

# FDG PET/CT Pitfalls in Gynecologic and Genitourinary Oncologic Imaging<sup>1</sup>

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**Abbreviations:** CA-125 = ovarian carcinoma antigen 125, EANM = European Association of Nuclear Medicine, FDG = fluorodeoxyglucose, MIP = maximum intensity projection, RCC = renal cell carcinoma, SUV = standardized uptake value, SUV<sub>max</sub> = maximum standardized uptake value

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The role of whole-body positron emission tomography (PET)/computed tomography (CT) with fluorodeoxyglucose (FDG) is now established in the assessment of many gynecologic and genitourinary malignant tumors. FDG PET/CT has been widely adopted for staging assessments in patients with suspected advanced disease, in cases of suspected disease recurrence, and for determining prognosis in a number of malignancies. A number of pitfalls are commonly encountered when reviewing FDG PET/CT scans in gynecologic and genitourinary cases; these pitfalls can be classified into those that yield potential false-positive or false-negative results. Potential false positives include physiologic uptake of FDG by the endometrium and ovaries in premenopausal patients, physiologic renal excretion of FDG into the ureters and the urinary bladder, and increased FDG activity in benign conditions such as uterine fibroids, pelvic inflammatory disease, and benign endometriotic cysts. Potential false negatives include low-level FDG uptake by necrotic, mucinous, cystic, or low-grade tumors and the masking of serosal and peritoneal disease by adjacent physiologic bowel or bladder activity. In addition, there are inherent technical limitations—such as motion artifact (from respiratory motion and bowel peristalsis) and the limited spatial resolution of PET—that may limit the assessment of small-volume malignant disease. Knowledge of the key imaging features of physiologic and nonphysiologic FDG uptake, in addition to understanding the principles of adequate patient preparation and PET scanning protocols, is important for accurate interpretation of gynecologic and genitourinary oncologic FDG PET/CT studies.

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## SA-CME LEARNING OBJECTIVES

*After completing this journal-based SA-CME activity, participants will be able to:*

- Understand the role of FDG PET/CT in the multimodality investigation of gynecologic and genitourinary cancers.
- List the common causes of physiologic and nonphysiologic FDG uptake that complicate FDG PET/CT of gynecologic and genitourinary malignancies.
- Describe the pathophysiologic mechanisms leading to potential false-positive and false-negative assessments in patients with gynecologic and genitourinary malignancies, explaining methods to minimize reporting pitfalls.

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## TEACHING POINTS

- Endometrial or ovarian FDG activity in postmenopausal women should be regarded as suspicious; further correlation with clinical history and transvaginal US and/or MR imaging should be performed to exclude malignancy.
- It is always important to correlate cystic and mucinous lesions at US and/or MR imaging, as they are potentially false negative at FDG PET/CT.
- In patients with ovarian cancer, it is important to review the CT component of the study for peritoneal nodularity and to also be aware that FDG uptake in peritoneal carcinomatosis can be masked by tracer activity within the bowel.
- As primary RCCs generally have low-level tracer uptake at FDG PET/CT, the kidneys should be a review area and correlation with contrast-enhanced CT is important.
- When there is vesicovaginal fistulation to the urinary tract, contamination from urinary FDG excretion can lead to an overestimation of activity within malignant disease, or, conversely, may mask disease.

## Introduction

Positron emission tomography (PET)/computed tomography (CT) is a molecular imaging technique that involves the intravenous administration of short-lived radiolabeled positron-emitting molecules to image biologic processes in vivo. The most frequently used tracer is 2-deoxy-2-fluorodeoxyglucose (FDG). Whole-body PET/CT using FDG is an established tool in the multimodality imaging assessment of gynecologic and genitourinary malignancies. It has been shown to be effective in disease staging, detection of early disease recurrence, and determining prognosis in a number of malignancies.

FDG is a glucose analog that is taken up by cells and phosphorylated by hexokinase to FDG-6-phosphate. As FDG-6-phosphate is not a substrate for glycolysis and does not undergo further metabolism, it remains within the cell (1). Most tumor cells take up FDG intensely by virtue of increased glucose metabolism due to upregulated expression of the glucose transporter proteins (the SLC2A [or GLUT] family) and increased hexokinase activity (2,3).

Current evidence-based guidelines outline several indications for FDG PET/CT in gynecologic and urologic cancers, including malignancy detection, staging, and assessment for recurrence. Table 1 outlines the current indications from the Royal College of Radiologists, Royal College Physicians, and U.S. National Comprehensive Cancer Network (NCCN) (4,5). In 2008, the U.S. National Oncologic PET Registry (6) reported that 10.2% of PET studies were performed for patients with gynecologic malignancies.

As the use of FDG PET/CT rapidly grows, increasing numbers of radiologists are becoming

involved in FDG PET/CT interpretation as primary reporters, or by reviewing FDG PET/CT studies to aid interpretation when reporting oncologic CT and MR imaging cases. It is therefore important to have a working knowledge of FDG PET/CT and potential interpretation pitfalls to ensure the safe and accurate evaluation of these studies.

In this article, we review imaging protocols, patient preparation, and common pitfalls in the use of FDG PET/CT for assessment of gynecologic and genitourinary tumors (summarized in Table 2). In addition, we provide teaching points to minimize false interpretation.

## FDG PET/CT Imaging Protocol

Satisfactory scanning technique and patient preparation is necessary to allow accurate assessment of PET/CT while keeping patient radiation exposure levels as low as reasonably possible.

Detailed patient preparation guidelines and institutional FDG PET/CT protocols are beyond the scope of this article; the reader is referred to the Society of Nuclear Medicine (SNM) 2006 (7) and the European Association of Nuclear Medicine (EANM) 2014 (8) guidelines. The following points highlight aspects of particular relevance to gynecologic and genitourinary imaging:

Sufficient prehydration is required to ensure a low concentration of FDG in the urine. Patients are asked to void just before image acquisition and are scanned in a caudal-to-cranial direction to reduce the radiation dose to the bladder and help reduce artifact within the pelvis that may mask disease. The use of small doses of diuretic at the time of tracer injection may also be helpful (9,10). On occasion, a catheter may be useful to drain the bladder and limit tracer accumulation within the pelvis (11). This may be particularly useful in cases of suspected bladder fistulas, which may mask disease.

When using FDG PET/CT for radiation therapy planning in patients with gynecologic and genitourinary malignancies, it is essential that patient positioning mimics that used at radiation therapy; close liaison with the radiation therapy department is therefore imperative. Patients are imaged in the radiation therapy treatment position, lying supine on a flatbed palette, with their arms positioned down, and using immobilization aids as needed (12).

The timing of posttherapeutic FDG PET/CT for response assessment in gynecologic and genitourinary malignancies is often crucial. The EANM guidelines recommend waiting 3 months following radiation therapy to avoid mistaking posttherapeutic changes for residual or recurrent

**Table 1: Indications for FDG PET/CT in Gynecologic and Genitourinary Malignancies**

**Indications in gynecologic malignancy**

- Staging of locally advanced cervical cancer being considered for radical chemoradiotherapy
- Response assessment of locally advanced cervical cancer after radical chemoradiotherapy
- Suspected recurrent cervical, endometrial, or vulval carcinoma when other imaging is equivocal
- Staging or restaging of patients with cervical, endometrial, or vulval carcinoma before exenterative surgery
- Suspected recurrent ovarian carcinoma with rising CA-125 levels and equivocal or negative CT and MR imaging

**Indications in genitourinary malignancy**

- Staging RCC in cases with equivocal findings at other imaging (but ~50% of RCC may not be FDG avid and the tracer is excreted into the urinary tract)
- Staging advanced muscle-invasive bladder carcinoma being considered for radical treatment
- Aiding a management decision in selected cases of metastatic RCC and ureteric carcinoma when standard CT and MR imaging is inconclusive
- Recurrent metastatic testicular seminoma or teratoma with elevated or rising tumor markers and equivocal or normal CT or MR imaging
- Restaging of patients with testicular seminoma and teratoma with residual masses after chemotherapy (but mature differentiated teratoma may not be FDG avid and cannot be excluded with a negative scan)

Note.—CA-125 = ovarian carcinoma antigen 125, MR = magnetic resonance, RCC = renal cell carcinoma. Sources.—References 4 and 5.

**Table 2: Summary of Limitations and Potential Pitfalls in FDG PET/CT Interpretation of Gynecologic and Genitourinary Malignancies**

Potential False Positives	Potential False Negatives
Physiologic FDG activity in ovaries and endometrium during ovulation and menstruation may mimic disease	Some necrotic, mucinous, cystic, or low-grade tumors may show low-level FDG activity and be less readily detected
Benign lesions such as uterine fibroids and benign endometriotic cysts can be metabolically active	Limited spatial resolution of PET and motion artifact may mask small-volume peritoneal disease and small lymph nodes
Focal ureteric activity or focal bladder activity can mimic disease	Physiologic bowel activity may mask peritoneal disease, serosal disease, and small lymph nodes
Vesicovaginal fistulas may limit disease evaluation by overestimating SUV	Perivesical disease may be masked by high physiologic activity excreted within the urinary bladder

disease (8). However, if there is clinical concern for disease outside of the radiation therapy field, early posttherapeutic PET/CT should proceed. In fact, there is increasing evidence that early FDG PET/CT during radiation therapy in patients undergoing chemoradiation therapy for locally advanced cervical cancer can provide prognostic information, although this is not yet in routine clinical practice (13,14).

**Technical Pitfalls**

**Attenuation Correction**

Attenuation correction algorithms are used to correct for the reduction in activity of the annihilation photons as they pass through tissues of varying density within the body. For PET/CT scans, the CT component is used for attenuation correction. This can lead to the introduc-

tion of attenuation artifacts, whereby there is overcorrection of photopenic areas corresponding to high-attenuation structures or material on the CT images, for example, hip prostheses, barium contrast medium within the bowel, surgical clips, pacemakers, and, rarely, intrauterine contraceptive devices (15,16). Attenuation artifacts can also arise in the presence of large areas of radioactivity such as the urinary bladder, resulting in adjacent areas of photopenia.

Attenuation artifact can thus both mimic and mask disease. It is therefore essential when reporting FDG PET/CT studies that both the attenuation- and non-attenuation-corrected images are reviewed to overcome this potential pitfall. Any apparent increased activity related to the presence of high-attenuation structures should not be evident on the non-attenuation-corrected images when there is no disease (17).

## Misregistration

PET/CT misregistration is a potential cause for a false-negative assessment of malignant disease. PET/CT misregistration is the anatomic malalignment of the PET and CT datasets that results in the superimposition of FDG activity onto the incorrect anatomic structures demonstrated on the CT component (18). This can be caused by respiratory motion, patient motion, bowel motility, and/or differences in bladder distention between the CT and PET acquisitions (19).

Reducing the time between the PET and CT acquisitions is the main technique to prevent misregistration, as it minimizes patient motion between the scans. In addition, the patient should be instructed on the importance of staying still and be placed in a comfortable position at the start of the study. Patients are usually scanned with their arms above their head to prevent truncation artifacts. If they are unable to tolerate this for the duration of the study, they should be scanned with their arms crossed over their chest or by their sides. When there has been misregistration, it is important that the reporting physician is able to recognize it and attempt to correct it using specialist software. However, in severe cases of misregistration artifact due to patient motion, repeated imaging of the bed positions involved may be required.

As the PET component of the study requires several minutes per bed position to acquire, it is not feasible to perform breath-hold CT, as is normal practice for diagnostic thoracic imaging. Therefore, both the CT and PET components of the study are typically performed during free respiration. This can lead to respiratory motion artifact, particularly in the lower lobes of the lung and peridiaphragmatic regions; this may limit assessment of pulmonary nodules, peridiaphragmatic liver lesions, and subphrenic peritoneal disease (20). Close scrutiny of the CT component of the study and any available contrast medium-enhanced CT or MR imaging can help to minimize this pitfall.

Motion artifact may also occur due to bowel motility secondary to peristalsis, which is of particular importance with pelvic malignancies in the detection of serosal peritoneal disease (21). Antiperistaltic agents have been used to try to reduce bowel activity, but their effect on misregistration has not been specifically studied (22).

Differences in urinary distention between the CT and the PET components can cause misregistration. This is minimized by performing the PET study in a caudal-to-cranial direction so that the urinary bladder is imaged early, hopefully before further distention.

## Limitations and Pitfalls of Gynecologic and Genitourinary Oncologic FDG PET/CT

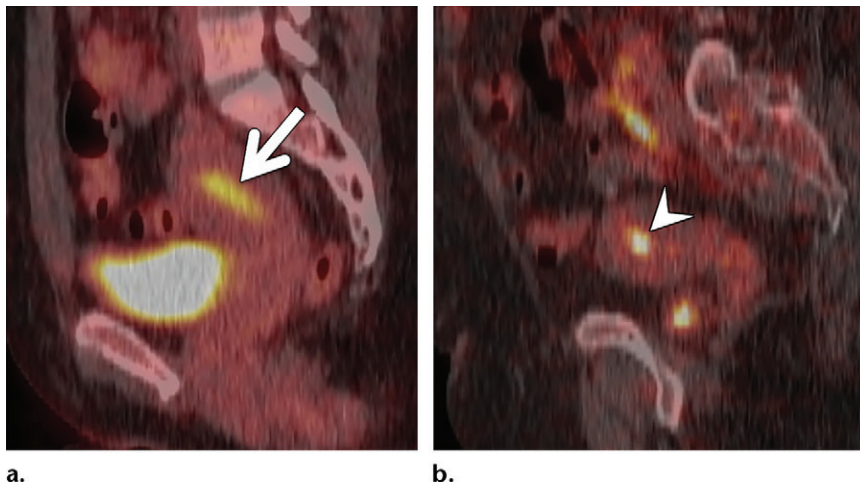
Table 1 demonstrates several indications for FDG PET/CT in assessment of gynecologic and genitourinary malignancies (4,5). Although there is relatively high sensitivity of FDG PET/CT in these malignancies, it is important to note that glucose metabolism is not specific to malignancy and that physiologic activity, benign conditions, and inflammatory processes can both mimic and mask disease. We will demonstrate potential pitfalls in the assessment of these conditions with potential false positives and false negatives.

### Physiologic Pitfalls

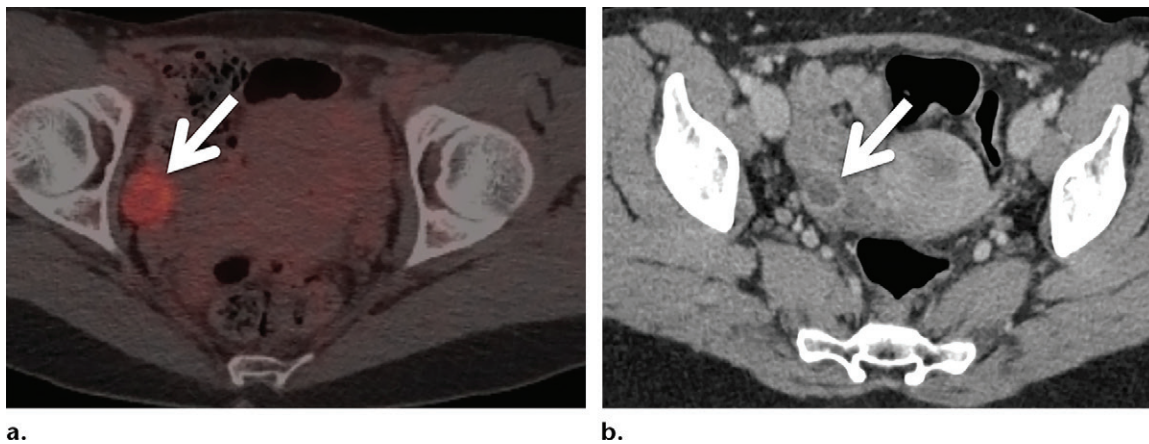
#### Endometrial and Ovarian Uptake

In premenopausal women, there can be physiologic FDG uptake within the endometrium that varies with the menstrual cycle. There are two peaks of potentially increased endometrial FDG uptake: during the menstrual flow phase (typically days 0–4 of the menstrual cycle) and ovulation (approximately day 14 of the menstrual cycle). The proliferative phase of the menstrual cycle is typically days 7–13 and the secretory phase is typically days 15–28. Lerman et al (23) reported that endometrial FDG uptake activity was higher in the menstrual (maximum standardized uptake value [SUV<sub>max</sub>] = 5.0 ± 3.2) and ovulatory (3.7 ± 0.9) phases of the cycle than in the proliferative (2.6 ± 1.1) and secretory (2.5 ± 1.1) phases. This is particularly relevant in patients with cervical cancer, as endometrial FDG uptake may not reflect infiltration of the tumor into the uterus. The pattern of tracer uptake and distribution in the endometrium can give a clue to the cause. When there is physiologic endometrial activity, FDG uptake is typically in a diffuse uniform pattern (Fig 1a), whereas in cases of endometrial cancer the FDG uptake is usually more focal (Fig 1b).

In premenopausal women, ovarian physiologic FDG uptake can be seen during ovulation and in relation to corpus luteal cysts (24). Physiologic uptake in the ovary manifests as ovoid with smooth margins or sometimes a rim of activity with a photopenic center. At contrast-enhanced CT, this may appear to be a small rim-enhancing cyst (Fig 2). The mechanism of physiologic ovarian uptake has been postulated to be due to an inflammatory reaction involving cytokines during the ovulatory process to increase glucose uptake to meet the metabolic demands of the growing follicle and the ovulated oocyte (25). Physiologic increased FDG activity



**Figure 1.** Physiologic and pathologic endometrial FDG uptake. **(a)** Physiologic endometrial uptake in a 34-year-old premenopausal woman during the menstrual flow phase of her menstrual cycle. Sagittal fused FDG PET/CT image demonstrates uniform increased tracer uptake (arrow) along the endometrium. **(b)** Endometrial cancer in a 64-year-old postmenopausal woman under investigation for a solitary pulmonary nodule. Sagittal fused FDG PET/CT image demonstrates incidental focal uptake (arrowhead) in the endometrium. Subsequent pelvic ultrasonography (US) (not shown) demonstrated a thickened endometrium, and pathologic analysis after biopsy allowed confirmation of the cancer.



**Figure 2.** Physiologic ovarian uptake in a 35-year-old woman. **(a)** Axial fused FDG PET/CT image demonstrates physiologic ringlike uptake (arrow) in the right adnexa, in keeping with a corpus luteal cyst. **(b)** Axial contrast medium-enhanced CT image acquired separately demonstrates the corpus luteal cyst (arrow) with peripheral rim enhancement.

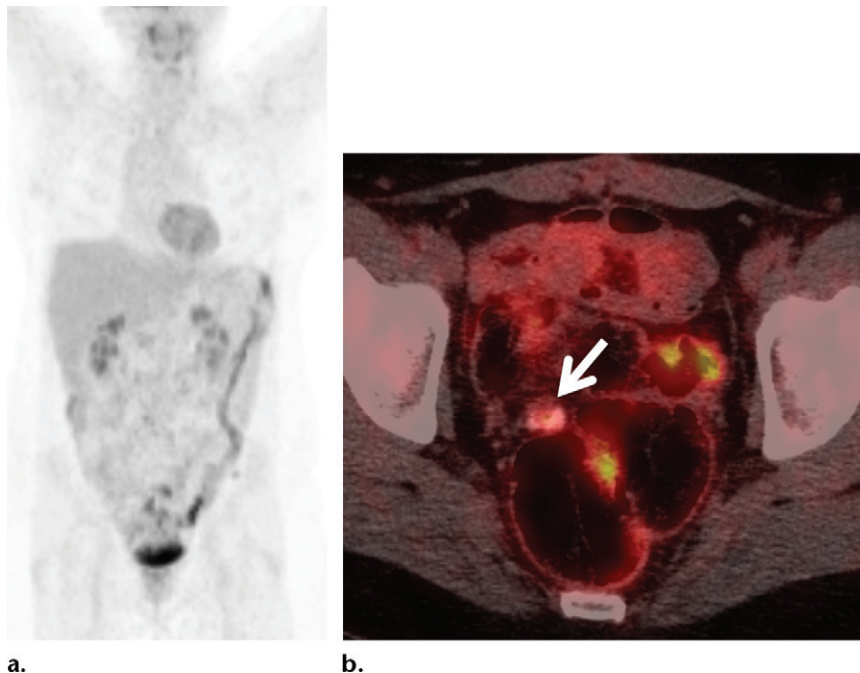
in the ovaries or uterus is not likely to occur in postmenopausal women. Endometrial or ovarian FDG activity in postmenopausal women should be regarded as suspicious; further correlation with clinical history and transvaginal US and/or MR imaging should be performed to exclude malignancy (Fig 1b).

The patient's menstrual history, including the date of the last menstrual period, should be routinely documented to aid interpretation of ovarian and endometrial activity. Premenopausal women who are *BRCA1*- or *BRCA2*-positive have an increased risk of developing ovarian cancer; ovarian FDG activity in these patients therefore needs to be viewed with caution and requires correlation with US or MR imaging (26).

### Bowel Activity

Physiologic FDG activity in the gastrointestinal tract is highly variable and can be intense, particularly in the right colonic, cecal, and rectosigmoid regions (27). Although this can lead to potential false positives in interpretation, it can also mask adjacent disease, particularly peritoneal carcinomatosis, resulting in a false-negative assessment (Fig 3). The mechanism of physiologic FDG activity in the bowel is not fully understood but is thought to include activated smooth muscle and mucosal uptake, FDG secretion, and microbial overgrowth (28). Intense and diffuse bowel FDG activity has also been described in type 2 diabetic patients taking the oral hypoglycemic biguanide, metformin (29). The

**Figure 3.** Peritoneal carcinomatosis in a 48-year-old woman that was masked due to increased colonic activity caused by metformin. (a) Coronal maximum intensity projection (MIP) PET image shows diffuse increased uptake within the descending and sigmoid colons. (b) Axial fused FDG PET/CT image demonstrates a partly calcified peritoneal deposit (arrow) that was masked on the MIP image by adjacent increased bowel activity.



exact mechanism whereby metformin results in increased bowel activity is unclear, but in animal studies it has been found to enhance the transfer of glucose from the vascular compartment into the intestinal mucosal cells and increase glucose utilization (30). Activation of adenosine monophosphate-activated protein kinase (AMPK), which induces the upregulation of glucose transporters (GLUT1, GLUT2, and GLUT4), may also play a role (31). Despite the association between increased gastrointestinal tract activity and metformin use, the current EANM guidelines recommend that metformin should be continued for blood sugar control unless intravenous contrast medium is to be administered, in which case metformin should be stopped for 48 hours to reduce the risk of lactic acidosis (8).

Physiologic activity within the bowel is typically diffuse and linear, whereas pathologic uptake is often focal. The pattern of focal colonic FDG uptake has a high sensitivity, specificity, and negative predictive value for colonic malignancy, but a lower positive predictive value for the same (32). Focal activity can also occur with premalignant polyps and benign inflammatory conditions such as inflamed diverticula, hemorrhoids, and focal colitis (33,34). Careful scrutiny of the CT component of the study and any accompanying diagnostic imaging to identify serosal and peritoneal disease or features of inflammation such as diverticulitis and colitis can help to avoid misinterpretation.

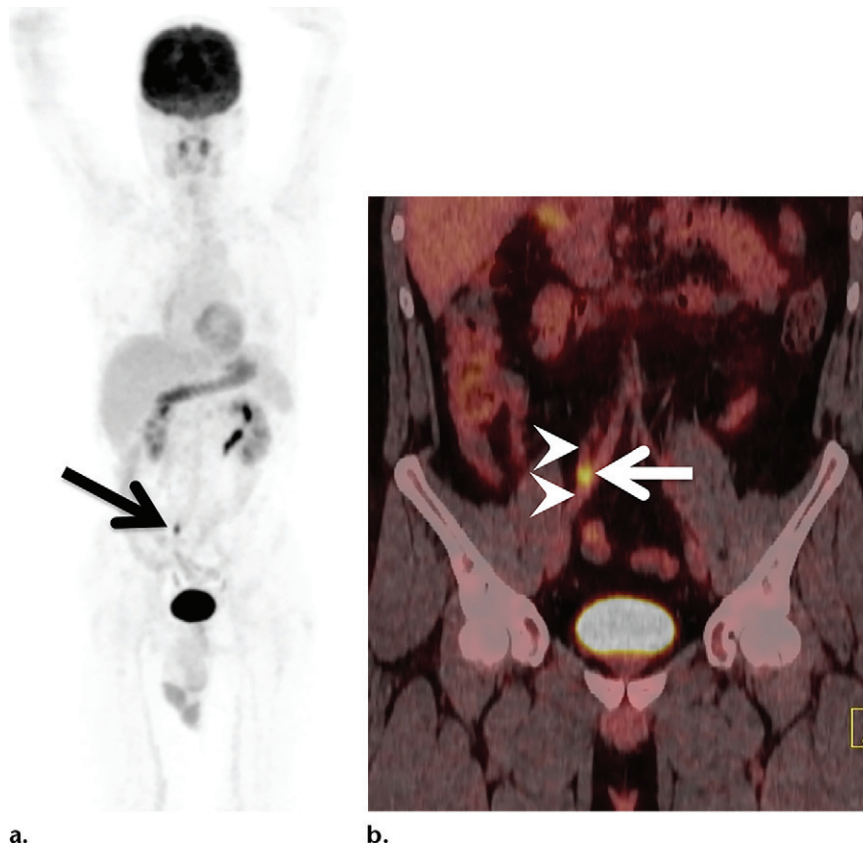
### Tracer Excretion

Although glucose is usually completely reabsorbed in the proximal tubules of the kidneys,

FDG is not and it therefore undergoes excretion into the urinary tract. The accumulation of the radiotracer in the urine can mimic disease, particularly on axial images if there are areas of focal ureteric activity. It is important to correlate focal activity with the coronal and sagittal planes of the fused FDG PET/CT images for accurate anatomic localization, where the focal ureteric activity is often elongated rather than rounded or ovoid as seen in a node (Fig 4). In addition, reviewing any prior FDG PET/CT images for previous ureteric activity definition may be helpful. Some centers advocate routine diuretic use with intravenous furosemide injection during scanning to help flush out excreted FDG, reducing focal ureteric activity and thereby reducing artifacts (35).

### Brown Adipose Tissue Uptake

Brown adipose tissue (BAT) can be found both above and below the diaphragm, but is typically located within the supraclavicular, midaxillary, posterior mediastinal, paraesophageal, and paraspinal regions (36). Sympathetic stimulation results in hypermetabolic BAT, which causes an increase in FDG activity on PET/CT images and has the potential for both masking and mimicking nodal disease. Careful evaluation of the CT component is required to differentiate BAT from disease, confirming the presence of fatty attenuating tissue in the anatomic region corresponding to the area of increased FDG uptake. Although BAT is typically more problematic in the cervical and thoracic regions, it can be prominent in the paraaortic region (Fig 5). The example in Figure



**Figure 4.** Focal ureteric activity mimicking a pathologic lymph node at surveillance FDG PET/CT in a 56-year-old man with previous thoracic sarcoma. (a) Coronal MIP PET image shows no thoracic disease but demonstrates focal activity (arrow) in the right hemipelvis. (b) Coronal fused FDG PET/CT image shows that the focus of activity (arrow) in the right hemipelvis is within the distal right ureter (arrowheads) and is due to physiologic FDG excretion.

5 demonstrates a patient with a paraganglioma who has extensive paraaortic FDG uptake in the BAT, which can be mistaken for, or mask, nodal disease. The increase in catecholamines due to paragangliomas has been reported to stimulate hypermetabolic brown fat (37).

Hypermetabolic BAT occurs more commonly in children than in adults and is more prevalent in females than in males overall. It is also more frequently encountered in cold weather and in patients with a low body mass index (38). To limit brown fat activity, the patient should be kept warm during the FDG injection and uptake time, and in severe cases administration of diazepam or a  $\beta$ -blocker should be considered (39,40).

### Low-Level FDG Uptake

There are several types of gynecologic and genitourinary malignancy with low-level glucose metabolism that demonstrate low-level, or even no, FDG uptake, thus potentially leading to false-negative assessments for malignancy.

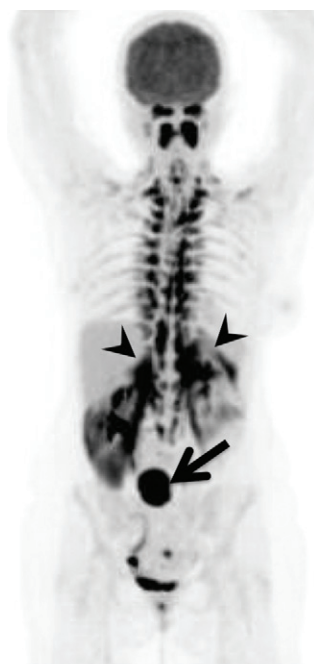
### Prostate Cancer

Most primary prostate cancers have low glucose metabolism, and therefore the primary tumor or metastases may demonstrate only low FDG avidity (41,42) (Fig 6). In addition, there is significant overlap in FDG uptake between prostate

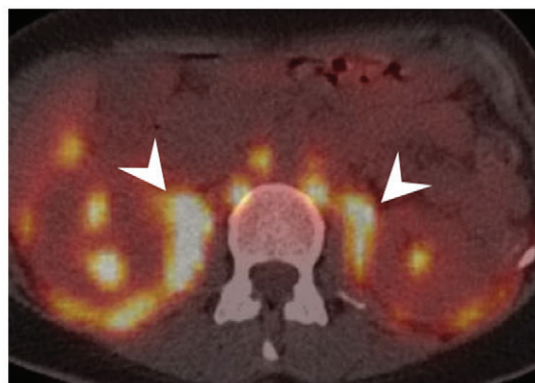
cancer and benign prostatic hyperplasia (43). Therefore, FDG PET/CT has a limited role in the assessment of prostate cancer, except perhaps in castration-resistant tumors, which tend to be FDG avid (44). Other non-FDG tracers, such as fluorine 18 fluorocholine and gallium 68 prostate-specific membrane antigen, are more promising than FDG (45). However, incidental prostatic activity can be encountered on FDG PET/CT scans. In a retrospective study of 3236 men, Seino et al (46) found incidental FDG uptake within the prostate in 53 patients (2%). Of those, 16% were found to have prostate cancer, whereas the majority (84%) had benign results. Incidental prostatic FDG activity therefore requires further investigation with prostate-specific antigen levels, dedicated pelvic MR imaging, and biopsy.

### Cystic and Mucinous Tumors

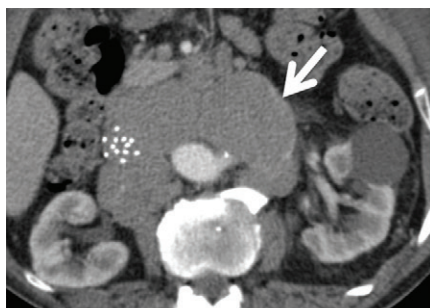
Malignancies with a clear cell or mucinous histologic pattern have been reported to have low-level FDG uptake (47) (Figs 7, 8). Therefore, the sensitivity of FDG PET/CT for the detection of mucinous neoplasms has been shown to be relatively low, with one retrospective study, from Berger et al (48), documenting a sensitivity of 59%. They postulated that mucinous tumors have proportionally low tumor cellularity because they contain more clear gelatinous fluid (mucin), which can be



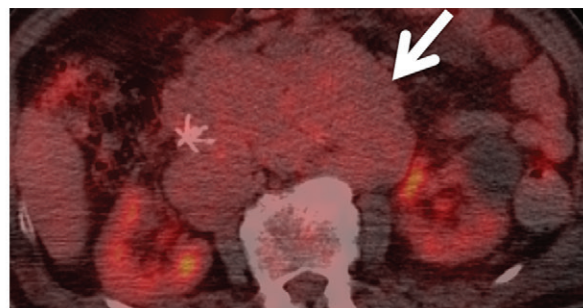
a.



b.



a.



b.

**Figure 6.** Low-level activity in retroperitoneal lymph nodes in a patient with prostate cancer. (a) Axial contrast-enhanced CT image demonstrates extensive retroperitoneal lymphadenopathy (arrow) that was thought to be due to lymphoma. A biopsy was performed and histopathologic results were of lymph node metastases from prostate cancer. (b) Axial fused FDG PET/CT image shows only low-level metabolic activity (arrow) in these metastatic lymph nodes and no increased FDG uptake in the prostate gland (not shown).

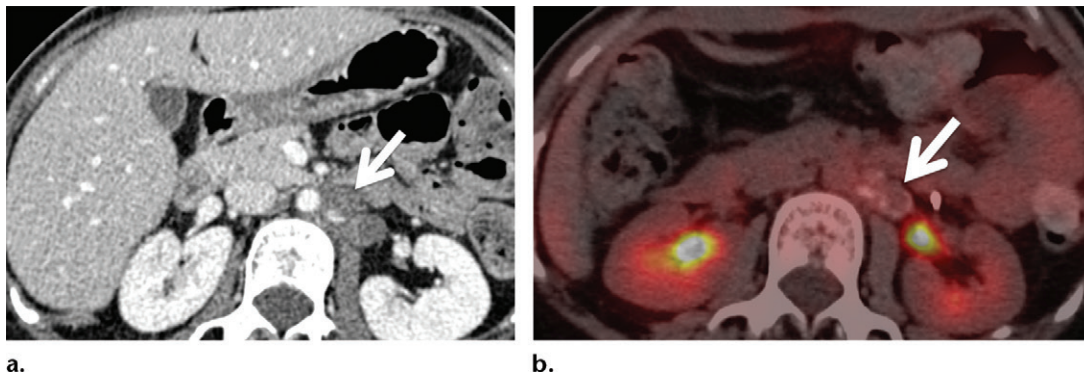
intracellular or extracellular. In vitro studies have shown that FDG uptake directly correlates with the number of viable cancer cells; mucinous tumors with lower proportions of viable cancer cells may therefore not demonstrate increased FDG avidity (49). Similarly, tumors with large cystic or necrotic components can also yield false-negative results at FDG PET/CT, due to the reduced cellular proportion of these tumors, which therefore contain fewer viable cancer cells. It is always important to correlate cystic and mucinous lesions at US and/or MR imaging, as they are potentially false negative at FDG PET/CT.

### Necrotic Lymph Nodes

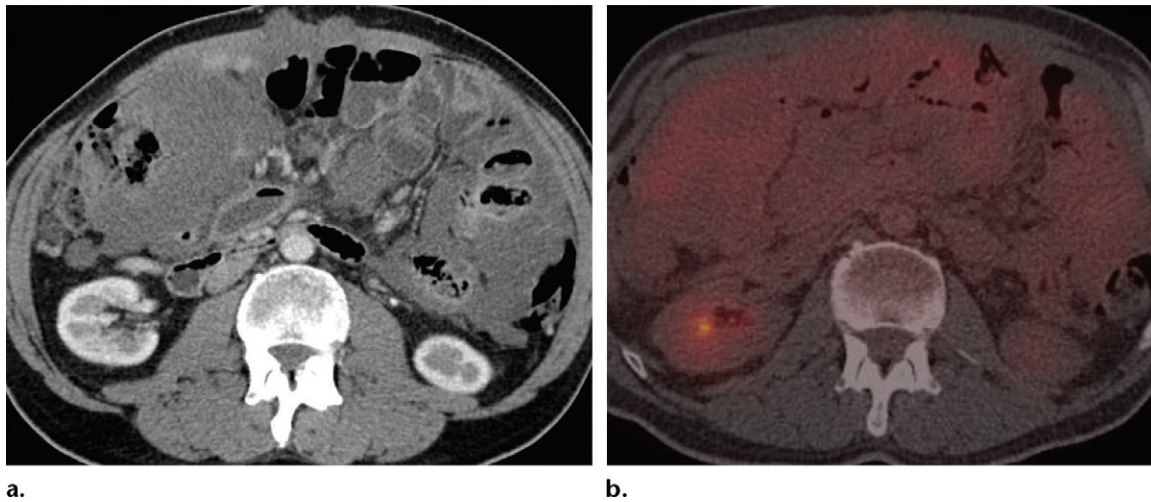
Assessment of lymph node involvement in the staging of gynecologic and genitourinary ma-

lignancies is one of the important roles of FDG PET/CT. Lymph nodes from squamous cell carcinoma are often necrotic; 85% of cervical cancers are of the squamous cell histologic subtype, as it is associated with exposure to the human papilloma virus (50). Involved lymph nodes from cervical cancer may therefore demonstrate central necrosis. A prospective study of 49 women with biopsy-proven cervical cancer demonstrated central necrosis in 27% and 17% of all abnormal nodes at CT and MR imaging, respectively, and a positive predictive value of 100% for metastases (51). The study also showed that most of the necrotic nodes had a maximal axial diameter of greater than 2 cm. However, given the reduced number of viable cancer cells, these malignant nodes may demonstrate little or no FDG uptake





**Figure 7.** Low-level FDG uptake in a 30-year-old woman with an ovarian mucinous tumor and rising tumor markers. (a) Axial contrast-enhanced CT image demonstrates a hypoattenuating partly calcified left paraaortic lymph node (arrow). (b) Axial fused FDG PET/CT image demonstrates low-level FDG uptake only in this node (arrow), which was proven to be metastatic at postsurgical histologic analysis.



**Figure 8.** Low-level FDG uptake in a 55-year-old woman with mucinous adenocarcinoma of the ovary. (a) Axial contrast-enhanced CT scan demonstrates mucinous contents within the abdominal cavity, in keeping with pseudomyxoma peritonei. (b) On an axial fused FDG PET/CT image, the mucinous area demonstrates low-level FDG uptake.

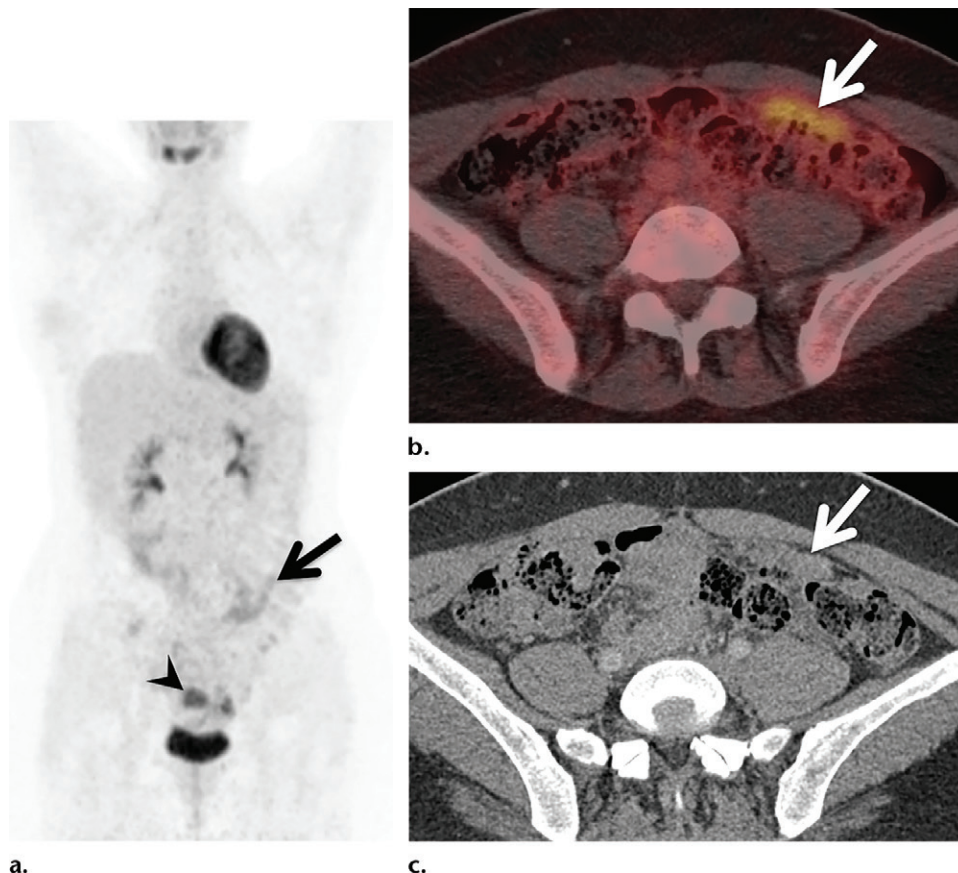
and therefore it is always important to inspect the CT component in cervical cancer.

### Peritoneal Carcinomatosis

In developed countries, ovarian cancer is the second most common but most lethal gynecologic malignancy (52). One significant reason for the relatively poor prognosis in that group is that the majority of patients with early-stage disease are asymptomatic, and by the time of presentation and diagnosis most patients have advanced-stage disease, often with peritoneal metastases. The presence of peritoneal carcinomatosis is one of the most important prognostic markers in patients with ovarian cancer; it is therefore important to detect peritoneal involvement as early as possible to initiate the appropriate oncologic or surgical therapy. Detection of peritoneal spread can be challenging at diagnostic CT and MR imaging. The limited spatial resolution of PET means that it is less useful than contrast-

enhanced CT for the detection of small-volume peritoneal disease and such peritoneal disease may demonstrate only low-level avidity, as activity can be underestimated in small nodules. A recent meta-analysis by Li et al (53) showed that the pooled sensitivity for the detection of peritoneal disease at PET/CT (84%) was significantly higher than at PET (60%).

Integrated FDG PET/contrast-enhanced CT has been reported to be more accurate than contrast-enhanced CT alone in predicting the surgical staging (54,55). However, false negatives may occur, typically with subcentimeter lymph nodes, peritoneal nodules measuring less than 7 mm, and cystic and mucinous lesions (as previously mentioned). A study of 62 patients with suspected peritoneal carcinomatosis was performed with histologic correlation of findings at laparotomy. Contrast-enhanced CT in 26 of 31 patients, PET alone in 25 of 31 patients, and integrated PET/contrast-enhanced CT in 30 of



**Figure 9.** Peritoneal disease mimicking bowel activity in a 32-year-old woman with ovarian adenocarcinoma with rising CA-125. (**a, b**) Coronal MIP PET image (**a**) shows bowel serosal disease (arrowhead) in the pelvis. Increased activity (arrow) in the left iliac fossa on both the MIP PET and axial fused FDG PET/CT (**b**) images was initially thought to represent bowel activity. (**c**) However, on scrutinizing the corresponding axial contrast-enhanced CT image, this area (arrow) corresponded to peritoneal nodularity, consistent with peritoneal disease.

31 patients allowed detection of peritoneal seeding with sensitivities of 88%, 88%, and 100%, respectively (55). In patients with ovarian cancer, it is important to review the CT component of the study for peritoneal nodularity and to also be aware that FDG uptake in peritoneal carcinomatosis can be masked by tracer activity within the bowel (Fig 9).

## Ovarian, Tubal, and Uterine Disease

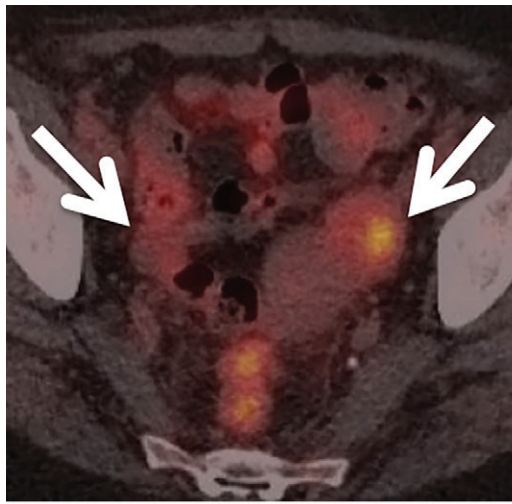
### Ovarian and Tubal Disease

Primary and secondary ovarian tumors can demonstrate increased FDG uptake (56). Although there is no routine role for FDG PET/CT in the characterization of adnexal masses, for which US and MR imaging are the modalities of choice, focal adnexal activity may be encountered incidentally. Ovarian uptake in postmenopausal women with another primary malignancy should therefore be regarded as suspicious for malignancy, either primary tumors, or metastases such as Krukenberg tumors where the primary site is typically the gastrointestinal tract or breast (Fig 10).

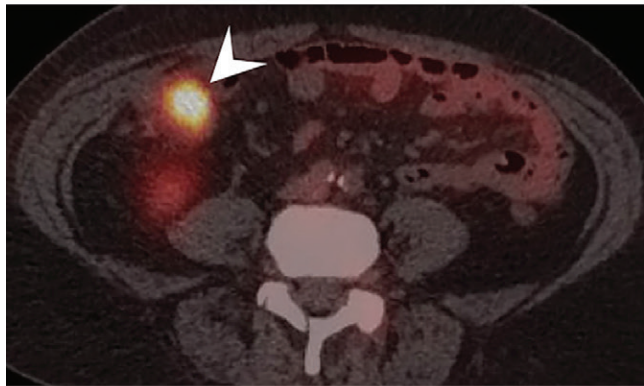
Although malignant ovarian lesions tend to be more FDG avid, there is an overlap in the level of metabolic activity between benign, borderline, and malignant lesions, with no reliable standardized uptake value (SUV) cutoff to differentiate between benign and malignant adnexal masses (57).

In patients with ovarian masses, there are a number of benign inflammatory conditions that may yield false-positive results with increased adnexal and/or tubal FDG uptake, such as pelvic inflammatory disease, tuboovarian abscesses, and endometriomas (58) (Fig 11). Other benign pelvic masses such as benign cystadenomas, teratomas, and schwannomas may also demonstrate increased FDG activity and give false-positive findings (59).

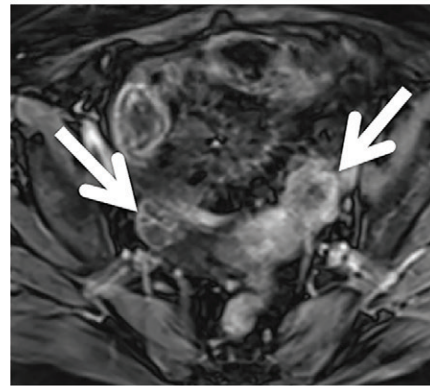
Gestational trophoblastic disease is a rare and aggressive tumor that is usually very chemosensitive; however, conventional US and MR imaging is often limited in differentiating between residual disease and necrosis. FDG PET/CT has been shown to help identify sites of primary and/or metastatic disease in patients with persistently high levels of  $\beta$ -human chorionic gonadotropin



a.



b.



c.

**Figure 10.** Pathologic FDG ovarian uptake in a 68-year-old woman with a primary cecal adenocarcinoma, in keeping with a Krukenberg tumor. (a, b) Axial fused FDG PET/CT images show increased FDG uptake in both ovaries (arrows in a) and the primary cecal adenocarcinoma (arrowhead in b). (c) Axial postcontrast T1-weighted fat-saturated MR image demonstrates enhancing ovarian lesions (arrows). Histologic analysis of the adnexal lesions confirmed metastatic lesions from the cecal primary tumor.

( $\beta$ -hCG) after first-line chemotherapy and may therefore be helpful in guiding management with alternative treatment (60) (Fig 12).

### Uterine Disease

Benign uterine leiomyomas (uterine fibroids) show a wide range of variable FDG activity; there can even be heterogeneous FDG uptake within the same fibroid (Fig 13). This phenomenon is thought to be regulated by different characteristics of the leiomyomas, including hormonal dependency, cellularity, vascularity, and the expression of GLUT transporter proteins and hexokinase (61). Benign leiomyomas with increased FDG activity are more common in premenopausal women (62). It is therefore important to correlate increased FDG uptake within the pelvis with other imaging, as many nonmalignant pathologic conditions may demonstrate increased tracer uptake.

### Kidney and Urinary Tract Disease

#### Kidney

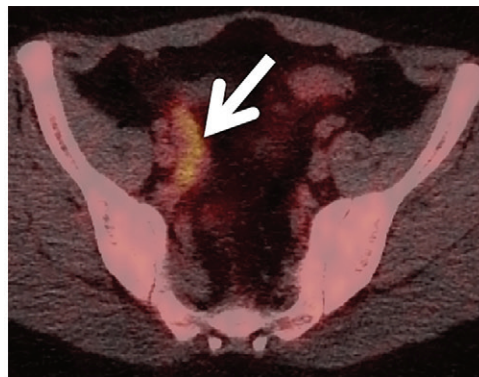
The role of FDG PET/CT is limited by its low sensitivity in the detection of RCC. A retrospective study of 66 patients by Kang et al (63)

showed that for primary RCC tumors, FDG PET/CT showed sensitivity and specificity of 60% and 100%, respectively, versus 92% and 100% for contrast-enhanced CT. In addition, they found that for retroperitoneal lymph node metastases and/or renal bed recurrence, FDG PET/CT showed 75% and 100% sensitivity and specificity, respectively, versus 93% sensitivity and 98% specificity for contrast-enhanced CT. As primary RCCs generally have low-level tracer uptake at FDG PET/CT, the kidneys should be a review area and correlation with contrast-enhanced CT is important. There may also be differential FDG uptake in primary RCC and secondary metastases. Where there is a significant difference, the metastases are more likely to demonstrate increased metabolic activity compared with the primary renal tumor (64) (Fig 14).

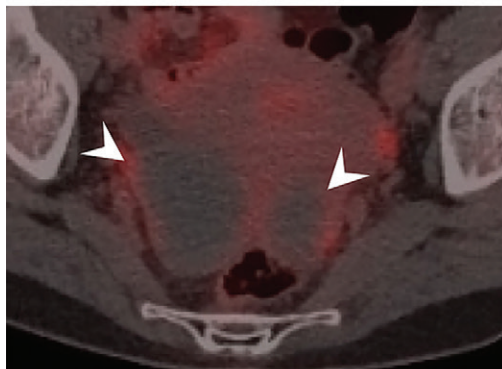
#### Urinary Tract

It is important to scrutinize the pattern of urinary excretion of FDG, as this can often suggest possible disease recurrence adjacent to the vesico-ureteric junctions that may otherwise have been difficult to visualize due to pooling of the excreted tracer within the urinary bladder (Fig 15).

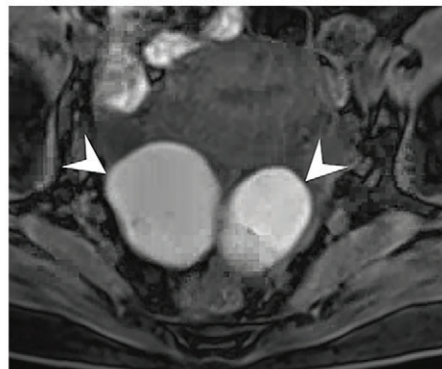
**Figure 11.** Benign conditions demonstrating increased FDG uptake. **(a)** Pelvic inflammatory disease in a 20-year-old woman with a known history of the condition. Axial fused FDG PET/CT image shows increased FDG activity (arrow) along the right fallopian tube. **(b, c)** Bilateral endometriomas in a 32-year-old woman. **(b)** Axial fused FDG PET/CT image shows bilateral pelvic masses with central photopenia and peripheral rim increased activity (arrowheads). **(c)** Axial T1-weighted fat-saturated MR image demonstrates high T1 signal intensity (arrowheads), in keeping with blood products and peripheral hemosiderin, consistent with the diagnosis.



a.

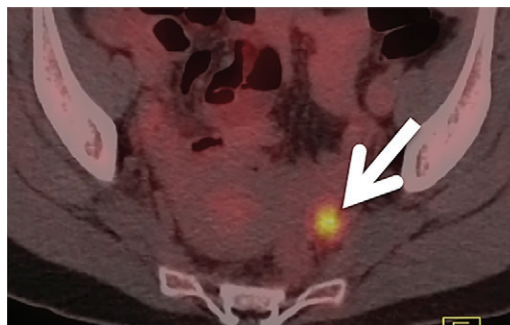


b.



c.

**Figure 12.** Tubal choriocarcinoma in a 29-year-old woman with elevated  $\beta$ -hCG level, negative initial US and MR imaging, and primary gestational trophoblastic disease. FDG PET/CT was used to identify the site of the disease; an axial image shows intense focal FDG uptake (arrow) in the left adnexa. This could not be physiologic uptake, as the patient's last menstrual period was 3 months prior, and therefore it was regarded as suspicious. The lesion was proven at histologic analysis.

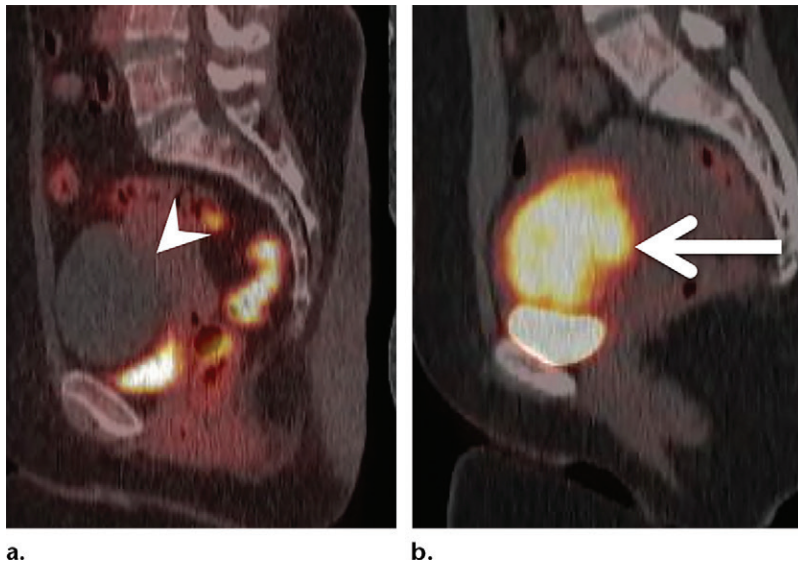


The example in Figure 15 demonstrates disease recurrence at the vaginal vault, causing upstream hydronephrosis. This manifests as a persistent nephrogram on the MIP PET images (Fig 15a).

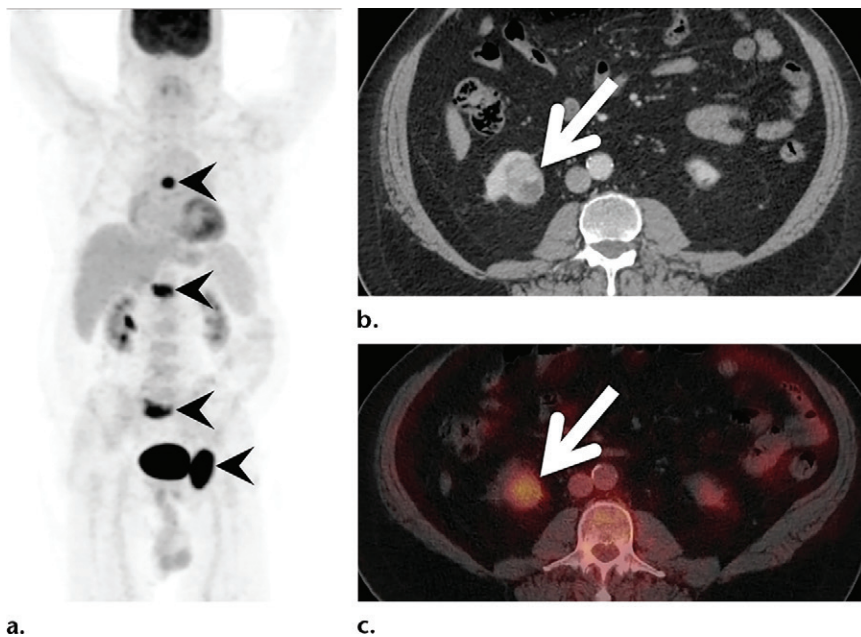
Fistulation is a documented complication in gynecologic malignancy that may occur as a consequence of advanced-stage disease, surgery, or radiation therapy. Vesicovaginal (including ureterovaginal) fistulas are among the most common types seen in association with gynecologic malignancies (65). When there is vesicovaginal fistulation to the urinary tract, contamination from urinary FDG excretion can lead to an overestimation of activity within malignant disease or, conversely, may mask disease (Fig 16). Therefore, care should be taken when assessing these patients, with close correlation with recent CT and MR imaging.

FDG PET/CT has previously been considered to be of limited utility in the detection of localized bladder cancers and perivesical lymph

nodes due to the urinary excretion of FDG (66,67). The activity of excreted FDG within the urinary bladder has been thought to make the evaluation of bladder wall lesions extremely difficult by masking disease. However, some studies have found that the detection of bladder tumors can be improved with delayed imaging after use of intravenous injection of the diuretic furosemide and oral hydration (68). We have also found that widening windows when interpreting FDG PET/CT studies often yields important information regarding activity around the urinary bladder. Figures 17 and 18 show two examples where widening the windows from the conventional  $SUV_{max}$  of 10 to 15 or higher can reveal increased pathologic FDG uptake in lesions suspicious for primary bladder tumors and disease recurrence in pelvic malignancies.



**Figure 13.** Variable FDG uptake within uterine fibroids. (a) Sagittal fused FDG PET/CT image in a 45-year-old woman demonstrates no FDG avidity in the large anterior uterine fibroid (arrowhead). (b) Sagittal fused FDG PET/CT image in a 36-year-old woman demonstrates markedly increased and heterogeneous FDG uptake (arrow) within the single lesion, which had imaging features consistent with a benign fibroid at US (not shown).



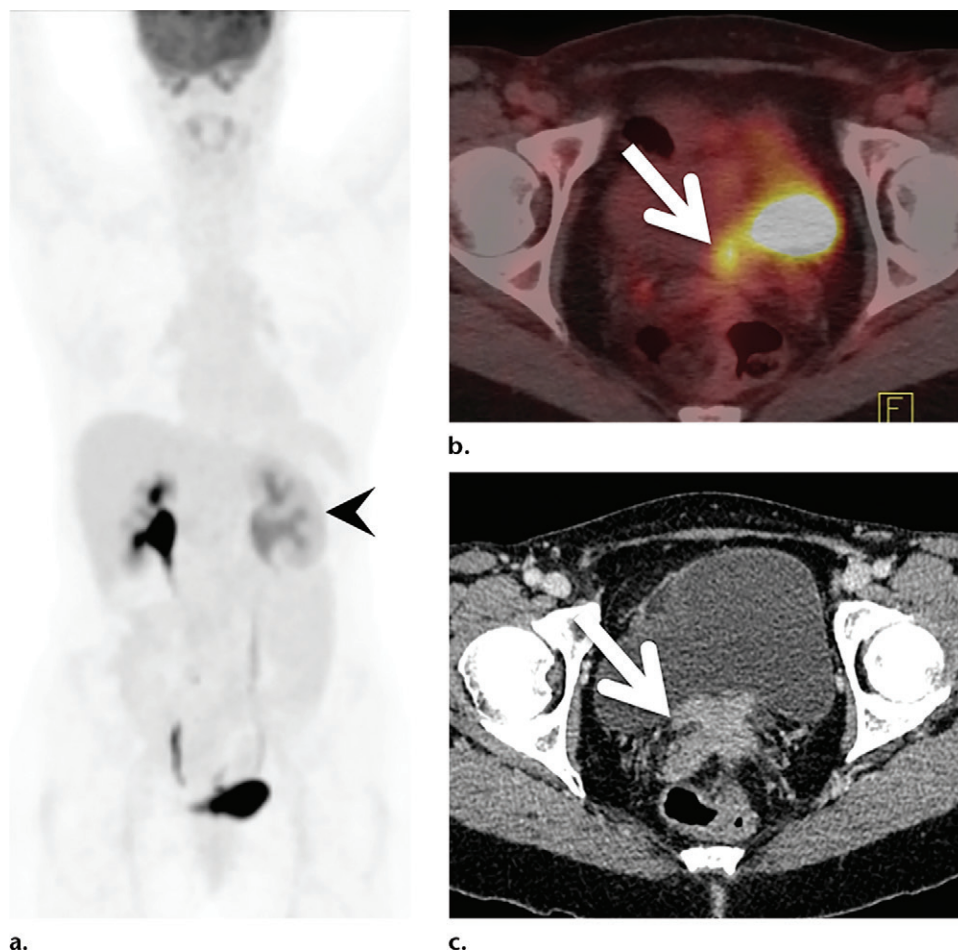
**Figure 14.** Low-level FDG uptake in an RCC in a 68-year-old man. (a) MIP PET image shows lytic bone metastases (arrowheads) with an unknown primary tumor. No obvious primary tumor is demonstrated on the image. (b) Axial contrast-enhanced CT image demonstrates a heterogeneously enhancing lesion at the lower pole of the right kidney (arrow), in keeping with an RCC. (c) Axial fused FDG PET/CT image shows subtle increased FDG uptake in the RCC (arrow).

Urinary bladder diverticula are generally asymptomatic and are found incidentally at anatomic imaging. Focal retention of FDG within a urinary bladder diverticulum can be a potential false positive by mimicking disease in the pelvis (67,69). Urinary bladder herniation represents 0.5%–3% of all lower abdominal hernias, and the bladder is involved in 1%–4% of all inguinal hernias (70). Herniation of the urinary bladder into the inguinal canal represents another potential pitfall in pelvic FDG PET/CT interpretation, as it can mimic a metastatic inguinal lymph node (71).

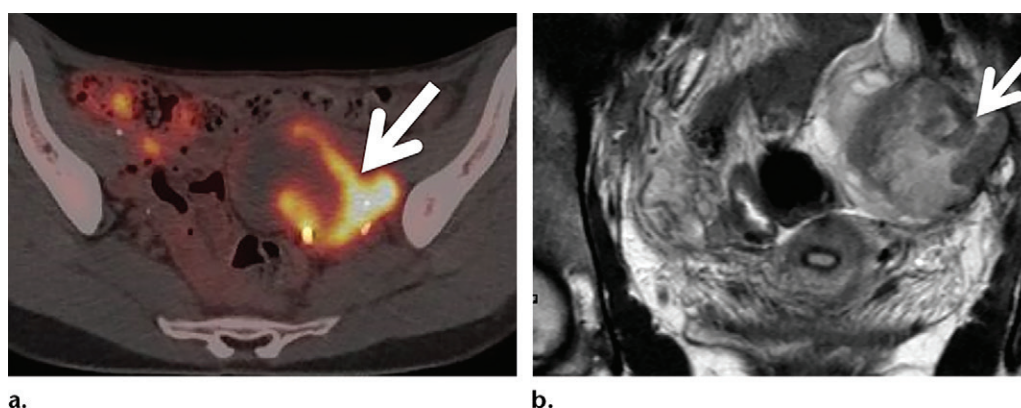
Further potential pitfalls in assessment of PET/CT studies occur when there is postsurgical anatomic distortion, particularly in patients with urinary diversions and/or bladder surgery. Patients with bladder carcinoma who have

undergone cystectomy and formation of an ileal conduit will demonstrate physiologic excretion of tracer through the ileal conduit and into a stoma, which can potentially mask adjacent peritoneal disease or local disease recurrence at the cystectomy bed. Patients with urinary diversions will also have increased risk of urinary contamination on the skin and around the stoma site, which can yield potential false-positive appearances on the MIP PET images. Conversely, vaginal disease can be dismissed as urinary contamination (Fig 19). It is therefore important to cross-correlate focal areas of activity demonstrated on MIP images with the fused axial images.

Women undergoing pelvic surgery are at risk for developing pelvic adhesions postoperatively



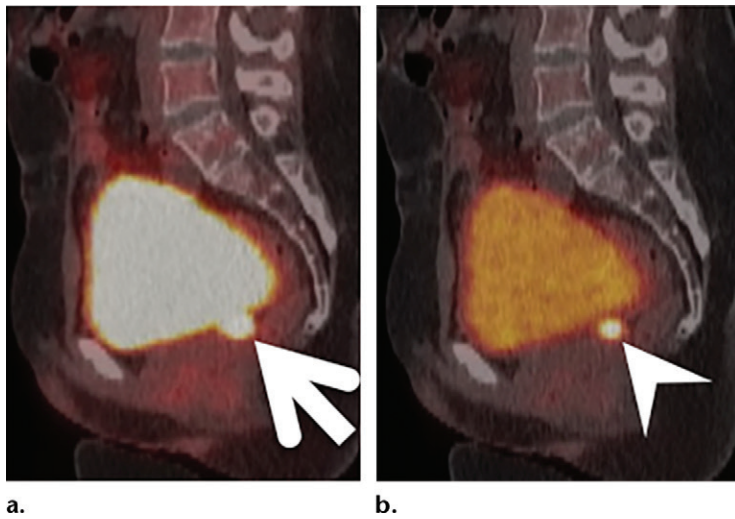
**Figure 15.** Pattern of urinary excretion suggesting recurrence at the bladder base in a 57-year-old woman with metastatic colorectal cancer. (a) MIP PET image shows a persistent left-sided nephrogram (arrowhead) due to hydronephrosis. (b, c) Axial fused FDG PET/CT (b) and contrast-enhanced CT (c) images show recurrence of the cancer (arrow), which is responsible for the left-sided hydronephrosis, at the vaginal vault adjacent to the bladder base.



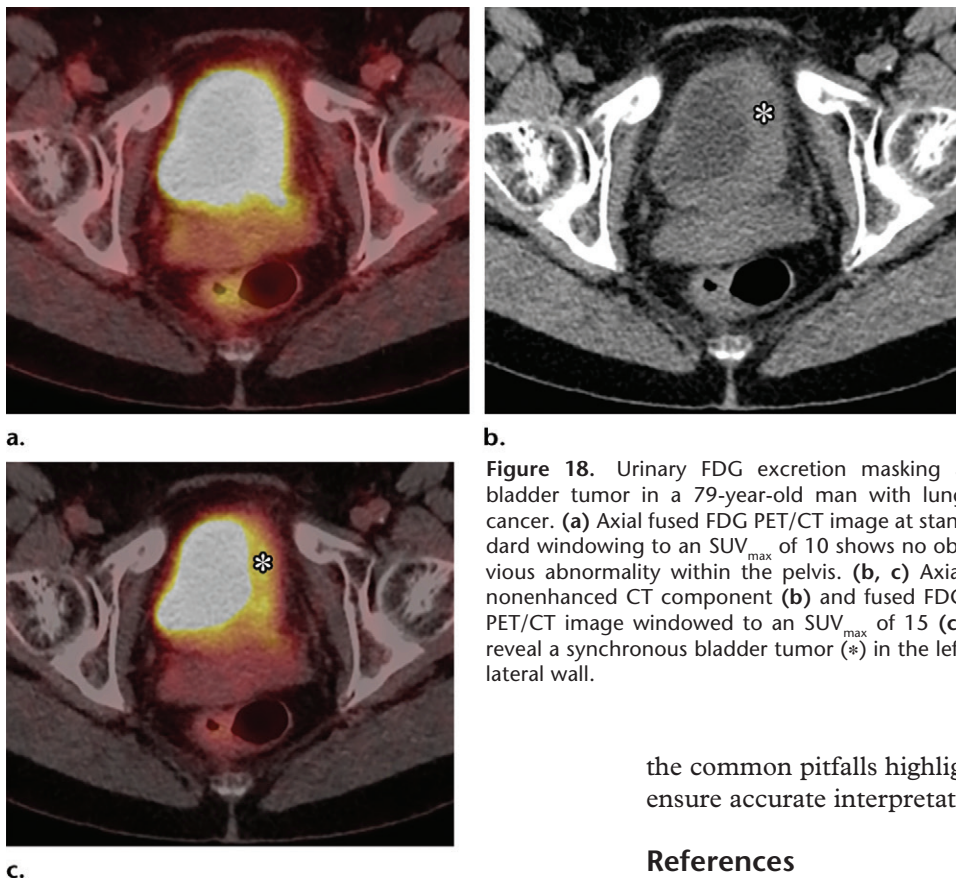
**Figure 16.** Overestimation of SUV due to disease fistulation, with the urinary tract causing urinary contamination, in a 45-year-old woman with cervical cancer relapse after trachelectomy. (a) Axial fused FDG PET/CT image shows increased FDG activity (arrow) within the left hemipelvis. (b) Coronal oblique T2-weighted MR image shows local recurrence of the cervical cancer (arrow), with invasion of the left pelvic sidewall and fistulation with the left ureter.

(72). Pelvic adhesions are often a precursor to problems such as bowel obstruction, pain, and infertility. They can also cause tethering of organs to each other or to the pelvic wall.

The process of tethering can result in anatomic distortion of the pelvic organs, which can lead to potential pitfalls in FDG PET/CT interpretation (Fig 20). It is always important to correlate



**Figure 17.** Urinary FDG excretion within the bladder masking adjacent disease in a 68-year-old woman with treated sigmoid cancer and rising tumor markers. **(a)** Sagittal fused FDG PET/CT image at standard windowing to an  $SUV_{max}$  of 10 shows focal uptake adjacent to the bladder (arrow), initially thought to represent a bladder diverticulum. **(b)** Sagittal fused FDG PET/CT image windowed to an  $SUV_{max}$  of 15 reveals focal uptake (arrowhead) at the vaginal vault, which was proven at histologic analysis to be recurrence of the sigmoid cancer.



**Figure 18.** Urinary FDG excretion masking a bladder tumor in a 79-year-old man with lung cancer. **(a)** Axial fused FDG PET/CT image at standard windowing to an  $SUV_{max}$  of 10 shows no obvious abnormality within the pelvis. **(b, c)** Axial nonenhanced CT component **(b)** and fused FDG PET/CT image windowed to an  $SUV_{max}$  of 15 **(c)** reveal a synchronous bladder tumor (\*) in the left lateral wall.

FDG PET/CT with other imaging modalities to assess patients for postsurgical anatomic distortion.

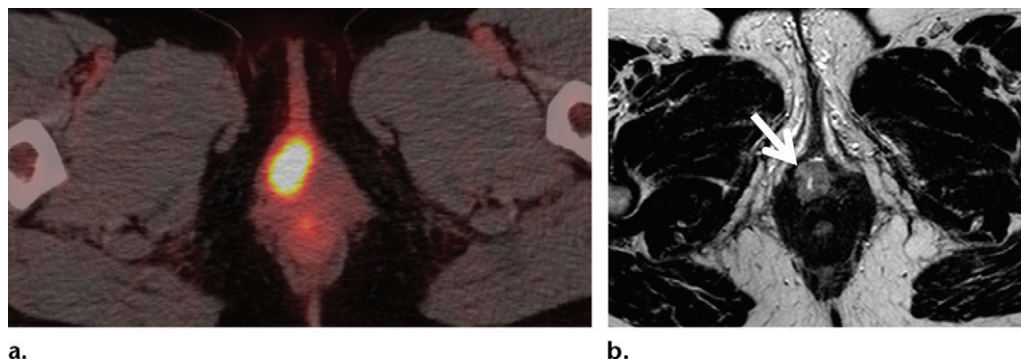
**Conclusion**

The increased use of FDG PET/CT has proved invaluable in detection, staging, and response assessment in gynecologic and genitourinary malignancies. As more clinicians are exposed to these studies, they should have knowledge of

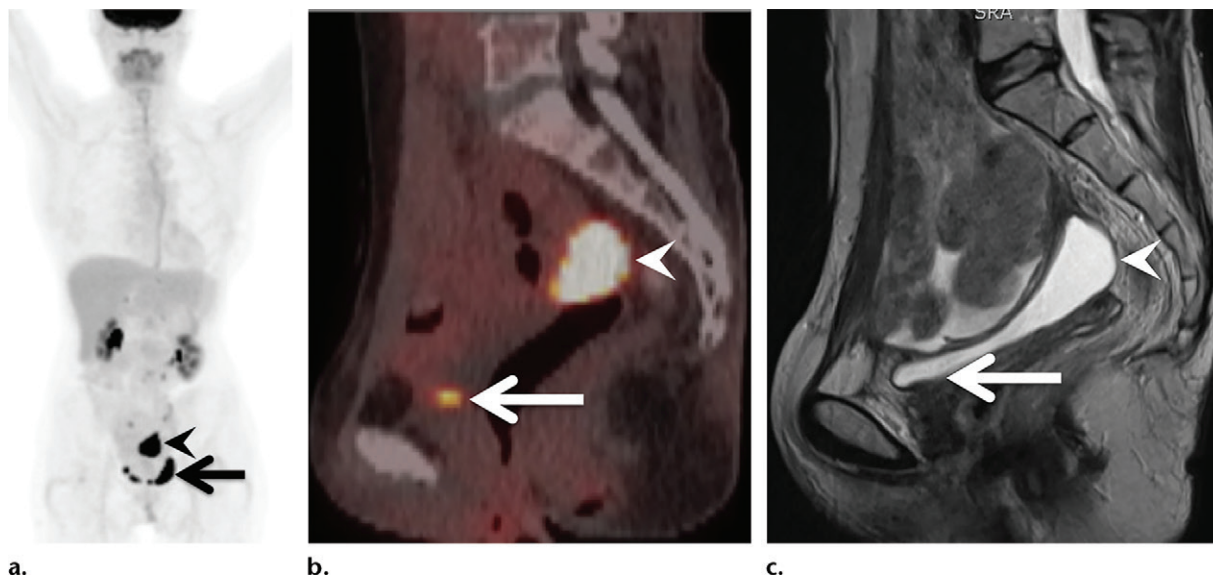
the common pitfalls highlighted in this article to ensure accurate interpretation.

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**Figure 19.** Vaginal metastasis initially mistaken for urinary activity in a patient with anal cancer. (a) Axial fused FDG PET/CT image demonstrates FDG uptake at the vaginal introitus, initially thought to be due to pooling of urine. (b) Axial T2-weighted MR image aids in confirmation of a lesion (arrow) in the vagina, proven to be a metastasis at histologic analysis.



**Figure 20.** Postsurgical anatomic distortion in a 43-year-old woman after total abdominal hysterectomy and bilateral salpingo-oophorectomy. (a, b) Coronal MIP PET (a) and sagittal fused FDG PET/CT (b) images show a focus of increased FDG activity (arrowhead) separate from the urinary bladder (arrow), in the region of the vaginal vault. This was thought likely to represent tethered bladder due to its intensity, but there was no clear connection between the two, so MR imaging was performed to exclude disease recurrence. (c) Sagittal T2-weighted MR image confirms that the activity is due to a tongue (arrowhead) of urinary bladder (arrow) tethered posteriorly due to previous surgery and adhesions.

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