PET-CT of Gynecological Malignancies and Ovarian Cancer

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Contents

Abbreviations

CA 125	Cancer antigen 125
CT	Computed tomography
DWI	Diffusion-weighted imaging
^{18}FDG	F-18-fluoro-deoxy-glucose
FIGO	International Federation of Gynecology and Obstetrics
MRI	Magnetic resonance imaging
PET	Positron emission tomography
SUV	Standardized uptake ratio
TVUS	Transvaginal ultrasound

34.1 Ovarian Cancer

Among gynecologic cancers, ovarian cancer is the second most common malignancy after endometrial cancer in developed countries but causing more deaths than the remaining gynecological cancers added together [1].

The high mortality reflects advanced stage at presentation with extrapelvic peritoneal disease and/or abdominopelvic lymphadenopathy or parenchymal metastases. Ovarian cancer can spread by intraperitoneal seeding, direct invasion, or through the lymphatic and vascular circulation. Peritoneal seeding is the most common route of dissemination [2].

Functional imaging with ^{18}FDG-PET benefits from the increased utilization of glucose by malignant cells and their high uptake of glucose compared to normal ones, opening a new field in clinical oncologic imaging. ^{18}FDG PET/CT makes

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it possible to acquire both metabolic and anatomic imaging data using a single device in a single diagnostic session and provides precise anatomic localization of suspicious areas of increased ^{18}FDG uptake [3]. In this clinical setting, ^{18}FDG PET/CT has achieved a significant improvement in diagnostic accuracy and exerted a considerable impact on patient management including diagnosis, staging, optimization of treatment, restaging, therapy monitoring, and prognostic prediction of various malignant tumors [4].

34.1.1 Diagnosis and Staging

The first approach to the study of ovarian tumors is based on gynecological examination, specific serum tumor markers like CA 125, and transvaginal ultrasound (TVUS). When a lesion is confirmed, other imaging techniques such as computed tomography (CT) and/or magnetic resonance imaging (MRI) are performed [5]. The differentiation between malignant and benign ovarian tumors is better obtained with contrast-enhanced pelvic MRI thanks to its excellent spatial and contrast resolution according to recently reported good diagnostic performance of 92–100 % sensitivity and 76–94 % specificity using a 3 T magnet [6].

Also ^{18}FDG PET/CT shows a relatively good diagnostic accuracy in differentiating malignant and benign ovarian tumors (87–100 % sensitivity, 74–100 % specificity, and 92–97 % accuracy) [7]. Ovarian lesions will show variable increase in ^{18}FDG uptake on PET/CT. In a study by Castellucci et al., a focally increased standardized uptake value (SUV) of three or higher in the ovary was considered positive for ovarian malignancy, whereas an SUV of 2.7 or lower was considered consistent with a benign finding. Moreover, differentiation between benign and malignant uptake on PET can be aided by the contemporaneously acquired CT scan on the basis of the characteristic pattern and location of ^{18}FDG uptake and the lack of discrete lymph nodes in patients with benign lesions [8].

But ^{18}FDG PET/CT hardly detects low-grade and early adenocarcinomas and borderline tumors with small volume or low cellular density, and false-positive results have also been reported in cases of serous cystadenoma, endometrioma, teratoma, and fibroma [9].

In premenopausal women undergoing surveillance imaging for other malignancies, hypermetabolic ovarian uptake is seen in the late follicular to early luteal cyst phases and has been mistaken for metastases to the ovaries or pelvic sidewall nodes [10]. In contrast, hypermetabolic ovarian uptake in a postmenopausal woman is abnormal and should be considered suspicious for malignancy. Thus, in interpreting PET images, ovarian tracer uptake should be correlated with the patient's menstrual status and phase [11].

In this manner, ^{18}FDG PET/CT had a good diagnostic value in differentiating between malignant and benign tumors and a low diagnostic value in differentiating between borderline malignant and benign tumors [12].

However, because of its high specificity, ^{18}FDG PET/CT may be used to confirm the diagnosis and rule out the presence of metastases before the patient undergoes surgical evaluation.

Ovarian cancer is staged by exploratory laparotomy according to the International Federation of Gynecology and Obstetrics (FIGO) and/or TNM staging systems [13] (Table 34.1). The surgery options include the staging laparoscopy or extensive surgery, including large resections or port implantation for intraperitoneal chemotherapy. An accurate staging at the time of diagnosis is extremely important in order to plan adequate therapy and is the most important prognostic factor in this cancer.

For preoperative staging of ovarian cancer, MRI has been accepted as being the most useful imaging technique in the assessment of the pelvis for local extent of primary disease and the relationship of tumor with surrounding vascular and lymphatic structures [14].

In fact, high-resolution MRI including dynamic postcontrast acquisition and diffusion-weighted imaging (DWI) may remain as the best imaging technique also in detecting tiny lesions and disseminated initial peritoneal lesions [15, 16]. Moreover, to obtain the initial staging and therapeutic decision, it is necessary to perform a chest and abdominal CT, for assessment of lymphatic extension of the disease, not only in the pelvic site but also in the abdomen and thorax. The main

Table 34.1 International Federation of Obstetric Gynecology (FIGO) and TNM Staging Systems for Ovarian Cancer

TNM	FIGO stage	Description
Primary tumor (*T*)		
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
T1	I	Tumor limited to the ovaries (one or both)
T1a	IA	Tumor limited to one ovary; intact capsule, no tumor on ovarian surface; no malignant cells in ascites or peritoneal washings
T1b	IB	Tumor limited to both ovaries; intact capsule, no tumor on ovarian surface; no malignant cells in ascites or peritoneal washings
T1c	IC	Tumor limited to one or both ovaries with any of the following: ruptured capsule(s), tumor on ovarian surface, malignant cells in ascites or peritoneal washings
T2	II	Tumor involves one or both ovaries with pelvic extension
T2a	IIA	Extension and/or implants on uterus and/or fallopian tube(s); no malignant cells in ascites or peritoneal washings
T2b	IIB	Extension to other pelvic tissues; no malignant cells in ascites or peritoneal washings
T2c	IIC	Pelvic extension (T2a or T2b) with malignant cells in ascites or peritoneal washings
T3	III	Tumor involves one or both ovaries with peritoneal metastasis outside the pelvis
T3a	IIIA	Microscopic peritoneal metastasis beyond the pelvis (no macroscopic tumor)
T3b	IIIB	Macroscopic peritoneal metastasis beyond the pelvis $\leq$ 2 cm in greatest dimension
T3c	IIIC	Macroscopic peritoneal metastasis beyond the pelvis >2 cm in greatest dimension and/or regional lymph node metastasis
Regional lymph nodes (*N*)		
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1	IIIC	Regional lymph node metastasis
Distant metastasis (*M*)		
M0		No distant metastasis
M1	IV	Distant metastasis (excludes peritoneal metastasis)

Notes:
The presence of nonmalignant ascites is not classified. The presence of ascites does not affect staging unless malignant cells are present
Liver capsule metastasis is T3/stage III; liver parenchymal metastasis, M1/stage IV. Pleural effusion must have positive cytology for M1/stage

pathways of lymphatic spread are along the ovarian vessels to the upper common iliac and para-aortic lymph nodes and along the broad ligament and parametria to the external iliac and obturator nodes [17].

The inability of CT and MRI to detect cancer in normal-sized lymph nodes or to discriminate between hyperplastic lymph nodes and metastases remains a major problem in conventional oncologic imaging [18]. In this case, we can use ^{18}FDG PET/CT for ovarian cancer staging. In fact, it has mainly been used to assess lymph node and distant metastasis, rather than to determine tumor extension and its relationship with surrounding tissues. PET/CT has an effective role in staging patients with advanced stage, providing useful information on involvement of extra-pelvic sites, such as either supraclavicular and para-aortic lymph nodes or peritoneum, omentum, bone, and muscle metastasis.

Recent studies have shown that ^{18}FDG PET, when used in conjugation with CT, is useful in evaluating distant metastases as well as equivocal lesions [8, 17]. PET/CT has high sensitivity in identifying peritoneal deposits larger than 1 cm and lymph nodes larger than 7 mm (Fig. 34.1). It has been shown to increase the pretreatment staging accuracy to 69–75 % compared with 53–55 %

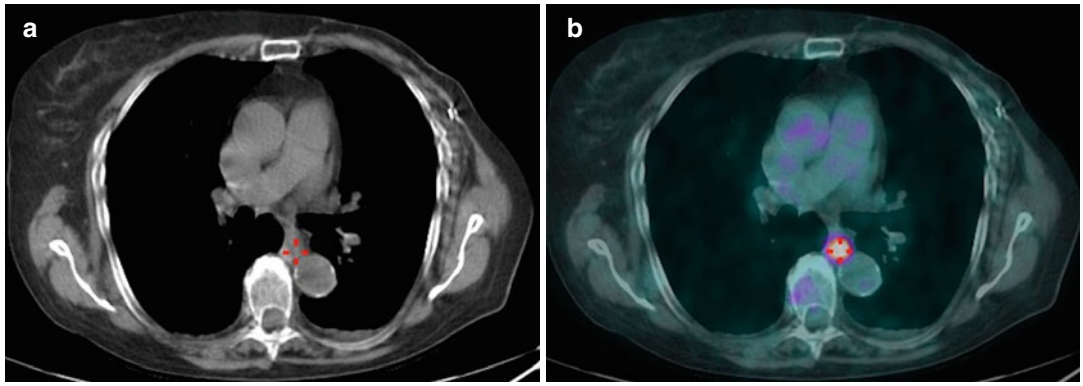

Fig. 34.1 A 62-year-old female with ovarian cancer diagnosed by CT and MRI. (**a**) Low-dose CT images and (**b**) ^{18}FDG PET/CT fusion images show a supradiaphragmatic ^{18}FDG-avid lymph node (markers), consistent with metastatic origin

obtained with CT alone [8]. Although both of these studies [8, 17] show definite evidence of improved accuracy in staging with the use of PET/CT, they also suggest that PET/CT is particularly useful in distinguishing patients with stages IIIC–IV ovarian cancer from those with stages I–IIIB cancer. For this classification, the specificity, sensitivity, and accuracy of ^{18}FDG PET/CT were 91, 100, and 98 %, respectively, in comparison with 64, 97, and 88 % for CT alone.

Thus, PET/CT can help in identifying the clinically important group of patients for whom optimal debulking is not possible and who thus need to undergo preoperative chemotherapy.

34.1.2 Monitoring Chemotherapy

Neoadjuvant chemotherapy has been used to improve the outcome of patients with initial inoperable cancer, and ^{18}FDG PET/CT has been proposed for the monitoring of cytoreductive therapy.

Conventional anatomical imaging is commonly used to assess the response to treatment by evaluating changes in tumor size as for other tumors, but this approach is limited in detecting the early response after the initiation of therapy because anatomic changes are usually seen only 2 or 3 months after the start of therapy. Metabolic changes often precede morphologic changes in tumor response and, therefore, ^{18}FDG-PET can demonstrate this response sooner than CT and MRI.

^{18}FDG-PET is thought to be useful in the detection of nonresponders to chemotherapy at an earlier stage during treatment. Identification of nonresponders would significantly improve patient management by reducing the use of ineffective therapies, preventing adverse effects, reducing the delay before administering more effective treatment, and minimizing costs.

Nishiyama et al. demonstrated that ^{18}FDG PET/CT-derived parameters, including SUV and percentage change, have the potential to predict response to chemotherapy or chemoradiotherapy in patients with advanced gynecologic cancer (uterine cancer, $n = 13$; ovarian cancer, $n = 8$) [19]. Based on histopathologic analysis of the specimens obtained at surgery, 10 patients were found to be responders and 11 to be nonresponders. When an arbitrary SUV of 3.8 was taken as the cutoff for differentiating between responders and nonresponders after therapy, ^{18}FDG PET/CT showed a sensitivity of 90 %, a specificity of 63.6 %, and an accuracy of 76.2 %. When an arbitrary percentage change of 65 % was taken as the cutoff, ^{18}FDG PET/CT showed a sensitivity of 90 %, a specificity of 81.8 %, and an accuracy of 85.7 %.

34.1.3 Restaging

The survival of patients after first line of treatment has improved significantly as a result of

advances in surgical procedures and chemotherapy. However, this extended survival has simultaneously increased the incidence of recurrence, even after surgery and adjuvant chemotherapy in early stage tumors, and it has been reported that 75 % of patients with ovarian cancer have a likelihood of disease relapse [20].

Early diagnosis of recurrence and exact anatomic localization of metastatic disease are crucial for determination of the best treatment strategy. Therefore, a close follow-up is essential utilizing noninvasive techniques such as tumor marker levels and imaging tests.

The monitoring of CA 125 tumor marker shows a high sensitivity for early diagnosis of recurrence in ovarian cancer, but it does not give any information about the extent or location of recurrence. Moreover, it has a poor negative predictive value. Currently, CA 125 level less than 35 U/mL is accepted as normal [21], and the existence of recurrence is based on higher levels in patients with normalization after the primary treatment or elevation of the nadir levels in patients with an elevated serum marker that never normalized after primary treatment [22].

There is an open debate in the literature regarding cutoff value of serum markers in women treated for ovarian cancer, since CA 125 has a good overall accuracy (80 %) but a low negative predictive value.

Nanni et al. analyzed the role of ^{18}FDG PET/CT in a cohort of patients with suspected relapse of ovarian cancer and correlated the results with serum levels of CA 125. They demonstrated that ^{18}FDG PET/CT was able to detect active disease at relatively low levels of CA 125, thereby facilitating the early diagnosis of recurrence or residual disease. In particular the optimal cutoff point of CA 125 after treatment to reflect active disease on PET/CT was 18 U/mL achieving a detection rate of 85.6 %. There was no relation between PET/CT negativity and the histological type of the tumor [23].

In a study by Mangili et al., ^{18}FDG PET/CT was compared with CT for the detection of ovarian cancer recurrence. A change in the clinical management was observed in 44 % of the patients when ^{18}FDG PET/CT information was added to conventional follow-up findings, as PET/CT increases the detection of tumor relapse compared to CT alone [24].

In particular, in women with recurrent disease, with previously treated ovarian carcinoma, ^{18}FDG PET-CT can alter management in close to 60 % of patients, detect more sites of active disease than abdominal and pelvic CT, as it is superior in the detection of nodal, peritoneal, and subcapsular liver disease, and also offer the opportunity for technology replacement in this setting [25] (Fig. 34.2).

Because PET/CT has a high contrast between tumor and background, in the case of hypermetabolic tumor implants, especially in subdiaphragmatic or subhepatic locations, on serosal surfaces of the bowel, or in small nodes, it has been reported to have better diagnostic accuracy than CT and MRI in these clinical situations (73–100 % sensitivity, 71–100 % specificity, and 83–100 % accuracy). In addition, it is difficult to detect small local recurrence, lymph node metastasis, small peritoneal dissemination, and bone/muscle metastasis for CT [26] (Fig. 34.3).

PET/CT not only helps in diagnosing recurrence, but also affects subsequent management. With its ability to precisely localize the lesion, as well as the extent of recurrence and distant metastases, PET/CT plays an important role in restaging of recurrent ovarian cancer. Fagotti et al. studied the ability of PET/CT to predict the possibility of optimal cytoreduction in recurrent ovarian cancer and reported an accuracy of 79 %, sensitivity of 93 %, specificity of 56 %, positive predictive value of 77 %, and negative predictive value of 83 % and, hence, good efficacy of PET/CT in planning surgical treatment of patients with recurrent ovarian cancer [27]. In another study, PET/CT was found to be comparable to staging laparoscopy for this purpose. Again, the false-negative results on PET/CT in that study were small peritoneal implants <7 mm in size [28].

34.2 Cervical Cancer

Despite advances in screening and prevention, cervical cancer remains as a major threat to women's health, however; actually, it tends to present

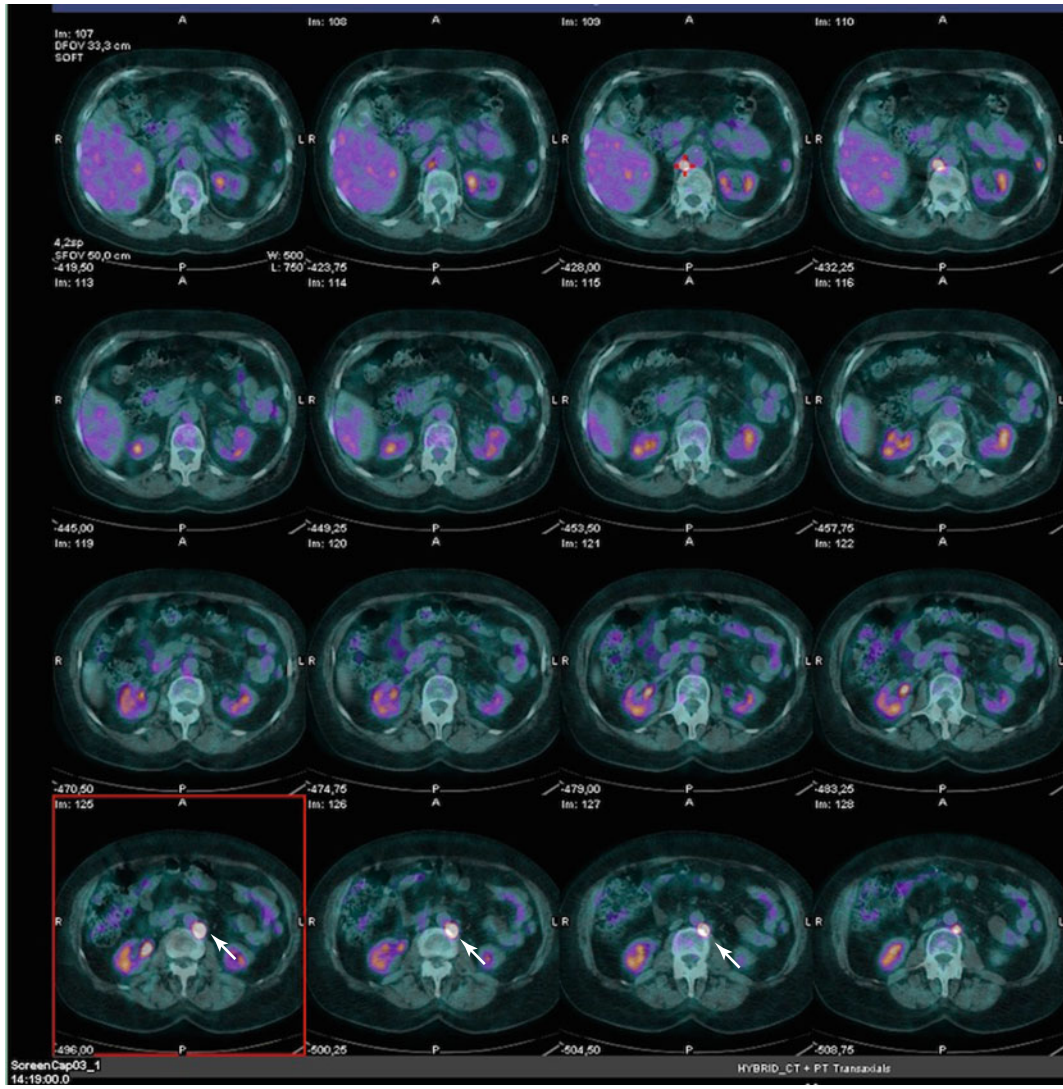

Fig. 34.2 A 56-year-old female with ovarian cancer already treated by surgery and chemotherapy. Follow-up ^{18}FDG PET/CT demonstrates a lumbo-aortic recurrent lymph node (*arrows*)

clinically before and, then, to have better survival rates [1]. Functional imaging with ^{18}FDG PET/CT can be used in initial staging (Table. 34.2), detection of recurrent disease, and evaluation of therapy response in patients with cervical cancer.

34.2.1 Diagnosis and Staging

In regard to the definition of the primary tumor, PET/CT does not appear to be very accurate in detecting the margins of the tumor. Tumors with a diameter <7 mm are negative for metabolic evaluation and areas of necrosis or fluid collections/bleeding/purulent content are not ^{18}FDG avid [29]. In the case of infiltration of the bladder or rectum, PET-CT, even with the difficulties related to the physiological accumulation of the tracer in the bladder, can detect increased uptake of the radiopharmaceutical as a nodular thickening at the involved viscera.

Since ultrasound and MRI allow visualization of even small-size cervical neoplasia, both techniques are adequate for the evaluation of tumor size and degree of stromal invasion.

Table 34.2 International Federation of Obstetric Gynecology (FIGO) and TNM Staging Systems for Cervical Cancer

TNM	FIGO stage	Description
Primary tumor (*T*)		
Tx		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Tis	0	Carcinoma in situ (preinvasive carcinoma)
T1	I	Invasive carcinoma confined to the cervix
T1a	IA	Diagnosed only by microscopy
T1a1	IA1	Micro-invasive carcinoma with stromal invasion ≤3 mm in depth, ≤7 mm width
T1a2	IA2	Micro-invasive carcinoma between 3 and 5 mm in depth, ≤7 mm width
T1b	IB	Clinically visible or microscopic lesion>IA2
T1b1	IB1	Clinical lesion ≤4 cm
T1b2	IB2	Clinical lesion >4 cm
T2	II	Extension beyond cervix but not to sidewall or to lower third of the vagina
T2a	IIA	Involvement of upper two-thirds of vagina
T2b	IIB	Parametrial involvement
T3	III	Extension to pelvic wall and/or lower third of vagina; hydronephrosis or non-functioning kidney
T3a	IIIA	Involvement of lower third of vagina, no extension to pelvic wall
T3b	IIIB	Pelvic sidewall involvement; hydronephrosis or non-functioning kidney
T4	IV	Extension beyond true pelvis or involving bladder or rectum (bullous edema is not sufficient to classify a tumor as T4) and/or distant metastases
T4a	IVA	Involvement of bladder or rectal mucosa
Regional lymph nodes (*N*)		
Nx		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Regional lymph node metastasis
Distant metastasis (*M*)		
Mx		Distant metastasis cannot be assessed
M0		No distant metastasis
M1	IVB	Distant metastasis (excludes peritoneal metastasis)

In recent comparative studies between intracavitary ultrasound and MRI, it has been reported a similar accuracy between the two techniques in this task [30]. In the evaluation of lymph node metastases, MRI and CT scan showed a comparable diagnostic accuracy with relatively low sensitivity and specificity rates. From the recent literature, it can be concluded that ^{18}FDG-PET provides a higher sensitivity than MRI in the diagnosis of lymph node metastases. In a recent meta-analysis, PET-CT showed a sensitivity (79–84 %) and specificity (95–99 %) higher than those obtained by CT (sensitivity of 47–50 % and specificity of 92–97 %) and MRI (sensitivity of 56–72 % and specificity of 92–96 %) [31]. The limited use of anatomical imaging in cervical cancer has led to the use of ^{18}FDG-PET for the evaluation of pelvic and para-aortic lymph nodes, not only in assessing the extent of disease but also with a prognostic role (Fig. 34.3).

Grigsby et al. compared the results of CT and ^{18}FDG-PET in the pretreatment N-staging of 101 patients with cervical carcinoma [32]. Patients were treated with a combination of radiotherapy and chemotherapy. CT demonstrated abnormally enlarged pelvic lymph nodes in 20 (20 %) and para-aortic lymph nodes in seven (7 %) of the 101 patients. PET demonstrated abnormal ^{18}FDG uptake in 67 (67 %) pelvic lymph nodes, in 21 (21 %) para-aortic lymph nodes, and in eight (8 %) supraclavicular lymph nodes. All positive lymph nodes on CT were also detected in PET

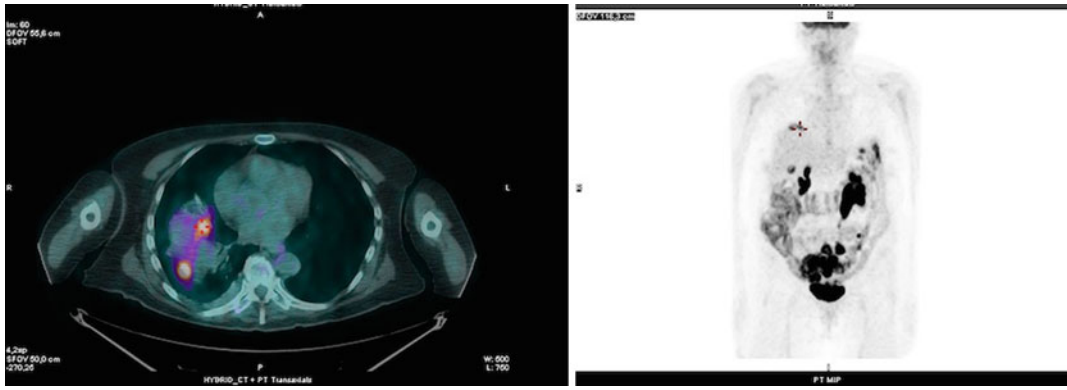

Fig. 34.3 A 49-year-old female submitted to perform an ^{18}FDG PET/CT for cervical cancer staging. ^{18}FDG PET/CT depicts a distant metastasis on liver capsule (markers)

scans. The disease-free survival at 2 years, based solely on para-aortic lymph nodes status, was 64 % in patients with negative CT and PET, 18 % in patients with negative PET and positive CT, and 14 % in patients with positive CT and PET. In conclusion, based on this study, ^{18}FDG hyperfixation to lumbo-aortic lymph nodes is the most important factor predictive of disease progression.

Singh et al. used ^{18}FDG-PET in patients with cervical cancer in clinical stage IIIB [33]. Three-year survival was that of 79 % in patients without lymph node involvement at presentation, while in patients with pelvic lymph node involvement was 58 % and in patients with positive para-aortic lymph nodes only 29 %. They concluded that PET should be performed in all patients with carcinoma of the cervix before treatment, to detect the presence of disease in para-aortic and pelvic lymph nodes. As normal-sized nodes may be metastatic, they can be negative in CT but show ^{18}FDG uptake.

34.2.2 Restaging

About one-third of patients with advanced-stage disease will develop recurrent or progressive cervical cancer, which usually occurs within the first 2 years after completion of primary treatment. The likelihood of recurrence depends on tumor stage, histologic findings, and lymph node status at the time of initial diagnosis, as well as treatment efficacy [34].

Recurrent disease is defined as tumor development at least 6 months after the treated lesion has regressed. Routine abdominopelvic CT is not particularly helpful for the detection of recurrent disease [35]. While ^{18}FDG-PET has excellent sensitivity and specificity for the evaluation of initial local recurrence and lymph node relapse. In particular, Ryu et al. reported that the sensitivity and specificity of ^{18}FDG-PET for the detection of recurrent disease were 90 and 76 %, respectively, and the positive and negative predictive values were 35 and 98 %, respectively, in the evaluation of local recurrence for patients surgically treated (Fig. 52.9) [34].

Cervical cancer relapse can affect abdominal and pelvic lymph nodes but also supradiaphragmatic (phrenic and supraclavicular) ones. About 20 % of patients present lung and bone metastasis, predominantly involving the pelvic bones and the lumbar and thoracic spine (Fig. 34.3).

Liu et al. [36] demonstrated the superiority of ^{18}FDG-PET over CT and MR imaging in detecting hematogenous bone metastasis in patients with advanced cervical cancer. ^{18}FDG PET/CT is also useful in identifying recurrent cervical cancer in both asymptomatic and symptomatic patients with elevated tumor markers and negative imaging findings (squamous cell carcinoma antigen >1.5 ng/mL) [37].

In another study by Unger et al., ^{18}FDG-PET detected recurrent disease in 31 % of asymptomatic women [38]. In this way, with the use of ^{18}FDG-PET in the follow-up of treated patients, it is possible to intervene in the recovery of recur-

rences that would previously have been discovered in more advanced stages. In fact, Brooks et al. showed that 3-year survival for symptomatic recurrences was 19 % versus 59 % for asymptomatic recurrences [39].

34.2.3 Radiotherapy Planning

^{18}FDG-PET can play an important role in patients with cervical cancer that are candidates for radiation therapy. The introduction of functional data in the planning of radiotherapy treatment is currently under clinical development. The combination of PET and CT in a single system allows having an imaging modality that may be used in the calculation of the tumor volume and in the definition of treatment plans, particularly when integrated with the virtual simulation. In addition, ^{18}FDG-PET imaging can provide data on metabolically active tumor volume.

These functional data have the potential to change the volume of treatment. Initial studies on the use of ^{18}FDG-PET in radiation treatment planning involved fusion of PET and CT images, including images obtained later (in a different moment) [40].

Dolezelova et al. studied 51 patients with advanced cervical cancer (stage IIB-IIIB) treated with a combination of external beam radiotherapy and brachytherapy, with or without concomitant cisplatin. The radiation treatment plans of lymphatic metastasis were based on fused PET/CT images. ^{18}FDG-PET images led to a change in the extent of disease in 19 (37 %) patients and of radiation fields in 9 (17.5 %) patients compared to CT planning [41].

In addition, ^{18}FDG-PET has been shown to provide useful additional information for planning brachytherapy in patients with gynecological malignancies. Lin et al. studied 11 patients with ^{18}FDG PET/CT in conjunction with their first, middle, or last brachytherapy treatment. A total of 31 intracavitary brachytherapy treatments were performed. The percent coverage of the target isodose surface for the first implant with and without optimization was 73 and 68 % ($p=0.21$), and the dose to 2 and 5 cm^3 of both the bladder and rectum were not significantly different. The authors concluded that this technique has the potential to improve tumor coverage in patients with cervical cancer, saving critical structures at the same time [42]. Therefore, ^{18}FDG-PET based treatment planning allowed for improved dose coverage of the tumor without significantly increasing the dose to the bladder and rectum. Furthermore, in patients who have undergone radiation therapy, PET/CT can be effective in distinguishing postoperative changes or radiation fibrosis from recurrent tumor.

34.3 Endometrial Cancer

Overall, endometrial cancer is the fourth most common malignancy in women and the eighth most common cause of death in women [43]. The majority of cases occur in postmenopausal women with the highest incidence in the seventh decade of life. Abnormal uterine bleeding is the most frequent clinical presentation of endometrial cancer, leading to early diagnosis in the majority of patients.

34.3.1 Diagnosis and Staging

A TVUS is recommended to obtain an impression of the endometrial layer or suspicious lesions in the female pelvis. The diagnosis of endometrial cancer is usually established by histology from endometrial biopsy with hysteroscopy, while for staging it is necessary to evaluate the extent of the primary tumor, regional lymph node involvement, and presence or absence of distant metastases as described by FIGO classification (Table 34.3).

In fact, endometrial cancer is also surgically staged, but accurate assessment by pretreatment imaging can potentially optimize surgical and nonsurgical treatment, particularly with regard to the use of preoperative, neoadjuvant therapy in advanced disease. MRI is used to evaluate the depth of myometrial and cervical invasion, which affects overall prognosis [44]. ^{18}FDG PET/CT imaging has been shown to be more accurate in identifying metastatic lymph nodes, particularly in nodes considered normal by size criteria.

Early data suggest that combined ^{18}FDG PET/CT may be useful in the management of endome-

Table 34.3 International Federation of Obstetric Gynecology (FIGO) and TNM Staging Systems for Endometrial Cancer

TNM	FIGO stage	Description
Primary tumor (*T*)		
Tis		Carcinoma in situ (preinvasive carcinoma)
T1	I	Tumor confined to corpus uteri
T1a	IA	Tumor limited to endometrium or invades less than one half of the myometrium
T1b	IB	Tumor invades one half or more of the myometrium
T2	II	Tumor invades stromal connective tissue of the cervix but does not extend beyond uterus (Endocervical glandular involvement should only be considered as stage I and no longer as stage II)
T3a	IIIA	Tumor involves serosa and/or adnexa (direct extension or metastasis)
T3b	IIIB	Vaginal (direct extension or metastasis) and/or parametrial involvement
	IIIC	Metastases to pelvic and/or para-aortic lymph nodes
	IV	Tumor invades bladder mucosa and/or bowel mucosa, and/or distant metastases
T4	IVA	Tumor invades bladder mucosa and/or bowel mucosa (bullous edema is not sufficient to classify a tumor as T4)
Regional lymph nodes (*N*)		
Nx		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1	IIIC1	Regional lymph node metastasis to pelvic lymph nodes
N2	IIIC2	Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes
Distant metastasis (*M*)		
M0		No distant metastasis
M1	IVB	Distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, or lung, liver, or bone metastases; it excludes metastasis to para-aortic lymph nodes, vagina, pelvic serosa, or adnexa)

trial cancer, particularly in the preoperative detection of pelvic and para-aortic metastatic lymphadenopathy [45]. Picchio et al. studied 32 consecutive patients with histological diagnosis of primary high-risk endometrial cancer with ^{18}FDG PET/CT. ^{18}FDG PET/CT findings were correlated with pathological findings on a patient-by-patient basis after surgery. In this study, sensitivity of ^{18}FDG PET-CT was 90.6 %, for primary tumor detection, 88.5 % for assessment of lymph node involvement, and 96.9 % for distant metastasis depiction. In particular, while the suspicion of distant metastases was documented by conventional imaging in only two patients, ^{18}FDG PET/CT correctly identified metastatic lesions in seven patients (21.9 % of cases) [46].

34.3.2 Recurrence and Follow-up

Recurrent carcinoma of endometrium has a poor prognosis. However, successful salvage treatment with long-term survival has been achieved after hormone therapy, radical surgery, and radiotherapy/chemotherapy in patients with recurrent disease. Conventional imaging and tumor markers have limited accuracy for detecting recurrence in these patients, while functional imaging can show earlier a recurrence.

In a retrospective study of Sharma et al., a total of 101 patients were evaluated with ^{18}FDG PET/CT for suspected recurrence and compared with CT and with clinical/imaging follow-up and/or histopathology. ^{18}FDG PET/CT was positive for recurrence in 51 (50.5 %) patients and negative in 50 (49.5 %), with an accuracy of 92.1 %. In addition, ^{18}FDG PET/CT showed a strong positive correlation with final diagnosis based on reference standard. Compared to CT, ^{18}FDG PET/CT has much higher specificity (62 % vs. 96.4 %), and accuracy (76.3 % vs. 92.1 %), with comparable sensitivity (85.1 % vs. 89.5 %) [47] (Fig. 34.4).

Conclusion

In all gynecological cancers, functional imaging with ^{18}FDG PET/CT appears to be a prominent and complementary method to morphological radiological techniques, allowing a complete evaluation of all types of cancers at all stages of natural history.

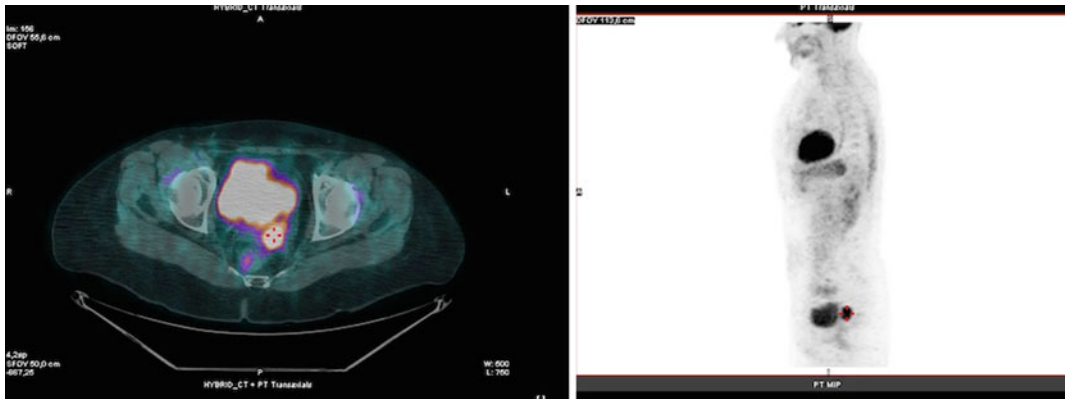

Fig. 34.4 Local recurrence of endometrial cancer in a 72-year-old female patient previously treated with surgery is demonstrated on a ^{18}FDG PET/CT study (markers)

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