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The Reproductive Tract

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Diagnostic imaging has played a major role in the evaluation of patients with the cancers of the reproductive tract. The imaging modalities have included ultrasonography, computed tomography, magnetic resonance imaging, hysterosalpingography, and scintigraphy with radiolabeled monoclonal antibodies. Positron emission tomography (PET) with [F-18]fluorodeoxyglucose also has been shown to be useful in the imaging evaluation of these patients. Clinical applications have included initial staging and posttherapy restaging of disease, detecting metastatic disease, differentiating posttherapy anatomic alterations from recurrent or residual disease, and predicting and evaluating treatment response. In this article, we review the diagnostic utility of dedicated PET and combined PET-computed tomography systems in the imaging assessment of reproductive tract malignancies (excluding prostate cancer) in both sexes with an emphasis on fluorodeoxyglucose applications.

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Cancers of the reproductive tract in both sexes account for a total of 313,600 new cases and a total of 56,300 cancer deaths in 2003. The majority of both the new cancer cases and the cancer deaths in males are from the prostate gland. In females, the majority of the new cancer cases are from the uterus, but the most deaths occur from ovarian cancer.[1] Diagnostic imaging has played a major role in the evaluation of patients with the cancers of the reproductive tract. The imaging modalities have included ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), hysterosalpingography, and scintigraphy with radiolabeled monoclonal antibodies. Positron emission tomography (PET) also has been shown to be useful in the imaging evaluation of these patients. As opposed to the anatomic imaging modalities, PET is a functional imaging modality that provides valuable diagnostic information regarding the biochemistry of the tissue of interest. [F-18]fluorodeoxyglucose (FDG) is the most common PET radiotracer. FDG tracks the glucose metabolic activity of the tissues through the physiologic actions of the facilitative cellular membrane glucose transporters (mainly GLUT-1) and the enzymatic activity of the hexokinase (mainly HK-II). Tumors often display increased glucose metabolism and thereby demonstrate high FDG accumulation. In this article, we review the diagnostic utility of dedicated PET and hybrid PET-computed tomography (PET-CT) systems in the imaging assessment of reproductive tract malignancies (excluding prostate cancer) in both sexes with an emphasis on FDG applications.

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Female Reproductive Tract

The reproductive tract is a common site for cancer in women. The estimated new gynecologic cancer cases and cancer deaths for 2003 were 83,700 cases and 26,800 cases, respectively.[1] Screening of asymptomatic women has had a major impact on the detection of cancers in an early stage, which in turn has been associated with high cure rate. Virtually all gynecologic cancers are curable if treated in the in situ or precancerous stage, and cure rates as high as 80% may be achieved if the cancer is confined to the primary site of disease.[2] In women with the cancers of the reproductive tract, PET has been shown to be useful in the initial staging and the posttherapy restaging of disease, in detecting metastatic disease, in differentiating posttherapy anatomic alterations from recurrent or residual disease, and in predicting and evaluating treatment response.

Cervical Cancer

Cervical cancer accounted for 12,200 new cancer cases and 4100 cancer deaths in 2003.[1] Screening with the Papanicolaou (Pap) smear has resulted in a sharp decline in the mortality from cervical cancer. However, cervical cancer still remains a leading cause of deaths in relatively young women in the developing countries, where screening is less prevalent.[2] Early detection is the key to cure. Most cervical cancers are squamous cell carcinomas but some are adenocarcinomas. Staging provides important information about the choice of treatment protocol and about prognosis. The staging of disease is based on the International Federation of Gynecology and Obstetrics (FIGO) classification. In general, carcinoma in situ is stage 0, carcinoma confined to the cervix is stage I, carcinoma extending beyond the cervix but not onto the pelvic wall or the lower one-third of vagina is stage II, carcinoma extending to the pelvic wall is stage III, and carcinoma extending to the adjacent organs or spreading to the distant sites is stage IV. The cure rate is nearly 100%

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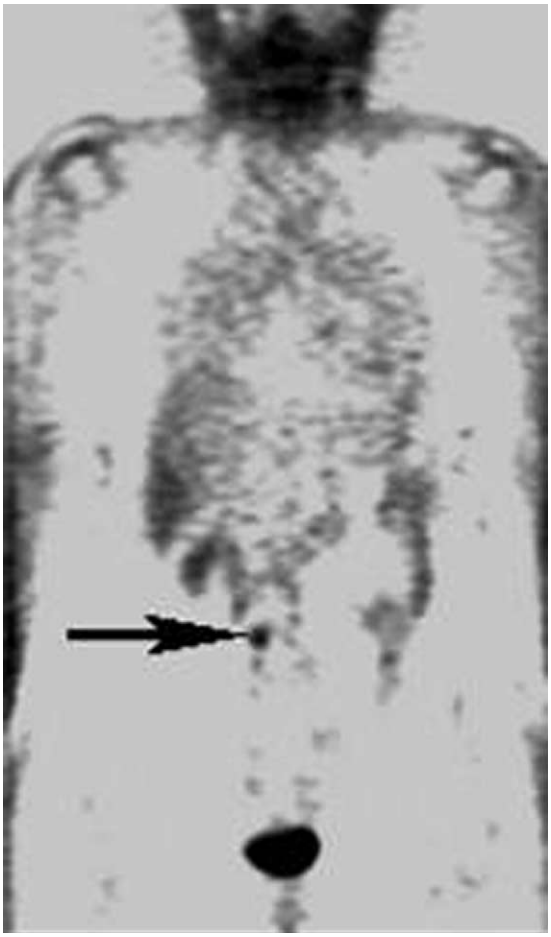

Figure 1 A 51-year-old female with history of cervical cancer treated initially with hysterectomy followed later by internal radiotherapy and bilateral oophorectomy. Three years after the last treatment, the patient presented with elevated serum carcinoembryonic antigen tumor marker. Coronal PET image demonstrates focal hypermetabolism in the retroperitoneum, which was confirmed to correspond to a metastatic retroperitoneal lymph node.

in early stage disease whereas it is less than 5% in the late stages. Choice of therapy, including surgery, radiation therapy, and chemotherapy, depends primarily on the disease stage. The disease-free interval after treatment depends on the initial stage of the tumor and the adequacy of the initial treatment. In recurrent disease, the tumors tend to appear in the central pelvis, in the retroperitoneum, and at the distant sites. Recurrent disease is associated with a poor prognosis and a high mortality within a few years.[2]

The utility of FDG PET in staging of cervical carcinoma has been studied by several investigators.[3-9] Early studies showed high accumulation of FDG in both the primary tumor and the metastatic lesions (Fig. 1).[7,8] The high FDG uptake is related to the overexpression of glucose transporter 1 (Glut-1) in the tumor and does not correlate with the initial grade of histologic differentiation and FIGO staging.[10] Lesion visualization in the pelvis is improved by obtaining postvoid FDG PET images, which substantially reduce the bladder urinary activity.[7] PET has been demonstrated to have a competitive advantage over CT in the diagnostic imaging evaluation of cervical cancer, although CT provides important information on the anatomic localization of the lesions (Fig. 2). In one study, PET was shown to be useful in detecting nodal disease involvement when CT was negative.[11] In a study of 50 patients with advanced cervical cancer confined to the pelvis and negative abdominal CT studies for nodal disease, FDG PET demonstrated a sensitivity of 86% and a specificity of 94% in detecting para-aortic lymph nodal disease with retroperitoneal surgical exploration as the diagnostic gold standard. In a similar study by the same group of investigators in 42 patients with advanced cervical cancer and negative abdominal MRI studies for nodal disease, FDG PET showed a sensitivity of 83% and specificity of 97% for assessment of para-aortic lymph node metastases.[12] MRI appears to have insufficient accuracy for nodal staging whereas high positive predictive value of PET can obviate the need for nodal sampling with the caveat that microscopic disease may be missed by either imaging modality.[13,14] In another study, PET demonstrated a sensitivity of 75%, a specificity of 92%, a positive predictive value of 75%, and a negative predictive value of 92% for detection of para-aortic nodal metastasis.[6] FDG PET has been shown to be not only more accurate than CT for lymph node staging but also a better predictor of survival in patients with cervical cancer.[15] Specifically, a multivariate analysis has demonstrated that the

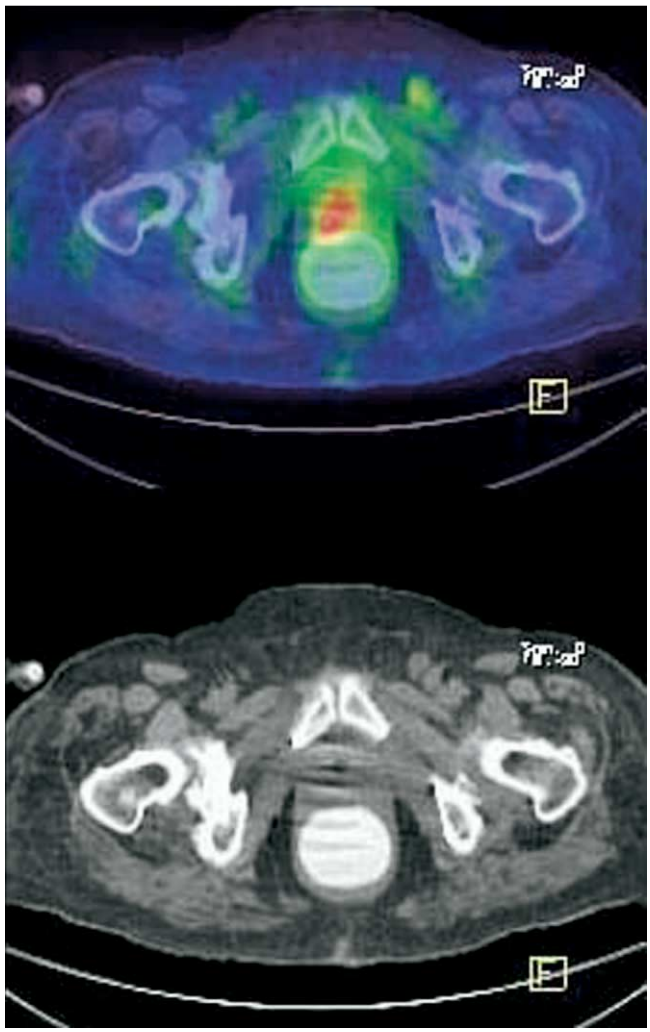

Figure 2 A 60-year-old female with newly diagnosed history of cervical cancer referred for staging. Axial CT alone (bottom) and fused PET-CT (top) images show focal hypermetabolism corresponding to a subcentimeter left inguinal lymph node. Imaging guided biopsy confirmed metastatic disease. The primary cervical tumor also showed marked hypermetabolism (not shown). (Color version of figure is available online.)

most significant determinant of progression-free survival is the presence of positive para-aortic lymph nodes on PET.[15]

Several studies have shown the utility of FDG PET in the diagnosis of recurrent and metastatic disease.[16-22] In a recent investigation, feasibility of FDG PET in the early detection of recurrent disease was evaluated retrospectively in 249 patients without evidence of cervical cancer after therapy.[23] The sensitivity and specificity of PET for detection of early recurrence were 90% and 76%, respectively. The sensitivity was higher in the spine, liver, and the mediastinal, hilar and scalene lymph node basins and relatively lower in the lung and retrovesical and para-aortic lymph node chains. Whether the ability of PET in detecting early recurrence in cervical cancer translates into potential improvements in the long-term patient outcome will need to be investigated. Havrilesky and coworkers evaluated the role of FDG PET in the detection of recurrent cervical cancer in 28 patients.[19] Diagnostic validation was determined by tissue biopsy within 3 months of the PET scan or no clinical evidence of recurrence within 6 months after the PET scan. PET demonstrated a sensitivity of 86% and a specificity of 87% for detecting recurrent cervical cancer. In another retrospective study comparing CT and PET in the detection of recurrent disease, the sensitivity and specificity were 78% and 83% for CT and 100% and 94% for PET, respectively.[20] Sun and coworkers reported on the diagnostic performance of PET in relation to specific sites of disease.[21] The sensitivity and specificity of FDG PET were 90% and 100% for detecting local recurrence, 100% and 94% for pelvic lymph node metastases, 100% and 100% for para-aortic lymph node metastases, and 100% and 100% for distal metastases, respectively. In other studies, dual-phase FDG PET scanning at 40 min and at 3 h after tracer administration followed by calculation of a lesion retention index (defined as subtraction of the 40-mi lesion standardized uptake value [SUV] from that at 3 h) was shown to be not only highly accurate but also significantly superior to MRI and CT in detecting metastases.[24,25] The performance of PET may also be improved with PET-CT in view of precise localization of hypermetabolic lesions.[26-28]

Belhocine and coworkers investigated the impact of PET on the management of cervical cancer.[29] Staging based on PET significantly influenced the choice of treatment in 18% of patients and overall PET agreement with the final diagnosis was significantly better than that of routine protocol, which included the FIGO staging and pelvis MRI. FDG PET can also provide important information for radiation treatment planning, which improves isodose tumor coverage and spares the nearby critical structures.[30] Similar findings have also been reported with the use of semiquantitative measures such as SUVs corrected for lean body mass in detecting active cervical cancer after radiation and in monitoring therapy response in metastatic disease.[31,32] PET may measure tumor volume accurately in patients with advanced disease. Although the PET-measured volume does not appear to correlate with the presence of lymph node disease but it does provide important information about prognosis including the progression-free survival and the overall survival.[33]

PET has been shown to be valuable in predicting the outcomes of patients with cervical cancer. Singh and coworkers evaluated the utility of pretreatment PET scan in predicting overall and cause-specific survival rates in 47 patients with FIGO stage IIIb cervical cancer who then underwent therapy with external beam radiation, intracavitary brachytherapy, and cisplatin.[34] Based on the PET detection of the extent of lymph node metastatic involvement, the 3-year cause-specific survival was 73% for those patients without lymph node metastases, 58% for those with only pelvic lymphadenopathy, 29% for those with pelvic and para-aortic lymph node metastases, and 0% for those with pelvic, para-aortic, and supraclavicular metastatic nodal disease. Posttreatment surveillance monitoring of cervical cancer by FDG PET has also been studied. Grigsby and coworkers did a retrospective review of 76 patients with cervical cancer who had undergone pre- and posttreatment FDG PET scans.[35] The 2-year progression-free survival rate was 86% for patients with unremarkable FDG PET scans, 40% for those with persistent abnormal FDG uptake, and 0% for those with new sites of hypermetabolic disease. The same group of investigators devised a simple visual analysis scoring scheme for characterizing the primary tumor at the time of initial diagnosis.[36] The total score was based on the sum of the subscores of tumor size, tumor shape, tumor FDG uptake heterogeneity, and the presence of abnormal lymph nodes. The higher total scores were associated with poor prognosis.

Other pathophysiological parameters have also been studied with PET in patients with cervical cancer. Tumor hypoxia is associated with poor response to radiation therapy and some forms of chemotherapy. In vivo imaging of tumor hypoxia would provide clinically relevant information in predicting tumor response to therapy. Dehdashti and coworkers performed PET with FDG and with Cu-60-diacetyl-bis(N(4)-methylthiosemicarbozone (60Cu-ATSM) before therapy in 14 patients with biopsy-proven cervical cancer.[37] Tumor uptake of 60Cu-ATSM was inversely related to progression-free survival and to overall survival. Moreover, tumor FDG uptake did not correlate with 60Cu-ATSM uptake, and no significant difference was observed in the tumor FDG uptake between those patients with hypoxic tumors and those with normoxic tumors. Therefore, 60Cu-ATSM provided incremental unique diagnostic information unavailable by FDG alone.

Uterine Cancer

Endometrial tumor is not only the most common type of uterine cancer but also the most common type of female genital cancer in the United States. Other less-common uterine malignancies include rhabdomyosarcoma, leiomyosarcoma, hemangioendothelioma, mixed mesodermal tumors, and sarcoma of the endometrium.[2] Endometrial adenocarcinoma is the predominant malignant neoplasm of the uterus and accounted for 40,100 new cancer cases and 6800 cancer deaths in women in 2003. The tumor tends to spread along the surface of the uterine cavity before penetrating the uterine corpus. Metastases may spread via the blood vessels, through the lymphatic system, or may seed the peritoneum via the fallopian tube. The cure rate for endometrial cancer is high. Hysterectomy is the primary treatment. However, radiation therapy, hormonal therapy, and chemotherapy also may be used in infrequent inoperable cases.[2]

Several single case studies and case-series studies have reported on the usefulness of PET in endometrial cancer.[38-43] Belhocine and coworkers performed posttherapy surveillance FDG PET scans in 34 patients with endometrial cancer.[42] Using PET, they detected unsuspected asymptomatic recurrences in 12% of cases but missed microscopic lung metastases in one patient. PET demonstrated a sensitivity of 96%, a specificity of 78%, a positive predictive value of 89%, a negative predictive value of 91%. PET findings also altered the treatment choice by detecting unsuspected distant metastases. Although FDG PET appears to be very useful for the imaging evaluation of endometrial carcinoma, benign uterine conditions, such as uterine myoma, may also result in relatively high FDG accumulation and be cause for false-positive finding.[44] The physiologic endometrial FDG uptake also may change cyclically, increasing during the ovulatory and menstrual phases.[45,46]

PET may also be useful in the evaluation of the less common uterine sarcomas by demonstrating relatively high FDG accumulation in the tumor with an SUV of 4.5 ± 1.3 (mean $\pm$ sd; Fig. 3). FDG

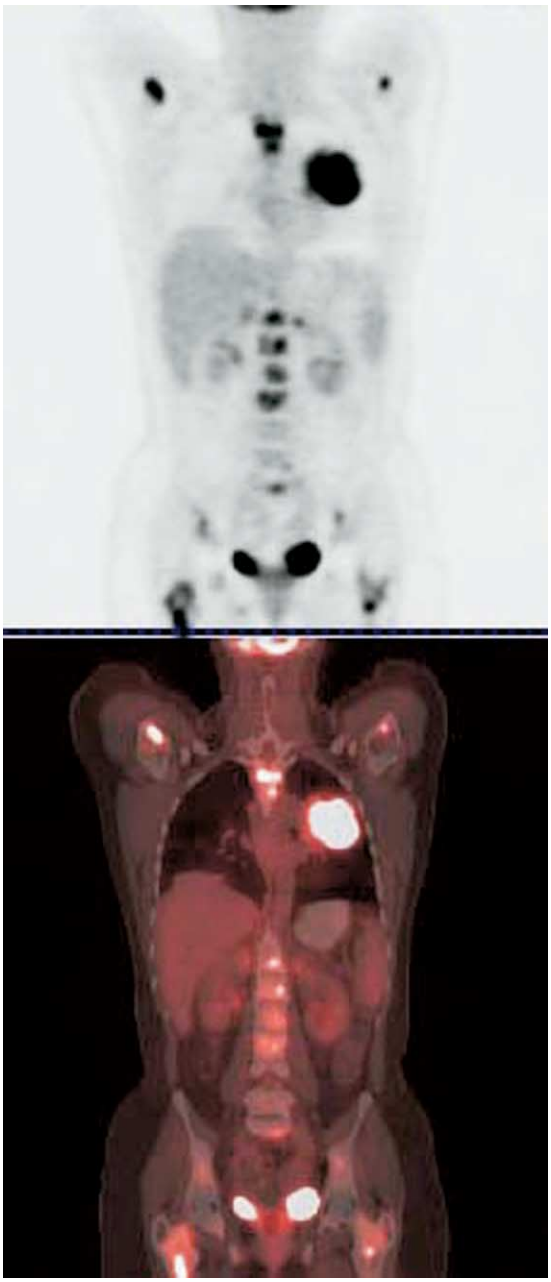

Figure 3 A 32-year-old woman with uterine sarcoma who was treated with hysterectomy and right oophorectomy. Coronal PET alone (top) and fused PET-CT (bottom) images show multifocal distant metastatic disease, including a large left lung and multiple skeletal lesions. (Color version of figure is available online.)

PET appears to have some competitive diagnostic advantage over MRI and US in the imaging assessment of uterine sarcoma.[47,48] A case report of the diagnostic utility of a combined PET-CT imaging system in uterine sarcoma has also been recently reported.[49]

Non-FDG radiotracers also have been investigated in the imaging evaluation of uterine carcinoma. Lapela and coworkers reported on the utility of C-11 methionine in 14 patients with primary uterine malignancy (8 with endometrial carcinoma, 6 with cervical carcinoma).[39] All patients demonstrated high tracer accumulation in the tumor with mean SUV of 8.4 in comparison to the mean SUV of 4.6 for the normal endometrium. Poorly differentiated carcinomas accumulated more tracer than the well-differentiated tumors. In another study, C-11 acetate also was found to be useful for the detection of recurrent endometrial cancer, with a sensitivity and specificity of 88% and 89%, respectively.[50]

Ovarian Cancer

Ovarian carcinoma is one of the deadliest and the most difficult of all gynecologic cancers to control because it often presents in the late stages of disease.[2] In 2003, ovarian carcinoma accounted for 25,400 new cancer cases and 14,300 cancer deaths in women.[1] Epithelial malignancy is the far more common type of ovarian cancer. Routine gynecologic examinations help in detecting the tumor early when it may still be curable. Clinical symptoms such as abdominal distension and discomfort develop when the disease is well advanced. Serum tumor markers such as carbohydrate-antigen 125 (CA-125) are useful in patients with epithelial ovarian cancer. Staging is according to the FIGO classification scheme. Definitive staging usually includes abdominal surgery accompanied by biopsy of suspicious areas and cytologic evaluation of the ascetic fluid, and the washings of the cul-de-sac, the lateral and paracolic gutters, and the subdiaphragmatic areas, as well as scrapings of the visceral and the parietal surfaces. Ovarian cancer spreads most commonly by intraperitoneal implantation and growth along the surfaces of the organs. Cytoreductive surgery is used with the goal to remove as much of the tumor as possible. Postoperative treatment includes chemotherapy and/or radiotherapy. Second-look surgical exploration has been used to determine the need for further therapy in patients who appear to be free of clinically evident disease. The choice of postoperative therapy is dependent on the properties of the tumor, the age and reproductive status of the patient, and the comorbid conditions. Intraperitoneal administration of chemotherapeutic agents, whole abdomen external radiotherapy, and hormonal therapy are other therapeutic alternatives.[2] Survival depends on the initial stage of disease, the lesion grade, and the amount of residual disease after therapy. The 5-year survival is about 70% in patients with stage I disease and about 4% in patients with stage IV disease.[2]

The diagnostic utility of PET in ovarian carcinoma has been investigated relatively extensively (Fig. 4).[51] Most reported studies with FDG use postvoid pelvis images to reduce bladder urine activity and do not incorporate bladder irrigation, although such maneuver may be helpful.[52] In premenopausal women, normal ovaries may demonstrate relatively high FDG uptake that appears to be related to the menstrual cycle.[46] A group of investigators compared the diagnostic performances of US, MRI, and FDG PET with histopathology as the standard of reference for the detection of malignancy in patients with asymptomatic adnexal masses.[53,54] The overall sensitivities and specificities were 58% and 76% for PET, 92% and 60% for US, 83% and 84% for MRI, and 92% and 85% for the combined imaging modalities, respectively. The combination of all three modalities was considered the method of choice for the imaging assessment of asymptomatic adnexal masses for malignancy. Similarly, the addition of FDG PET to CT increases accuracy in staging ovarian cancer.[55] An overall good diagnostic performance for FDG PET, with a sensitivity of 90% and a specificity of 90%, has been reported but these parameters excluded the detection of peritoneal carcinomatosis.[56] Although imaging detection of peritoneal carcinomatosis can be difficult on both CT and PET, attention to certain characteristic scintigraphic patterns, including the presence of either nodular or diffuse peritoneal activity, can be helpful for recognition of peritoneal pathology (Fig. 5).[57] Overall, the encouraging results of the diagnostic performance of FDG PET have rendered significant impact on the clinical staging (18%–57%) and the clinical management (17%-67%) of patients with ovarian cancer.[58]

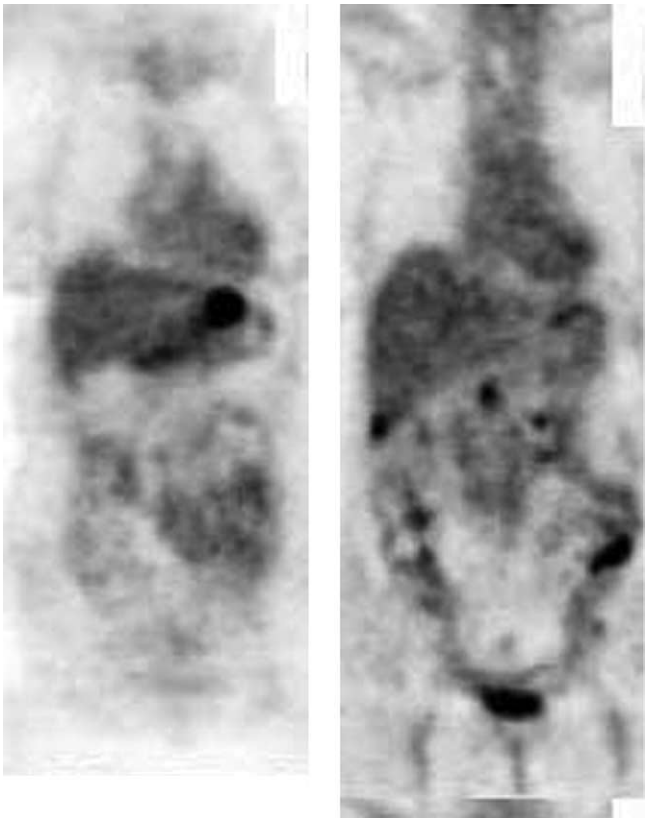

Figure 4 A 69-year-old female with history of ovarian cancer treated with Cytoxan and presents with elevated serum CA-125 level. The coronal PET images show multifocal hypermetabolic metastatic disease involving the left hepatic lobe (left panel), the inferior tip of the right hepatic lobe as well as a cluster of celiac lymph node (right panel).

Incremental value of PET to CT was investigated in 25 women who had undergone debulking surgery followed by chemotherapy.[59] Second-look laparoscopy or laparotomy was used for histological confirmation. The combination of PET and CT was associated with improved diagnostic performance in comparison to CT alone. The lesion-based sensitivity, specificity, and negative predictive value were 70%, 83%, and 59%, respectively, for CT alone and 83%, 92%, and 73%, respectively, for combined PET and CT. Although PET imaging may be useful for identifying macroscopic disease when other imaging modalities are negative or equivocal, but both PET and the other imaging modalities are limited in detecting the peritoneal micrometastases as well as the low grade malignancies and cannot currently substitute for second-look operation.[60-67] The use of SUV may however help in differentiating the physiological bowel activity from the intraperitoneal metastases.[68]

FDG PET and CT have also been compared for detection of early small tumor recurrence. Both FDG PET and CT were performed in 31 patients 1 month before second-look surgery, which served as the standard of reference for the detection of recurrent disease.[69] Both CT and PET demonstrated very high sensitivity (>99%) and specificity (91%) without a statistical difference between them, although the detection rates of tumor nodules found on CT was greater than on PET when the nodule size was 0.3 to 0.7 cm. The utility of the new hybrid PET-CT imaging system has also been assessed in the detection of recurrent ovarian and fallopian tube carcinoma in a recent retrospective study.[70] Recurrent disease was correctly identified in 62% of patients who had negative CT and positive PET-CT studies, which suggested such patients may directly proceed to salvage treatment and avoid the morbidity and expense of surgical evaluation.[70] Other studies also have documented the incremental diagnostic utility of PET-CT in comparison with PET alone.[71-73] In one study, PET-CT identified additional lesions compared with CT in 80% and changed management in 73% of the patients.[72]

Other studies have reported that FDG PET has limited utility for detecting persistent small-volume disease. Rose and coworkers evaluated the predictive value of FDG PET in determining a complete response in patients with advanced ovarian carcinoma who had a complete response based on clinical and radiologic remission and a normal serum CA-125 level following primary chemotherapy.[74] Intravenous hydration with diuresis and bowel preparation was used to reduce background activity. The findings of FDG PET were compared with second-look laparotomy. PET was falsely negative in all of the cases with microscopic peritoneal disease and true positive in only 25% of the sites of macroscopic disease with an overall sensitivity of 10% and a specificity of 42%. Therefore, it appears that although a positive PET is useful in detecting recurrent disease and in this respect may have a competitive advantage over the other imaging modalities, a negative PET cannot exclude small-volume disease and cannot replace second-look surgery for that purpose.[75-77] Despite this limitation, however, other studies have suggested that not only the diagnosis of recurrent disease based on PET precedes the diagnosis by the other conventional procedures (median 6 months) but also that a negative PET scan during the follow-up period after the primary treatment predicts longer relapse-free interval than a positive PET scan does.[78] FDG PET also has been found cost-effective in the therapeutic management of patients with ovarian cancer.[79-81]

PET has been found to be more sensitive than CT in the evaluation of patients with suspected recurrent disease based on elevated serum tumor marker CA-125 (>35 U/mL).[82,83] In a study of 28 patients with asymptomatic elevated serum tumor marker and equivocal or negative other imaging studies, FDG PET detected sites of recurrent disease with a sensitivity of 95% and specificity of 88%.[84] In a similar study of 25 patients, FDG PET was found to be accurate in detecting ovarian cancer recurrence with a sensitivity of 80% and a specificity of 100% in comparison with sensitivities and specificities of 55% and 100%, respectively, for conventional imaging (CT and MRI), and 75% and 100%, respectively, for CA-125 serum tumor marker.[85] Yen and coworkers reported similar findings for PET, CT/MRI, and CA-125 in the detection of recurrent disease with a same sensitivity of 91% for all the three diagnostic procedures and different specificities of 92%, 77%, and 46%, respectively.[86] In patients with rising CA-125 levels within the normal range, FDG PET may also be useful in detecting early small region of relapse even when the other imaging studies and the physical examination are unremarkable.[87-89] Other reports suggest that combined conventional imaging and PET results in the highest diagnostic yield for detecting the sites of recurrent disease.[90,91] There also are recent encouraging reports on the utility of combined PET-CT imaging systems for localizing and differentiating pathologic activity from physiologic activity in women with recurrent ovarian carcinoma.[92,93] Specifically, PET-CT imaging has a high predictive value of 94% in detecting recurrent disease equal to or larger than 1 cm among patients with biochemical evidence of recurrence and negative or equivocal conventional CT findings (Fig. 6). The PET-CT detection of macroscopic recurrent lesions may thus facilitate complete surgical cytoreduction.[93]

The utility of C-11 choline PET has also been investigated. The

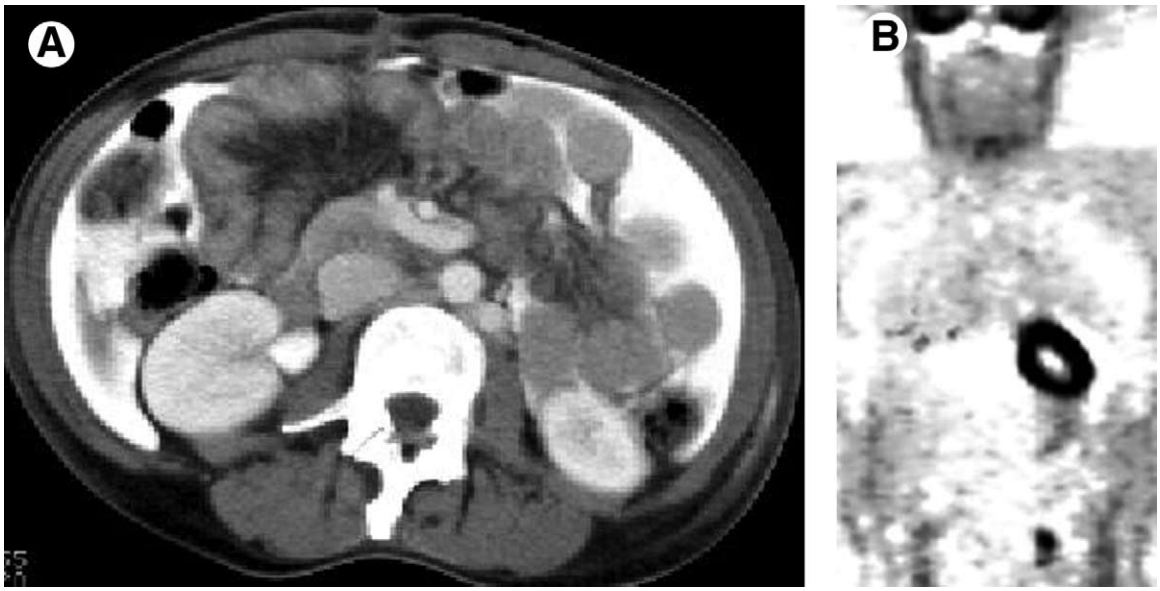

Figure 5 A 61-year-old patient with history of ovarian carcinoma s/p TAH-BSO and chemotherapy. After the end of therapy, a PET scan and an abdominal and pelvis CT were performed to evaluate response to therapy. Serum CA-125 was normal at 30 U/mL. (A) Abdomen and pelvis CT with intraperitoneal and intravenous contrasts showed mesenteric strandiness without masses or definite evidence for peritoneal carcinomatosis. (B) PET scan showed mild diffuse abdominal activity with subtle areas of hypermetabolic nodularity, largest located in the left upper quadrant, considered highly suspicious for peritoneal carcinomatosis, which was confirmed by subsequent second-look surgery.

biological basis for radiolabeled choline uptake in tumors is the malignancy-induced up-regulation of choline kinase, which leads to the incorporation and trapping of choline in the form of phosphatidylcholine (lecithin) in the tumor cell membrane in proportion to the rate of tumor duplication. In a recent study, Torizuka and coworkers compared C-11 choline and FDG PET in 18 patients with untreated primary and 3 patients with suspected recurrent ovarian cancer. C-11 choline detected the primary tumor in 16 of 18 patients whereas FDG was positive in 14 patients.[94] For the diagnosis of recurrent disease both C-11 choline and FDG were true positive in one case whereas they were both false-negative in the remaining two cases as the result of cystic and microscopic peritoneal disease. Mean tumor SUV was significantly higher for FDG than for C-11 choline (9.1 ± 3.8 versus 4.6 ± 1.6). The lack of urinary activity in C-11 choline images was beneficial, although the background bowel activity hampered the assessment for abdominal nodal disease.

C-11 methionine has also been investigated as a potential PET radiotracer in evaluating ovarian carcinoma.[95] Benign or borderline malignant tumors did not accumulate the tracer while all carcinomas had high tracer localization with a mean SUV of 7. However, both the physiological accumulations and the other methodological factors limited the value of C-11 methionine PET in staging ovarian cancer.[95]

Fallopian Tube, Vaginal, and Vulvar Cancers

Primary carcinoma of the fallopian tube is rare and can occur at all ages. It accounts for less than 2% of all gynecologic cancers. The most frequent histology is papillary adenocarcinoma.[2] Treatment consists of cytoreductive surgery, including abdominal hysterectomy and bilateral salpingo-oophorectomy. Radiotherapy also is frequently used whereas chemotherapy may be used when both radiation and surgery fail. Few case studies have reported the diagnostic utility of PET in tubal malignancy.[96-98] There are no reports on the diagnostic utility of FDG PET in vaginal cancer. However, a recent case report of vaginal atresia with hematometrocolpos showed hypometabolic masses on FDG PET that aided the patient management by excluding malignancy.[99]

Vulvar cancer accounted for 4000 new cancer cases and 800 cancer deaths in 2003.[1] The primary histology is squamous cell carcinoma.[2] It is more common in older women. Lesions usually occur on the labia majora, clitoris, and the periurethral areas. In the advanced stages, the tumor may manifest as a fungating mass extending into the urethra, vagina, and the rectum. The cancer spreads primarily by lymphatic dissemination. Radical vulvectomy with or without groin lymph node dissection is the primary treatment. There is limited data on the diagnostic utility of FDG PET in vulvar cancer.[100,101] A recent study from Washington University evaluated prospectively the usefulness of PET in detecting groin node metastases in 15 patients with vulvar cancer before surgical exploration.[102] On a groin-by-groin basis, PET had a sensitivity of 67% a specificity of 95%, a positive predictive value of 86%, and a negative predictive value of 86%. On a patient-by-patient basis, PET had a sensitivity of 80%, a specificity of 90%, a positive predictive value of 80%, and a negative predictive value of 90% in demonstrating the metastases. PET was more accurate in detecting extranodal metastases than in detecting groin node disease. PET was therefore considered relatively insensitive in predicting groin lymph node metastases while the high specificity of PET suggested a potential role in radiation treatment planning.

Male Reproductive Tract

The reproductive tract is a common site for cancer in men. The estimated new male genital cancer cases and cancer deaths for 2003 were 229,000 cases and 29,500 cases, respectively.[1] The great majority of these cases are attributable to the prostate gland, which will not be discussed here. In this section, our primary focus of discus-

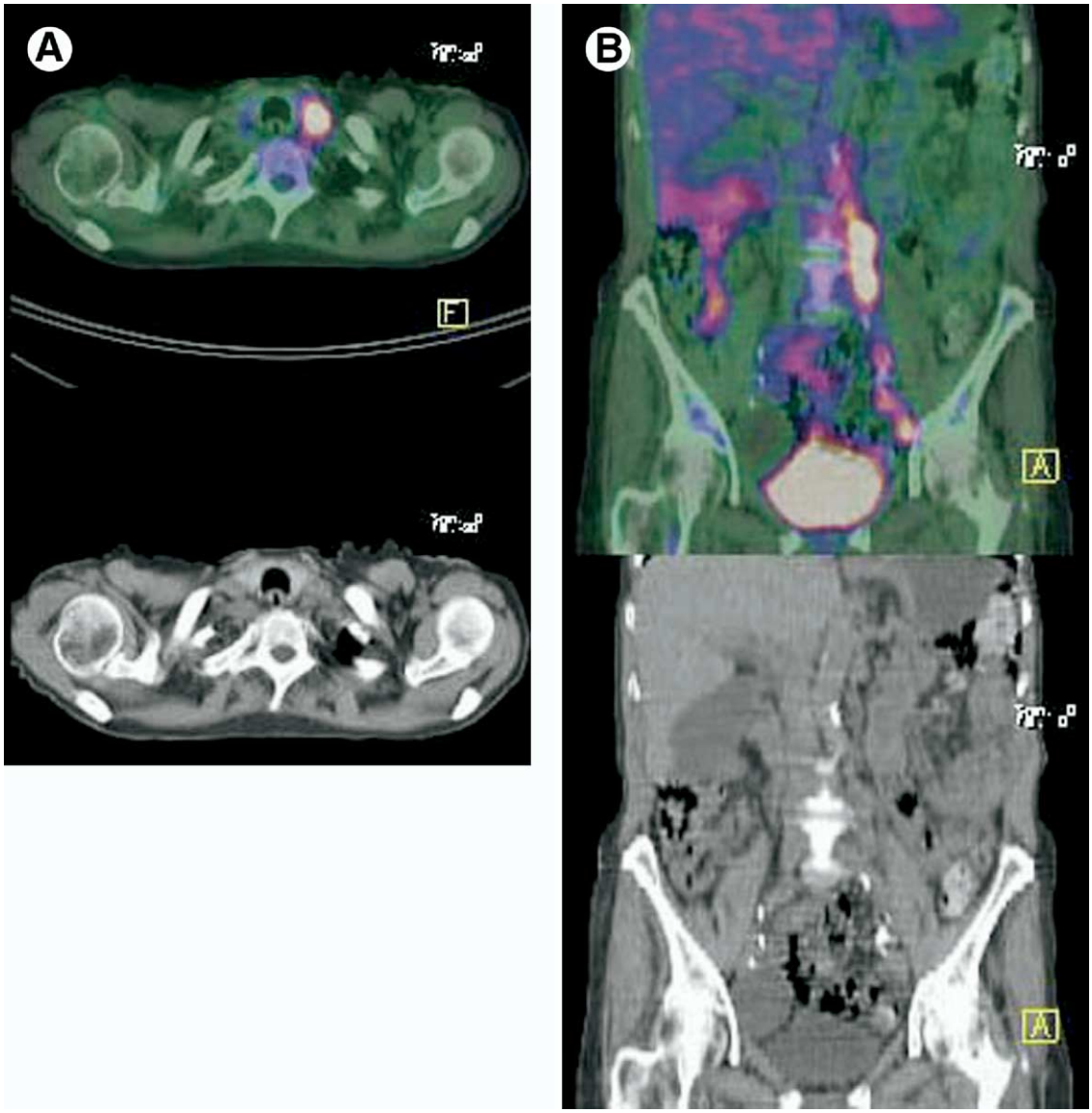

Figure 6 A 74-year-old female with history of metastatic ovarian cancer treated with TAH/BSO, omentectomy, and chemotherapy. PET-CT was performed in view of rising serum CA-125 tumor marker level. PET-CT demonstrated hypermetabolic metastatic lymphadenopathy in the (A) left supraclavicular (images shown in axial plane), as well as (B) left paraaortic and left iliac nodal basins (images shown in coronal plane). In both sets of images, the fused PET-CT images are shown on the top and the CT alone images are shown at the bottom. (Color version of figure is available online.)

sion will be on the diagnostic utility of PET in testicular cancer. PET has been shown to be particularly useful in detecting metastatic disease, in restaging the disease, in differentiating posttherapy scar from recurrent or residual disease, and in predicting and evaluating treatment response.

Testicular Cancer

Testicular cancer represents about 1% of all cancers in males, but it is one of the most frequent cancers in young adult men and is more common in whites than in blacks.[103] In 2003, testicular cancer accounted for 7600 new cancer cases and 400 cancer deaths in men.[1] Testicular cancer is highly curable. With adoption of the current sophisticated treatment strategies, overall cure rates of approximately 95% may be achieved with acceptable morbidity.[104] Typical disease presentation is an asymptomatic testicular mass. In advanced stages, symptoms and signs may include an abdominal mass, ureteral obstruction from para-aortic lymphadenopathy, or pulmonary symptoms from metastases. Diagnostic procedures include physical examination, serum tumor marker (alpha-fetoprotein, human chorionic gonadotropin) assays, and imaging. Scrotal US can assess and delineate the intrascrotal mass. Chest and abdominal CT studies are used for staging.[103] Treatment and prognosis depends on the anatomic staging and the histologic typing of the cancer. Surgery with bilateral retroperitoneal lymph node dissection is usually performed in seminoma. Chemotherapy-induced debulking usually precedes surgery in the presence of bulky nodal involvement. Nodal irradiation to the level of the diaphragm may be employed in seminomas. In nonseminomas, cytoreductive surgery and chemotherapy has replaced radiation therapy in the low stage disease, although irradiation of the nonresectable localized metastatic

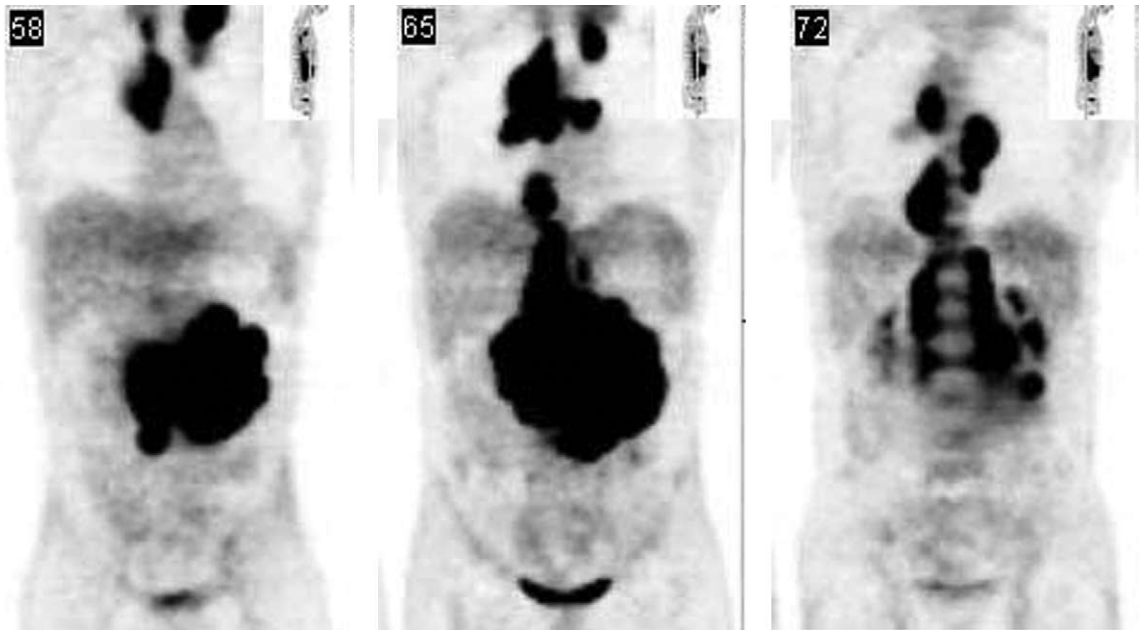

Figure 7 A 25-year-old male with history of testicular cancer initially treated with left orchiectomy presented with elevated is serum β-human chorionic gonadotropin and alpha-fetoprotein. PET scan demonstrated extensive contiguous intensely hypermetabolic metastatic lymphadenopathy involving the nodal basins of the neck, thorax, and abdomen.

disease may be helpful. Salvage chemotherapy may also be used in patients with relapse or in patients who are refractory to the initial chemotherapy. Overall, many cases of testicular cancer are potentially curable. Complete remission can be obtained in up to 70% of patients with metastatic disease by chemotherapy alone. In another 10% to 15% of patients may become disease-free by surgical excision of the residual tumor.[103] After first-line chemotherapy, the 5-year progression-free survival rates are 78%, 67%, and 66%, for the resultant posttreatment histologies of necrosis, differentiated teratoma, and undifferentiated tumor, respectively.[105]

The normal testis demonstrates variable FDG accumulation. The range of SUV varies from a minimum of 0.9 to a maximum of 5.7 with a mean of 2.2.[106] Although this latter study showed no significant change in normal testicular FDG uptake with age, other stud-

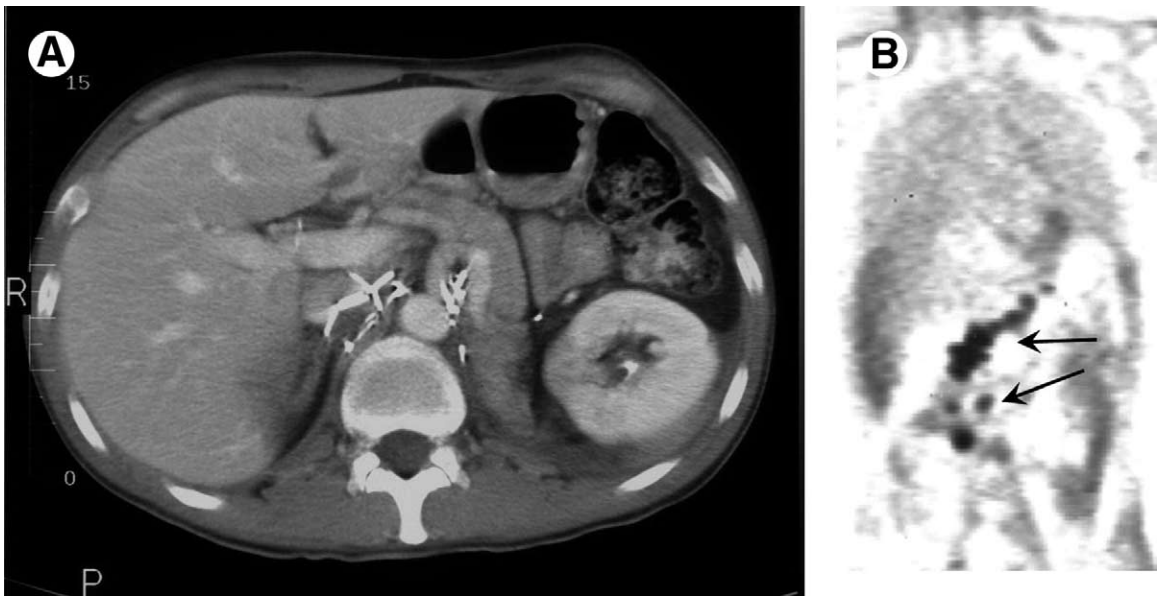

Figure 8 A 36-year-old male with history of nonseminomatous testicular cancer initially treated with orchiectomy followed by retroperitoneal lymph nodal dissection and chemotherapy. He presented with elevated serum βhcG. (A) Axial CT showed postsurgical changes in relation to retroperitoneal lymph nodal dissection. (B) PET revealed contiguous chain of hypermetabolic lymphadenopathy in the upper- and mid-abdomen compatible with recurrent metastatic disease. The patient underwent additional chemotherapy based on the PET demonstration of disease.

ies have demonstrated a moderate correlation between decreasing testicular FDG uptake and increasing age.[107] The decline in the testicular FDG localization is believed to reflect the age-related decline in the androgen production and its effect on the normal testicular function. The diagnostic utility of PET in testicular cancer has been evaluated by many investigators.[108-111] Hain and coworkers investigated the role of FDG PET in the initial staging of testicular cancer in 31 patients (13 seminoma, 18 nonseminoma).[112] PET had a positive predictive value of 100% and a negative predictive value of 76% or 91% depending on the classification of a number of cases as either false-negative or true-negative PET when the CT studies were regarded as suspicious, although the clinical follow-up was inconclusive. In a similar study of 50 patients, the sensitivities and specificities were 87% and 94% for PET, 73% and 94% for CT, and 67% and 100% for serum tumor markers.[113] The FDG uptake in the tumors was very heterogeneous with an SUV ranging from as low as 1.8 to as high as 17.3. However, in general it appears that seminomas accumulate more FDG than nonseminomas.[114]

Sanchez and colleagues compared CT and PET in the follow-up of nonseminomatous germ cell tumors in the retroperitoneum of 15 patients.[115] PET not only detected the retroperitoneal relapse earlier than CT but also demonstrated mature teratomas in residual retroperitoneal masses more accurately than CT. Lassen and coworkers also reported similar results that demonstrated the diagnostic advantage of FDG PET over the conventional staging procedures for detection of retroperitoneal relapse within 1 year of orchiectomy in patients with stage I nonseminomatous germ cell tumors.[116] Another study investigated the role of PET in the initial staging of clinical stage I and II nonseminomatous germ cell tumors and in the restaging of both nonseminomatous and seminomatous germ cell tumors after chemotherapy.[117] FDG PET demonstrated no benefit over CT in primary staging but showed an advantage over CT in restaging with a high negative predictive value in predicting treatment-related fibrosis. However, other studies have shown the potential for false-positive PET findings early after chemotherapy due to reactive inflammatory processes.[118] Despite this potential pitfall, FDG PET appears to be more advantageous than CT and serum tumor markers in assessing early response to chemotherapy and in identifying those patients who may benefit from high-dose salvage chemotherapy (Fig 7).[119] Similarly, in patients with bulky seminoma who have been treated with chemotherapy, FDG PET performs well in detecting residual viable tumor, especially those greater than 3 cm, with a sensitivity of 89%, a specificity of 100%, a positive predictive value of 100% and a negative predictive value of 97%.[120] In a subset of patients with raised serum tumor markers alone, a positive predictive value of 92% and a negative predictive value of 50% have been reported (Fig 8).[121] However, few earlier studies have found no diagnostic benefit for PET in this clinical setting which may have been influenced at least in part by the heterogeneity of the patient population in these studies.[122,123] Despite the potential for false-positive findings (eg, sarcoidosis), PET appears to be useful for the detection of malignant nodes that do not meet the size criteria at CT or when the lack of retroperitoneal fat makes it difficult to identify retroperitoneal nodes with CT.[124,125] FDG PET is also more advantageous than CT in evaluating treatment response, although early imaging posttherapy may result in high false-positive rate because of inflammation.[114,126-133] It has been suggested that FDG PET must be performed at least 2 weeks after completion of chemotherapy to reduce the false-positive findings.[114] In a difficult case when there is an urgent therapeutic ramification, FDG PET may also be useful in directing CT-guided needle biopsy of the residual intrathoracic lesions for distinguishing viable tumor or teratoma from residual fibrosis and necrosis.[134]

PET radiotracers other than FDG have also been investigated in testicular carcinoma. Kole and coworkers reported on the utility of C-11 tyrosine in the prechemotherapy imaging evaluation of 10 patients with retroperitoneal nonseminoma testicular germ cell tumors metastases.[135] Most of the tumors showed low or no tracer uptake with a SUV ranging from 0.3 to 2.9. The authors concluded that C-11 tyrosine in not a suitable PET radiotracer in testicular cancer given the low tracer localization in the tumor. A single clinical case of the diagnostic utility of FDG PET in Sertoli cell tumor has also been recently reported.[136]

Penile Cancer

Penile cancer is an uncommon male genital cancer. In 2003, penile and other male genital cancers, excluding the cancers of the prostate gland and the testis, accounted for 1400 new cancer cases and 200 cancer deaths in males. Squamous cell carcinoma is the most common histological type of invasive penile cancer. Although organ-sparing surgery is an option, it may not be feasible. The treatment of choice is partial or total penectomy for invasive disease. Because inguinal lymph nodes may be enlarged as the result of inflammation, assessment for the possible nodal metastatic involvement is difficult by conventional imaging techniques. Ravizzini and coworkers present a single case report of the diagnostic utility of FDG PET in the detection of metastatic penile squamous cell carcinoma in a patient who had previously undergone partial penectomy.[137] High FDG accumulation was noted in multiple locations that corresponded to the sites of metastatic disease.

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