Published in final edited form as:

PET Clin. 2015 July ; 10(3): 361–374. doi:10.1016/j.cpet.2015.03.002.

PET/CT in renal, bladder and testicular cancer

Kirsten Bouchelouche,

Department of Nuclear Medicine & PET Centre, Aarhus University Hospital, Denmark

Chief Physician, M.D., DMSc, and

Department of Nuclear Medicine & PET Centre, Aarhus University Hospital, Denmark

Peter L. Choyke, M.D., F.A.C.R. [Chief]

Molecular Imaging Program, Center for Cancer Research, National Cancer Institute (NCI), Bethesda, MD, USA

Abstract

Imaging plays an important role in the clinical management of cancer patients. Hybrid imaging with PET/CT is having a broad impact in oncology, and in recent years PET/CT is beginning to have an impact in uro-oncology as well. In both bladder and renal cancer there is a need to study the efficacy of other tracers than F-18 fluorodeoxyglucose (FDG), particularly tracers with only limited renal excretion. Thus, new tracers are being introduced in these malignancies. This review focuses on the clinical role of FDG and other PET agents in renal, bladder and testicular cancer.

Keywords

PET/CT; renal cancer; bladder cancer; testicular cancer

INTRODUCTION

Positron emission tomography (PET)/computed tomography (CT) has become one of the most important imaging modalities for patients with cancer and PET/CT with F-18 fluorodeoxyglucose (FDG) has become ubiquitous as a tool for staging and follow-up of many cancer patients. In urology, FDG is the most common PET radiotracer used in renal, bladder and testicular cancer but its role is hampered by physiological excretion of FDG through the urinary system masking FDG uptake in primary renal and bladder carcinomas. Thus, new PET agents have been introduced and tested in both malignancies. In this review, we focus on the role of PET/CT in staging, detection of recurrent and metastatic disease, response assessment and prognosis in renal, bladder and testicular cancer.

Corresponding author: Kirsten Bouchelouche, Chief Physician, MD, DMSc, Department of Nuclear Medicine & PET Centre, Aarhus University Hospital, Skejby, Brendstrupgaardsvej 100, DK-8200 Aarhus, Denmark, kirsbouc@rm.dk, Phone: +45 20 29 19 03.

The Authors have nothing to disclose.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

USE OF PET IN RENAL CELL CARCINOMA

Overview of RCC

Renal cell carcinoma (RCC) represents approximately 3% of human cancers. With the advent of widespread cross sectional imaging, the detection of small renal cancers has increased, and the majority of these are well differentiated and are cured by surgical resection¹. Nonetheless, renal cancer remains a significant cause of cancer death due to the variable aggressiveness of some tumors. Renal cancers are categorized as clear cell (60–80%), papillary (10%), chromophobe-oncocyctic (5%) and other tumors such as sarcomatoid, squamous cell and leiomyosarcoma. Accompanying the increase in small RCCs, there has been an increase in the diagnosis of small benign tumors such as oncocytomas and angiomyolipomas that can mimic RCC¹. Since RCCs can be highly lethal it is important to identify them, characterize and stage them and then monitor them during treatment. A decade ago PET played almost no role in RCC. In recent years a fuller understanding of the role of PET in the management of RCC has been realized.

Renal cancers can be stratified as localized, locally advanced and metastatic. Here, we consider the role of FDG PET in each of these settings. In the final section we will consider other PET agents that have been proposed to evaluate RCC.

Primary RCC

Traditionally, FDG PET has played a minor role in the diagnosis of RCC. Contrast enhanced CT and MRI have proven very effective at detecting solid renal masses suspicious for RCC. However, both modalities are non-specific and cannot distinguish benign and malignant lesions. For many small lesions that are indeterminant, a biopsy is recommended to rule out benign disease prior to intervention, although this recommendation is often not followed¹. It would be tempting to use FDG PET in this setting however, PET/CT has a sensitivity of only approximately 60% for RCC although it is 90% specific for malignancy². Thus, a negative FDG PET is not clinically helpful. This is in part due to the lower metabolic status of many RCCs but also because FDG PET is primarily excreted thru the kidneys making RCCs isointense with renal parenchyma³. If they were located elsewhere in the body, where the background was lower, they might be considered positive, but in the kidney they are often difficult to detect. The uptake of FDG in renal tumors is size dependent³. FDG is exquisitely sensitive for type II papillary renal cancers (Fig 1&2) especially when found in conjunction with the Hereditary Leiomyoma Renal Cell Carcinoma (HLRCC) syndrome³. Sarcomatoid tumors are also reliably PET avid³. However, in general, FDG has modest uptake and can also be taken up in benign renal tumors³. Thus, FDG PET has played a minor role in primary RCC evaluation. Moreover, FDG has proven insensitive in cystic renal masses due to the low burden of solid tissue in such lesions⁴. Interestingly C-11 acetate has been reported to be useful in this setting, having a 100% positive predictive value (PPV), although a sensitivity of only 50%. C-11 acetate is excreted via the pancreas and therefore avoids the confusion of renal parenchymal enhancement found with FDG. In any case, C-11 acetate is limited to masses >1.5cm in diameter⁴ and has the unavoidable disadvantage of a short half-life ($t_{1/2}$ =20 minutes), limiting the study to sites with cyclotrons and radiochemistry. Occasionally a FDG PET scan performed for another malignancy will

reveal a lesion within the kidney. It is uncertain whether this lesion represents a metastasis or another primary tumor⁵. Unfortunately, uptake in the lesion is not specific in this regard, and a biopsy is usually performed to clarify this dilemma. Thus, FDG PET plays a minor role in the diagnosis of primary RCC. Diagnosis is generally made on CT and/or MRI and if questions arise, a biopsy is usually recommended. FDG plays an important role in particular subtypes of renal cancer such as type II papillary and sarcomatoid.

Staging of RCC

FDG PET also plays a relatively minor role in the initial staging of RCC. The majority of cancers discovered on CT or MRI is small and localized with a low risk of metastases, therefore additional studies are unwarranted. Higher risk, larger tumors are more FDG PET avid. For local staging FDG PET has been found useful in determining whether thrombus in the renal vein and inferior vena cava is malignant or “bland”⁶, a distinction that is considered important by some surgeons⁷. In general CT, MRI and bone scan in symptomatic patients are considered sufficient staging studies to clear a patient for surgery. Occasionally, when an isolated potential metastasis is detected, FDG PET can be used to confirm metabolic activity thereby confirming the diagnosis of metastatic disease (Fig 3). However, in general FDG PET is not widely used for RCC staging. Surveillance imaging after surgery is also discouraged as there is no level 1 evidence that early intervention improves survival⁸. American Urologic Association guidelines suggest that more advanced initial tumors may warrant increased surveillance and FDG PET could play a role here, although this has not been studied⁸.

Metastatic RCC

FDG PET in RCC is most often used in patients with metastatic disease who are on novel targeted therapies. Renal cancer is not responsive to conventional chemotherapy and thus, this therapy is rarely, if ever, employed. A variety of targeted therapies, which include tyrosine kinase inhibitors such as sorafenib and sunitinib that have antiangiogenic mechanisms and MTOR inhibitors such as everolimus, have demonstrated efficacy and small but important improvements in overall survival. These targeted agents do not generally behave in the same manner as conventional cytotoxic agents. Although tumor size measurements, embodied in the RECIST criteria, have proven adequate for monitoring chemotherapy, for other cancers with modern targeted therapies, there is often little change in the size of the lesions and some metastases even increase even while the drug is prolonging survival⁹. Thus, FDG PET activity could play a role in monitoring the effectiveness of targeted therapies with tyrosine kinase inhibitors.

Ferda et al demonstrated that initial uptake of lesions correlated with prognosis, with patients whose renal tumors exhibit SUVmax >10 having significantly worse survival than those with SUV max <10¹⁰. Decreases in FDG uptake also correlated with outcome⁹⁻¹¹ and were independent of where the lesion was located (e.g. bone, lung, node etc.). More dramatic decreases in SUV max correlated with better progression free survival (PFS) and overall survival (OS)². The advantage of FDG PET over conventional modalities is most apparent in bone and musculoskeletal metastases, which are difficult to assess on CT and MRI because the bone damage continues to be seen even when the lesion is responding.

There is a trend toward using a total metabolic volume or total lesion glycolysis (TLG) as an overall measure of disease burden^{12,13} rather than individual SUVmax scores. This is calculated by multiplying the SUVmax and the number of lesions. Thus, FDG PET is increasingly used to monitor the efficacy of treatment of patients with metastatic disease who are receiving tyrosine kinase inhibitors and other targeted therapies.

Other agents for RCC

A number of other PET agents have been used for renal cancer. Sodium fluoride PET has not been commonly reported in RCC but recent reports suggest it will be more sensitive than conventional bone scans, much as it in other malignancies. This is true even for predominantly lytic renal cancer bone metastases¹⁴.

Over 95% of clear cell renal cancers express carbonic anhydrase IX on their cell membrane. An antibody, cG250, was developed as a potential therapeutic agent, but results of early trials showed modest or no benefit¹⁵. However, it was thought that labeling the antibody with I-124 could produce an effective imaging agent for clear cell carcinoma¹⁵. The REDECT trial of I-124 Girentuximab (cG250) showed an 86% sensitivity and 86% specificity for clear cell carcinoma¹⁵. The agent was not as useful for lesions <2cm in diameter or in non-clear-cell renal cancers. The advantages of this agent are that it is specific for clear cell carcinoma and has a sensitivity comparable to biopsy¹⁵ but the disadvantage is that less common, but nevertheless aggressive cancers may be negative. It may play a role in patients too ill to undergo biopsy or in those patients for whom adequate conventional studies cannot be obtained. However, the study requires 3–7 days because of the long clearance time of the antibody and this may make it impractical⁶. Moreover, it is unclear whether the niche applications of this agent would make it economically sustainable. Suggestions have been made to exchange the I-124 with Zr-89, which may result in better imaging, but this does not clarify the actual clinical role of this agent^{6,16}.

F-18 MISO has also been suggested as an imaging agent for RCC based on the level of hypoxia in many renal tumors, however, this agent has not been extensively studied and early reports show only modest uptake in RCCs and it was not predictive of response to therapy¹⁷. Interestingly, initial studies show a decrease in hypoxia after initiating TKI therapy likely due to “vascular normalization”, followed by an increase in hypoxia as antiangiogenic effects begin to predominate¹⁷.

As mentioned earlier C-11 acetate has been proposed as an alternative agent for imaging RCC as it is not excreted through the kidney. However, the technical limitations of this agent are likely to inhibit its widespread use.

Summary

FDG PET/CT is not widely used in most primary RCCs although particular RCC subtypes are quite avid for the agent. In high risk, larger patients FDG PET may be useful in pre-operative staging and is particularly useful when conventional imaging is negative or there is a potential tumor thrombus. In metastatic RCC, FDG PET/CT is increasingly used to monitor targeted molecular therapies such as tyrosine kinase inhibitors. Sodium fluoride PET appears to be a useful method in detecting subtle bone metastases but it has not yet

replaced conventional bone scan. Several other PET agents targeting carbonic anhydrase IX, hypoxia and fatty acid synthesis have been proposed and tested but none are in widespread use.

USE OF PET IN BLADDER CANCER

Overview of bladder cancer

Bladder carcinoma (BC) is the ninth most common cancer worldwide and the most frequent type of cancer of the urinary tract¹⁸. Painless haematuria is the most common presenting complaint¹⁹. More than 90% of BCs are urothelial (transitional cell) carcinomas, 5% are squamous cell carcinomas, and less than 2% are adenocarcinomas¹⁹. At presentation, approximately 30% of patients have muscle invasive BC¹⁸. Muscle invasive BC is an aggressive epithelial tumor with a high rate of early systemic dissemination. The common sites of metastatic disease include liver, lung, bone, and adrenal glands. The standard method of diagnosing BC continues to be based on direct visualization of the bladder with cystoscopy and subsequent biopsy/resection. The optimal management of these patients is dependent on accurate staging and detection of metastatic disease. Generally, muscle invasive bladder confined BC is treated with radical cystectomy with pelvic lymph node dissection (PLND), whereas metastatic disease is treated with cisplatin based combination chemotherapy¹⁹. The extent of extravesical involvement determines whether the patient is a candidate for neoadjuvant chemotherapy before definitive treatment.

Primary bladder cancer

Both CT and MRI are widely used for imaging of primary BC. For local tumor assessment, MRI is reported to be more accurate than CT¹⁸. MRI is superior to CT for determining depth of bladder wall infiltration²⁰. Both CT and MRI have limited capability for detecting microscopic invasion of the perivesical fat, but they may be used to find T3b disease or higher with good diagnostic accuracy²¹. The role of FDG PET/CT in the detection of localized BC is limited because of the difficulty in differentiating radiotracer activity excreted into the urine from tumor activity in the bladder. Several methods have been proposed to overcome radioactivity interference in urine, i.e., FDG wash out, early images, late images after voiding, dual phase imaging, catheterization, bladder irrigation, and forced diuresis^{22–29}. A recent meta-analysis evaluated the diagnostic accuracy of FDG PET/CT for detecting bladder lesions³⁰. Six studies met the inclusion criteria. The pooled sensitivity and specificity of PET or PET/CT for the detection of BC was 80.0% and 84.0%, respectively. When compared with results of MRI and CT published in other studies, FDG PET/CT showed no superiority in detecting local bladder lesions³⁰.

Staging

Assessment of lymph node (LN) metastases based solely on size is limited by the inability of both CT and MRI to identify metastases in normal-sized or minimally enlarged nodes. Thus, the sensitivity for detection of LN metastases is low for both imaging modalities²⁰. Specificity is also low because nodal enlargement may be due to benign disease. Given the ability of PET to detect metabolic activity, investigators have begun exploring the use of PET in staging BC^{31–37} (Fig 4& 5). A recent meta-analysis of FDG PET/CT for the staging

and restaging of bladder cancer, found that the pooled sensitivity was 82%, the pooled specificity was 89%, and the global accuracy was 92%³⁸. FDG PET/CT detects more malignant disease than conventional CT/MRI in 20–40% of patients^{32,33}, and FDG PET/CT may change the clinical management in up to 68% of the patients³². Upstaging is more frequent than downstaging³³. For diagnosing LN positive disease, Swinnen et al reported the accuracy, the sensitivity, and the specificity of 84%, 46%, and 97% for FDG PET/CT, respectively³⁴. When analyzing the results of CT alone, there was an accuracy of 80%, sensitivity of 46%, and specificity of 92%. The study found no advantage for combined FDG PET/CT over CT alone for LN staging of invasive BC. FDG PET/CT has also been compared to MRI for LN-staging in patients with BC(n=18)³¹. The specificities for detection of LN metastases for MRI and FDG PET/CT were 80% and 93.33%, respectively. The negative predictive values (NPV) were 80% and 87.5% for MRI and FDG PET/CT, respectively. The differences in specificity and NPV were not statistically significant. However, the trend of the data indicates an advantage of FDG PET/CT over MRI³¹. Larger prospective studies are needed to further elucidate the clinical role of FDG PET/CT in LN staging of BC.

Restaging

The overall prognosis for recurrent BC is poor. However, additional salvage and/or palliative therapies are prompted when disease is discovered. Accurate restaging is therefore important before additional costly and toxic therapies are considered. There are few data available regarding the utility of FDG PET/CT in assessing for recurrence and metastatic disease in patients who have previously undergone treatment for their primary BC^{39–41}. Jadvar et al retrospectively assessed the diagnostic ability of FDG PET or PET/CT in recurrent and metastatic BC⁴¹. In the study all 35 patients were previously treated for their primary disease. The metastatic sites detected in the study included mediastinum, lung, and bone. FDG PET/CT affected the clinical management in 17% of patients, by prompting either additional therapy or a wait-and-watch strategy. The few studies indicate that FDG PET may be useful for the detection of recurrent tumor in the pelvis, differentiation between local recurrent disease versus postsurgical or post irradiation fibrosis/necrosis and for the detection of distant metastases.

Response to therapy

In muscle invasive BC neoadjuvant chemotherapy is an established standard treatment that improves the overall survival of patients with BC⁴². However, the non-response rate is relative high. Monitoring the LN response to neoadjuvant chemotherapy may enable patient selection for surgery. Evaluation of the LN response with conventional imaging modalities is usually difficult and inaccurate. This is mainly due to difficulty with identifying viable tumor in residual (necrotic) masses and small tumor deposits in LNs of normal size. Recently, FDG PET/CT was used for monitoring the response of pelvic LN metastasis to neoadjuvant chemotherapy for BC (n=19)⁴³. Metabolic response was assessed according to EORTC (European Organization for Research and Treatment of Cancer) recommendations based on the change in FDG uptake on FDG PET/CT. Radiological response was assessed on CT according to RECIST (Response Evaluation Criteria in Solid Tumors). All patients underwent PLND with histopathological evaluation of LNs. PET/CT and CT correctly

distinguished responders (95%) from nonresponders (79%) and complete responders (68%) from patients with residual disease (63%). Although no definitive conclusions can be drawn from these preliminary data, PET/CT appeared feasible for evaluating the LN response to neoadjuvant chemotherapy. However, this has to be confirmed in large clinical trials.

Prognostic value

Only two studies have focused on the prognostic value of FDG PET/CT. Kibel et al, reported sensitivity, specificity, PPV and NPV of 70%, 94%, 78% and 91%, respectively, for FDG PET/CT in 42 patients with BC⁴⁴. Median follow-up was 14.9 months. FDG PET/CT detected occult metastatic disease in 17% (7/42) of the patients with negative conventional preoperative evaluations. Recurrence free survival, OS and disease free survival (DSS) were all significantly poorer in the patients with positive FDG PET/CT than in those with negative FDG-PET/CT. In the study, FDG PET/CT was strongly correlated with survival. Recently, Mertens et al, also investigated the association between extravesical FDG avid lesions on PET/CT and mortality in patients with muscle invasive BC⁴⁵. Of the 211 patients included in the study, 98 (46.4%) had one or more extravesical lesions on PET/CT, 113 (53.5%) had a negative PET/CT. Conventional CT revealed extravesical lesions in 51 patients (24.4%). Median follow-up was 18 months. Patients with a positive PET/CT had a significantly shorter OS and DSS (median OS: 14 vs 50 months, $P = .001$; DSS: 16 vs 50 months, $P < .001$). In multivariable analysis, the presence of extravesical lesions on PET/CT was an independent prognostic indicator of mortality. This association was not statistically significant for conventional CT. The results indicate that the presence of extravesical FDG-avid lesions on PET/CT might be considered an independent indicator of mortality.

Other agents for Bladder Cancer

Investigators have attempted to improve the sensitivity of PET by using tracers that are not excreted in the urine like FDG. Tracers like C-11 choline, C-11 acetate and C-11 methionine have been used for that purpose. Furthermore, sodium fluoride has been used for detection of bone metastasis.

Choline—Few data are available on the role of C-11 choline PET/CT in BC^{46–52}. The sensitivity for detection of LN metastasis is relative low^{49,51,52}. Recently, Brunocilla et al investigated the diagnostic accuracy of choline PET/CT in preoperative LN staging of BC suitable for radical cystectomy and extended PLND⁵¹. Overall, 844 LNs were evaluated, and 38 of them (4.5%) showed metastatic involvement. On a patient-based analysis, choline PET/CT showed a sensitivity of 42% and specificity of 84%, whereas, CT showed a sensitivity of 14% and specificity of 89%. On a LN based analysis, choline PET/CT showed a sensitivity of 10% and specificity of 64%, whereas CT showed a sensitivity of 2% and specificity of 63%. In contrast, another study ($n=44$), choline PET/CT was not able to improve the diagnostic efficacy in preoperative LN staging compared with CT⁴⁶. C-11 choline PET may be more useful for restaging of BC suspected of relapse, especially for LN evaluation and distant metastases⁵³. Recently, the prognostic value of choline PET/CT in preoperative staging of muscle invasive BC was investigated⁵⁴. In this prospective study, 44 patients with localized BC were staged with choline PET/CT before radical cystectomy with

PLND. The results of imaging were correlated to OS and CSD. There was no statistically significant difference in OS and CSD between the patient groups when stratified for organ confined versus non organ confined disease or LN involvement defined by either choline PET/CT or CT. The authors concluded that neither CT nor choline PET/CT was able to sufficiently predict OS or CSD in BC patients treated with radical cystectomy. However, a major limitation of the study is the relative small number of patients included.

Methionine—C-11 methionine uptake in tissue is an indication of amino acid transport and metabolism, which is often increased in malignant tumors. In a small study, methionine was superior to FDG, however, tumor was identified with a sensitivity of 78% (18/23) only with methionine PET⁵⁵. Methionine uptake was correlated to tumor grade. However, methionine did not improve staging of BC. In another study, methionine PET was used for the evaluation of therapy response in 44 patients with varying stages of BC treated with chemotherapy⁵⁶. The diagnostic accuracy of PET was poor and the technique could not monitor the therapeutic effect of neoadjuvant chemotherapy, producing results that correlated with therapy outcome.

Acetate—Another tracer with little or no urinary excretion is C-11 acetate. A small study (n=16) prospectively evaluated MRI, acetate PET/CT and CT for staging of BC⁵⁷. MRI, acetate PET/CT and CT demonstrated similar levels of accuracy. For all modalities, a history of intravesical and/or systemic chemotherapy affected staging accuracy. In another small study (n=14), acetate PET/CT was compared with choline PET/CT in BC⁵⁸. Acetate and choline scans were performed within one week. The two tracers demonstrated equivalent results in the preoperative evaluation.

Sodium fluoride—Lytic bone metastases of BC may be better detected using sodium fluoride PET scans, as compared with conventional 99mTc-MDP bone scan. Recently, sodium fluoride PET was compared with MDP bone scan in the detection of skeletal metastases in BC⁵⁹. In this prospective study, 48 patients with BC underwent PET and bone scan within 48 hours. Skeletal metastases diagnosed on each of these techniques was compared against a final diagnosis based on CT, MRI, skeletal survey, clinical follow up and histological correlation. The sensitivity, specificity, positive PPV, NPV, and accuracy of MDP planar bone scan were 82.35%, 64.51%, 56%, 86.95%, and 70.83%; of MDP SPECT/CT were 88.23%, 74.19%, 65.21%, 92%, and 79.16%; and of fluoride PET/CT were 100%, 87.09%, 80.95%, 100%, and 91.66%, respectively. In the study, fluoride PET/CT was superior to both MDP planar bone scan and MDP SPECT/CT. Fluoride PET/CT identified bony metastases and changed the management in 17 of 48 patients (35%).

Summary

FDG PET/CT is not used for evaluation of primary tumor in the bladder because of urinary excretion of FDG. Several methods have been proposed to overcome interference from radioactivity in urine. However, FDG PET/CT is increasingly used for staging and restaging in muscle invasive BC, and FDG PET/CT may add important prognostic information. Tracers with no or little urinary excretion have been proposed and tested in BC, but are not recommended in international guidelines.

USE OF PET IN TESTICULAR CANCER

Overview of testicular cancer

Testicular cancer represents between 1% and 1.5% of male cancers and 5% of urological tumors, with 3–10 new cases occurring per 100,000 males/per year⁶⁰. Over the last 30 years, the incidence of testicular cancer has increased⁶¹. Only 1–2% is bilateral at diagnosis. The histological type varies; although there is a clear predominance (90–95%) of germ cell tumors (GCT)⁶⁰. Testicular cancers are classified as seminomas, which account for approximately 40% of GCT or nonseminomatous germ cell tumors (NSGCT), which account for approximately 60%⁶². The clinical management of testicular GCT depends on the pathology, staging, and prognostic stratification⁶³. Testicular tumors show excellent cure rates⁶². This is mainly due to careful staging at the time of diagnosis, adequate early treatment based on chemotherapeutic combinations, with or without radiotherapy and surgery; and very strict follow-up and salvage therapies. Testicular cancer typically spreads by the lymphatic route through channels along testicular vessels to the retroperitoneum⁶⁴. Hematogenous spread is predominantly to the lungs. Testicular cancer normally appears as a painless, unilateral scrotal mass⁶². In approximately 20% of cases, the first symptom is scrotal pain. Orchidectomy and pathological examination of the testis are necessary to confirm the diagnosis and to define the local extension⁶⁰. Serum tumor markers (AFP, hCG, LDH) are prognostic factors and contribute to diagnosis and staging⁶⁰. Imaging plays an important role in the clinical management of testicular cancer. In the following we give an overview of PET/CT in testicular cancer.

Primary Testicular Cancer

Currently, diagnostic ultrasound (US) serves to confirm the presence of a testicular mass and to explore the contralateral testis⁶⁵. The sensitivity of US to detect testicular tumor is almost 100%, and it has an important role in determining whether a mass is intra- or extratesticular⁶⁵. MRI offers higher sensitivity and specificity than US for diagnosing tumors^{65,66}. MRI of scrotum has a sensitivity of 100% and a specificity of 95–100%⁶⁷, but its high cost does not justify its clinical use. FDG PET/CT does not have a role in the primary evaluation of a scrotal mass.

Staging

In order to determine the presence of metastatic disease, the LN pathway must be screened and the presence of visceral metastases must be determined⁶⁰. Retroperitoneal and mediastinal LNs are most often assessed by CT. The supraclavicular nodes can be assessed by physical examination. CT has a sensitivity of 70–80% in determining the state of the retroperitoneal LN, and MRI produces similar results to CT⁶⁰. However, MRI is not recommended for routine imaging in staging of testicular cancer because of the high cost and limited access to MRI, but MRI may be useful when CT and US are inconclusive, when the patient has an allergy to CT contrast media or in cases where the radiation dose should be reduced. FDG PET is a potentially useful diagnostic tool for initial staging in patients with GCT. Studies have suggested improved diagnostic accuracy of FDG PET compared with CT imaging in a range of settings^{68–71}. In one study, 70% of patients with normal-sized nodes who subsequently developed relapse could be identified at presentation by the use of

PET⁶⁹. Recently, Ambrosini et al, performed a retrospective study in 51 seminoma and 70 NSGCT⁷². FDG demonstrated good sensitivity and specificity for seminoma lesions (92% and 84%, respectively), but its sensitivity was lower for NSGCT (sensitivity and specificity were 77% and 95%, respectively). The FDG scan influenced the clinical management of 92% (47/51) seminomas, and 84% (59/70) NSGCT. Sharma et al demonstrated high diagnostic accuracy of FDG PET/CT for restaging both seminomatous and non-seminomatous malignant GCTs in a large patient population (n=96)⁷³. FDG PET/CT showed sensitivity, specificity, PPV, NPV and accuracy of 94.2%, 75.0%, 83.0%, 90.9% and 85.8% overall; 90.0%, 74.0%, 72.0%, 90.9% and 80.8% in seminomatous GCT; and 96.8%, 76.9%, 91.1%, 90.9% and 91.1% in non-seminomatous GCT, respectively⁷³. The difference in PET/CT accuracy for seminomatous and non-seminomatous GCTs was not significant. The results support the potential usefulness of FDG PET/CT for the assessment of patients with GCT.

Residual disease

In patients with metastatic seminoma, post chemotherapy residual masses are present in 55%–80%. In lesions > 3 cm, viable tumor is expected in 11%–37% of cases. Surgery is technically demanding due to fibrosis and it is often incomplete and associated with increased morbidity. Thus, it is important to discriminate between residual tumor and fibrosis/necrosis. CT and MRI cannot adequately predict the histology of residual masses⁷⁴. For many years, FDG PET has been considered as the gold standard for discriminating between residual tumors and necrosis/fibrosis (Fig 6). Several prospective and retrospective studies evaluated the diagnostic performance of FDG-PET or PET/CT in the post chemotherapy management of patients with GCT^{70,72,75–84}. Recently, Treglia et al published a meta-analysis about the diagnostic performance of FDG PET and PET/CT in the post chemotherapy management of patients with seminoma⁸⁵. Nine studies including 375 scans were included. The pooled analysis demonstrated sensitivity 78%, specificity 86%, PPV 58%, NPV 94%, and accuracy 84%. A better diagnostic accuracy of FDG PET or PET/CT in evaluating residual/recurrent lesions > 3 cm compared to those < 3 cm was found. However, possible sources of false negative and false positive results for post chemotherapy residual/recurrent seminoma at FDG PET or PET/CT should be kept in mind. False negative findings may be due to small lesions (with size below the resolution of the method) or with low proliferative activity (and consequently low FDG uptake). False positive results may be due to inflammatory lesions. The results of the meta-analysis support the role of FDG PET or PET/CT in the post chemotherapy management of patients with seminoma. Bachner et al, performed a retrospective validation of the large SEMPET trial published in 2004^{75,79}. A total of 11 Centers participated and a total of 127 FDG PET studies were evaluated. The authors compared PET scans carried out before and after a cut-off level of 6 weeks after the end of the last chemotherapy cycle. PET sensitivity, specificity, negative predictive value (NPV), and positive predictive value were 50%, 77%, 91%, and 25%, respectively, before the cut-off and 82%, 90%, 95%, and 69% after the cut-off. PET accuracy significantly improved from 73% before to 88% after the cut-off (P = 0.032).

The presence of vital carcinoma and mature teratoma is common (55%) in residual masses in patients with NSGCT. In patients with metastatic NSGCT, residual masses after cisplatin-based combination chemotherapy consist of necrosis in 40%, persisting vital carcinoma in 20%, and mature teratoma in 40% of patients⁸⁶. Oechsle et al conducted a large prospective multicenter study in order to evaluate the accuracy of FDG PET in NSGCT for the prediction of histology compared with CT and serum tumor markers⁸². A total of 121 patients with stage IIC or III NSGCT scheduled for secondary resection after cisplatin based CTX were included. FDG PET was performed after completion of CTX. Prediction of tumor viability with FDG PET was correct in 56%, which did not reach the expected clinically relevant level of 70%, and was not better than the accuracy of CT (55%) or serum tumor markers (56%). Sensitivity and specificity of FDG PET were 70% and 48%. PPV were not significantly different (55%, 61%, and 59% for CT, STM and PET, respectively). Judging only vital carcinoma as true malignant finding, the NPV increased to 83% for FDG PET. The results indicate that in NSGCT, FDG-PET is less helpful in predicting histology in residual masses after chemotherapy than in patients with pure seminomatous GCT. Whether NSGCT has lower FDG uptake than seminoma remains to be evaluated further in the future in prospective large-scale studies.

Other agents for testicular cancer—Until recently, FDG has been the only radiotracer used for PET imaging of GCT. Increased uptake of FDG is regarded as an indicator of viable tumor. However, FDG uptake is not specific for tumor; inflammatory and granulomatous tissues also show FDG accumulation. The role of FDG PET in staging nonseminomatous GCT residues is limited because FDG PET cannot differentiate mature teratoma from necrosis and fibrosis. The thymidine analog F-18-fluorothymidine (FLT) is a cell proliferation marker. Recently, A small study (n=11) investigated the addition of FLT PET to FDG PET for early response monitoring and prediction of the histology of residual tumor masses in patients with metastatic GCT⁸⁷. The authors concluded that despite the lower incidence of false-positive results with FLT PET than with FDG PET, PET-negative residual masses after chemotherapy of metastatic nonseminomatous GCT still require resection, because the low negative predictive value of FDG PET cannot be improved by application of the proliferation marker FLT⁸⁷.

Summary

FDG PET/CT has no role in primary evaluation of a scrotal mass, but can be used for staging in GCT. However, FDG PET is not yet included in the international guidelines for staging of testicular cancer. For detection of residual disease, FDG PET/CT is an accurate diagnostic method in the post chemotherapy management of patients with seminoma.

ABBREVIATIONS

AFP	alpha-fetoprotein
BC	bladder cancer
CSD	cancer specific death

CT	computed tomography
FDG	fluorodeoxyglucose
FLT	fluorothymidine
GCT	germ cell tumor
hCG	human chorionic gonadotropin
LDH	lactate dehydrogenase
LN	lymph node
MRI	magnetic resonance imaging
NPV	negative predictive value
NSGCT	non seminomatous germ cell tumor
OS	overall survival
PFS	progression free survival
PPV	positive predictive value
RECIST	response evaluation criteria in solid tumors
RCC	renal cell carcinoma
SUV	standardized uptake value
TLG	total lesion glycolysis

References

1. Sahni VA, Silverman SG. Imaging management of incidentally detected small renal masses. *Semin Intervent Radiol.* 2014; 31:9. [PubMed: 24596435]
2. Caldarella C, Muoio B, Isgro MA, Porfiri E, Treglia G, Giovannella L. The role of fluorine-18-fluorodeoxyglucose positron emission tomography in evaluating the response to tyrosine-kinase inhibitors in patients with metastatic primary renal cell carcinoma. *Radiol Oncol.* 2014; 48:219. [PubMed: 25177235]
3. Makis W, Ciarallo A, Rakheja R, Probst S, Hickeson M, Rush C, et al. Spectrum of malignant renal and urinary bladder tumors on 18F-FDG PET/CT: a pictorial essay. *Clin Imaging.* 2012; 36:660. [PubMed: 23153993]
4. Oyama N, Ito H, Takahara N, Miwa Y, Akino H, Kudo T, et al. Diagnosis of complex renal cystic masses and solid renal lesions using PET imaging: comparison of 11C-acetate and 18F-FDG PET imaging. *Clin Nucl Med.* 2014; 39:e208. [PubMed: 24217534]
5. Aras M, Dede F, Ones T, Inanir S, Erdil TY, Turoglu HT. Is The Value of FDG PET/CT In Evaluating Renal Metastasis Underestimated? A Case Report And Review of The Literature. *Mol Imaging Radionucl Ther.* 2013; 22:109. [PubMed: 24416629]
6. Czarnecka AM, Kornakiewicz A, Kukwa W, Szczyluk C. Frontiers in clinical and molecular diagnostics and staging of metastatic clear cell renal cell carcinoma. *Future Oncol.* 2014; 10:1095. [PubMed: 24941992]
7. Ravina M, Hess S, Chauhan MS, Jacob MJ, Alavi A. Tumor thrombus: ancillary findings on FDG PET/CT in an oncologic population. *Clin Nucl Med.* 2014; 39:767. [PubMed: 24999677]
8. Saldone MC, Uzzo RG. Balancing process and risk: standardizing posttreatment surveillance for renal cell carcinoma. *J Urol.* 2013; 190:417. [PubMed: 23688642]

9. Chen JL, Appelbaum DE, Kocherginsky M, Cowey CL, Rathmell WK, McDermott DF, et al. FDG-PET as a predictive biomarker for therapy with everolimus in metastatic renal cell cancer. *Cancer Med.* 2013; 2:545. [PubMed: 24156027]
10. Ferda J, Ferdova E, Hora M, Hes O, Finek J, Topolcan O, et al. 18F-FDG-PET/CT in potentially advanced renal cell carcinoma: a role in treatment decisions and prognosis estimation. *Anticancer Res.* 2013; 33:2665. [PubMed: 23749925]
11. Kakizoe M, Yao M, Tateishi U, Minamimoto R, Ueno D, Namura K, et al. The early response of renal cell carcinoma to tyrosine kinase inhibitors evaluated by FDG PET/CT was not influenced by metastatic organ. *BMC Cancer.* 2014; 14:390. [PubMed: 24885730]
12. Farnebo J, Gryback P, Harmenberg U, Laurell A, Wersall P, Blomqvist LK, et al. Volumetric FDG-PET predicts overall and progression-free survival after 14 days of targeted therapy in metastatic renal cell carcinoma. *BMC Cancer.* 2014; 14:408. [PubMed: 24906441]
13. Yoon HJ, Paeng JC, Kwak C, Park YH, Kim TM, Lee SH, et al. Prognostic implication of extrarenal metabolic tumor burden in advanced renal cell carcinoma treated with targeted therapy after nephrectomy. *Ann Nucl Med.* 2013; 27:748. [PubMed: 23818007]
14. Fuccio C, Spinapolic EG, Cavalli C, Palumbo R, D'Ambrosio D, Trifiro G. 18FFluoride PET/CT in the detection of bone metastases in clear cell renal cell carcinoma: discordance with bone scintigraphy. *Eur J Nucl Med Mol Imaging.* 2013; 40:1930. [PubMed: 23877634]
15. Divgi CR, Uzzo RG, Gatsonis C, Bartz R, Treutner S, Yu JQ, et al. Positron emission tomography/computed tomography identification of clear cell renal cell carcinoma: results from the REDECT trial. *J Clin Oncol.* 2013; 31:187. [PubMed: 23213092]
16. Cheal SM, Punzalan B, Doran MG, Evans MJ, Osborne JR, Lewis JS, et al. Pairwise comparison of 89Zr- and 124I-labeled cG250 based on positron emission tomography imaging and nonlinear immunokinetic modeling: in vivo carbonic anhydrase IX receptor binding and internalization in mouse xenografts of clear-cell renal cell carcinoma. *Eur J Nucl Med Mol Imaging.* 2014; 41:985. [PubMed: 24604591]
17. Ammari S, Thiam R, Cuenod CA, Oudard S, Hernigou A, Grataloup C, et al. Radiological evaluation of response to treatment: application to metastatic renal cancers receiving anti-angiogenic treatment. *Diagn Interv Imaging.* 2014; 95:527. [PubMed: 24906810]
18. Witjes JA, Comperat E, Cowan NC, De SM, Gakis G, Lebre T, et al. EAU guidelines on muscle-invasive and metastatic bladder cancer: summary of the 2013 guidelines. *Eur Urol.* 2014; 65:778. [PubMed: 24373477]
19. Kaufman DS, Shipley WU, Feldman AS. Bladder cancer. *Lancet.* 2009; 374:239. [PubMed: 19520422]
20. Bouchelouche K, Turkbey B, Choyke PL. PET/CT and MRI in Bladder Cancer. *J Cancer Sci Ther.* 2012; S14
21. Rajesh A, Sokhi HK, Fung R, Mulcahy KA, Bankart MJ. Bladder cancer: evaluation of staging accuracy using dynamic MRI. *Clin Radiol.* 2011; 66:1140. [PubMed: 21924408]
22. Mertens LS, Fioole-Bruining A, Vegt E, Vogel WV, van Rhijn BW, Horenblas S. Detecting primary bladder cancer using delayed (18)F-2-fluoro-2-deoxy-Dglucose- positron emission tomography/computed tomography imaging after forced diuresis. *Indian J Nucl Med.* 2012; 27:145. [PubMed: 23919066]
23. Mertens LS, Bruin NM, Vegt E, de Blok WM, Fioole-Bruining A, van Rhijn BW, et al. Catheter-assisted 18F-FDG-PET/CT imaging of primary bladder cancer: a prospective study. *Nucl Med Commun.* 2012; 33:1195. [PubMed: 22781846]
24. Chondrogiannis S, Marzola MC, Colletti PM, Rubello D. Proposal of a New Acquisition Protocol for Bladder Cancer Visualization With 18F-FDG PET/CT. *Clin Nucl Med.* 2014
25. Yildirim-Poyraz N, Ozdemir E, Uzun B, Turkolmez S. Dual phase 18Ffluorodeoxyglucose positron emission tomography/computed tomography with forced diuresis in diagnostic imaging evaluation of bladder cancer. *Rev Esp Med Nucl Imagen Mol.* 2013; 32:214. [PubMed: 23218514]
26. Yang Z, Cheng J, Pan L, Hu S, Xu J, Zhang Y, et al. Is whole-body fluorine-18 fluorodeoxyglucose PET/CT plus additional pelvic images (oral hydrationvoiding- refilling) useful for detecting recurrent bladder cancer? *Ann Nucl Med.* 2012; 26:571. [PubMed: 22763630]

27. Anjos DA, Etchebehere EC, Ramos CD, Santos AO, Albertotti C, Camargo EE. 18F-FDG PET/CT delayed images after diuretic for restaging invasive bladder cancer. *J Nucl Med*. 2007; 48:764. [PubMed: 17475965]
28. Harkirat S, Anand S, Jacob M. Forced diuresis and dual-phase Ffluorodeoxyglucose- PET/CT scan for restaging of urinary bladder cancers. *Indian J Radiol Imaging*. 2010; 20:13. [PubMed: 20351986]
29. Kosuda S, Kison PV, Greenough R, Grossman HB, Wahl RL. Preliminary assessment of fluorine-18 fluorodeoxyglucose positron emission tomography in patients with bladder cancer. *Eur J Nucl Med*. 1997; 24:615. [PubMed: 9169567]
30. Wang N, Jiang P, Lu Y. Is fluorine-18 fluorodeoxyglucose positron emission tomography useful for detecting bladder lesions? A meta-analysis of the literature. *Urol Int*. 2014; 92:143. [PubMed: 23941766]
31. Jensen TK, Holt P, Gerke O, Riehmman M, Svolgaard B, Marcussen N, et al. Preoperative lymph-node staging of invasive urothelial bladder cancer with 18F-fluorodeoxyglucose positron emission tomography/computed axial tomography and magnetic resonance imaging: correlation with histopathology. *Scand J Urol Nephrol*. 2011; 45:122. [PubMed: 21231796]
32. Apolo AB, Riches J, Schoder H, Akin O, Trout A, Milowsky MI, et al. Clinical value of fluorine-18 2-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography in bladder cancer. *J Clin Oncol*. 2010; 28:3973. [PubMed: 20679618]
33. Mertens LS, Fioole-Bruining A, Vegt E, Vogel WV, van Rhijn BW, Horenblas S. Impact of (18) F-fluorodeoxyglucose (FDG)-positron-emission tomography/computed tomography (PET/CT) on management of patients with carcinoma invading bladder muscle. *BJU Int*. 2013; 112:729. [PubMed: 23790129]
34. Swinnen G, Maes A, Pottel H, Vanneste A, Billiet I, Lesage K, et al. FDG-PET/CT for the preoperative lymph node staging of invasive bladder cancer. *Eur Urol*. 2010; 57:641. [PubMed: 19477579]
35. Kosuda S, Kison PV, Greenough R, Grossman HB, Wahl RL. Preliminary assessment of fluorine-18 fluorodeoxyglucose positron emission tomography in patients with bladder cancer. *Eur J Nucl Med*. 1997; 24:615. [PubMed: 9169567]
36. Bachor R, Kotzerke J, Reske SN, Hautmann R. Lymph node staging of bladder neck carcinoma with positron emission tomography. *Urologe A*. 1999; 38:46. [PubMed: 10081101]
37. Drieskens O, Oyen R, Van PH, Vankan Y, Flamen P, Mortelmans L. FDG-PET for preoperative staging of bladder cancer. *Eur J Nucl Med Mol Imaging*. 2005; 32:1412. [PubMed: 16133380]
38. Lu YY, Chen JH, Liang JA, Wang HY, Lin CC, Lin WY, et al. Clinical value of FDG PET or PET/CT in urinary bladder cancer: a systemic review and metaanalysis. *Eur J Radiol*. 2012; 81:2411. [PubMed: 21899971]
39. Anjos DA, Etchebehere EC, Ramos CD, Santos AO, Albertotti C, Camargo EE. 18F-FDG PET/CT delayed images after diuretic for restaging invasive bladder cancer. *J Nucl Med*. 2007; 48:764. [PubMed: 17475965]
40. Harkirat S, Anand S, Jacob M. Forced diuresis and dual-phase Ffluorodeoxyglucose- PET/CT scan for restaging of urinary bladder cancers. *Indian J Radiol Imaging*. 2010; 20:13. [PubMed: 20351986]
41. Jadvar H, Quan V, Henderson RW, Conti PS. [F-18]-Fluorodeoxyglucose PET and PET-CT in diagnostic imaging evaluation of locally recurrent and metastatic bladder transitional cell carcinoma. *Int J Clin Oncol*. 2008; 13:42. [PubMed: 18307018]
42. Meeks JJ, Bellmunt J, Bochner BH, Clarke NW, Daneshmand S, Galsky MD, et al. A systematic review of neoadjuvant and adjuvant chemotherapy for muscle-invasive bladder cancer. *Eur Urol*. 2012; 62:523. [PubMed: 22677572]
43. Mertens LS, Fioole-Bruining A, van Rhijn BW, Kerst JM, Bergman AM, Vogel WV, et al. FDG-positron emission tomography/computerized tomography for monitoring the response of pelvic lymph node metastasis to neoadjuvant chemotherapy for bladder cancer. *J Urol*. 2013; 189:1687. [PubMed: 23142689]

44. Kibel AS, Dehdashti F, Katz MD, Klim AP, Grubb RL, Humphrey PA, et al. Prospective study of [18F]fluorodeoxyglucose positron emission tomography/computed tomography for staging of muscle-invasive bladder carcinoma. *J Clin Oncol.* 2009; 27:4314. [PubMed: 19652070]
45. Mertens LS, Mir MC, Scott AM, Lee ST, Fioole-Bruining A, Vegt E, et al. 18Ffluorodeoxyglucose-- positron emission tomography/computed tomography aids staging and predicts mortality in patients with muscle-invasive bladder cancer. *Urology.* 2014; 83:393. [PubMed: 24468513]
46. Maurer T, Souvatzoglou M, Kubler H, Opercan K, Schmidt S, Herrmann K, et al. Diagnostic efficacy of [11C]choline positron emission tomography/computed tomography compared with conventional computed tomography in lymph node staging of patients with bladder cancer prior to radical cystectomy. *Eur Urol.* 2012; 61:1031. [PubMed: 22196847]
47. Graziani T, Ceci F, Lopes FL, Chichero J, Castellucci P, Schiavina R, et al. 11CCholine PET/CT for Restaging of Bladder Cancer. *Clin Nucl Med.* 2014
48. Maurer T, Horn T, Souvatzoglou M, Eiber M, Beer AJ, Heck MM, et al. Prognostic Value of C-Choline PET/CT and CT for Predicting Survival of Bladder Cancer Patients Treated with Radical Cystectomy. *Urol Int.* 2014; 93:207. [PubMed: 25012094]
49. Picchio M, Treiber U, Beer AJ, Metz S, Bossner P, van RH, et al. Value of 11Ccholine PET and contrast-enhanced CT for staging of bladder cancer: correlation with histopathologic findings. *J Nucl Med.* 2006; 47:938. [PubMed: 16741302]
50. Gofrit ON, Mishani E, Orevi M, Klein M, Freedman N, Pode D, et al. Contribution of 11C-choline positron emission tomography/computerized tomography to preoperative staging of advanced transitional cell carcinoma. *J Urol.* 2006; 176:940. [PubMed: 16890661]
51. Brunocilla E, Ceci F, Schiavina R, Castellucci P, Maffione AM, Cevenini M, et al. Diagnostic accuracy of (11)C-choline PET/CT in preoperative lymph node staging of bladder cancer: a systematic comparison with contrast-enhanced CT and histologic findings. *Clin Nucl Med.* 2014; 39:e308. [PubMed: 24458183]
52. de Jong IJ, Pruim J, Elsinga PH, Jongen MM, Mensink HJ, Vaalburg W. Visualisation of bladder cancer using (11)C-choline PET: first clinical experience. *Eur J Nucl Med Mol Imaging.* 2002; 29:1283. [PubMed: 12271408]
53. Graziani T, Ceci F, Lopes FL, Chichero J, Castellucci P, Schiavina R, et al. 11CCholine PET/CT for Restaging of Bladder Cancer. *Clin Nucl Med.* 2014
54. Maurer T, Horn T, Souvatzoglou M, Eiber M, Beer AJ, Heck MM, et al. Prognostic Value of C-Choline PET/CT and CT for Predicting Survival of Bladder Cancer Patients Treated with Radical Cystectomy. *Urol Int.* 2014; 93:207. [PubMed: 25012094]
55. Ahlstrom H, Malmstrom PU, Letocha H, Andersson J, Langstrom B, Nilsson S. Positron emission tomography in the diagnosis and staging of urinary bladder cancer. *Acta Radiol.* 1996; 37:180. [PubMed: 8600958]
56. Letocha H, Ahlstrom H, Malmstrom PU, Westlin JE, Fasth KJ, Nilsson S. Positron emission tomography with L-methyl-11C-methionine in the monitoring of therapy response in muscle-invasive transitional cell carcinoma of the urinary bladder. *Br J Urol.* 1994; 74:767. [PubMed: 7827849]
57. Vargas HA, Akin O, Schoder H, Olgac S, Dalbagni G, Hricak H, et al. Prospective evaluation of MRI, (1)(1)C-acetate PET/CT and contrast-enhanced CT for staging of bladder cancer. *Eur J Radiol.* 2012; 81:4131. [PubMed: 22858427]
58. Orevi M, Klein M, Mishani E, Chisin R, Freedman N, Gofrit ON. 11C-acetate PET/CT in bladder urothelial carcinoma: intraindividual comparison with 11Ccholine. *Clin Nucl Med.* 2012; 37:e67. [PubMed: 22391726]
59. Chakraborty D, Bhattacharya A, Mete UK, Mittal BR. Comparison of 18F fluoride PET/CT and 99mTc-MDP bone scan in the detection of skeletal metastases in urinary bladder carcinoma. *Clin Nucl Med.* 2013; 38:616. [PubMed: 23603596]
60. Albers P, Albrecht W, Algaba F, Bokemeyer G, Cohn-Cedermark G, Fizazi K, et al. EAU Guidelines on testicular cancer. Update 2011. *European Association of Urology. Actas Urol Esp.* 2012; 36:127. [PubMed: 22188753]

61. Manecksha RP, Fitzpatrick JM. Epidemiology of testicular cancer. *BJU Int.* 2009; 104:1329. [PubMed: 19840008]
62. Horwich A, Shipley J, Huddart R. Testicular germ-cell cancer. *Lancet.* 2006; 367:754. [PubMed: 16517276]
63. Flechon A, Rivoire M, Droz JP. Management of advanced germ-cell tumors of the testis. *Nat Clin Pract Urol.* 2008; 5:262. [PubMed: 18398406]
64. Jana S, Blafox MD. Nuclear medicine studies of the prostate, testes, and bladder. *Semin Nucl Med.* 2006; 36:51. [PubMed: 16356796]
65. Kim W, Rosen MA, Langer JE, Banner MP, Siegelman ES, Ramchandani P. US MR imaging correlation in pathologic conditions of the scrotum. *Radiographics.* 2007; 27:1239. [PubMed: 17848688]
66. Cassidy FH, Ishioka KM, McMahon CJ, Chu P, Sakamoto K, Lee KS, et al. MR imaging of scrotal tumors and pseudotumors. *Radiographics.* 2010; 30:665. [PubMed: 20462987]
67. Johnson JO, Mattrey RF, Phillipson J. Differentiation of seminomatous from nonseminomatous testicular tumors with MR imaging. *AJR Am J Roentgenol.* 1990; 154:539. [PubMed: 2106218]
68. Hain SF, O'Doherty MJ, Timothy AR, Leslie MD, Partridge SE, Huddart RA. Fluorodeoxyglucose PET in the initial staging of germ cell tumours. *Eur J Nucl Med.* 2000; 27:590. [PubMed: 10853816]
69. Lassen U, Daugaard G, Eigved A, Hojgaard L, Damgaard K, Rorth M. Wholebody FDG-PET in patients with stage I non-seminomatous germ cell tumours. *Eur J Nucl Med Mol Imaging.* 2003; 30:396. [PubMed: 12634968]
70. Hain SF, O'Doherty MJ, Timothy AR, Leslie MD, Harper PG, Huddart RA. Fluorodeoxyglucose positron emission tomography in the evaluation of germ cell tumours at relapse. *Br J Cancer.* 2000; 83:863. [PubMed: 10970686]
71. Cremerius U, Wildberger JE, Borchers H, Zimny M, Jakse G, Gunther RW, et al. Does positron emission tomography using 18-fluoro-2-deoxyglucose improve clinical staging of testicular cancer?--Results of a study in 50 patients. *Urology.* 1999; 54:900. [PubMed: 10565755]
72. Ambrosini V, Zucchini G, Nicolini S, Berselli A, Nanni C, Allegri V, et al. 18F-FDG PET/CT impact on testicular tumours clinical management. *Eur J Nucl Med Mol Imaging.* 2014; 41:668. [PubMed: 24265073]
73. Sharma P, Jain TK, Parida GK, Karunanithi S, Patel C, Sharma A, et al. Diagnostic accuracy of integrated (18)F-FDG PET/CT for restaging patients with malignant germ cell tumours. *Br J Radiol.* 2014; 87:20140263. [PubMed: 24896199]
74. Stomper PC, Kalish LA, Garnick MB, Richie JP, Kantoff PW. CT and pathologic predictive features of residual mass histologic findings after chemotherapy for nonseminomatous germ cell tumors: can residual malignancy or teratoma be excluded? *Radiology.* 1991; 180:711. [PubMed: 1651526]
75. Bachner M, Lorient Y, Gross-Goupil M, Zucali PA, Horwich A, Germa-Lluch JR, et al. 2-(1)(8)fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) for postchemotherapy seminoma residual lesions: a retrospective validation of the SEMPET trial. *Ann Oncol.* 2012; 23:59. [PubMed: 21460378]
76. Siekiera J, Malkowski B, Jozwicki W, Jasinski M, Wronczewski A, Pietrzak T, et al. Can we rely on PET in the follow-up of advanced seminoma patients? *Urol Int.* 2012; 88:405. [PubMed: 22507953]
77. Hinz S, Schrader M, Kempkensteffen C, Bares R, Brenner W, Kreges S, et al. The role of positron emission tomography in the evaluation of residual masses after chemotherapy for advanced stage seminoma. *J Urol.* 2008; 179:936. [PubMed: 18207171]
78. Lewis DA, Tann M, Kesler K, McCool A, Foster RS, Einhorn LH. Positron emission tomography scans in postchemotherapy seminoma patients with residual masses: a retrospective review from Indiana University Hospital. *J Clin Oncol.* 2006; 24:e54. [PubMed: 17135635]
79. De SM, Becherer A, Bokemeyer C, Stoiber F, Oechsle K, Sellner F, et al. 2- 18fluoro-deoxy-D-glucose positron emission tomography is a reliable predictor for viable tumor in postchemotherapy seminoma: an update of the prospective multicentric SEMPET trial. *J Clin Oncol.* 2004; 22:1034. [PubMed: 15020605]

80. Spermon JR, De Geus-Oei LF, Kiemeny LA, Witjes JA, Oyen WJ. The role of (18)fluoro-2-deoxyglucose positron emission tomography in initial staging and re-staging after chemotherapy for testicular germ cell tumours. *BJU Int.* 2002; 89:549. [PubMed: 11942962]
81. Ganjoo KN, Chan RJ, Sharma M, Einhorn LH. Positron emission tomography scans in the evaluation of postchemotherapy residual masses in patients with seminoma. *J Clin Oncol.* 1999; 17:3457. [PubMed: 10550142]
82. Oechsle K, Hartmann M, Brenner W, Venz S, Weissbach L, Franzius C, et al. [18F]Fluorodeoxyglucose positron emission tomography in nonseminomatous germ cell tumors after chemotherapy: the German multicenter positron emission tomography study group. *J Clin Oncol.* 2008; 26:5930. [PubMed: 19018083]
83. Becherer A, De SM, Karanikas G, Szabo M, Bokemeyer C, Dohmen BM, et al. FDG PET is superior to CT in the prediction of viable tumour in post-chemotherapy seminoma residuals. *Eur J Radiol.* 2005; 54:284. [PubMed: 15837411]
84. De SM, Bokemeyer C, Becherer A, Stoiber F, Oechsle K, Kletter K, et al. Predictive impact of 2-18fluoro-2-deoxy-D-glucose positron emission tomography for residual postchemotherapy masses in patients with bulky seminoma. *J Clin Oncol.* 2001; 19:3740. [PubMed: 11533096]
85. Treglia G, Sadeghi R, Annunziata S, Caldarella C, Bertagna F, Giovannella L. Diagnostic performance of fluorine-18-fluorodeoxyglucose positron emission tomography in the postchemotherapy management of patients with seminoma: systematic review and meta-analysis. *Biomed Res Int.* 2014; 2014:852681. [PubMed: 24963486]
86. Hartmann JT, Schmoll HJ, Kuczyk MA, Candelaria M, Bokemeyer C. Postchemotherapy resections of residual masses from metastatic nonseminomatous testicular germ cell tumors. *Ann Oncol.* 1997; 8:531. [PubMed: 9261521]
87. Pfannenberger C, Aschoff P, Dittmann H, Mayer F, Reischl G, von WC, et al. PET/CT with 18F-FLT: does it improve the therapeutic management of metastatic germ cell tumors? *J Nucl Med.* 2010; 51:845. [PubMed: 20484416]

KEYPOINTS

- PET/CT with F-18 fluorodeoxyglucose (FDG) is not widely used in most primary renal cancers; however, FDG PET/CT may be used in selected high-risk patients and when conventional imaging is negative or if there is a potential tumor thrombus.
- In metastatic renal cancer, FDG PET/CT is increasingly used to monitor targeted molecular therapies.
- FDG PET/CT is increasingly used for staging and restaging in muscle invasive bladder cancer, and the modality may add important prognostic information; PET tracers with no urinary excretion, especially C-11 choline, have been tested in clinical studies.
- FDG PET/CT may be used for staging, restaging, and follow up of testicular cancer and is especially useful for the evaluation of residual tumors in patients with seminoma.

Figure 1. Solitary renal cancer in the right upper pole. This patient had a Type II papillary renal cancer in the right kidney (A) and was considered high risk for metastatic disease. The FDG PET/CT demonstrates increased activity in the upper pole of the kidney corresponding the mass on CT (B) and no evidence of metastatic disease elsewhere. (C)

Figure 2. Patient with aggressive Type II Papillary Renal Cancer associated with Hereditary Leiomyoma Renal Cell Carcinoma syndrome which has recurred after left nephrectomy.

PET CT with F18-FDG demonstrates intense uptake in the left para-aortic adenopathy on transverse PET/CT (A) and coronal projection image (B) After therapy with a combination of targeted therapies, the activity and size of the adenopathy have dramatically decreased (C,D). The patient has maintained a good response for two years.

Figure 3.

Patient with history of clear cell renal cancer with recurrent disease in the axilla and retroperitoneum. Transverse CT scan shows several abnormal nodes in the left axilla (A). Retroperitoneal adenopathy is also seen (B). Coronal PET demonstrates extensive uptake in the Axilla and shoulder muscles as well as retroperitoneal adenopathy (C).

Figure 4.

Patient with newly diagnosed muscle invasive bladder cancer. Tumor in the bladder wall could not be visualized with FDG PET due to FDG activity in urine. However, unexpected focal increased FDG activity in the right ureter was seen (A,B), which was due to malignancy. A lymph node metastasis was also seen in the right side of pelvis (C).

Figure 5. Patient with newly diagnosed muscle invasive bladder cancer. A bone metastasis in right acetabulum can be seen on FDG PET/CT (A,B) but with only minimal changes on CT (C). A lymph node metastasis is seen in the right side of the pelvis (D).

Figure 6.

Patient with seminoma treated with chemotherapy, where a retroperitoneal residual mass was seen on CT. FDG PET/CT demonstrated moderate activity in a small area of the known residual mass (A). After a new cycle of chemotherapy FDG PET/CT showed complete regression of FDG activity in the residual mass (B). However, control FDG PET/CT 3 months later demonstrated relapse in the retroperitoneal mass (C) and multiples peritoneal metastases (D). After one more cycle of chemotherapy FDG PET/CT demonstrated complete regression (E). Only few benign inflammatory elements in cutis were seen.