenty-one post-operative patients with endometrial cancer received 30 FDG-PET examinations to evaluate recurrence or response to treatment. The findings of FDG-PET were compared with their serum levels of tumor markers, CT and/or MRI findings, and the final outcome. Results of FDG-PET were also correlated with the clinical course of each patient. **Results:** In detecting recurrent lesions and evaluating treatment responses, FDG-PET, with the help in anatomic information by CT/MRI, showed better diagnostic ability (sensitivity 100.0%, specificity 88.2%, accuracy 93.3%) compared with combined conventional imaging (sensitivity 84.6%, specificity 85.7%, accuracy 85.0%) and tumor markers (sensitivity 100.0%, specificity 70.6%, accuracy 83.3%). FDG-PET had no false-negative results, suggesting the possibility of its use as the first-line examination in a patient's follow-up. FDG-PET could detect unknown lesions in 4 cases, and, as reported for other malignancies, FDG-PET affected the patient management in one-third of the cases. Furthermore, the results of FDG-PET correlated well with the clinical outcome of the patients, with patients with negative PET results tending to show disease-free courses. **Conclusions:** These results suggest that, despite the limited number of patients studied, FDG-PET was accurate in detecting recurrence and evaluating therapeutic response, and could afford important information in the management of post-operative patients with endometrial cancer. FDG-PET also appeared to have a possibility to predict the outcome of each patient.

Key words: FDG-PET, endometrial cancer, recurrence, treatment response

INTRODUCTION

POSITRON EMISSION TOMOGRAPHY (PET) using ^{18}F -fluorodeoxyglucose (FDG) has been widely used in the assessment of patients with various malignancies such as lung cancer, cancer of the gastrointestinal tract and malignant

lymphoma.^{1–3} Since FDG-PET can afford metabolic information of the cancerous tissues irrespective of the morphological changes, it is expected to play a major role in differentiating malignant from benign lesions, in detecting recurrent lesions which were indistinguishable from normal structures or post-operative changes by morphological imaging, and so on. In addition, whole-body scan with short acquisition time is advantageous for detecting unexpected distant metastasis. FDG-PET has recently been applied also to patients with gynecological malignancies, and several studies have been published describing the usefulness of FDG-PET in the diagnosis of recurrent uterine cervical and ovarian cancers.^{4–8} For endometrial cancers, however, there have been very few

Received November 28, 2002, revision accepted February 10, 2003.

For reprint contact: Tsuneo Saga, M.D., Department of Nuclear Medicine and Diagnostic Imaging, Graduate School of Medicine, Kyoto University, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606–8507, JAPAN.

E-mail: saga@kuhp.kyoto-u.ac.jp

Table 1 Patient profile

#	age	stage	histology	aim of FDG-PET	final diagnosis	FDG-PET****	tumor marker **	CT/MRI**
1	54	Ia	endo G1	rec suspected	no rec	TN	CA125 normal	FP
2	70	Ia	endo G2/serous	follow up	no rec	TN	CA125 normal	N/A
3	82	Ib	endo G1	rec suspected	no rec	FP	CA19-9 elevated	TN
4	53	Ib	endo G1	follow up	no rec	TN	normal	N/A
5	44	Ib	endo G1	rec suspected	no rec	TN	CA19-9 elevated	TN
6-1				re-staging	local	TP	STN elevated	TP
6-2	66	Ib	endo G2	re-staging	local	TP	STN elevated	FN
6-3				follow up	no rec	TN	STN elevated	N/A
7	59	Ic	endo G1	therapeutic effect	no rec	FP	CA125 elevated	TN
8	66	Ic	serous	therapeutic effect	no rec	TN	CA125 normal	N/A
9-1				re-staging	local/LN	TP	CA125 elevated	TP
9-2	69	Ic	serous	re-staging	LN	TP	CA125 elevated	TP
10	56	IIb	endo G2	follow up	no rec	TN	CA125 normal	N/A
11-1				rec suspected	lung	TP	CA125 elevated	TP
11-2	67	IIIa	small cell	therapeutic effect	no rec	TN	CA125 normal	N/A
11-3				follow up	no rec	TN	CA125 normal	N/A
12	54	IIIa	endo G2	rec suspected	no rec	TN	CA19-9 elevated	N/A
13	54	IIIa	endo G2	therapeutic effect	no rec	TN	CA125 normal	TN
14	56	IIIc	endo G2	follow up	no rec	TN	CEA normal	N/A
15	77	IIIc	endo G1/clear	therapeutic effect	no rec	TN	CA19-9 normal	TN
16-1				re-staging	LN/dissemi	TP	CA125 elevated	TP
16-2	57	IIIc	serous	therapeutic effect	LN	TP	CA125 elevated	TP
17	65	IIIc	serous	re-staging	local/LN/ lung/bone	TP	CA125 elevated	TP
18	64	IVb	serous	re-staging	dissemi	TP	CA125 elevated	TP
19-1				therapeutic effect	liver	TP	CA125 elevated	TP
19-2				therapeutic effect	liver/LN	TP	CA125 elevated	TP
19-3	51	IVb	endo G3	re-staging	liver/lung/ LN/dissemi	TP	CA125 elevated	TP
20	58	IVb	serous	follow up	no rec	TN	CA125 normal	N/A
21-1				rec suspected	dissemi	TP	CA125 elevated	FN
21-2	77	IVb	serous/endo G3	therapeutic effect	no rec	TN	CA125 normal	TN

endo: endometrioid carcinoma, G: grade, serous: serous papillary carcinoma, clear: clear cell carcinoma, small cell: small cell neuroendocrine carcinoma, rec: recurrence, LN: lymph node metastasis, dissemi: dissemination, lung: lung metastasis, bone: bone metastasis, CT/MRI: available CT and/or MRI, TP: true positive, TN: true negative, FP: false positive, FN: false negative

*: FDG-PET was evaluated with the help of CT/MRI for anatomic information.

**: Examination-based diagnosis

studies describing the clinical application of FDG-PET, in which Belhocine et al. first described the usefulness of FDG-PET in the post-therapy surveillance.^{9,10} In the present study, to clarify the usefulness of FDG-PET in the management of patients with endometrial cancer, we retrospectively reviewed and evaluated the diagnostic ability of FDG-PET in detecting recurrent lesions and evaluating treatment response, and also studied the impact of FDG-PET on the management of post-operative patients with endometrial cancer.

MATERIALS AND METHODS

Patients

Twenty-one post-operative patients with uterine endometrial cancer were included in the present study (44 to 82 years, mean 62 years). Before being enrolled in this study,

each of the patients gave written informed consent, as required by the Kyoto University Human Study Committee. Table 1 summarizes the profiles of the patients. Clinical stages at operation were diagnosed as I in 9 patients, II in 1 patient, III in 7 patients and IV in 4 patients. The histology of endometrial cancer was confirmed as endometrioid adenocarcinoma in 10 patients, serous papillary carcinoma in 6 patients, small cell neuroendocrine carcinoma in 1 patient, mixed endometrioid and serous carcinoma in 2 patients and mixed endometrioid and clear cell carcinoma in 1 patient. All patients underwent FDG-PET examinations and evaluation of serial serum tumor marker levels, such as CA125, CA19-9, CEA, and STN (Sialyl TN antigen). CT and/or MRI images were obtained in 14 patients (19 examinations).

FDG-PET

Between April, 1999 and March, 2002, 30 FDG-PET examinations were performed for these 21 patients (3 patients received 3 examinations and 3 patients received 2 examinations). Twenty-one FDG-PET examinations were done to evaluate recurrence (re-staging recurrence, evaluating suspected recurrence, and follow-up study without suspicion of recurrence) and 9 examinations were conducted to evaluate the response to treatment.

Fluorine-18 FDG was synthesized by the nucleophilic substitution method with an ^{18}F -FDG-synthesizing instrument F-100 (Sumitomo Heavy Industries, Co. Ltd., Tokyo, Japan) and a cyclotron, CYPRIS-325R (Sumitomo Heavy Industries, Co. Ltd.).^{11,12}

All patients were examined with a high-resolution, whole-body PET scanner with an 18-ring detector arrangement (Advance, General Electric Medical Systems, Milwaukee, WI). The system permitted the simultaneous acquisition of 35 axial images with interslice spacing of 4.25 mm. Axial resolution was 4.2 mm full width at half-maximum intensity, allowing multidirectional reconstruction of the images without loss of resolution. The field of view and pixel size of the reconstructed images were 256 mm and 2 mm, respectively.

The patients fasted for more than 4 hours before the injection of FDG. Approximately 370 MBq of FDG was intravenously injected, and the acquisition of whole body PET images started 50 minutes later. Each emission scan was obtained for 3 minutes per single bed position and each post-emission transmission scan was obtained for 1 min per single bed position. To cover from the face to the upper thigh, 5 to 6 bed positions were scanned according to the height of each patient. In order to minimize the activity in the urinary bladder, emission data were obtained starting from thigh upward to the head just after urination. To patients who were hospitalized in the gynecological ward of our institution, we gave i.v. hydration (1,000 ml of saline) and 20 mg of furosemide, and placed a triple-lumen Foley catheter in the bladder for continuous irrigation and drainage before imaging the pelvis. Until June 2000 (5 examinations), only the emission scan was obtained and the non-attenuation corrected images were reconstructed using filtered-back projection algorithms. From June, 2000 (25 examinations), both emission and post-emission transmission scans were obtained and the attenuation corrected images were reconstructed using iterative reconstruction algorithms and segmented attenuation correction.

Conventional Imaging

CT scans were obtained with two helical scanners with and/or without intravenous contrast material (W3000, Hitachi Medico, Tokyo, Japan; or HiSpeed Advantage, General Electric Yokogawa Medical Systems, Tokyo, Japan). Patients were administered 100–150 ml of non-ionic contrast material via mechanical injection at a rate of

2 ml/sec, and the scanning began 2 minutes after the start of contrast material injection.

MR imaging was performed using a 1.5-T superconductive system (Signa, General Electric System; or Magnetom Symphony, Siemens, Erlangen, Germany) with a body coil, with which sagittal and axial T2-weighted fast-spin echo images and T1-weighted spin echo images were obtained. A Gd-enhanced T1-weighted image with fat-saturation was also obtained in some patients.

Image Analysis

Available conventional images, such as CT and MRI, were interpreted by the consensus of at least three experienced radiologists who were unaware of the PET findings. PET images were interpreted by at least three experienced nuclear medicine physicians with all available clinical information and correlative conventional imaging as an anatomic guidance. In the present study, PET images were evaluated only qualitatively, where focal accumulation of FDG, which could be distinguished from physiologic accumulation, was regarded as abnormal.

The FDG-PET findings were compared with that of the

Table 2 Examination-based diagnostic ability of FDG-PET, conventional imaging and tumor markers

	FDG-PET*	CT/MRI	TM
TP	13	11	13
TN	15	6	12
FP	2	1	5
FN	0	2	0
(number of cases)			
sensitivity (%)	100.0	84.6	100.0
specificity (%)	88.2	85.7	70.6
accuracy (%)	93.3	85.0	83.3

TP: true positive, TN: true negative, FP: false positive, FN: false negative, CT/MRI: available CT and/or MRI, TM: tumor markers. *: FDG-PET was evaluated with the help of CT/MRI for anatomic information.

Table 3 Lesion location-based diagnostic ability of FDG-PET and conventional imaging

	FDG-PET*	CT/MRI
TP	22	18
TN	15	6
FP	4	1
FN	0	3
(number of locations)		
sensitivity (%)	100.0	85.7
specificity (%)	78.9	85.7
accuracy (%)	90.2	85.7

TP: true positive, TN: true negative, FP: false positive, FN: false negative, CT/MRI: available CT and/or MRI. *: FDG-PET was evaluated with the help of CT/MRI for anatomic information.

combination of conventional imaging and tumor markers, and were related to the final diagnosis obtained by histopathology, response to treatment, and further clinical follow up for at least 5 months including imaging studies and the check-ups of tumor marker levels. Diagnostic ability was determined on a patient-basis and also on lesion location-basis (local, various metastasis sites such as lymph node (LN), bone, liver, and lung). In addition to determining the diagnostic accuracy of FDG-PET, the ability of FDG-PET to give additional lesions that could

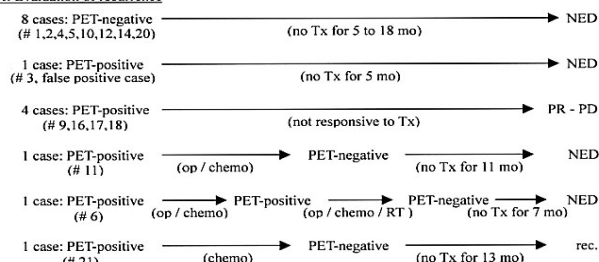
Table 4 Diagnostic ability of abdominal lesions

	CT	CT + MRI	FDG-PET*
TP	13	15	18
TN	4	6	15
FP	1	1	3
FN	5	3	0
	(number of lesions)		
	CT	CT + MRI	FDG-PET*
sensitivity (%)	72.2	83.3	100.0
specificity (%)	80.0	85.7	83.3
accuracy (%)	73.9	84.0	91.7

*: FDG-PET was evaluated with the help of CT/MRI for anatomic information.

Clinical outcome of patients related to the purpose of FDG-PET examination.

A: Evaluation of recurrence



B: Evaluation of treatment response

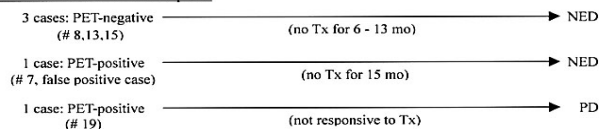


Fig. 1 Clinical outcome of patients related to the purpose of the FDG-PET examination. Tx: treatment, op: operation, chemo: chemotherapy, NED: no evidence of disease, PR: partial response, PD: progressive disease, rec.: recurrence

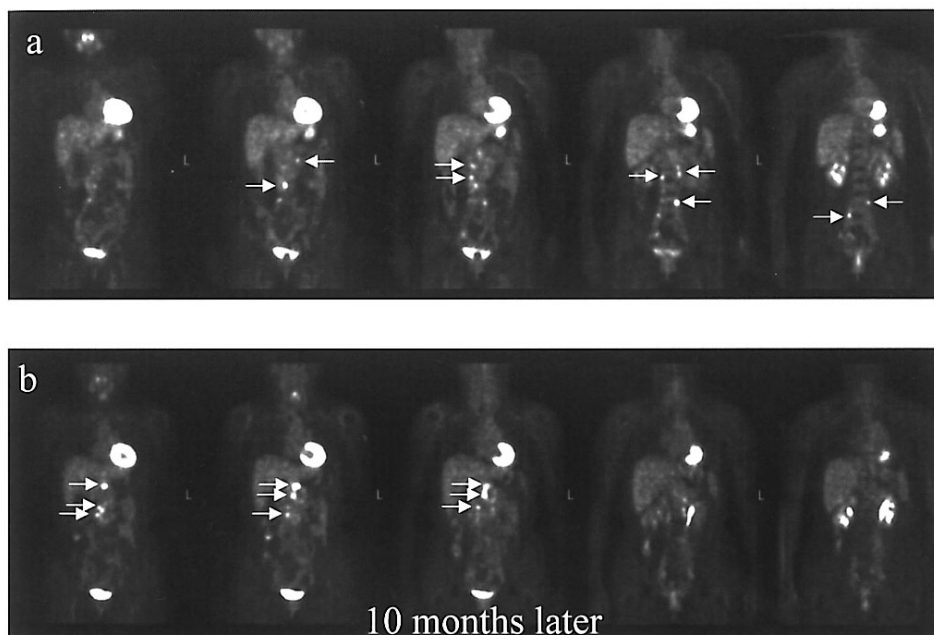


Fig. 2 Serous papillary adenocarcinoma, initial stage IIIc (#16). The first FDG-PET, examined when the patient had a high serum CA125 level and was diagnosed as recurrence by CT and MRI, showed multiple uptakes (white arrows) in the abdomen suggesting LN metastases (a). She received repeated systemic chemotherapy and also radiation therapy to the LN metastasis invading the 4th lumbar vertebra. The second FDG-PET, examined 2 months after the last treatment to evaluate the treatment response, showed decreased FDG uptake in the lower abdomen and pelvis suggesting a therapeutic effect, but also showed increased FDG uptakes (white arrows) in the upper abdomen (lymph node metastases) which was outside the field of radiation therapy (b).

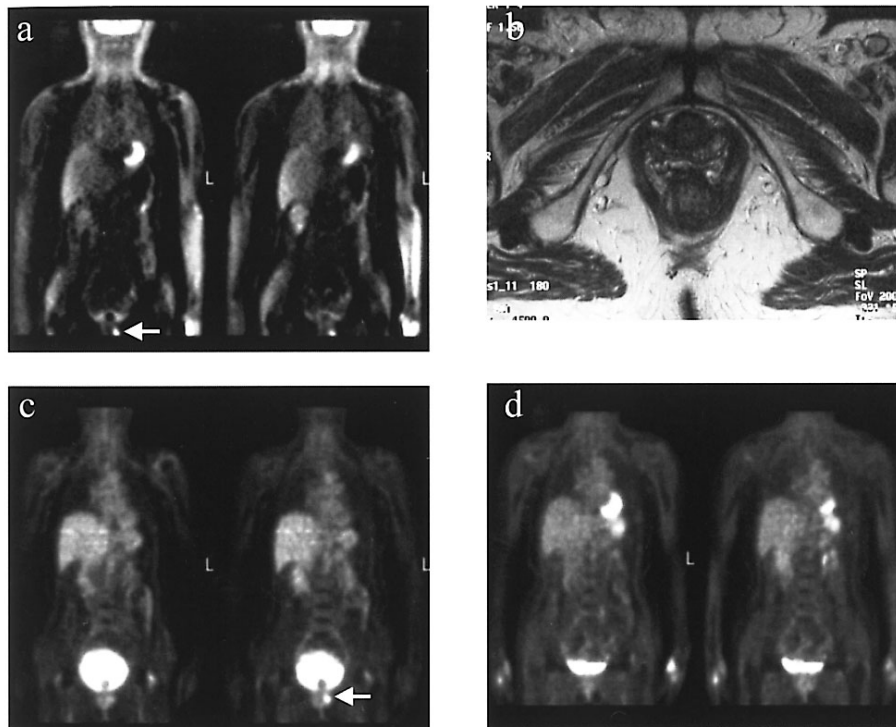


Fig. 3 Endometrioid adenocarcinoma Grade 2, initial stage Ib (#6). The first FDG-PET, examined before the resection of local recurrence, clearly showed the recurrent focus in the vagina (a, white arrow), which was also detected by MRI. After resection and 2 courses of systemic chemotherapy, she developed another recurrent lesion in the vagina, which was unclear by MRI (b, T2WI) but was detected by FDG-PET (c, white arrow). After the operation, post-operative irradiation, and chemotherapy, the follow-up FDG-PET became negative (d) and she remained disease-free thereafter.

not be detected by conventional imaging, and the impact of FDG-PET on the management of each patient were evaluated. Furthermore, we also correlated the results of FDG-PET with the clinical outcome (responsiveness to treatment, duration of disease free-survival, etc.) of each patient.

RESULTS

Among 21 patients, the diseases of 8 patients were finally diagnosed as recurrent lesions or viable lesions after therapy. Six of these 8 patients had non-endometrioid histology and 1 patient had high-grade (G3) endometrioid adenocarcinoma (Table 1). On an examination-basis, the sensitivity, specificity and accuracy of FDG-PET were 100.0%, 88.2% and 93.3%, respectively, which were better than those of the imaging results of available CT and/or MRI (84.6%, 85.7%, 85.0%) and tumor markers (100.0%, 70.6%, 83.3%) (Table 2). Interestingly, FDG-PET and tumor markers had no false-negative cases, while CT/MRI showed fewer false-positive cases than FDG-PET and tumor markers. On a lesion location-basis, FDG-PET also showed better sensitivity and accuracy than CT/MRI results (sensitivity: 100.0% vs. 85.7%, accuracy: 90.2% vs. 85.7%) (Table 3).

The ability to detect abdominal lesions by abdominal CT, combined abdominal CT and pelvic MRI, and FDG-PET was also compared (Table 4). Abdominal CT was less accurate for detecting a recurrent lesion in the abdomen (sensitivity 72.2%, specificity 80.0%, accuracy 73.9%) than FDG-PET (sensitivity 100.0%, specificity 83.3%, accuracy 91.7%). By combining the results of pelvic MRI with those of abdominal CT, the diagnostic ability improved (sensitivity 83.3%, specificity 85.7%, accuracy 84.0%), but was still worse than FDG-PET.

FDG-PET could detect unknown lesions in 4 cases. Among them, bone metastases and peritoneal dissemination were detected only by FDG-PET. Lung and LN metastases were later confirmed by conventional imaging. In addition, the results of FDG-PET changed the management of 7 patients (33.3%). In 3 patients, recurrence was confirmed by FDG-PET and treatment started. In 1 patient, the results of FDG-PET changed the treatment planning by correctly determining the lesion distribution. In the remaining 3 patients, suspected recurrence was excluded by FDG-PET, and they were followed without treatment.

Although we did not experience any false-negative cases of FDG-PET, false-positive lesions were observed in 4 cases. Physiological uptake in the intestine was

misinterpreted as dissemination or LN metastasis in 3 cases, and the heterogeneously increased uptake in the bone marrow after G-CSF administration for chemotherapy-induced neutropenia was misinterpreted as bone metastasis in 1 case.

Figure 1 schematically summarized the clinical outcome of 21 patients who received FDG-PET in relation to the aim of the FDG-PET and its result.

Among 16 patients, who were evaluated for recurrent lesions, 8 patients were PET-negative and all remained disease-free without treatment during the follow-up period. One additional patient, whose PET result was falsely positive, with intense intestinal uptake falsely diagnosed as dissemination, also remained disease-free. In 4 patients, who were PET-positive, treatment was not successful, and they showed only a partial response or disease-progression. Figure 2 illustrates the case of multiple LN metastases that could not be controlled by treatment. In 2 patients with positive PET results, recurrent lesions detected by FDG-PET were successfully treated and the follow-up PET became negative, and they were disease-free thereafter. Figure 3 illustrates the patient with local recurrence, who finally became disease-free after repeated treatment. In the last patient, a peritoneal disseminated lesion detected by FDG-PET could be successfully treated, and the follow-up FDG-PET became negative. However, after more than 1-year follow up without treatment, the patient's tumor markers started to rise again and she developed new peritoneal disseminated lesions.

When FDG-PET was used to evaluate the response to therapy, PET could correctly evaluate the viability of the disease. Three patients with negative PET findings and 1 patient, whose PET finding was falsely positive, remained disease-free without additional treatment during the follow-up period. However, in 1 patient, who showed a positive PET finding, additional treatment could not fully control the residual viable disease.

DISCUSSION

Endometrial cancer is known to have a better prognosis than uterine cervical cancer, especially in the early stage.¹³ However, in patients with advanced stage disease (> stage III), high-grade endometrioid adenocarcinoma, and those having non-endometrioid histology such as serous papillary and clear cell carcinomas, the prognosis is not always good and they sometimes develop recurrence and metastasis in the post-operative course.^{14,15} In the present study, 6 of 8 patients with recurrent lesion had non-endometrioid histology and 1 of the remaining 2 patients had high-grade (G3) endometrioid adenocarcinoma. The clinical stages of these 8 patients were I in 2, III in 3, and IV in 3 patients. From these findings, it appears that endometrial cancer patients with non-endometrioid histology or high-grade (grade 3) endometrioid adenocarcinoma, and with advanced clinical stage at initial surgery

(> stage III) require particularly strict follow up.

In detecting recurrent lesions, FDG-PET, with the help of anatomic information by CT/MRI, showed the best diagnostic ability among the three modalities tested (FDG-PET, combined conventional imaging results, and tumor markers). Interestingly, FDG-PET showed no false negative cases with a high negative predictive value, while conventional imaging showed fewer false positive cases with a high positive predictive value. These results favor the use of FDG-PET as the first-line diagnostics in the follow up of post-operative patients with endometrial cancer.

Serum tumor markers also showed a specificity of 100%, but also many false positive cases, resulting in the lowest specificity among the three modalities compared. This is not surprising since elevation of serum tumor markers also occurs in non-malignant conditions, such as inflammation and benign tumors. Furthermore, tumor markers cannot localize the site of recurrence.

In contrast to the high negative predictive value of FDG-PET in the present study, we experienced 4 false positive lesions resulting from physiological intestinal uptake and increased bone marrow uptake by the use of G-CSF after chemotherapy. Close comparison of the FDG uptake sites with anatomical images and full knowledge of the clinical information are important to minimize these false positive lesions.

In the evaluation of patients with gynecological malignancies, pelvic MRI is the examination of choice for the local status in the pelvis, and abdominal CT is usually conducted for the examination of the whole abdomen to detect metastasis and dissemination. However, the diagnostic ability of abdominal CT in the detection of recurrent lesions in the abdomen was not sufficiently high, and even with the combination of abdominal CT and pelvic MRI, the diagnostic ability was less than that of FDG-PET. FDG-PET appears to have the possibility to serve as the initial examination to detect suspected recurrence and to evaluate the treatment response, although CT or MRI should be conducted to clarify the anatomic and morphologic nature of the suspected lesion.

In addition, FDG-PET could detect unknown lesions. In one-third of the patients, the results of FDG-PET affected the management of the patients, which similar to the experience reported for other malignancies.^{16,17}

Long-term follow up of these patients showed that the results of FDG-PET correlated well with the clinical outcome of the patients. All patients with negative PET findings in the initial examination were disease-free during the follow up period. In addition, even if the initial PET was positive, if the follow up PET became negative after treatment, those patients remained disease-free during the follow up period, although 1 patient with peritoneal dissemination finally developed a new disseminated lesion after a 1-year disease-free period. This suggests that the results of FDG-PET can be used to evaluate the

treatment response, and a negative PET result is a predictor of favorable prognosis, although the number of such patients should be increased to give a definite conclusion. This is in contrast to the follow-up of ovarian cancer patients with FDG-PET. In ovarian cancer, especially in patients with advanced clinical stage at the initial treatment, negative PET results may not always imply a disease-free status, but may simply mean the absence of macroscopic disease, with recurrence occasionally encountered in the follow up of these patients.¹⁸ It is also reported that the sensitivity of FDG-PET in detecting small-volume disease before second-look laparotomy is low.¹⁹ This difference, probably reflecting the different nature of recurrence in the two diseases, may favor the use of FDG-PET in the follow up of endometrial cancer patients, while we should be more cautious in the interpretation of negative PET results in ovarian cancer patients. In the case of ovarian cancer, the presence of microscopic disseminated lesions is the diagnostic challenge.

Belhocine et al. recently published a paper describing the usefulness of FDG-PET in the post-treatment follow-up.¹⁰ In their study, the sensitivity, specificity, and accuracy of FDG-PET in detecting recurrence were 96%, 78%, and 89%, respectively, which were comparable to our results. They also reported that most (11 of 12) patients with negative PET studies remained disease-free in the follow-up period. In 35% of patients with confirmed recurrences, the PET findings significantly altered the treatment choice. Our present data gave additional support to these findings.

In conclusion, although the number of patients was limited, the present study showed that FDG-PET was accurate in detecting recurrences, and was useful in the follow up of post-operative patients with endometrial cancer, and warrants further studies with large number of patients. FDG-PET also appears to have the potential for evaluating the treatment response and to be useful in predicting the prognosis after treatment.

REFERENCES

1. Delbeke D, Martin WH. Positron emission tomography imaging in oncology. *Radiol Clin North Am* 2001; 39: 883–917.
2. Delbeke D. Oncological applications of FDG PET imaging: brain tumors, colorectal cancer, lymphoma and melanoma. *J Nucl Med* 1999; 40: 591–603.
3. Lowe VJ, Fletcher JW, Gobar L, Lawson M, Kirchner P, Valk P, et al. Prospective investigation of positron emission tomography in lung nodules. *J Clin Oncol* 1998; 16: 1075–1084.
4. Sugawara Y, Eisbruch A, Kosuda S, Recker BE, Kison PV, Wahl RL. Evaluation of FDG PET in patients with cervical cancer. *J Nucl Med* 1999; 40: 1125–1131.
5. Rose PG, Adler LP, Rodriguez M, Faulhaber PF, Abdul-Karim FW, Miraldi F. Positron emission tomography for evaluating para-aortic nodal metastasis in locally advanced cervical cancer before surgical staging: a surgicopathologic study. *J Clin Oncol* 1999; 17: 41–45.
6. Zimny M, Siggelkow W, Schroder W, Nowak B, Biemann S, Rath W, et al. 2-[Fluorine-18]-fluoro-2-deoxy-d-glucose positron emission tomography in the diagnosis of recurrent ovarian cancer. *Gynecol Oncol* 2001; 83: 310–315.
7. Torizuka T, Nobezawa S, Kanno T, Futatsubashi M, Yoshikawa E, Okada H, et al. Ovarian cancer recurrence: role of whole-body positron emission tomography using 2-[fluorine-18]-fluoro-2-deoxy-D-glucose. *Eur J Nucl Med Mol Imaging* 2002; 29: 797–803.
8. Nakamoto Y, Saga T, Ishimori T, Mamede M, Togashi K, Higuchi T, et al. Clinical value of positron emission tomography with FDG for recurrent ovarian cancer. *Am J Roentgenol* 2001; 176: 1449–1454.
9. Nakahara T, Fujii H, Ide M, Mochizuki Y, Takahashi W, Yasuda S, et al. F-18 FDG uptake in endometrial cancer. *Clin Nucl Med* 2001; 26: 82–83.
10. Belhocine T, De Barsey C, Hustinx R, Willems-Foidart J. Usefulness of ¹⁸F-FDG PET in the post-therapy surveillance of endometrial carcinoma. *Eur J Nucl Med* 2002; 29: 1132–1139.
11. Hamacher K, Coenen HH, Stocklin G. Efficient stereospecific synthesis of no-carrier-added 2-[¹⁸F]-fluoro-2-deoxy-D-glucose using aminopolyether supported nucleophilic substitution. *J Nucl Med* 1986; 27: 235–238.
12. Kitano H, Magata Y, Tanaka A, Mukai T, Kuge Y, Nagatsu K, et al. Performance assessment of O-18 water purifier. *Ann Nucl Med* 2001; 15: 75–78.
13. Irvin WP, Rice LW, Berkowitz RS. Advances in the management of endometrial adenocarcinoma. A review. *J Reprod Med* 2002; 47: 173–189.
14. Mariani A, Webb MJ, Keeney GL, Aletti G, Podratz KC. Assessment of prognostic factors in stage IIIA endometrial cancer. *Gynecol Oncol* 2002; 86: 38–44.
15. Sakuragi N, Hareyama H, Todo Y, Yamada H, Yamamoto R, Fujino T, et al. Prognostic significance of serous and clear cell adenocarcinoma in surgically staged endometrial carcinoma. *Acta Obstet Gynecol Scand* 2000; 79: 311–316.
16. Arulampalam T, Costa D, Visvikis D, Boulos P, Taylor I, Ell P. The impact of FDG-PET on the management algorithm for recurrent colorectal cancer. *Eur J Nucl Med* 2001; 28: 1758–1765.
17. Yap CS, Seltzer MA, Schiepers C, Gambhir SS, Rao J, Phelps ME, et al. Impact of whole-body ¹⁸F-FDG PET on staging and managing patients with breast cancer: the referring physician's perspective. *J Nucl Med* 2001; 42: 1334–1337.
18. Saga T, Ishimori T, Nakamoto Y, Higashi T, Mamede M, Higuchi T, et al. Clinical follow up of patients with gynecological malignancies who underwent FDG-PET without imaging finding of recurrence. *J Nucl Med* 2001; 42: 285p. (abstract)
19. Rose PG, Faulhaber P, Miraldi F, Abdul-Karim FW. Positive emission tomography for evaluating a complete clinical response in patients with ovarian or peritoneal carcinoma: correlation with second-look laparotomy. *Gynecol Oncol* 2001; 82: 17–21.