Cancer Imaging (2007) **7,** S130–S138
DOI: 10.1102/1470-7330.2007.9015

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PET/CT and cross sectional imaging of gynecologic malignancy

Revathy B. Iyer, Aparna Balachandran and Catherine E. Devine

Department of Diagnostic Radiology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Corresponding address: Revathy B. Iyer, MD, 1515 Holcombe Boulevard, Unit 368, Houston, TX 77030, USA.
Email: riyer@mdanderson.org

Abstract

Gynecologic cancers are a common cause of morbidity and mortality in women of all ages. While many gynecologic cancers are staged clinically using the International Federation of Gynecology and Obstetrics (FIGO) staging system, imaging can be a useful adjunct to clinical staging. Cross sectional imaging techniques such as ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) have been used to detect and follow patients with gynecologic cancer. These imaging modalities can show anatomic detail and morphologic changes in the female genitourinary tract to good advantage. Positron emission tomography (PET) differs in that it shows functional information that is not easily obtained by the other cross sectional imaging techniques. The fusion of PET with CT allows anatomic localization of functional abnormalities in the female genital tract and thereby allows the detection of gross disease in many malignant conditions both within and outside the confines of the female pelvis. The utility and limitations of imaging common gynecologic tumors such as cervical, ovarian and endometrial cancer are discussed with particular emphasis on PET/CT imaging.

Keywords: *Cervical cancer; ovarian cancer; endometrial cancer; imaging.*

Introduction

Positron emission tomography (PET) has been used in oncologic imaging for about three decades now, however in the last several years scientific data has consolidated the utility of this biologic imaging technique in the diagnosis and management of patients with cancer. While many radiotracers have been studied, ^{18}F-fluoro-deoxyglucose (^{18}F-FDG) PET is most widely in clinical use. ^{18}F-FDG has a physical half-life of 110 min and is widely available, which makes it ideally suited for imaging. Elevated glucose metabolism in most tumor cells causes increased accumulation of this radiopharmaceutical. FDG competes with glucose for transport into the cell and is subsequently phosphorylated and trapped in the cell. The power of PET imaging comes from the ability to detect biological or functional characteristics of tumor cells rather than morphology alone.

While ^{18}F-FDG is a good radiotracer, it is not entirely specific for malignancy. High physiologic uptake may be seen in metabolically active normal tissues such as the brain, bowel, genitourinary tract, salivary glands, and lymphoid tissue. Inflammation or infection can also be metabolically active. Evaluation of the abdomen and pelvis can be particularly challenging because of FDG activity in the urinary collecting systems, ureters, and bladder as well occasional intense uptake in the cecum and rectosigmoid colon. The liver typically has a mottled appearance with moderate uptake while the spleen is typically less metabolically active and more homogeneous in appearance. In pre-menopausal women, physiological uptake is normal in the ovaries and uterus during various phases of the menstrual cycle and should not be confused with tumor.

The development of combined PET/computed tomography (CT) scanners allows the use of CT as the attenuation map to correct the FDG emission data. CT allows accurate anatomic definition of areas of increased FDG update and allows better differentiation of benign from malignant lesions yielding a more specific report. Lesion characterization on CT is also improved in the setting of low FDG uptake in some tumors such as mucinous adenocarcinomas. Mucinous lesions and associated

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calcification are well detected on CT but not demonstrated easily on FDG PET. Small, sub-centimeter lesions are also better characterized on CT since the metabolic rate in small lesions is often underestimated because of limits of resolution of PET scanners. FDG PET clearly has a role in the evaluation and management of patients with cancer. The following sections describe the role of FDG PET in the evaluation of patients with gynecologic malignancy.

Cervical cancer

Cervical cancer is the third most common gynecologic malignancy in the US with more than 10,000 new cases diagnosed each year resulting in an estimated 3700 deaths in 2007[1]. The histologic subtype that occurs most commonly is squamous cell carcinoma in about 90% of cases. Squamous cell carcinomas arise from the squamo-columnar junction near the external os in younger patients, resulting in exophytic lesions. As the squamo-columnar junction migrates toward the uterine body in older women, these tumors grow from the endocervix and may become quite large before they are diagnosed. Adenocarcinoma and adenosquamous carcinoma account for about 10% of cervical cancer cases with unusual histologies such as sarcoma and lymphoma being quite rare.

Staging and treatment

Cervical cancer invades the cervical stroma and then spreads by direct invasion of parametrial tissues, uterus and vagina. Adjacent organs in the pelvis such as the bladder and rectum may be involved in more advanced disease. Hematogenous spread to the lungs, liver or bone is unusual at initial presentation although it may occur with advanced disease or recurrence. Lymphovascular invasion results in metastatic lymphadenopathy which is quite common. Metastatic nodes are typically seen along the internal iliac and external iliac chains in the pelvis with subsequent spread to the retroperitoneum. Inguinal adenopathy may be seen with lower vaginal involvement. Retrocrural, mediastinal and supraclavicular spread of adenopathy is seen with bulky disease in the abdomen.

When tumor is confined to the cervix and the overall tumor volume is small, surgical management can be curative and radical hysterectomy is typically performed. As tumor size increases and spread beyond the cervix into the parametrial tissues occurs, definitive radiotherapy and chemotherapy are generally used. Once a diagnosis of invasive cervical cancer is made, accurate staging is of great importance for treatment planning. Clinical staging relies primarily on physical examination, which may be difficult and erroneous particularly in those patients with advanced disease. The role of imaging is therefore to document the presence of extra-cervical spread to better define management of these patients (Table 1).

Table 1 Cervix cancer FIGO staging

Stage 0	Carcinoma in situ, CIN
Stage I	Invasive carcinoma confined to the cervix
Stage I	Diagnosed only by microscopy
IA1	Micro-invasive carcinoma with stromal invasion <3 mm depth, <7 mm width
IA2	Micro-invasive carcinoma <5 mm depth, <7 mm width
Stage IB	Clinically visible or microscopic lesion >IA2
IB1	Clinical lesion <4 cm
IB2	Clinical lesion >4 cm
Stage II	Extension beyond cervix but not to sidewall
IIA	Involvement of upper two-thirds of vagina
IIB	Parametrial involvement
Stage III	Extension to pelvic wall and/or lower third of vagina; hydronephrosis
IIIA	Involvement of lower third of vagina
IIIB	Pelvic sidewall involvement; hydronephrosis
Stage IV	Extension beyond true pelvis or involving bladder or rectum
IVA	Involvement of bladder or rectal mucosa
IVB	Spread outside true pelvis or metastasis to distant organs

Imaging

Magnetic resonance imaging (MRI), with its superior soft tissue contrast resolution and multi-planar capabilities is well suited to image cervical cancer. T2 weighted MR images provide excellent detail of normal uterine and cervical anatomy and also demonstrate the primary tumor and its extent. Since the absence of parametrial invasion by tumor is important in determining if the patient may be a surgical candidate, MRI can be used to predict parametrial invasion with a negative predictive value of 95%[2]. Endocervical tumors may be difficult to evaluate clinically, but are well demonstrated by MR imaging. Stromal invasion by the primary tumor is also well delineated by MRI. The overall accuracy of MR staging of cervical cancer is reported to be about 90%[2,3].

CT is also used for evaluation of advanced disease, nodal involvement and distant metastasis although CT has had a limited role in evaluating the primary cervical tumor as tumors may be isodense to the normal cervix. FDG PET cannot be reliably used to determine the extent of local tumor invasion but definitely plays a role in the evaluation of metastatic disease, particularly lymph node metastases (Fig. 1).

Although the presence or absence of pelvic lymph node metastasis does not affect the FIGO clinical stage, lymphadenopathy is an important prognostic factor in patients with cervical carcinoma. While CT and MRI have been used to detect local extent of tumor, both of these cross sectional imaging modalities primarily rely on morphologic changes such as nodal size and therefore have difficulty detecting metastatic disease in 'normal sized' lymph nodes (short axis diameter <1 cm)[4,5]. Other criteria such as inherent tissue contrast and contrast enhancement are also unreliable[6].

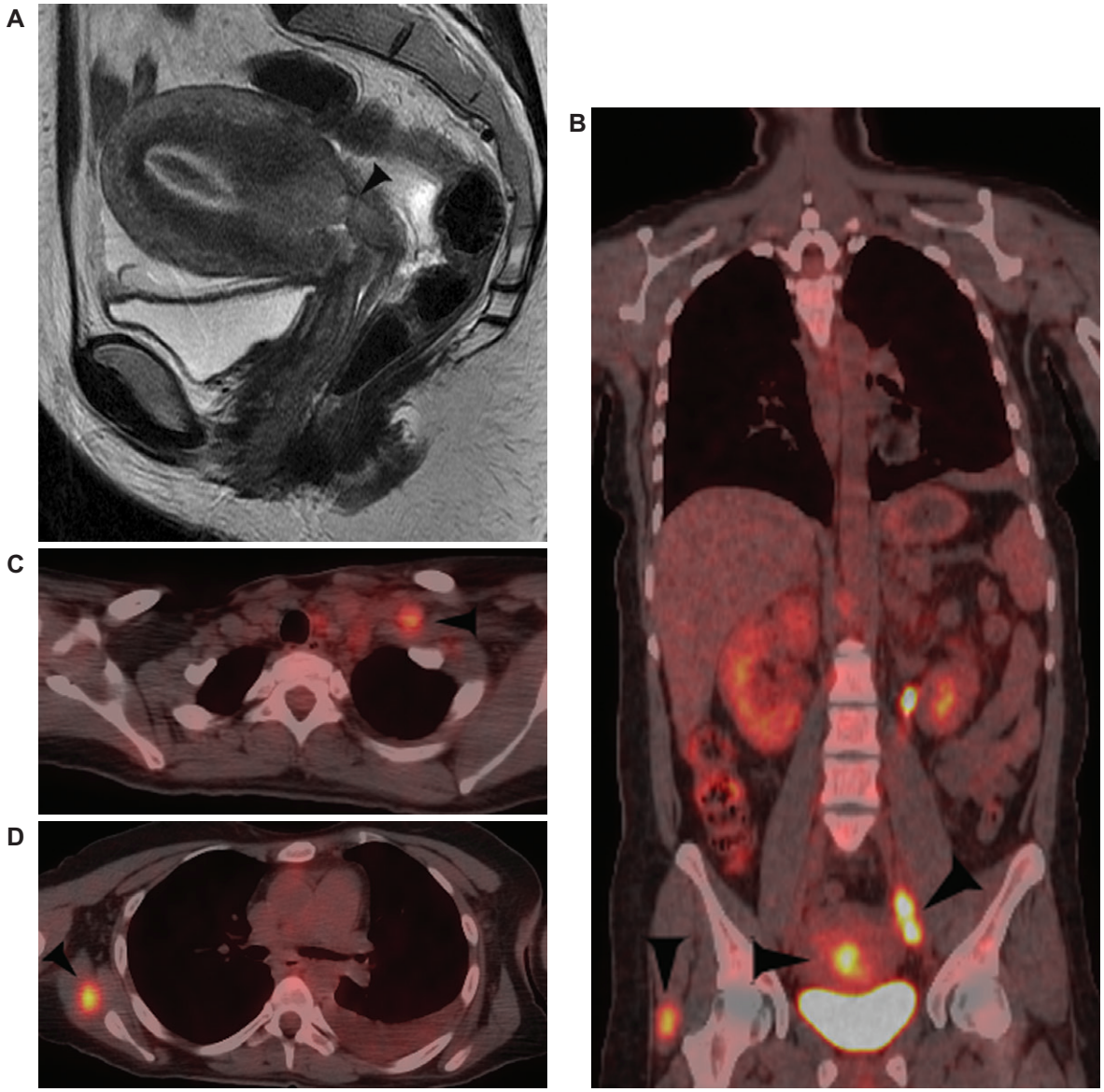

Figure 1 **A 37-year-old female with newly diagnosed squamous cell carcinoma of the cervix. (a) Sagittal T2-weighted MRI of the pelvis shows cervical tumor (arrowhead); (b) coronal fused PET/CT shows FDG avid primary tumor and adenopathy in the pelvis as well as uptake adjacent to the right hip (arrowheads), subsequently proven soft tissue metastasis; (c) axial fused PET/CT shows FDG avid adenopathy in the left supraclavicular fossa (arrowhead); (d) axial fused PET/CT also shows another FDG avid soft tissue metastasis in the right periscapular region (arrowhead).**

Lymphangiography, CT, and MRI have been shown to perform similarly in the detection of lymph node metastasis from cervical cancer with an overall accuracy estimated to be about 85%[7].

Since FDG PET can demonstrate metabolically active sites of tumor spread, it has been shown to have a role in the staging and evaluation of lymph node involvement in patients with cervical cancer. PET has shown some promise in detecting lymph node metastases in the pelvis and retroperitoneum[8,9]. Sironi *et al.*[10] found that PET/CT proved to be valuable for lymph node staging in patients with early-stage cervical cancer with short-axis diameter greater than 0.5 cm being the size threshold for accurate depiction of metastatic nodes. Bladder and ureteral activity can mask disease in the pelvis and can be overcome by having patient void or using continuous bladder irrigation. Focal areas of ureteral activity should not be confused with nodal disease

FDG PET may also be useful for determining treatment response and prognostication of patients. FDG PET has been used to predict survival in patients with cervical cancer. Grigsby *et al.*[11] found that 2-year progression free survival was 64% in CT-negative, PET-negative patients; 18% in CT-negative, PET-positive patients; and dropped to 14% in CT-positive, PET-positive patients.

Approximately 1/3 of patients with invasive cervical cancer have recurrence after treatment. Conventional imaging cannot differentiate recurrence from treatment related fibrosis. PET activity may help distinguish tumor recurrence from post-therapy changes after the acute post-therapy changes have subsided in the pelvis.

In summary, the role of FDG PET is promising for primary staging of cervical carcinoma particularly since it appears to be more accurate than cross-sectional imaging (CT/MRI) for determining lymph node involvement. It is also helpful for determining prognosis of disease and finding recurrent disease. It is important to keep in mind the limitations of PET. It may not resolve 'small' lesions such as lung lesions that are <6 mm, liver lesions that are <1 cm and brain metastases due to the inherent high glucose uptake in the normal brain. Diffuse peritoneal carcinomatosis can be difficult to detect because of bowel activity. FDG avid lesions may also be benign such as acute infections, as well as granulomatous processes such as tuberculosis and sarcoid. It is also important to keep in mind false negative lesions that may not take up FDG such as mucinous tumors.

Ovarian cancer

Ovarian cancer is the second most common gynecological malignancy accounting for about 22,220 new cases per year[1]. It is, however, the most common cause of cancer related death from gynecological malignancy and the fifth leading cause of cancer related death in women[1]. While most cases are sporadic, risk factors include nulliparity, early menarche, and late menopause. Many patients with ovarian cancer present with non-specific symptoms such as abdominal bloating and increased distension. These non-specific symptoms lead to a delay in diagnosis and later stage of disease at presentation[12].

The majority of ovarian cancers, up to 85%, arise from the surface epithelium of the ovary[13]. Of the epithelial tumors, the most common type is serous adenocarcinoma. The remaining 15% of all ovarian cancers are germ cell tumors (such as teratomas, dysgerminomas and yolk sac tumors), sex cord stromal tumors (such as fibromas and thecomas) and least commonly, metastatic ovarian cancer from other primary tumors, particularly those of gastric, colonic and pancreatic origin (Table 2).

Imaging ovarian masses

Ultrasound is the study of choice in the initial evaluation of known or suspected adnexal masses[14]. It is sensitive in detection, inexpensive and widely available. Suspicious features seen on ultrasound include the presence of thick nodular walls or septations (>3 mm), papillary projections and echogenic loculations or solid areas[15–18]. The sensitivity of gray scale ultrasound criteria in predicting malignancy in ovarian tumors has been shown to be between 85 and 97%, whereas its specificity ranges from 56 to 95%. In addition to the gray scale evaluation, color and pulsed Doppler ultrasound have also been used in the evaluation of ovarian masses, although overlap of Doppler indices between malignant and benign lesions limits the usefulness of this technique[19–23].

MRI can be used to further evaluate sonographically indeterminate ovarian masses due to the better tissue contrast resolution seen with MR imaging. MRI is useful in the diagnosis of benign lesions, such as mature cystic teratomas (containing fat), endometriomas (containing blood products), and non-degenerative leiomyomas in the adnexa[24,25]. The findings most predictive of malignancy on MRI are papillary projections, necrosis in a solid tumor, and septations, which can be readily detected on contrast-enhanced MRI.

Table 2 Ovarian cancer staging

FIGO Stage	TNM stage	Disease extent
I	T1	Tumor limited to ovaries
IA	T1a	Tumor limited to one ovary, no malignant ascites, no tumor on the external surface, capsule intact
IB	T1b	Tumor limited to both ovaries, no malignant ascites, no tumor on the external surface, capsule intact
IC	T1c	Stage IA or IB with malignant ascites or capsule rupture or with tumor on the surface of one or both ovaries or with positive peritoneal washings
II	T2	Tumor involves one or both ovaries with pelvic extension
IIA	T2a	Extension to involve the uterus or fallopian tubes, no malignant ascites
IIB	T2b	Extension to other pelvic tissues, no malignant ascites
IIC	T2c	Stage IIB or IIC with malignant ascites, or capsule rupture or with tumor on the surface of one or both ovaries or with positive peritoneal washings
III	T3	Tumor involves one or both ovaries with microscopic peritoneal metastases outside the pelvis
IIIA	T3a	Microscopic peritoneal metastasis beyond the pelvis and nodes are negative
IIIB	T3b	Macroscopic peritoneal metastasis beyond the pelvis, 2 cm or less in size and nodes are negative
IIIC	T3c	Peritoneal metastasis greater than 2 cm in size and/or retroperitoneal or ±N1 inguinal lymph node metastasis
IV	M1	Distant metastasis including involvement of liver parenchyma

CT can be used in the staging of ovarian cancer, but is of limited utility in the characterization of a known ovarian mass. CT is of help in characterizing mature cystic teratomas containing fat.

PET using FDG has been evaluated for the diagnosis and characterization of ovarian masses. Hypermetabolic ovarian lesions, which were more intense than physiologic liver uptake have been considered positive for malignancy in most studies. Some of the studies used a cut off value of standardized uptake value (SUV) greater than or equal to 3 to be highly suggestive of malignancy. However, in menstruating women, false positive FDG uptake has been seen in follicular cysts and in corpus luteum cysts, between day 10 and day 25 of the menstrual cycle. Scanning pre-menopausal women before day 10 of the cycle can help distinguish physiologic uptake in the ovaries. False positive findings have also been seen in benign cystadenomas, teratomas, schwannomas, endometriomas and other inflammatory processes of the ovary. FDG uptake in the ovaries in post-menopausal women is usually concerning and must be further evaluated, typically with ultrasound.

In early studies, PET imaging demonstrated high sensitivity and specificity for the diagnosis of ovarian malignancy. This may have been due to lack of pathological proof in the earlier studies. In subsequent studies, the sensitivities and specificities of FDG PET in the diagnosis of ovarian cancer has been between 58 and 86% and 54 and 86% respectively in women with adnexal masses[26,27]. In a study by Kawahara *et al*.[28], a total of 38 patients were evaluated. PET imaging showed a sensitivity of 78% and a specificity of 87% compared with 91% and 87% respectively for MRI. False positive results were seen for cystadenomas and dermoid tumors and false negative results were seen in borderline ovarian tumors and mucinous adenocarcinoma of the ovary. In a study by Grab *et al*.[29], 101 asymptomatic adnexal masses were evaluated by ultrasound, MRI and PET. The sensitivity and specificity of PET was 58% and 80% compared with 90% and 60% with ultrasound and 83% and 84% with MRI. False positive results in benign cystadenomas and endometriosis were noted in this study with false negative results in the case of borderline tumors of the ovary. In a study of Fenchel *et al*.[30], false negative PET findings were obtained in cystadenocarcinoma and ovarian tumors with low malignant potential, and false positive PET results were obtained in acute inflammatory processes, benign schwannoma, teratoma, cystadenoma, and endometriomas. FDG accumulation in the ovary can also occur related to follicular and corpus luteum cysts resulting in false positive imaging results. This was shown to occur in 20% of pre-menopausal women in a study by Kim *et al*.[31].

Due to the false positive results in benign ovarian conditions and the false negative results in borderline tumors and early stage ovarian cancer, the role of FDG PET imaging for the initial diagnosis of ovarian cancer is limited.

Clinical staging and treatment

Once a diagnosis of ovarian cancer has been established, accurate staging is critical in planning treatment. The prognosis and 5-year survival in patients with ovarian cancer is dependent on the stage at diagnosis and ranges from 80% for stage I disease to 8% for stage IV disease. Ovarian cancer can spread locally within the pelvis, with subsequent spread within the peritoneal cavity to the rest of the abdomen. Tumor spread can also occur via lymphatics and hematogenously. Lymphadenopathy can be seen in the inguinal, pelvic and para-aortic regions. Hematogenous sites of spread include the liver and lung.

The standard of care for suspected early ovarian cancer is a comprehensive staging laparotomy which also provides tissue to establish a histologic diagnosis. A comprehensive staging laparotomy consists of a total abdominal hysterectomy, bilateral salpingooophorectomy, infracolic omentectomy, random sampling of multiple peritoneal sites (including pelvic side walls, paracolic gutters, cul-de-sac, and surface of bladder, rectum, and diaphragm), and pelvic and para-aortic lymphadenectomy. Optimal debulking refers to the surgical resection of all tumor sites to a maximal diameter of less than 1 cm[32]. Clinical trials have shown that optimal surgical debulking is associated with a more favorable response to post-operative chemotherapy and, therefore, prolonged survival. The role of pre-operative imaging in identifying patients who are potential candidates for optimal debulking surgery is extremely important.

Imaging and staging

There are few studies evaluating the additional role of PET imaging to CT imaging in the pre-operative staging of ovarian cancer. Yoshida *et al*.[33] evaluated 15 patients who underwent PET in addition to CT to detect tumor spread. The sensitivity and specificity of CT alone was 72% and 81% compared with 76% and 82% with the addition of PET. The accuracy of staging improved from 53% with CT alone to 87% with CT and PET. This study concluded that the addition of PET to CT improved the diagnostic accuracy in the staging of ovarian cancer. This study also showed increased FDG uptake in malignant but normal sized para-aortic nodes. Yuan *et al*.[34] in a study of five patients with recurrent ovarian cancer also demonstrated that PET imaging can detect metastases even in normal sized lymph nodes. The detection of sub-centimeter peritoneal implants is limited both on CT and on PET imaging. PET imaging in addition is limited by the spatial resolution and the physiologic activity seen in the bowel, ureters and bladder. Physiologic FDG uptake in the ureters, bladder,

and bowel can mimic peritoneal implants. Some authors have suggested the use of hydration, diuretics and voiding prior to image acquisition in order to minimize the effects from ureteric and bladder activity. The use of combined PET/CT can also help decrease false positives related to by better anatomic localization of normal structures.

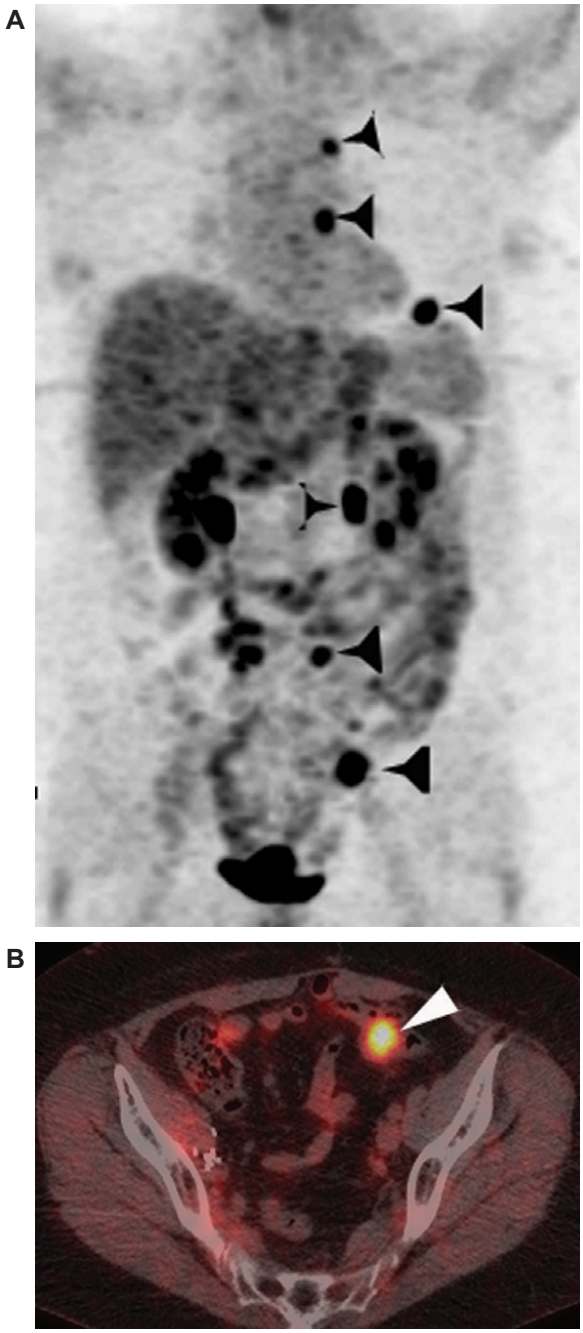

Figure 2 **A 56-year-old female with recurrent ovarian cancer. (a) Coronal PET image shows multiple sites of FDG recurrent disease in the chest, abdomen and pelvis (arrowheads); (b) axial fused PET/CT localizes one site of FDG uptake to the sigmoid colon which proved to be metastatic ovarian cancer involving the colon.**

Recurrent ovarian cancer

CT imaging is the most commonly used imaging modality in patients with suspected recurrent ovarian cancer. With the advent of thin section, multidetector CT, smaller metastatic deposits are diagnosed on CT. However, the accuracy of CT drops to 25–50% for peritoneal implants less than 1 cm in size[35]. Studies have reported that PET imaging may be of help in patients to detect recurrence due to the high tumor to background FDG uptake. The sensitivity of PET ranges from 80 to 100% and the specificity ranges from 42 to 100%. Some of these studies were performed on patients with elevated tumor marker levels and negative/equivocal CT imaging.

PET imaging is also limited in the ability to detect small metastatic deposits and can be limited due to physiologic bowel and bladder activity. In a study by Nakomoto *et al.*[36], the overall sensitivity improved from 72.7 to 92.3% and specificity improved from 75 to 100% with the addition of PET to CT imaging. Picchio *et al.*[37] showed increase in sensitivity from 70 to 83% and increase in specificity from 83 to 92% with the addition of PET to CT compared with CT imaging alone. Bristow *et al.*[38] evaluated combined PET/CT in the detection of tumor recurrence. The sensitivity and accuracy was 83% and 82% respectively. There is a definite role for PET imaging in patients with elevated tumor marker levels (CA 125 levels) and negative/equivocal CT imaging. With the increasing use of combined PET/CT imaging, the additive roles of PET and CT imaging can be utilized in patients undergoing follow up with elevated tumor marker levels (Fig. 2). Future prospective studies evaluating these patients along with histopathologic correlation maybe beneficial.

Endometrial carcinoma

Endometrial cancer is a common gynecologic malignancy which develops in approximately 142,000 women and is responsible for an estimated 42,000 deaths worldwide each year[39]. In the United States, endometrial cancer is the fourth most common malignancy in women overall and the most common gynecologic cancer and is the eighth most common cause of death in women[1].

The majority of cases occur in post-menopausal 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. The overall 5-year survival of patients with endometrial cancer is around 80%, but there is a substantial prognostic difference depending on stage, myometrial invasion, and histological type[39]. The overall prognosis is poor in advanced or recurrent endometrial carcinoma[40].

Diagnosis, staging, treatment

The diagnosis of endometrial cancer is usually established by histology from endometrial biopsy. Staging is based on extent of the primary tumor, regional lymph node involvement, and presence or absence of distant metastases. The FIGO staging of endometrial cancer is used and patients are typically staged surgically[39]. Lymphatic spread is via obturator nodes or internal iliac nodes, and subsequently to retroperitoneal nodes with rare direct para-aortic spread without pelvic disease[41].

Treatment for endometrial cancer is total abdominal hysterectomy with or without lymph node dissection. Systemic treatment is used for palliative purposes in the setting of metastatic or advanced disease[39]. Neo-adjuvant therapy chemotherapy may be used in select cases for pre-operative down-staging (Table 3).

Table 3 TNM staging system for endometrial carcinoma (American Joint Committee on Cancer, 2002)

TNM category	FIGO stages	Description
Primary tumor (T)		
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Tis	0	Carcinoma *in situ*
T1	I	Tumor confined to corpus uteri
T1a	IA	Tumor limited to endometrium
T1b	IB	Tumor invades less than one-half of the myometrium
T1c	IC	Tumor invades one-half or more of the myometrium
T2	II	Tumor invades cervix but does not extend beyond uterus
T2a	IIA	Tumor limited to the glandular epithelium of the endocervix; there is no evidence of connective tissue stromal invasion
T2b	IIB	Invasion of the stromal connective tissue of the cervix
T3	III	Local and/or regional spread as defined below
T3a	IIIA	Tumor involves serosa and/or adnexa (direct extension or metastasis) and/or cancer cells in ascites or peritoneal washings
T3b	IIIB	Vaginal involvement (direct extension or metastasis)
T4	IVA	Tumor involves 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	IIIC	Regional lymph node metastasis to pelvic and/or para-aortic nodes
Distant metastasis (M)		
MX		Distant metastasis cannot be assessed
M0		No distant metastasis
M1	IVB	Distant metastasis (includes metastasis to abdominal lymph nodes other than para-aortic, and/or inguinal lymph nodes; excludes metastasis to vagina, pelvic serosa, or adnexa)

Imaging

Endometrial cancer is surgically staged, but accurate assessment by pre-treatment imaging can potentially optimize surgical and non-surgical treatment particularly with regard to the use of pre-operative, neo-adjuvant therapy in advanced disease[42]. MR imaging is used to evaluate the depth of myometrial invasion and cervical invasion, which affects overall prognosis. The likelihood of lymphovascular invasion is greater with greater myometrial penetration of tumor. CT or MR may also be used to assess nodal involvement[43,44]. CT and MRI criteria for metastatic lymphadenopathy are based mostly on size criteria. PET imaging has been shown to be more accurate in identifying metastatic lymph nodes, particularly in nodes considered normal by size criteria (Fig. 3)[45,46].

Like most neoplasms, endometrial carcinoma does demonstrate an increased rate of glycolysis and takes up FDG[47]. There have been case reports of endometrial cancer diagnosed incidentally by PET[48,49]. Malignant uptake in the endometrium has been shown to have a mean SUV of 18.8 ± 9[45].

Non-malignant, physiologic causes of increased ^{18}F-FDG uptake in the endometrium must be taken into account in the routine interpretation of PET/CT images. In pre-menopausal patients, normal endometrial uptake of ^{18}F-FDG varies cyclically, increasing during the menstrual and ovulatory phases of the cycle[40,45].

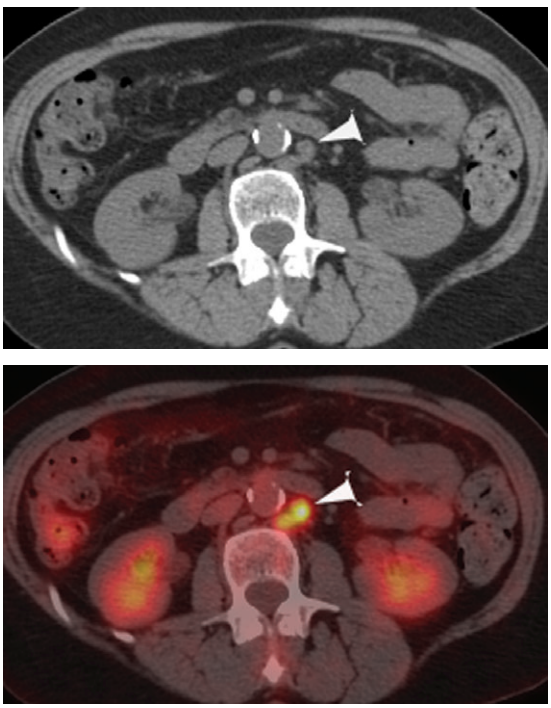

Figure 3 **A 74-year-old female with endometrial cancer. (a) CT shows small retroperitoneal nodes that measure less than 1 cm; (b) axial PET/CT shows FDG uptake in these nodes, subsequently proven metastases.**

Assessment of physiologic endometrial uptake has demonstrated mean SUVs of 5 ± 3.2 and 3.7 ± 0.9 in menstruating and ovulating patients, respectively, and 2.6 ± 1.1 and 2.5 ± 1.1 in patients in the proliferative and secretory phases, respectively[45]. Pre-menopausal patients using oral contraceptives have endometrial uptake values similar to the non-ovulating, non-menstruating phases of the cycle, likely due to the suppressive effects of contraceptives on the endometrium[45,50]. To avoid a false positive interpretation of endometrial malignancy, the menstrual history should be correlated in pre-menopausal patients[45]. If there is a question of physiologic activity, repeat PET imaging may be performed in the early follicular phase of the menstrual cycle[40,45].

Cyclic abnormalities also affect endometrial activity on FDG PET. Oligomenorrhea in pre-menopausal patients has been associated with increased uptake with a mean SUV of 3.4 ± 1.4[45]. In patients with amenorrhea, endometrial uptake resembles the values in post-menopausal patients[45]. Post-menopausal patients not receiving hormonal therapy have been shown to have a mean endometrial SUV of 1.7 ± 0.5[45]. Hormonal therapy in post-menopausal patients has not been shown to significantly affect endometrial uptake, but has not been conclusively studied[45].

Early data suggest that combined PET/CT may be useful in the management of endometrial cancer, particularly in the pre-operative detection of pelvic and para-aortic metastatic lymphadenopathy[40,47,51]. FDG PET has been used for detecting and evaluating recurrent endometrial cancer, with the advantage of imaging the entire body in a single study[51,52]. Initial investigations have suggested that whole-body FDG PET in conjunction with CT and MRI may facilitate optimal management of endometrial cancer in well-selected cases[40]. The routine use of PET/CT for endometrial cancer staging is unwarranted. The clinical applications of PET/CT in patients with endometrial carcinoma are emerging and further studies will be required to delineate its effect on outcome[45,46]. In the routine interpretation of PET/CT studies, knowledge of physiologic endometrial activity and correlation with the patient's menstrual phase are useful to avoid false positive interpretation of endometrial malignancy.

Conclusion

Cross sectional imaging can be an important adjunct to clinical evaluation of patients with cervical, ovarian and endometrial cancer in the appropriate setting. FDG PET/CT imaging further allows functional information to be correlated with anatomic abnormalities. This information has been used to assist in staging and surveillance of disease. FDG PET/CT has also been used to predict survival of patients particularly with regard to nodal and distant spread of disease in patients with cervical cancer. The pitfalls and limitations of FDG PET/CT imaging should always be considered when evaluating patients with gynecologic malignancies. With the development of additional radiotracers, molecular imaging techniques may provide even greater sensitivity and specificity for imaging the female genital tract in the future.

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