Usefulness of ^{18}F-FDG PET in the post-therapy surveillance of endometrial carcinoma

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Abstract. The aim of this study was to assess the usefulness of fluorine-18 fluoro-2-deoxy-D-glucose positron emission tomography (FDG PET) in the post-therapy surveillance of endometrial carcinomas. Forty-one fully corrected whole-body PET studies were performed in 34 women with previously treated endometrial cancers as a part of their follow-up programme. In 28 studies, FDG PET was indicated to localise a recurrence suspected at the control visits on the basis of clinical examination and/or radiological abnormalities (chest X-ray, CT or MRI) and/or elevated tumour marker levels (CA125, CEA). Another 13 studies were performed as a simple surveillance procedure. Overall, in 26 studies PET detected recurrent disease, which was confirmed either by histology (n=7) or by clinical and radiological outcomes (n=19). In 88% of the cases, the PET findings confirmed recurrence suggested by routine follow-up. In the remaining 12% of cases, PET detected asymptomatic recurrences that were unsuspected at the control visits. Whole-body PET accurately localised the site of confirmed recurrences as being above and below the diaphragm in 50%, only below the diaphragm in 35% and only above the diaphragm in 15%. In one patient, however, PET missed microscopic lung metastases shown on thoracic CT, and in three studies, metabolic imaging results were not confirmed. In 11 of 12 negative PET studies, no subsequent clinical or radiological recurrences were observed with a median follow-up of 10 months. Overall, the results of PET agreed well with the final diagnosis (Cohen's kappa coefficient =0.78). In 9/26 patients (35%) with confirmed recurrences, the PET findings significantly altered the treatment choice by detecting either clinically or radiologically unsuspected distant metastases. The sensitivity, specificity, diagnostic accuracy and positive and negative predictive values of FDG PET imaging in the post-therapy surveillance of endometrial carcinomas were 96%, 78%, 90%, 89% and 91%, respectively. Indeed, the high likelihood ratio for a positive test result (4.5) and the low likelihood ratio for a negative test result (0.05) demonstrated the clinical utility of metabolic imaging in "ruling in" disease as well as "ruling out" recurrence. In conclusion, whole-body FDG PET appears useful in the post-therapy surveillance of endometrial cancers, both for the accurate localisation of suspected recurrences and for the detection of asymptomatic recurrent disease.

Keywords: Endometrial carcinomas – FDG PET – Post-therapy surveillance

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Introduction

The post-therapy surveillance of women previously treated for an endometrial carcinoma routinely includes complete physical examination at the control visits and conventional imaging procedures when clinically indicated [1]. Patients with localised recurrences are classically treated by surgery and/or radiation, while those with disseminated recurrent disease are good candidates for hormonal therapy or systemic chemotherapy regimens [2, 3]. With the routine protocol, however, the detection of recurrences has been shown to be suboptimal, particularly in asymptomatic patients [4, 5, 6]. Indeed, soon after treatment and sometimes later in follow-up, the accuracy of morphological imaging techniques such as computed tomography (CT) or magnetic resonance imaging (MRI) for the diagnosis of recurrences may be limited by the post-surgical or post-radiation changes. As a consequence, tissue sampling may be required to definitely differentiate treatment-related scarring or fibrosis from recurrent disease [7, 8, 9, 10, 11]. Post-treatment serum levels of CA125 and, to a lesser extent, CA19.9 have been shown to be useful indicators of active recur-

rences. So far, however, these tumour markers are unable to localise the site of disease [12, 13].

On the other hand, the early detection of recurrences in asymptomatic patients may have a significant impact on survival [2, 3]. Additionally, the appropriate use of combined therapy modalities could improve the treatment efficacy for recurrences confined to the pelvis or showing extension beyond the pelvic wall [14, 15, 16, 17]. This provides an important rationale for the introduction of more effective diagnostic tools in the post-therapy management of women with endometrial carcinomas.

Fluorine-18 fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) is a high technology imaging method using a glucose analogue as a metabolic tracer. The value of FDG PET in oncology has been firmly established [18, 19]. In particular, its performance in the post-treatment evaluation of many cancers, including gynaecological malignancies such as breast cancer, ovarian cancer and cervical cancer, is well documented [20, 21, 22, 23, 24, 25, 26]. To date, however, nearly no data have been reported on the usefulness of metabolic imaging in endometrial cancer. In this study, we retrospectively assessed the contribution of FDG PET in the post-therapy surveillance of women with endometrial carcinoma.

Materials and methods

Patient population. Between September 1997 and November 2001, 34 women (mean age 65±10 years) previously treated for proven endometrial carcinoma underwent 41 FDG-PET studies in their follow-up programme. Five women had two PET studies and one had three PET studies. According to the International Federation of Gynaecology and Obstetrics (FIGO) staging system, the disease was initially classified from stage IB to stage IVA. In 12 asymptomatic women, the PET studies (n=13) were performed as a part of the post-therapy surveillance, which routinely included complete physical examination at the control visits and oriented morphological imaging procedures (chest X-ray, CT or MRI). In 22 patients, the PET studies (n=28) were indicated to localise a recurrence suspected on the basis of clinical and/or radiological abnormalities and/or elevated tumour marker levels (CA125, CEA). The mean follow-up time after performance of the PET studies was 10±4 months.

PET imaging procedure. All of the patients underwent fully corrected whole-body FDG PET studies. A Penn Pet 240H scanner (UGM Philadelphia, Pa., USA) was used in 24 patients and a C-Pet scanner (Adac, Philips Medical System, Milpitas, Calif., USA) in ten. Patients fasted for at least 4–6 h before injection to reduce serum glucose and insulin levels to near basal concentrations. In order to avoid bladder and ureteral artefacts, intravenous injection of diuretics (Lasix, 10 mg) was preferred to the use of Foley catheters and continuous hydration. The PET studies were performed an average of 65±10 min (46–96 min) after intravenous injection of a mean activity of 240.5 MBq (6.5 mCi) of ^{18}F-FDG. On average, women explored on the Penn Pet received 259 MBq (7 mCi) while those studied on the C-Pet received 166.5 MBq (4.5 mCi). Patients were kept at rest and were asked to void just before starting the acquisition. Scanning was carried out from the inguinal region to the neck. In all cases, a whole-body segmented attenuation correction was performed using single photon transmission scans with a caesium-137 external point source. Images were reconstructed using an iterative algorithm based on OS-EM (ordered subset – expectation maximisation). The total scanning time was 45–60 min. UGM software was used for both data acquisition and reconstruction. For visual interpretation, the images were displayed on transversal, sagittal and coronal slices, and also in rotating fashion.

Morphological imaging procedures. Following our routine surveillance policy, only those women presenting with suspicion of recurrence at the physical examination and/or elevated tumour marker levels underwent conventional imaging procedures. For this purpose, MRI was performed using a 1.0-T Signa MR/Hispeed (GE Medical Systems; Milwaukee, Wis., USA) before and after intravenous injection of 0.1 mmol/kg of gadolinium (Magnevist, Schering Laboratories, Germany). CT of the thorax and/or the abdominopelvic region was performed using contrast agents (PQ 1500-PQ 2000, 4th generation; Picker, Cleveland, USA).

Image interpretation. In all cases, the clinical records of the patients were retrospectively reviewed and the results of each imaging modality (PET, CT or MRI) were faithfully reported as initially interpreted by the nuclear physicians and radiologists. For PET analysis, only ^{18}F-FDG uptake abnormalities were considered as pathological, while the physiological distribution of tracer was not taken in account. Overall, the lesions detected by FDG-PET imaging were reported according to the anatomical sites and then grouped with regard to their location above and/or below the diaphragm. Accordingly, recurrences located below the diaphragm included pelvic lesions involving central organs or recurrent disease extending to the pelvic wall and also nodal foci, peritoneal deposits and liver metastases. Recurrences located above the diaphragm included lung metastases as well as mediastinal and supraclavicular nodal disease.

Evaluation of the PET results. The recurrences detected by FDG PET imaging were most often confirmed by clinical and radiological outcomes (19 PET studies), particularly in cases of disseminated disease. Otherwise, in those patients who underwent surgical resection for recurrences confined to the pelvis and targeted biopsies of superficial nodes or liver metastases, the results of PET were confirmed histologically (seven PET studies). In three studies, the PET findings were invalidated after comparison with morphological imaging results. On the other hand, patients with negative PET (12 studies) had routine post-therapy surveillance with a median follow-up of 10±4 months. The results were considered as true-negatives after a minimum follow-up period of 6 months without any clinical or radiological recurrences.

Statistics. To assess the performances of PET imaging in the post-therapy surveillance of endometrial carcinomas, we calculated the sensitivity, the specificity, the diagnostic accuracy and the predictive values according to the classical definitions. The likelihood ratios were then inferred from the following formulae:

- Likelihood ratio for a positive test result = sensitivity/1–specificity
- Likelihood ratio for a negative test result = 1–sensitivity/specificity

Estimates are presented with the 95% confidence interval (95% CI).

The agreement of PET with the final diagnosis was also determined by means of the Cohen's kappa coefficient (κ). The closer the value of κ to 1, the better the agreement.

For statistical analysis, we used the latest website version provided by the Department of Gynaecology and Obstetrics from the University of Hong Kong located at: http://www.obg.cuhk.edu.hk/.

Results

Whole-body FDG PET imaging was able to detect a confirmed recurrence in 26 out of the 41 studies performed in 34 women previously treated for endometrial carcinomas. In 23/26 studies (88%), there was also suspicion of recurrence using the routine surveillance protocol, which included clinical and/or radiological abnormalities and/or elevated tumour marker levels. In the three remaining PET studies demonstrating a recurrence, the women were asymptomatic (12%). In the present series, 85% of the women (22/26) presenting with confirmed recurrences had FIGO stages II–IV. More specifically, five patients had FIGO stage II (two IIA and three IIB), nine had FIGO stage III (four IIIA and five IIIB) and eight had FIGO stage IVA. Additionally, four women (15%) with FIGO stage IB had recurrent disease detected by FDG PET imaging.

The site of recurrence was both above and below the diaphragm in 50% of cases (Fig. 1), and only above the diaphragm in 15% (Fig. 2). Recurrences confined to below the diaphragm (i.e. abdominopelvic recurrences) were detected in 35% of studies (Fig. 3).In 13 patients with disseminated recurrent disease, PET detected 55 metastatic sites including 37 nodal metastases and 18 visceral recurrences (Table 1). Four women had only supradiaphragmatic metastatic sites (Table 2) and nine had localised infradiaphragmatic recurrences(Table 3).

In terms of patient management, PET had an impact on treatment options in 9 of the 26 patients with confirmed recurrences (35%). This included six women with symptomatic disease in whom the conventional imaging

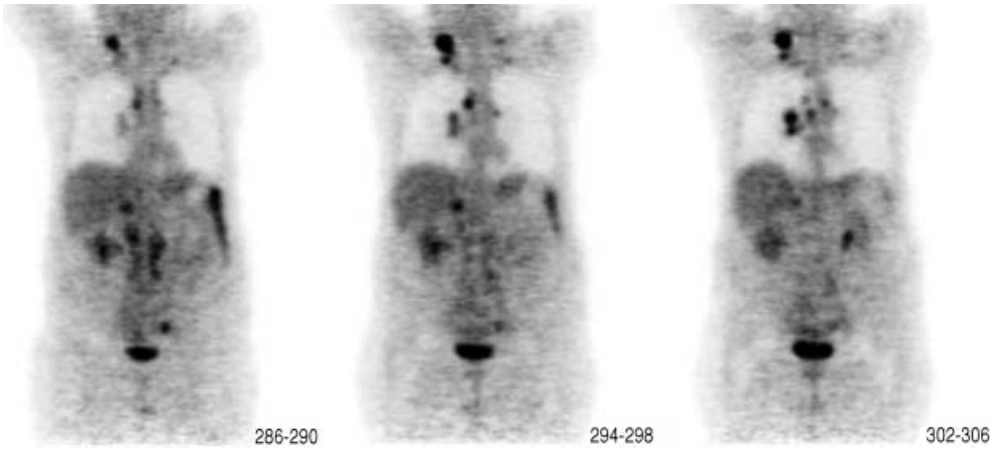

Fig. 1. A case of disseminated recurrent endometrial cancer. Whole-body FDG PET detected supraclavicular, mediastinal, hilar and para-aortic nodal metastases (coronal slices)

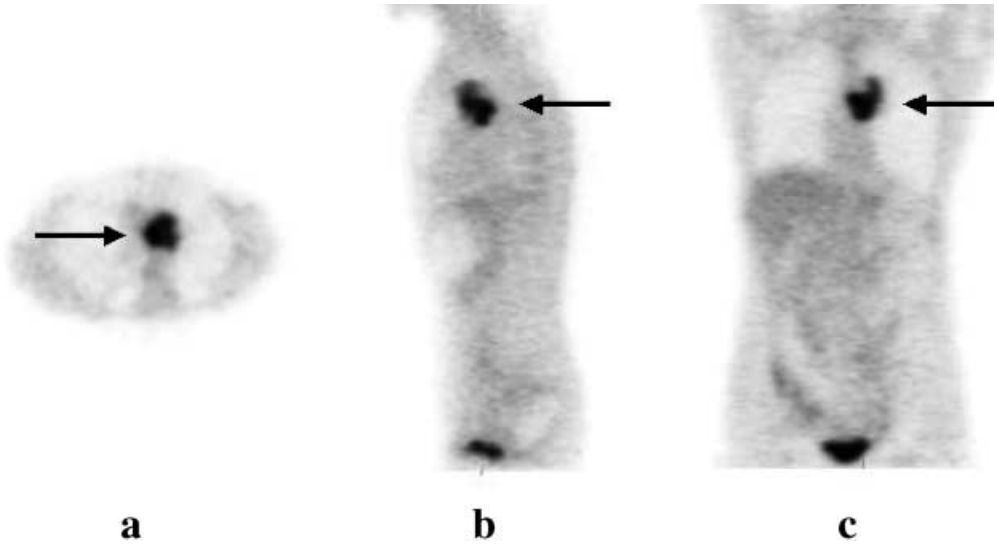

Fig. 2. A case of recurrence from endometrial carcinoma located at the mediastinal level (*arrow*), seen on transaxial (**a**), sagittal (**b**) and coronal slices (**c**). No other abnormality was found below the diaphragm

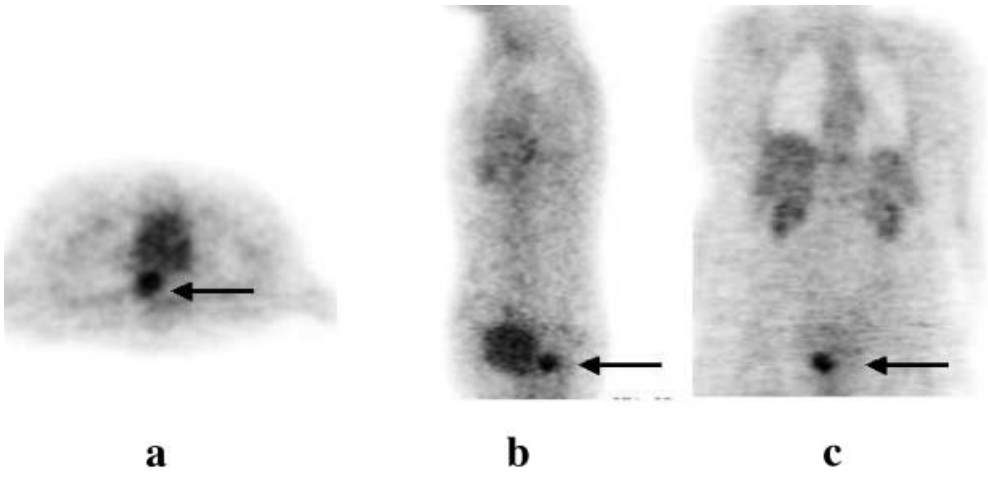

Fig. 3. A case of endometrial cancer presenting with a recurrence (*arrow*) confined to the pelvis (**a, b, c**: transaxial, sagittal and coronal slices)

Table 1. Sites of recurrence detected by FDG PET in patients with disseminated recurrent disease (*n*=13)

Anatomical area	No.
Lung/pleura	5
Liver	3
Bone	4
Peritoneum	3
Central pelvis	2
Ureter	1
Supradiaphragmatic nodes	
Supraclavicular	8
Mediastinal	6
Hilar	5
Infradiaphragmatic nodes	
Para-aortic	10
Iliac	5
Inguinal	3

Table 2. Sites of recurrence detected by FDG PET in patients with recurrent disease located only above the diaphragm (*n*=4)

Anatomical area	No.
Lung	1
Mediastinal nodes	1
Supraclavicular nodes	2

Table 3. Sites of recurrence detected by FDG PET in patients with recurrent disease located only below the diaphragm (*n*=9)

Anatomical area	No.
Central pelvis	3
Pelvic wall	4
Abdominopelvic nodes	3
Liver	3
Peritoneum	3

work-up showed recurrence confined to the pelvis whereas whole-body PET detected extrapelvic foci. The treatment strategy was thus changed from a surgery-based approach to chemotherapy regimens ± radiation. In three patients, only PET was able to detect recurrent disease, the recurrence being unsuspected both clinically and radiologically. Interestingly, PET was also useful in five of ten women who presented with a strong suspicion of recurrence on the basis of the physical examination and/or elevated tumour marker levels. In these cases, it provided valuable information by localising the sites of disease above and below the diaphragm. The impact of PET on staging and patient management is summarised in Table 4.

On the other hand, in 11 of 12 PET studies, a negative result allowed confirmation of complete remission with a minimum follow-up period of 6 months. However, PET yielded three false positive results corresponding to focal abdominal ^{18}F-FDG uptake not confirmed to represent malignancy by histology and/or by follow-up. Furthermore, in one patient, metabolic imaging missed microscopic lung metastases detected by thoracic CT. As indicated by the kappa coefficient value (κ=0.78), the results of PET agreed quite well with the final diagnoses. Overall, in the post-therapy surveillance of women with endometrial cancers, FDG PET had a 96% sensitivity, a 78% specificity, a 90% diagnostic accuracy, an 89% positive predictive value and a 91% negative predictive value. The likelihood ratio for a positive test result of 4.5 (1.6–12.2) and the likelihood ratio for a negative test result of 0.05 (0.007–0.31) demonstrated the capability of PET to "rule in" disease as well as to "rule out" recurrence. The results (with 95% CI) are detailed in Table 5.

Discussion

Adenocarcinoma of the endometrium is the most frequent gynaecological cancer in post-menopausal women [2]. Although the FIGO recommendations provide a practical framework for the staging of newly diagnosed primary tumours [3], to date no consensual guidelines exist regarding the appropriate post-therapy surveillance of patients previously treated for endometrial carcinomas. As a consequence, routine follow-up strategies are

Table 4. Impact of FDG PET findings on staging and management of patients with confirmed recurrent endometrial carcinoma (*n*=26)

Patient no.	FIGO stage	Sites of PET findings	Routine protocol results	Treatment
1	IIIB	Local	Clin +/TM +	Surgery
2	IIA	Local + distant	Clin +/Rx + (local)	Chemotherapy + radiation
3	IIIA	Local + distant	Clin +/TM +	Surgery + chemotherapy
4	IIB	Local	Clin +	Surgery
5	IVA	Local + distant	Clin +/Rx + (local)	Surgery + chemotherapy
6	IVA	Distant	Clin +/Rx + (distant)	Surgery + chemotherapy
7	IVA	Distant	Clin +/Rx + (distant)	Chemotherapy
8	IVA	Local + distant	Clin +/TM +	Chemotherapy
9	IVA	Local	Clin –/TM –/Rx –	Chemotherapy
10	IIB	Distant	Clin +/Rx + (distant)	Chemotherapy
11	IIIB	Local	Clin +	Chemotherapy
12	IIIB	Local + distant	Clin +/TM +	Chemotherapy
13	IIIB	Local + distant	Clin +/TM +/Rx + (local)	Chemotherapy + radiation
14	IIIA	Local	Clin +/TM +	Chemotherapy
15	IIIB	Local + distant	Clin +	Chemotherapy
16	IIA	Local + distant	Clin +/Rx + (local)	Surgery + chemotherapy
17	IB	Local	Clin +/Rx + (local)	Surgery + radiation
18	IB	Local + distant	Clin +	Chemotherapy
19	IVA	Local	Clin +/Rx + (local)	Chemotherapy
20	IVA	Local	Clin +/Rx + (local)	Chemotherapy
21	IVA	Distant	Clin +/Rx + (distant)	Chemotherapy
22	IB	Local + distant	Clin +/Rx + (local)	Chemotherapy
23	IB	Local + distant	Clin +/Rx + (local)	Chemotherapy
24	IIIA	Local	Clin –/Rx –	Surgery + radiation
25	IIIA	Local + distant	Clin +/TM +	Chemotherapy
26	IIB	Local + distant	Clin –/Rx –	Chemotherapy

Local, Recurrences confined to the pelvis; distant, recurrences located beyond the pelvis; Clin, clinical symptoms; Rx, radiological suspicion; TM, tumour markers (CA125 or CEA)

Table 5. Overall results

	FDG PET results	95% CI
Sensitivity	0.96	0.89–1.03
Specificity	0.78	0.57–1.00
Diagnostic accuracy	0.90	0.81–0.99
Negative predictive value	0.91	0.76–1.07
Positive predictive value	0.89	0.78–1.00
Likelihood ratio for a positive test result	4.5	1.6–12.2
Likelihood ratio for a negative test result	0.05	0.007–0.31

based on institutional experiences, but their effectiveness is a matter of controversy. While most recurrences from endometrial cancer occur within the first 2 years following treatment, the conventional work-up at control visits, including gynaecological examination ± vaginal Pap smears, chest X-rays and ultrasonography, is rarely effective in diagnosing asymptomatic recurrences [4, 5, 6]. After recent surgery or radiation therapy, the detection of recurrent disease only on the basis of CT or MRI may be extremely difficult given the acute oedema or inflammation surrounding the site of primary tumour. Later in the course of the follow-up, the persistence of treatment-related fibrosis may also hamper accurate evaluation of the disease status [7, 8, 9, 10, 11]. An elevated serum level of CA125 after initial treatment has been shown to be highly specific in detecting recurrences from endometrial carcinoma [12, 13]. However, tumour markers are unable to localise the site of the disease. For all these reasons, more effective diagnostic methods are required for the post-treatment surveillance of endometrial carcinomas.

FDG PET imaging has been shown to be of great value for the diagnosis, staging, re-staging and post-treatment monitoring of various malignancies [27, 28]. Many gynaecological cancers, such as breast cancer, ovarian cancer,and cervical cancer, are now recognised as good indications for PET imaging using ^{18}F-FDG. The value of FDG PET has been verified for the pre-treatment evaluation of primary cancers as well as for the surveillance of previously treated tumours [20, 21, 22, 23, 24, 25, 26]. Nonetheless, very few data are available on the utility of metabolic imaging in the exploration of endometrial cancers. Lapela et al. first reported the feasibility of PET using carbon-11 methionine for the imaging of uterine carcinomas. These authors studied 14 such carcinomas by this means, including eight endometrial cancers and six cervical carcinomas. However, they

underlined the poor quality of the images, which were sometimes impaired by urinary artefacts at the bladder level [29]. Recently, FDG PET was reported to be able to image both the primary tumour and lung metastases in a 60-year-old woman suffering from a histologically proven endometrial carcinoma [30]. In a series of nine women previously treated for endometrial carcinoma, Grigsby et al. also showed the usefulness of metabolic imaging in detecting lung metastatic sites that were undetected by conventional imaging studies [31]. This led to significant changes in the management of individual patients. In an older study, Spellman et al. measured the levels of seven enzymes in endometrium from 208 women with regular cycles. A physiological increase in the activity of all seven enzymes was found during the secretory phase. The enzymes included hexokinase and glucose-6-phosphate dehydrogenase, two key enzymes of the glycolytic pathway and thus of the ^{18}F-FDG tissue uptake process [32]. Other basic studies showed that oestrogens increase the activity of glucose-6-phosphate dehydrogenase and pyruvate kinase in rat uterus [33, 34].

These preclinical and clinical reports warranted further investigations in the use of FDG PET in women presenting with endometrial carcinoma, an oestrogen-dependent cancer. Additionally, tumour changes detected at the metabolic level usually precede macroscopic features evidenced by morphological imaging procedures [18, 19, 20, 21, 22, 23, 24, 25, 26]. The goal of the present study was to specifically address the issue of the role of ^{18}F-FDG PET imaging in the post-therapy surveillance of endometrial carcinomas. The lack of a standardised follow-up programme and the relatively low sensitivity of the protocols routinely used in gynaecological practice for the detection of recurrences stress the need for more efficient diagnostic tools.

Our results demonstrate the usefulness of PET imaging using ^{18}F-FDG in the post-therapy surveillance of patients with previously treated endometrial carcinoma. For instance, metabolic imaging confirmed the presence of recurrent disease in 88% of patients with suspicion of recurrence at control visits. However, unlike the routine follow-up protocol, whole-body FDG PET was able to accurately localise the sites of recurrence over the entire body within a single imaging procedure. Moreover, the value of PET was further illustrated by its ability to detect unsuspected recurrences in 12% of women with confirmed recurrent disease: by contrast, the sensitivity of routine follow-up in detecting asymptomatic recurrences is known to be very low [4, 5, 6].

Although all stages of disease may recur locally and/or at distant sites, on the basis of pathological factors a woman may be classified as having a low, intermediate or high risk of recurrence [35]. In the present series, 85% of the women (22/26) presenting with confirmed recurrences had FIGO stages II–IV disease (Table 4). These findings suggest that the optimal role for PET could be in this subgroup of patients with a high risk of recurrence (stage II, III or IV disease or serous or clear-cell carcinoma). Nonetheless, four women (15%) with FIGO stage IB also had recurrent disease detected by FDG PET imaging. This suggests that PET may also play a role in patients initially classified as having a "low or intermediate risk" of recurrence (stage I, grade 1 or 2 non-serous and non-clear-cell adenocarcinoma with invasion of the myometrium). It is likely, however, that the frequency of the PET controls should be modulated according to the risk of recurrence. Further controlled studies are warranted to specifically assess the contribution of PET for each stage of the disease.

Owing to its limited spatial resolution, in one patient PET missed lung micrometastases detected by thoracic CT. Metabolic imaging also yielded three false-positive results, which rather impaired the specificity of the technique. Although the clinical context and the medical history of the patient can help in achieving an accurate diagnosis, the inherent pitfalls of metabolic imaging cannot be avoided in all circumstances. For instance, some benign tumours or infectious diseases may also take up ^{18}F-FDG, examples including leiomyoma, benign serous cystadenoma, benign fibroids, endometriosis and endometrioma [36, 37, 38]. Similarly, the inflammatory changes that follow the primary therapy (recent surgery or radiation therapy) can induce intense uptake of the metabolic tracer [39]. Other false-positive results are related to the physiological retention of the tracer in the urinary system or the bowels. These situations are not infrequent in the context of gynaecological malignancies. To help overcome the limited specificity of FDG PET, reference can be made to the post-treatment serum levels of CA125: increases in comparison with baseline have been shown to reflect, at an early stage, the presence of active recurrences of endometrial carcinoma [40]. In equivocal cases (ureteral uptake versus nodal metastases, or normal intestinal uptake versus tumour mass), recently introduced PET-CT devices may also contribute in accurately distinguishing a "true" recurrence from physiological or benign uptake. Indeed, such combined devices may be of great utility in anatomically localising a metabolically active recurrence for the purpose of targeted radiation [41, 42, 43]. On the basis of these considerations, we believe that the judicious combination of a single whole-body imaging technique such as FDG PET with pre- and post-treatment measurement of the serum level of a highly specific tumour marker such as CA125 could avoid both the cost of repeated conventional imaging studies and the disagreement to which they give rise. Morphological imaging would be performed when PET results are negative but tumour marker levels are abnormally elevated, or to precisely define the anatomical margins of the disease for the purpose of targeted radiation therapy. Theoretically, this protocol should be focussed particularly on the first 2 or 3 years following the primary tumour therapy, when the prevalence of recurrence is highest. Further multicentre studies are, how-

ever, necessary to confirm our encouraging results and also to determine the optimal timing of FDG PET during the post-therapy surveillance.

The results of this study, like those reported by Grigsby et al., indicate that whole-body FDG PET offers added value in terms of staging and treatment choices in endometrial carcinoma (Table 4). For instance, the utility of a whole-body technique is shown by the fact that 50% of the recurrences occurred both above and below the diaphragm, while 15% occurred only above the diaphragm and 35% only below it. These results are in line with the pattern of recurrence commonly reported in the literature [1, 2, 3, 4, 5, 6, 34]. Currently, in patients with endometrial carcinoma, systemic chemotherapy and/or progesterone therapy is advocated for disseminated recurrent disease [2, 16, 17]. Localised pelvic recurrences may be treated by surgery and/or targeted radiation [2, 3, 14, 35]. Additionally, it has been shown that pelvic exenteration may be performed with relative success in a subset of patients with failure of prior radiation [15].

In the present study, PET had an actual treatment impact in 35% (9/26) of the women with confirmed recurrent disease, either by detecting extrapelvic foci (6/9) or by detecting clinically and radiologically unsuspected recurrences (3/9). As a result, PET significantly altered the treatment options from surgery ± radiation to chemotherapy ± radiation. Metabolic imaging also allowed the initiation of treatment in those asymptomatic women in whom it identified recurrent disease. Owing to the high rate of extrapelvic and metastatic recurrences in our series, the majority of patients underwent systemic therapies rather than surgical treatment. Therefore, most of the recurrences were confirmed by the clinical and radiological outcomes rather than by systematic histological analyses. In other words, in these patients with multiple foci, the non-invasive nature of PET imaging and its high diagnostic accuracy could allow the avoidance of invasive surgical procedures. As recently reported by Beggs et al. in a study of 50 oncology patients, PET findings suggesting disseminated disease may be considered as "a metabolic biopsy" [44]. On the other hand, the early detection by whole-body PET imaging of recurrences confined to the pelvis would warrant more aggressive therapies. Last but not least, metabolic imaging has the capability to reliably exclude recurrent disease. As evidenced by the low likelihood ratio for a negative test result (<0.1), even negative PET had a clinical value since in 11 of the 12 negative PET studies no recurrence was observed with a median follow-up duration of 10 months.

In conclusion, whole-body FDG PET is a valuable tool in the post-therapy surveillance of women previously treated for endometrial carcinoma. The capability of PET to detect suspected and unsuspected recurrences, in one session, enables non-invasive follow-up of patients by means of a single procedure. The optimal timing of FDG PET during the follow-up programme and the way in which it should be combined with other diagnostic modalities, such as tumour marker determinations and morphological imaging, remain to be defined. Further prospective studies are also necessary to assess the cost-effectiveness of the technique and its impact on patient survival.

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