Review

DOI: 10.4274/uob.galenos.2018.1132

Bull Urooncol 2019;18:80-88

Nuclear Medicine Applications in Diagnosis of Urological Tumors

Mine Araz MD[1], Yüksel Ürün MD[2]

[1]*Ankara University Faculty of Medicine, Department of Nuclear Medicine, Ankara, Turkey*
[2]*Ankara University Faculty of Medicine Department of Medical Oncology, Ankara, Turkey*

Abstract

Except for prostate carcinoma, there is limited data in the literature on the role of nuclear imaging methods in the management of urological cancers. 18F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) is generally the most widely used method in oncological imaging. However, the diagnostic power of this radiopharmaceutical in urological tumors is weakened partially due to its physiological urinary excretion. For this reason, some other 18F-labeled molecules, especially Ga-68 prostate-specific membrane antigen for prostate cancer and 18F-sodium fluoride for bone metastases, have recently gained importance. In addition, characterization of renal masses with Tc-99m methoxy isobutyl isonitrile (MIBI), a nonspecific tumor agent, and detection of bone metastases with whole-body Tc-99m methylene diphosphonate (MDP) bone scintigraphy are still used. In this review, scintigraphic methods and PET/CT imaging used in diagnosis and follow-up of urological tumors will be discussed.

Keywords: Urological neoplasms, radionuclide imaging, radiology

Introduction

Computerized tomography (CT) is the most commonly used imaging method for diagnosis, staging, treatment planning and follow-up of kidney tumors and bladder tumors. Magnetic resonance imaging (MRI) can provide more detailed information about local advanced disease. In particular, the use of multiparametric MRI in prostate cancer is increasing (1).

Nuclear imaging methods can provide information on the function, behavior and receptor status of tumoral tissue, unlike anatomical imaging. 18F-fluorodeoxyglucose (18F-FDG) is the most commonly used metabolic agent in oncologic PET/CT studies and provides whole-body evaluation in one step. Although urinary excretion of 18F-FDG in urological tumors is intense and thus its role in local disease evaluation is limited, it provides a significant advantage by demonstrating extent of disease. Imaging studies with new radiopharmaceuticals undergoing lower urinary excretion continue.

Kidney Tumors

18F-FDG PET/CT

Sensitivity of 18F-FDG PET/CT has been reported between 50% and 60% in the primary diagnosis and determination of kidney tumors. For this purpose, it has not been shown to have a significant contribution to conventional imaging methods such as CT and MRI. In the literature, although imaging after forced diuresis or dual-phase delayed imaging method have been tried in order to reduce the effect of physiological urine activity, no superiority was achieved with these methods over routine imaging protocol. In addition, it was found that there was no correlation between the amount of GLUT 1 expression and 18F-FDG uptake after surgical excision of the primary tumor (2,3,4).

Routine use of 18F-FDG PET/CT in the staging of kidney tumors is not recommended in standard protocols and guidelines. The most important reason for this is that 18F-FDG has a high rate of false negativity for the primary tumor due to the intense physiological urine activity. However, it has been reported that it may be useful in demonstrating extrarenal metastatic disease in risky patients (5,6).

Early detection and treatment of recurrence after nephrectomy shows a certain survival benefit for some patients. As a whole-body imaging method, 18F-FDG PET/CT can make a significant contribution to patient management during the restaging phase. Metabolic characterization can provide more accurate diagnosis in patients with recurrent or metastatic suspicious findings in postoperative follow-up radiological imaging results. In addition, it is more successful in detecting bone metastases than whole-body bone scintigraphy. The studies published in the literature are small sample studies and mostly retrospective. Recently, a meta-analysis of the results of 1158 patients in 15 studies was published and the sensitivity and the specificity of

Address for Correspondence: Mine Araz MD, Ankara University Faculty of Medicine, Department of Nuclear Medicine, Ankara, Turkey
Phone: +90 312 595 64 45 **E-mail:** minesoylu@yahoo.com **ORCID-ID:** orcid.org/0000-0001-6467-618X
Received: 06.11.2018 **Accepted:** 08.11.2018

18F-FDG PET/CT were 86% and 88%, respectively (7,8,9,10). The sensitivity and specificity of 18F-FDG PET/CT in restaging in 104 patients with renal cell carcinoma (RCC) at postoperative 2nd year were 74% and 80%, respectively. In this series, follow-up treatment strategies were changed in 43% of patients with 18F-FDG PET/CT. In this study, patients with and without pathologic uptake in 18F-FDG PET/CT were compared in terms of survival, and three-year progression-free survival and five-year overall survival rates were significantly lower in patients with positive PET/CT compared to patients with normal PET/CT (20% vs 67% for progression-free survival, 19% vs 69% for overall survival). Thus, 18F-FDG PET/CT can also be used as a prognostic marker in the follow-up of patients with kidney tumors, besides its ability to detect recurrence or metastasis (11). However, routine use is not recommended with existing data and the results of prospective studies to be performed in large patient groups are needed in order to better determine its role in the staging (Table 1).

In RCC, partial/radical nephrectomy or local ablative treatments are performed as definitive treatment in the presence of local disease. In advanced stage disease, anti-angiogenic agents or immune checkpoint inhibitors targeting the vascular endothelial growth factor pathway are used alone or in combination. Since these treatments are very expensive and require close follow-up in terms of the side effects profile, it is important to determine the patients who will benefit from the treatment in the early period in order to prevent both complications and unnecessary treatment costs. As the response evaluation criteria in solid tumors (RECIST) criteria predict, only size-based assessment may not reflect the actual clinical response in this patient group, especially in patients with bone metastasis. A clinical response can be achieved and survival may be prolonged, even if the lesion size is very small or the lesion is growing. Therefore, other methods were searched for the evaluation of the actual treatment response and 18F-FDG, which is the most frequently used agent for evaluating the metabolic response, was tried. When the data of a few studies were examined, it was demonstrated that its role might be important in the evaluation of response in patients using tyrosine kinase inhibitors, that the change between baseline maximum standardized uptake value (SUV_{max}) values and post-treatment SUV_{max} values could be prognostically significant and that the prognosis was worse in patients with higher activity in baseline 18F-FDG PET/CT study (12,13,14,15,16,17,18,19,20,21).

18F Florotymidine (18F-FLT) PET/CT

Another PET agent, which is tried for restaging in the follow-up of RCC, is 18F-FLT. 18F-FLT is a proliferation agent that remains in the cell by phosphorylation with thymidine kinase in proliferating tumors. Since thymidine is not a substrate of phosphorylase, it undergoes glucuronidation and is kept intensely in the liver and bone marrow in the body (22). In a multicenter study comparing the role of 18F-FDG PET/CT with 18F-FLT PET/CT in evaluating the treatment response of patients treated with sunitinib for diagnosis of metastatic RCC, it has been reported that baseline 18F-FDT PET/CT has a prognostic value, and that 18F- FLT PET/CT does not have such a benefit but it can be used much earlier in the evaluation of response to treatment than in 18F-FDG (1-2 weeks) (23).

Ga-68 Prostate-specific membrane antigen PET/CT

Renal cell cancers are highly vascular tumors. A high (75-97%) expression of PSMA was shown in the neovascularization bed (24). Therefore, Ga-68 PSMA was also tested in the diagnosis and follow-up of RCC. Although it is not effective in demonstrating primary tumor due to renal excretion, it is an agent that can be useful in the characterization of lesions that are considered as suspicious by conventional methods (25). Higher uptake is observed in clear cell carcinoma than in papillary type (26,27). In the literature, the data on this subject consisted of case reports and case series, and the sensitivity and positive predictive value of Ga-68 Prostate-specific membrane antigen (PSMA) PET/CT were better compared to CT (92% vs 69% and 97% vs 80%) (28).

Tc-99m Myocardial Perfusion Imaging Test SPECT/CT

Benign and malignant differentiation cannot be performed by conventional methods in 14% of operated T1 kidney masses (<4 cm), and pathological results of 20-30% of operated cases are reported as benign. Thus, although no PET agent can be shown for preoperative characterization of primary renal masses, there is a SPECT agent that may be useful. Tc-99m MIBI is a nonspecific tumor agent used for imaging by conventional gamma cameras. In benign and malignant tumors with increased metabolic rate, it is retained in mitochondria within the cell (29). Because oncocytomas contain more mitochondria than other types of RCC, they show higher Tc-99m MIBI uptake (30). When the results of the few studies on this subject were evaluated, Tc-99m MIBI was positive in almost all of the

Table 1. Diagnostic value of 18F-FDG PET/CT in staging and re-staging of renal tumors

Authors	Number of Patients	P/R	Indication	Sensitivity (%)	Specifity (%)	Accuracy rate (%)
Kang D et al. (5)	66	R	S	Primary tumor: 60, RPLN: 75, Distant metastasis: 75-77.3	Primary tumor: 100 RPLN: 100 Distant metastasis: 97-100	-
Özülker et al. T (8)	18	P	S	Primary tumor: 46.6	Primary tumor: 66.6	50
de Llano et al. S (9)	58	R	RS	80.56	86.36	58.7
Kumar et al. (10)	63	R	RS	90	91	90
Alongi P et al. (11)	104	R	RS	74	80	-

P: Prospective, R: Retrospective, S: Staging, RS: Restaging, RPLN: Retroperitoneal lymph node

patients who were diagnosed as oncocytoma pathologically and who were evaluated with Tc-99m MIBI SPECT/CT in the preoperative period, and Tc-99m MIBI uptake was not observed in patients diagnosed as having other RCC subtypes. Sensitivity for oncocytomas was reported as 83-100% (31). In a recent study, Tc-99m MIBI SPECT/CT was performed in 48 patients who had T1 tumors before the nephrectomy, and Tc-99m MIBI SPECT/CT was positive in nine patients with pre-operative benign diagnosis. Out of these nine patients, pathology report was compatible with oncocytoma in seven patients and chromophobe RCC in two patients. Five patients with negative Tc-99m MIBI SPECT/CT were confirmed to have RCC in the postoperative period (32).

Bladder Tumors

18F-FDG PET/CT

Its role in the detection of primary bladder tumor is limited due to urinary excretion of radiopharmaceuticals, as in all urologic tumors. No superiority to CT or MRI was demonstrated (33). In lymph node staging, the sensitivity was reported as 46-82%, the specificity was 89-97%, and the accuracy rate was reported as 84-92%. It was reported that it contributed to the conventional imaging methods in 20-40% of the patients and caused a change in treatment management in 68% (34,35,36,37). In order to determine its role in restaging after primary treatment, large series are needed. In a study conducted in 35 patients, it was reported that 17% of the patients had a change in the planned treatment strategy after 18F-FDG PET/CT (38,39). There are publications showing that it can be useful than conventional methods in the differentiation of residual tumor and necrosis for evaluation of neoadjuvant chemotherapy response (40,41). It was reported that occult metastases which cannot be demonstrated by radiological imaging methods in patients with muscle invasive bladder tumor could be demonstrated by 18F-FDG PET/CT and that preoperative 18F-FDG PET/CT positive patients have worse survival compared to negative patients (median overall survival 14 vs 50 months, progression-free survival 16 vs 50 months, $p<0.001$). In addition, the presence of extravesical lesion was shown to be an independent prognostic marker by multiple variance analysis (42,43) (Table 2).

C-11 Choline PET/CT

C-11 choline is phosphorylated by choline kinase after being taken into the cell and incorporated into the structure of cell membrane phospholipids. C11-choline uptake was also increased in tumors with increased proliferation rates (44).

In the functional imaging of bladder tumors, agents with less urinary excretion than 18F-FDG were tested. Since C-11 choline is a radiopharmaceutical with short half-life, it is thought that the need for faster imaging after injection would minimize handicaps due to physiological urinary excretion. However, in a few studies, the sensitivity in demonstrating lymph node metastases before radical cystectomy was found to be low. For this purpose, its superiority to CT has not been proved. It may be more useful in patients with recurrence after cystectomy (Table 2) (45,46,47,48).

C-11 Acetate PET/CT

In the literature, the accuracy rates of CT and MRI and C-11 acetate PET/CT have been shown to be similar and it is stated that it is not superior to C-11 choline (49,50). In a recent study by Salminen et al. (51), C-11 acetate PET/MR has been reported to have high sensitivity and accuracy rates in detecting muscle invasive bladder cancer and response to neoadjuvant chemotherapy in these patients and to have limited success in lymph node staging (Table 2).

Prostate Cancer

Ga-68 PSMA PET/CT

Prostate-specific membrane antigen (PSMA) is an integral protein found in the neovascularized endothelial cell membrane, not in the tumor itself. In prostate cancer, it is 10 times more expressed than non-cancerous prostate. In the literature, there are studies conducted with more than one PSMA ligand labeled with Ga-68 and the most widely used is PSMA 11 (52,53,54).

Ga-68 PSMA uptake is known to increase in dedifferentiated, metastatic, hormone refractory disease. PSMA expression level is closely related to Gleason score, serum PSA level and prognosis (55,56,57). In demonstration of primary tumor in moderate-high-risk disease, the sensitivity and specificity of

Table 2. Diagnostic value of 18F-FDG, C-11 choline and C-11 acetate PET in staging and re-staging of bladder tumors

Authors	Number of Patients	P/R	Radio-pharmaceutical used	Indication	Sensitivity	Specifity (%)	Accuracy Rate (%)	Changes in clinical approach
Apolo AB et al. (34)	47	P	18F-FDG	S	87	88	-	-
Swinnen G et al. (36)	51	P	18F-FDG	S	46	97	84	-
Jadvar H et al. (38)	35	R	18F-FDG	RS	-	-	-	17
Kibel AS et al. (42)	43	P	18F-FDG	S	70	94	-	-
Drieskens O et al. (39)	40	P	18F-FDG	S	60	88	78	-
Gofrit et al. (46)	18	R	C-11 Choline	S	100	92	-	-
Brunocilla E et al. (47)	26	P	C-11 Choline	S	43	84	-	-
de Jong et al. (48)	18	R	C-11 Choline	S	67	100	-	-
Vargas et al. (49)	16	P	C-11 Acetate	S	100	71	-	-

P: Prospective, R: Retrospective, S: Staging, RS: Restaging

were 58% and 82%, respectively, and were 64% and 94%, respectively, for Ga-68 PSMA PET/CT. These values are even higher (76% and 97%) when Ga-68 PET imaging is combined with MRI, which is known to be superior to CT in soft-tissue imaging. This difference was found to be statistically significant between the successes of all three studies (p=0.03) (58). In the literature, there are new publications demonstrating the superiority of Ga-68 PSMA PET/MR combination only to MR (59,60). PET/MR studies, which can be performed in a single session of multiparametric MR, which is the anatomical imaging method with the highest accuracy and sensitivity in prostate cancer, with functional data provided by Ga-68 PSMA PET, are predicted to be used as a routine for imaging in prostate cancer patients in centers with PET/MRI facilities (61).

The most commonly used indication of Ga-68 PSMA PET/CT in prostate cancer is re-staging in patients with biochemical recurrence after primary treatment. The effectiveness of Ga-68 PSMA PET/CT at this stage has been demonstrated in numerous studies. In general, while the lesion detection rate is around 80%, there is a direct relationship between the serum PSA levels and the success of the examination. In a study, the detection rate was calculated as 58% in patients with serum PSA level of 0.2-1.0 ng/mL, 76% in patients with serum PSA level of 1-2 ng/mL and 95% in patients with serum PSA level of > 2 ng/mL. In a recent study, Ga-68 PSMA PET/CT was performed in 117 patients for biomechanical recurrence, and it was reported that Ga-68 PSMA PET/CT changed treatment strategy in 62-76% of patients and that 86% of these patients were given treatment for metastases detected by Ga-68 PET/CT (58). In these patients, Ga-68 PSMA PET/CT can show lymph node metastases in unexpected regions such as mesorectal, posterior pelvic region and supraclavicular region, and can detect occult metastases in lymph nodes below 1 cm that are not suspected radiologically (Figure 1). The sensitivity and specificity in lymph node assessment were 80% and 97%, respectively. It was found

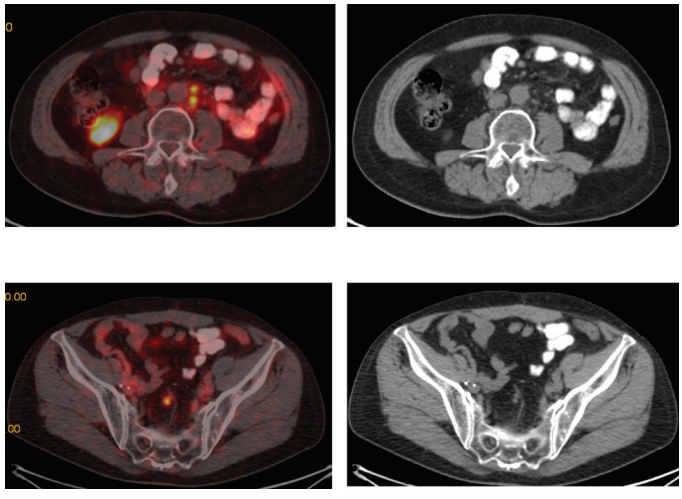

Figure 1. Millimetric lymph nodes in the paraaortic and presacral area in thoracoabdominopelvic CT of a 64-year-old patient who had pathology result of adenocarcinoma (Gleason 4+5) after radical prostatectomy and who developed PSA recurrence (tPSA=23.48 ng/mL) after radiotherapy. Ga-68 PSMA PET/CT showed intense pathological activity in these lymph nodes that did not reach the pathological dimension

to be more successful than bone scintigraphy in demonstrating bone lesions (62,63,64,65,66) (Table 3).

In a recently published meta-analysis, the effect of Ga-68 PSMA PET/CT on the treatment plan of the patients was investigated, and it was reported that Ga-68 PSMA PET/CT caused a change in the treatment plan in 54% of the patients, that the number of patients with systemic treatment decreased significantly and that the number of patients undergoing radiotherapy, focal therapy and surgery increased (67).

It has been reported that performing pre-treatment Ga-68 PSMA PET/CT for patients planned to receive primary or salvage RT may cause changes in the RT plan in 20-60% of patients. A better clinical response was found in patients with negative Ga-68 PSMA PET/CT before RT compared to positive results. A better response to RT is expected in patients with micrometastasis that is too small to be detected even with CT. It has been shown in a small number of small-scale studies that it was also successful in the evaluation of RT response in patients who developed biochemical recurrence after RT (68,69,70,71). It is also used to evaluate the response to treatment in patients under hormone therapy (Figure 2).

Although it has been introduced as a specific agent for prostate cancer, in recent years, incidental Ga-68 PSMA uptake has been reported in numerous benign and malign pathologies, except for prostate cancer. In patients diagnosed with prostate cancer, a secondary malignancy or benign events should be kept in mind in clinical interpretation when Ga-68 PSMA uptake is detected in atypical or unexpected localizations (72).

Although Ga-68 PSMA PET/CT is successful in showing occult lymph node metastases, <5 mm lymph nodes can be omitted with the partial volume effect under the PET resolution limit. Neuroendocrine differentiation was reported in prostate cancer as another cause of false negativity for Ga-68 PSMA PET/CT. In this group of patients, imaging with Ga-68 labeled DOTA peptides may be more appropriate (73,74,75,76,77).

C-11 Choline PET/CT

C-11 Choline is a PET agent that has been used for many years in prostate cancer, but there are many new studies reporting the superiority of Ga-68 PSMA PET/CT to C-11 Choline PET/CT in recurrent disease. While C-11 Choline seems to be advantageous because urinary excretion is less than that of Ga-68 PSMA, some lesions can be omitted because of its short half-life and need for imaging with short-term and rapid procedures. In addition, because it is a nonspecific agent compared to PSMA, numerous pathologies are known to cause false positivity (76,77).

F-18 Fluciclovin PET/CT

Anti-1-amino-3-F-18-fluorocyclobutane-1-carboxylic acid (Fluciclovin) is a synthetic amino acid analogue and is retained in prostate cancer through increased amino acid transport. It has been shown to be effective as a radiopharmaceutical in a large number of patients in prostate cancer and was approved by Food and Drug Administration (FDA) in 2016 for the re-staging of patients with PSA recurrence after primary treatment (78).

In a prospective clinical study comparing the role of Fluciclovin PET/CT, PET/MR and multiparametric MRI in the diagnosis of primary prostate cancer, it was shown that quantitative values obtained from Fluciclovin PET images were correlated with Gleason score but were not superior to multiparametric MR in detecting lesion. In this case, it was concluded that hybrid PET/MR images may be useful in prostate biopsies (79).

In a prospective study of 24 patients in whom biochemical response could not be obtained despite a primary treatment other than prostatectomy, the diagnostic power of Fluciclovin PET/CT was found to be significantly higher than multiparametric MRI (94.7% vs 31.6-36.8%). It was reported that this difference was particularly evident in the demonstration of extraprostatic disease, however, the sensitivity of Fluciclovin PET/CT for primary prostate tumor after treatment and the specificity of multiparametric MRI were higher (80).

In a prospective, multicentric study of the data of 213 patients, the efficacy of Fluciclovin PET/CT was investigated in the examination of biochemical recurrence after curative treatment, and in 57% of the patients, recurrence was shown in one or more foci with Flucyclovin PET/CT, and treatment approach was changed in 59% (81).

The most important advantage of Fluciclovin compared to other mentioned PET radiopharmaceuticals is that urinary excretion is significantly less. Thus, small foci present in the prostate bed and pelvic lymph nodes can be shown more easily. However, it has been reported that metastases in these areas may be omitted due to the relatively intense bone marrow and liver activity (78).

In a retrospective study demonstrating the efficacy of Fluciclovin PET/CT in 596 prostate cancer patients, it was reported as 41.4% even in patients with serum PSA levels <0.79 ng/mL. In a study comparing F-18 Fluciclovin PET/CT with Ga-68PSMA PET/CT in a small group of patients, Ga-68 PSMA PET/CT was positive in 7/10 patients, whereas Fluciclovin PET/CT was negative in 8/10 patients. While widespread disease could be demonstrated with Ga-68 PSMA PET/CT in 4/10 patients, it was reported that Fluciclovin PET/CT was negative in these patients (82).

Whole-Body Tc-99m MDP Bone Scintigraphy and 18F-NaF PET/CT

Tc-99m MDP and 18F-NaF are retained in bone lesions by binding to hydroxyapatite crystals. Although the mechanisms of retention are similar, Tc-99m MDP is a SPECT imaging agent used in conventional whole-body bone scintigraphy, and 18F-NaF is used as a positron spreading agent in PET/CT imaging. Generally, 18F-NaF is a more sensitive agent than Tc-99m MDP because of resolution superiority of PET imaging and its success in demonstrating both lytic and blastic lesions. However, because its relatively high cost, harder to obtain due to being a cyclotron product, and adequate and established success of Tc-99m MDP in demonstrating bone metastases in prostate cancer in the present protocols, 18F-NaF PET/CT is indicated only in suspected cases in this patient group. 18F-NaF PET/CT is

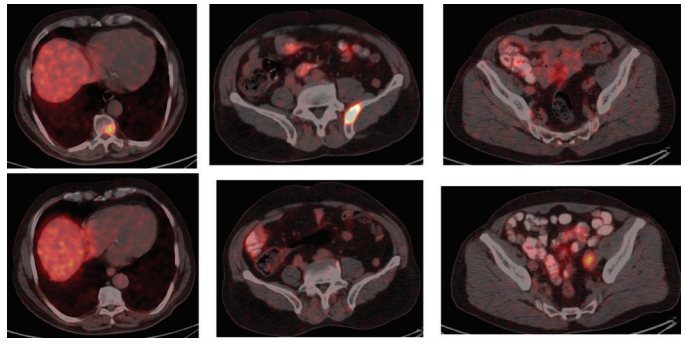

Figure 2. Pathological activity in multiple foci in skeletal system and left obturator lymph nodes in Ga-68 PSMA PET/CT performed in a 77-year-old patient with a prostate needle biopsy result compatible with acinar adenocarcinoma (Gleason 4+5) (First line). It was noted that activity in the bone lesions and lymph nodes defined in the Ga-68 PSMA PET/CT performed for the purpose of evaluating the response to treatment after hormoneotherapy decreased significantly (Second line)

Table 3. The diagnostic value of Ga-68 PSMA PET/CT and PET/MR in staging and re-staging of prostate tumors

Authors	Number of Patients	Indication	Method of screening	P/R	Sensitivity (%)	Specifity (%)	Accuracy Rate	Changes in treatment strategy (%)
Fendler WP et al. (53)	53	S	PET/MR	-	98	94	-	-
Soydal C et al. (57)	104	RS	PET/CT	R	92	80 (PSA <1.4 ng/mL) 90 (PSA <2 ng/mL)	-	-
Grubmüller B et al. (58)	117	RS	PET/CT and PET/MR	R	65 (PSA: 0.2-<0.5 ng/mL) 85.7 (PSA: 0.5-<1) 85.7 (PSA: 1-2) 100 (PSA ≥2)	-	-	74
Maurer t et al. (62)	130	RS	PET/CT and PET/MR	R	65.9	98.9	88.5	-
van Leeuwen PJ et al. (64)	30	RS	PET/CT	P	64	95	-	-
van Leeuwen PJ et al. (65)	70	RS	PET/CT	P	-	-	-	20
Bluemel C et al. (66)	45	RS	PET/CT	R	-	-	-	42.2
Calais J et al. (68)	101	RS	PET/CT	P	-	-	-	53
Habl G et al. (69)	100	RS	PET/CT and PET/MR	R	-	-	-	59

S: Staging, RS: Restaging, P: Prospective, RS: Retrospective, PSA: Prostate specific antigen

most commonly used for imaging before Ra-223 treatment and for evaluating post-treatment response (83,84,85,86).

Testicular Tumors

18F-FDG PET/CT

In the diagnosis of primary testicular tumors, the disease can be diagnosed correctly primarily by ultrasound and then MRI in almost all patients (87,88). It has been shown that metabolic imaging provides more accurate results in studies comparing 18F-FDG PET to conventional CT for staging in patients with primary testicular tumors. The success of detecting radiologically normal sized metastatic lymph nodes was reported as 70%, and this could significantly change the treatment approach in this patient group (89). The sensitivity in seminomatous germ cell tumors (SGCT) is slightly better in comparison with nonseminomatous germ cell tumors (NSGCT) (90-92% vs 77-96%) (90).

In the presence of metastatic disease, residual masses may continue in 55-80% of patients after chemotherapy. In particular, 11-37% of the masses >3 cm can still have live tumor tissue in seminoma cases. Surgical interventions after chemotherapy may be challenging and morbid due to fibrosis. For this reason, it is important to distinguish between live tumor tissue and fibrosis before surgery. 18F-FDG PET/CT has been used for many years for this indication and there are studies in the literature about its role in postoperative follow-up of testicular tumors (91,92,93). In a meta-analysis, for this purpose, sensitivity was reported as 78%, specificity as 86%, and overall accuracy rate as 84% in SGCT. 18F-FDG PET/CT has been shown to be more successful in lesions greater than three centimeters (94). The success in predicting live tumor tissue decreases to 56% in NSGCT (95). Since residual masses may contain up to 40% mature teratoma in this patient group, necrosis-live tissue distinction may not be clearly performed with 18F-FDG PET/CT (96). Prospective, large-scale studies are needed to clarify the role of 18F-FDG PET/CT in NSGCT (Table 4).

18F-FLT PET/CT

The fact that 18F-FDG uptake is observed in false positive lesions in inflammatory lesions has led to the hypothesis that more accurate results can be obtained with other tumor-specific agents in the differentiation of live tumor-necrosis or fibrosis. In a small-scale study of 18F-FLT, a cell proliferation marker, its success in evaluating early response to treatment was investigated. Although false positivity rates could be reduced by 18F-FLT in this study, the presence of live tumor tissue in residual masses could not be ruled out with 18F-FLT, as negative predictive value was not high enough (97).

Conclusion

• 18F-FDG PET/CT in RCC is successful in staging in high-risk disease and demonstrating response to treatment in patients with metastatic disease. However, there is a need for further studies on routine use. Tc-99m MIBI SPECT/CT has high sensitivity and specificity in the malignant-benign differentiation of indeterminate renal masses.

• 18F-FDG PET/CT has a role in staging and re-staging of muscle-invasive bladder cancer, and can provide an idea about prognosis.

• Although not involved in the metabolic characterization of primary scrotal masses, 18F-FDG PET/CT is useful in the staging, restaging and follow-up of testicular tumors, especially in the evaluation of seminoma patients with a >3 cm residual retroperitoneal lesion after treatment. The role of imaging with F-18 and C-11 labeled other radiopharmaceuticals in order to reduce the rate of false negativity associated with physiological renal clearance of 18F-FDG has not yet been elucidated.

• Ga-68 PSMA PET/CT in prostate cancer has high sensitivity in every stage, especially in patients with biochemical recurrence and its use is becoming more common. In addition, conventional bone scintigraphy with Tc-99m MDP is still sufficient for imaging bone metastases. 18F-NaF PET/CT can be used as a more expensive but more sensitive alternative in selective cases, such as patients who are scheduled for treatment with Ra-223.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.A., Y.Ü., Design: M.A., Y.Ü., Data Collection or Processing: M.A., Y.Ü., Analysis or Interpretation: M.A., Y.Ü., Literature Search: M.A., Y.Ü., Writing: M.A., Y.Ü.

Conflict of Interest: No conflict of interest was declared by the authors.

Table 4. Diagnostic value of 18F-FDG PET and PET/CT in staging and re-staging of testicular tumors

Authors	Number of Patients	P/R	Screening	Indication	Patology (S/NS)	Sensitivity (%)	Specifity (%)	Accuracy Rate (%)
Lassen U et al. (89)	46	R	PET	RS	NS	70	100	93
Ambrosini V et al. (90)	121	R	PET/CT	RS	S ve NS	S: 92 NS:77	S: 84 NS: 95	-
Oechsle K et al. (95)	121	P	-	RS	NS	70	48	-
Bachner et al. (91)	127	R	PET	RS	S	67	82	-
Siekiera et al. (92)	37	R	PET/CT	RS	S	100	94	-
Hinz S et al. (93)	20	P	PET	RS	S	100	47	-

P: Prospective, R: Retrospective, RS: Restaging S: Seminomatous, NS: Non-seminomatous tumor

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Bagheri MH, Ahlman MA, Lindenberg L et al. Advances in medical imaging for the diagnosis and management of common genitourinary cancers. Urol Oncol 2017;35:473-491. [doi: 10.1016/j.urolonc.2017.04.014]
2. Kamel EM, Jichlinski P, Prior JO et al. Forced diuresis improves the diagnostic accuracy of 18F-FDG PET in abdominopelvic malignancies. J Nucl Med 2006; 47:1803-1807.
3. Ozülker T, Ozülker F, Ozbek E et al. A prospective diagnostic accuracy study of F-18 fluorodeoxyglucose-positron emission tomography/computed tomography in the evaluation of indeterminate renal masses. Nucl Med Commun 2011;32:265-272.
4. Ferda J Ferdova E, Hora M et al. 18F-FDG-PET/CT in potentially advanced renal cell carcinoma: a role in treatment decisions and prognosis estimation. Anticancer Res 2013;33:2665-2672.
5. Kang DE, White RL, Zuger JH, et al. Clinical use of fluorodeoxyglucose F 18 positron emission tomography for detection of renal cell carcinoma. J Urol 2004;171:1806-1809.
6. Wang HY, Ding HJ, Chen JH, et al. Meta-analysis of the diagnostic performance of [18F] FDG-PET and PET/CT in renal cell carcinoma. Cancer Imaging 2012;12:464-474.
7. Ma H, Shen G, Liu B et al. Diagnostic performance of 18F-FDG PET or PET/CT in restaging renal cell carcinoma: a systematic review and meta-analysis. Nucl Med Commun 2017;38:156-163
8. Ozülker T, Ozülker F, Ozbek E, et al . A prospective diagnostic accuracy study of F-18 fluorodeoxyglucose-positron emission tomography/computed tomography in the evaluation of indeterminate renal masses. Nucl Med Commun 2011;32:265-272
9. de Llano S RM, Jiménez-Vicioso A, Mahmood S, et al. Clinical impact of (18)F-FDG PET in management of patients with renal cell carcinoma. Rev Esp Med Nucl 2010;29:12-19.
10. Kumar R, Shandal V, Shamim SA, et al. Role of FDG PET-CT in recurrent renal cell carcinoma. Nucl Med Commun 2010;31:844-850.
11. Alongi P, Picchio M, Zattoni F, et al. Recurrent renal cell carcinoma: clinical and prognostic value of FDG PET/CT. Eur J Nucl Med Mol Imaging 2016;43:464-473
12. Revheim ME, Winge-Main AK, Hagen G, et al. Combined positron emission tomography/computed tomography in sunitinib therapy assessment of patients with metastatic renal cell carcinoma. Clin Oncol 2011;23:339-343.
13. Vercellino L, Bousquet G, Baillet G, et al. 18F-FDG PET/CT imaging for an early assessment of response to sunitinib in metastatic renal carcinoma: preliminary study. Cancer Biother Radiopharm. 2009;24:137-144.
14. Caldarella C, Muoio B, Isgrò MA, et al . 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;48:219-227.
15. Kelly-Morland C, Rudman S, Nathan P., et al. Evaluation of treatment response and resistance in metastatic renal cell cancer (mRCC) using integrated 18 F–Fluorodeoxyglucose (18 F–FDG) positron emission tomography/magnetic resonance imaging (PET/MRI); The REMAP study. BMC Cancer 2017;17:392 [doi: 10.1186/s12885-017-3371-9]
16. Vasudev NS, Goh V, Juttla J K., et al. Changes in tumour vessel density upon treatment with anti-angiogenic agents: relationship with response and resistance to therapy. Br. J. Cancer 2013;109:1230-1242.
17. Ranieri G, Marech I, Niccoli Asabella A, et al. Tyrosine-kinase inhibitors therapies with mainly Anti-Angiogenic activity in advanced renal cell carcinoma: Value of PET/CT in Response Evaluation. Eur J Cancer 2009;45:228-247.
18. Gofrit ON, Orevi M. Diagnostic challenges of kidney cancer: a systematic review of the role of positron emission tomography-computerized tomography. J. Urol 2016;196:648-57.
19. van der Veldt AA, Meijerink MR, van den Eertwegh A J, et al. Sunitinib for treatment of advanced renal cell cancer: primary tumor response. Clin. Cancer Res 2008;14:2431-2436.
20. Namura K, Minamimoto R, Yao M, et al.. Impact of maximum standardized uptake value (SUVmax) evaluated by 18-Fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (18 F-FDG-PET/CT) on survival for patients with advanced renal cell carcinoma: a preliminary report. BMC Cancer 2010; 10:667
21. Kayani I, Avril N, Bomanji J, et al. Sequential FDG-PET/CT as a biomarker of response to sunitinib in metastatic clear cell renal cancer. Clin Cancer Res. 2011;17:6021-6028
22. Rasey JS, Grierson JR, Wiens LW et al.. Validation of FLT uptake as a measure of thymidine kinase-1 activity in A549 carcinoma cells. J Nucl Med 2002;43:1210-1217.
23. Horn KP, Yap JT, Agarwal N, et al. FDG and FLT-PET for early measurement of response to 37.5 mg daily sunitinib therapy in metastatic renal cell carcinoma. Cancer Imaging 2015;15:15.
24. Baccala A, Sercia L, Li J, et al. Expression of prostate-specific membrane antigen in tumor-associated neovasculature of renal neoplasms Urology 2007;70:385-390.
25. Sawicki LM, Buchbender C, Boos J, et al. Diagnostic potential of PET/CT using a 68 Ga-labelled prostate-specific membrane antigen ligand in whole-body staging of renal cell carcinoma: initial experience. Eur J Nucl Med Mol Imaging 2017;44:102-107
26. Backhaus P, Noto B, Avramovic N et al. Targeting PSMA by radioligands in non-prostate disease-current status and future perspectives Eur J Nucl Med Mol Imaging 2018;45:860-887.
27. Yin Y, Campbell SP, Markowski MC et al. Inconsistent detection of sites of metastatic Non-Clear Cell Renal Cell Carcinoma with PSMA-targeted [18F]DCFPyL PET/CT. Mol Imaging Biol 2018 Sep 14. doi: 10.1007/s11307-018-1271-1272.
28. Rhee H, Blazak J, Tham CM, et al. Pilot study: use of gallium-68 PSMA PET for detection of metastatic lesions in patients with renal tumour. EJNMMI Res 2016;6:76
29. Moretti JL, Hauet N, Caglar M, et al. To use MIBI or not to use MIBI? That is the question when assessing tumour cells. Eur J Nucl Med 2005;32:836-842.
30. Gormley TS1, Van Every MJ, Moreno AJ. Renal oncocytoma: preoperative diagnosis using technetium 99m sestamibi imaging. Urology 1996;48:33-39.
31. Reynolds MA, Porter KK. Characterizing indeterminate renal masses with molecular imaging: the role of 99mTc-MIBI SPECT/CT. Curr Urol Rep 2017;18:86
32. Sheikhbahaei S, Jones CS, Porter KK, et al. Defining the added value of 99mTc-MIBI SPECT/CT to conventional cross-sectional imaging in the characterization of enhancing solid renal masses Clin Nucl Med 2017;42:e188-e193
33. Zhang H, Xing W, Kang Q, et al. Diagnostic value of [18 F] FDG-PET and PET/CT in urinary bladder cancer: a meta-analysis. Tumor Biol. 2015;36(5):3209-3214.
34. Apolo AB, Riches J, Schöder H, 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;28:3973-3978.
35. Mertens LS, Fioole-Bruining A, Vegt E, et al. Impact of 18F-fluorodeoxyglucose (FDG)-positron-emission tomography/computed tomography (PET/CT) on management of patients with carcinoma invading bladder muscle. BJU Int 2013;112:729-734 [doi: 10.1111/bju.12109].
36. Swinnen G, Maes A, Pottel H, et al .FDG-PET/CT for the preoperative lymph node staging of invasive bladder cancer Eur Urol 2010;57:641-647.
37. Lu YY Chen JH, Liang JA, et al. Clinical value of FDG PET or PET/CT in urinary bladder cancer: a systemic review and meta-analysis. Eur J Radiol 2012; 81:2411-2416

38. Jadvar H, Quan V, Henderson RW, et al. [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(1):42-47
39. Drieskens O, Oyen R, Van Poppel H, et al. FDG-PET for preoperative staging of bladder cancer. Eur J Nucl Med Mol Imaging 2005;32:1412-7.
40. Meeks JJ, Bellmunt J, Bochner BH, et al. A systematic review of neoadjuvant and adjuvant chemotherapy for muscle-invasive bladder cancer Eur Urol 2012;62(3):523-533.
41. Mertens LS, Fioole-Bruining A, van Rhijn, 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(5):1687-1691.
42. Kibel AS, Dehdashti F, Katz M D, et al. Prospective study of [18F] fluorodeoxyglucose positron emission tomography/computed tomography for staging of muscle-invasive bladder carcinoma J Clin Oncol 2009;27(26):4314-4320.
43. Mertens LS, Mir MC, Scott AM, et al. 18F-fluorodeoxyglucose–positron emission tomography/computed tomography aids staging and predicts mortality in patients with muscle-invasive bladder cancer. Urology 2014;83:393-398.
44. Takesh M. Kinetic Modeling Application to (18)F-fluoroethylcholine positron emission tomography in patients with primary and recurrent prostate cancer using two-tissue compartmental model World J Nucl Med 2013;12(3):101-110.
45. Kim SJ, Koo PJ, Pak K et al. Diagnostic accuracy of C-11 choline and C-11 acetate for lymph node staging in patients with bladder cancer: a systematic review and meta-analysis. World Journal of Urology 2018;36:331-340.
46. Gofrit ON, Mishani E, Orevi M, et al. Contribution of 11C-choline positron emission tomography/computerized tomography to preoperative staging of advanced transitional cell carcinoma J Urol 2006;176:940-944.
47. Brunocilla E1, Ceci F, Schiavina R, 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:e308-312.
48. De Jong IJ, Pruim J, Elsinga PH, et al. Visualisation of bladder cancer using 11 C-choline PET: first clinical experience. Eur J Nucl Med Mol Imaging 2002; 29:1283-1288.
49. Vargas HA, Akin O, Schöder H, et al. Prospective evaluation of MRI, 11C-acetate PET/CT and contrast-enhanced CT for staging of bladder cancer. Eur J Radiol 2012;81:4131-4137.
50. Orevi M, Klein M, Mishani E, et al. 11C-acetate PET/CT in bladder urothelial carcinoma: intraindividual comparison with 11C-choline. Clin Nucl Med 2012;37:e67-e72.
51. Salminen A, Jambor I, Merisaari H. 11C-acetate PET/MRI in bladder cancer staging and treatment response evaluation to neoadjuvant chemotherapy: a prospective multicenter study (ACEBIB trial). Cancer Imaging 2018;18:25.
52. Silver DA, Pellicer I, Fair WR, et al. Prostate-specific membrane antigen expression in normal and malignant human tissues. Clin Cancer Res 1997;3:81-85.
53. Fendler WP, Eiber M, Beheshti M, et al. 68 Ga-PSMA PET/CT: Joint EANM and SNMMI procedure guideline for prostate cancer imaging: version 1.0. Eur J Nucl Med Mol Imaging 2017;44:1014-1024.
54. Ghosh A, Heston WD. Tumor target prostate specific membrane antigen (PSMA) and its regulation in prostate cancer. J Cell Biochem 2004;91:528-539.
55. Ross JS, Sheehan CE, Fisher HA, Correlation of primary tumor prostate-specific membrane antigen expression with disease recurrence in prostate cancer. Clin Cancer Res 2003;9:6357-6362.
56. Eiber M, Weirich G, Holzapfel K et al. Simultaneous 68Ga-PSMA HBED-CC PET/MRI Improves the Localization of Primary Prostate Cancer. Eur Urol 2016;70:829-836.
57. Soydal C, Urun Y, Suer E, et al. PSA levels as a predictor of 68Ga PSMA PET/CT positivity in patients with prostate cancer? Q J Nucl Med Mol Imaging 2018 May 10. doi: 10.23736/S1824-4785.18.03056-X.
58. Grubmüller B, Baltzer P, D'Andrea D, et al. 68 Ga-PSMA 11 ligand PET imaging in patients with biochemical recurrence after radical prostatectomy–diagnostic performance and impact on therapeutic decision-making Eur J Nucl Med Mol Imaging 2018;45:235-242.
59. Park SY, Zacharias C, Harrison C et al. Gallium 68 PSMA-11 PET/MR imaging in patients with intermediate- or high-risk prostate cancer. Radiology 2018;288:495-505.
60. Hicks RM, Simko JP, Westphalen AC et al. Diagnostic Accuracy of 68Ga-PSMA-11 PET/MRI compared with multiparametric MRI in the detection of prostate cancer. Radiology 2018;18:180788. doi: 10.1148/radiol.2018180788.
61. Civelek AC. 68Ga-PSMA-11 PET: better at detecting prostate cancer than multiparametric MRI? Radiology. 2018 Sep 18:181981. doi: 10.1148/radiol.2018181981.
62. Maurer T, Gschwend JE, Rauscher I, et al. Diagnostic efficacy of 68gallium-PSMA positron emission tomography compared to conventional imaging for lymph node staging of 130 consecutive patients with intermediate to high risk prostate cancer. J Urol 2016;195:1436-1443.
63. Hijazi S, Meller B, Leitsmann C, et al. See the unseen: Mesorectal lymph node metastases in prostate cancer. Prostate 2016;76(8):776-780.
64. Leeuwen PJ, Emmett L, Ho B, et al. Prospective evaluation of 68Gallium-prostate-specific membrane antigen positron emission tomography/computed tomography for preoperative lymph node staging in prostate cancer. BJU Int 2016;119:209-215.
65. van Leeuwen PJ, Stricker P, Hruby G, et al. (68) Ga-PSMA has a high detection rate of prostate cancer recurrence outside the prostatic fossa in patients being considered for salvage radiation treatment. BJU Int 2016;117:732-739.
66. Bluemel C, Linke F, Herrmann K, et al. Impact of 68 Ga-PSMA PET/CT on salvage radiotherapy planning in patients with prostate cancer and persisting PSA values or biochemical relapse after prostatectomy. EJNMMI Res 2016;6:78.
67. Han S, Woo S, Kim YJ et al. Impact of 68Ga-PSMA PET on the Management of Patients with Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol 2018;74:179-190.
68. Calais J, Fendler WP, Eiber M, Impact of 68Ga-PSMA-11 PET/CT on the Management of Prostate Cancer Patients with Biochemical Recurrence. J Nucl Med 2018;59:434-441.
69. Habl G, Sauter K, Schiller K, et al. 68Ga-PSMA-PET for radiation treatment planning in prostate cancer recurrences after surgery: Individualized medicine or new standard in salvage treatment Prostate 2017;77:920-927.
70. Hruby G, Eade T, Kneebone A, et al. Delineating biochemical failure with 68Ga-PSMA-PET following definitive external beam radiation treatment for prostate cancer. Radiother.Oncol 2017;122:99-102.
71. Afshar-Oromieh A, Haberkorn U, Eder M, et al. [68 Ga] Gallium-labelled PSMA ligand as superior PET tracer for the diagnosis of prostate cancer: comparison with 18 F-FECH. Eur J Nucl Med 2012;39:1085-1086.
72. Tosoian JJ, Gorin MA, Rowe SP, et al. Correlation of PSMA-targeted 18F-DCFPyL PET/CT findings with immunohistochemical and genomic data in a patient with metastatic neuroendocrine prostate cancer. Clin Genitourin Cancer 2016;15:e65-e68.
73. Chakraborty PS, Tripathi M, Agarwal KK, et al. Metastatic poorly differentiated prostatic carcinoma with neuroendocrine differentiation: negative on 68Ga-PSMA PET/CT. Clin Nucl Med 2015;40:163-166.
74. Gofrit ON, Frank S, Meirovitz A, et al. PET/CT with 68Ga-DOTA-TATE for diagnosis of Neuroendocrine: differentiation in patients with castrate-resistant prostate cancer. Clin Nucl Med 2017;42:1-6.
75. Umbehr MH, Müntener M, Hany T, et al. The role of 11C-choline and 18F-fluorocholine positron emission tomography (PET) and PET/CT

in prostate cancer: a systematic review and meta-analysis. Eur Urol 2013;64:106-117.

76. Evangelista L, Zattoni F, Guttilla A, et al. Choline PET or PET/CT and biochemical relapse of prostate cancer: a systematic review and meta-analysis. Clin Nucl Med 2013;38:305-314.
77. Beheshti M, Haim S, Zakavi R Impact of 18F-choline PET/CT in prostate cancer patients with biochemical recurrence: influence of androgen deprivation therapy and correlation with PSA kinetics. J Nucl Med 2013;54:833-840.
78. Hofman MS, Iravani A, Nzenza T, Advances in Urologic Imaging: Prostate-Specific Membrane Antigen Ligand PET Imaging. Urol Clin North Am 2018;45:503-524.
79. Jambor I, Kuisma A, Kähkönen E. et al. Prospective evaluation of 18F-FACBC PET/CT and PET/MRI versus multiparametric MRI in intermediate- to high-risk prostate cancer patients (FLUCIPRO trial) Eur J Nucl Med Mol Imaging 2018;45:355-364.
80. Akin-Akintayo O, Tade F, Mittal P et al. Prospective evaluation of fluciclovine (18F) PET-CT and MRI in detection of recurrent prostate cancer in non-prostatectomy patients. Eur J Radiol 2018 May;102:1-8. doi: 10.1016/j.ejrad.2018.02.006.
81. Andriole GL, Kostakoglu L, Chau A et al. The Impact of positron emission tomography with 18F-Fluciclovine on the management of patients with biochemical recurrence of prostate cancer: results from the LOCATE Trial. J Urol 2018;Sep1.pii:S0022-5347(18)43798-43786. [doi: 10.1016/j.juro.2018.08.050].
82. Bach-Gansmo T, Nanni C, Nieh PT, et al. Multisite Experience of the Safety, Detection Rate and Diagnostic Performance of Fluciclovine (18F) Positron Emission Tomography/Computerized Tomography Imaging in the Staging of Biochemically Recurrent Prostate Cancer J Urol 2017;197:676-683.
83. Even-Sapir E, Metser U, Mishani E, et al. The detection of bone metastases in patient with high risk prostate cancer: 99m Tc scintigraphy, SPECT and 18F-fluoride PET. J Nucl Med 2006;47:287-97.
84. Tateishi U, Morita S, Taguri M, et al. A meta-analysis of 18 F-Fluoride positron emission tomography for assessment of metastatic bone tumor Ann Nucl Med 2010; 24:523-31.
85. Apolo AB, Lindenberg L, Shih JH et al. Prospective Study Evaluating Na18F PET/CT in Predicting Clinical Outcomes and Survival in Advanced Prostate Cancer. Nucl Med 2016;57:886-892.
86. Yu EY, Duan F, Muzi M, et al. Castration-resistant prostate cancer bone metastasis response measured by 18F-fluoride PET after treatment with dasatinib and correlation with progression-free survival: results from American College of Radiology Imaging Network 6687 J Nucl Med 2015;56:354-60.
87. Kim W, Rosen MA, Langer JE, et al. US MR imaging correlation in pathologic conditions of the scrotum. Radiographics 2007;27:1239-1253.
88. Cassidy FH, Ishioka KM, McMahon CJ, ve ark.. MR imaging of scrotal tumors and pseudotumors. Radiographics 2010;30:665-683.
89. Lassen U, Daugaard G, Eigtved A, et al. Whole-body FDG-PET in patients with stage I non-seminomatous germ cell tumours. Eur J Nucl Med Mol Imaging 2003;30:396-402.
90. Ambrosini V, Zucchini G, Nicolini S, et al. 18F-FDG PET/CT impact on testicular tumours clinical management. Eur J Nucl Med Mol Imaging 2014;41:668-673.
91. Bachner M, Loriot Y, Gross-Goupil M et al. "2-18 Fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) for postchemotherapy seminoma residual lesions: a retrospective validation of the SEMPET trial," Annals of Oncology 2012;23:59-64.
92. Siekiera J, Małkowski B, Jóźwicki W. et al. Can we rely on PET in the follow-up of advanced seminoma patients? Urologia Internationalis 2012;88:405-409.
93. Hinz S, Schrader M, Kempkensteffen C, et al. The role of positron emission tomography in the evaluation of residual masses after chemotherapy for advanced stage seminoma, Journal of Urology 2008;3:936-940.
94. Treglia G, Sadeghi R, Annunziata S, et al. Diagnostic performance of fluorine-18-fluorodeoxyglucose positron emission tomography in the postchemo- therapy management of patients with seminoma: systematic review and meta-analysis. Biomed Res Int 2014;2014:852681.
95. Oechsle K, Hartmann M, Brenner W, et al. [18F]Fluo- rodeoxyglucose positron emission tomography in nonseminomatous germ cell tumors after chemo- therapy: the German multicenter positron emission tomography study group. J Clin Oncol 2008;26:5930-5935.
96. Hartmann JT, Schmoll HJ, Kuczyk MA, et al. Postchemotherapy resections of residual masses from metastatic non-seminomatous testicular germ cell tumors. Ann Oncol 1997;8:531-538.
97. Pfannenberg C, Aschoff P, Dittmann H, et al. PET/CT with 18F-FLT: PET/CT with 18F-FLT: does it improve the therapeutic management of metastatic germ cell tumors? J Nucl Med 2010;51:845-853.