HORMONES 2013, 12(3):327-333

Review

PET and PET/CT imaging in thyroid and adrenal diseases: an update

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ABSTRACT

Positron emission tomography (PET) and PET/computed tomography (PET/CT) with different tracers are imaging methods increasingly used in patients with thyroid and adrenal diseases. The aim of this article is to provide an overview based on literature data about the usefulness of PET imaging in this setting. PET and PET/CT with different tracers have been used in patients with thyroid diseases including differentiated thyroid carcinoma, medullary thyroid carcinoma, and poorly differentiated and anaplastic thyroid carcinoma. The usefulness of ^{18}F-FDG-PET and PET/CT in assessing indeterminate thyroid nodules at fine needle aspiration biopsy and the clinical relevance of thyroid incidental ^{18}F-FDG uptake has also been evaluated. Currently, great interest is being shown in a variety of PET tracers that target specific characteristics of adrenal gland function, allowing a more accurate characterization of adrenal masses and staging of adrenal tumors. Since PET/CT using different tracers is an expensive diagnostic tool which necessitates ionizing radiation exposure, cost-effectiveness studies are needed in order to define the appropriate use of this diagnostic method in various endocrine disorders.

Key words: Adrenal, Endocrine tumors, Endocrinology, Nuclear medicine, PET/CT, Positron emission tomography, Thyroid

INTRODUCTION

Positron emission tomography (PET) and PET/computed tomography (PET/CT) are established diagnostic tools in the management of many solid tumors. PET/CT is a hybrid technique which combines morphological information obtained by the CT component with functional data provided by PET imaging.[1] There is increasing evidence in the literature about the usefulness of PET and PET/CT imaging with different tracers in various endocrine disorders. Fluorine-18-Fluorodeoxyglucose (^{18}F-FDG) is the most frequently used PET tracer in oncology.[1] This glucose analogue is trapped by cells via the glucose transporters (GLUTs). GLUTs overexpression is particularly prevalent in aggressive endocrine tumors; in addition, overexpression of hexokinase-1 promotes ^{18}F-FDG uptake in cancer cells.[2] Several PET tracers

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Received 06-09-2012, Accepted 10-01-2013

other than ^{18}F-FDG have also been used in endocrinology to evaluate different metabolic pathways (Tables 1, 2). For example, Iodine-124 (^{124}I) has been used to study the iodine metabolism in thyroid tumors.[3] Fluorine-18-Dihydroxyphenylalanine (^{18}F-DOPA), which assesses the amino acid uptake, decarboxylation and storage,[4] and Gallium-68-somatostatin analogues (^{68}Ga-SMS), which evaluate the somatostatin receptor status,[5] are PET tracers particularly useful in medullary thyroid carcinoma, paraganglioma/pheochromocytoma and other neuroendocrine tumors (NETs). Fluorine-18-Dopamine (^{18}F-Dopamine) and Carbon-11-Hydroxyephedrine (^{11}C-HED) assess the catecholamine uptake and storage and are useful in NETs and in tumors of the adrenal medulla. Lastly, Carbon-11-Metomidate (^{11}C-Metomidate) and analogues are PET tracers used in the evaluation of lesions of the adrenal cortex.[6]

The aim of this article is to provide an overview about the role of PET and PET/CT with different tracers in thyroid and adrenal diseases

PET AND PET/CT IN THYROID DISEASES

During the last two decades PET and PET/CT with different tracers have been used increasingly in patients with thyroid diseases, including differentiated thyroid carcinoma (DTC), poorly differentiated and anaplastic thyroid carcinoma (PDTC and ATC), and medullary thyroid carcinoma (MTC). The usefulness of these techniques in assessing indeterminate thyroid nodules at fine needle aspiration biopsy (FNAB) and the clinical relevance of thyroid incidental ^{18}F-FDG uptake at PET imaging have been also evaluated.

- PET and PET/CT in differentiated thyroid carcinoma

DTC cells expressing the sodium-iodine symporter take up radioiodine. In a small percentage of DTC

Table 1. Most frequently used PET tracers in thyroid tumors

PET tracers	Function explored	Thyroid tumors evaluated
Fluorine-18 Fluorodeoxyglucose (^{18}F-FDG)	Glucose metabolism	Poorly differentiated and more aggressive thyroid tumors
Iodine-124 (^{124}I)	Iodine metabolism	Differentiated thyroid carcinoma
Fluorine-18-Dihydroxyphenylalanine (^{18}F-DOPA)	Amino acid uptake, decarboxylation and storage	Medullary thyroid carcinoma
Gallium-68-somatostatin analogues (^{68}Ga-SMS)	Somatostatin receptor expression	Medullary thyroid carcinoma

Table 2. Most frequently used PET tracers in adrenal tumors

PET tracers	Function explored	Adrenal tumors evaluated
Fluorine-18 Fluorodeoxyglucose (^{18}F-FDG)	Glucose metabolism	Poorly differentiated and more aggressive adrenal tumors
^{11}C-Metomidate (^{11}C-Metomidate)	Corticosteroids synthesis	Tumors of the adrenal cortex
Fluorine-18-Dihydroxyphenylalanine (^{18}F-DOPA)	Amino acid uptake, decarboxylation and storage	Paraganglioma/Pheochromocytoma
Gallium-68-somatostatin analogues (^{68}Ga-SMS)	Somatostatin receptor expression	Paraganglioma/Pheochromocytoma
Fluorine-18-Dopamine (^{18}F-Dopamine)	Catecholamine uptake and storage	Paraganglioma/Pheochromocytoma
Carbon-11-Hydroxyephedrine (^{11}C-HED)	Catecholamine uptake and storage	Paraganglioma/Pheochromocytoma

the cells are de-differentiated and the radioiodine uptake capacity is lost. These cells multiply more rapidly and are metabolically more active, while their glucose metabolism is increased.[7]

Low-risk patients with DTC are very unlikely to require ^{18}F-FDG-PET or PET/CT as part of initial staging or follow-up. Moreover, to date, ^{18}F-FDG-PET and PET/CT are not recommended for preoperative assessment of DTC.[8] Currently, the most valuable role of ^{18}F-FDG-PET and PET/CT in the work-up of DTC is to be seen in those patients who present with increasing serum thyroglobulin (Tg) levels and a negative diagnostic radioiodine whole-body scan post-thyroidectomy, according to the American Thyroid Association (ATA) guidelines.[8] If no disease sites are identified on conventional imaging or radioiodine whole-body scan or Tg levels are elevated out of proportion to minor disease found on conventional imaging, ^{18}F-FDG-PET or PET/CT should be performed to detect recurrent or metastatic disease.[7,8] A meta-analysis to determine the diagnostic accuracy of ^{18}F-FDG-PET and PET/CT in DTC patients who presented with elevated serum Tg levels post-thyroidectomy and negative radioiodine whole-body scan reported a good diagnostic accuracy of these methods with pooled sensitivity and specificity of 88.5% and 84.7%, respectively. The pooled values of sensitivity increased when only ^{18}F-FDG-PET/CT studies were considered in the analysis (93.5%), demonstrating a superior diagnostic accuracy of PET/CT compared to PET alone.[9]

The current ATA guidelines suggest that FDG-PET or PET/CT should be performed when Tg levels are >10 ng/mL.[8] In any case, no clear cut-off value of Tg can be established in clinical practice.[10]

Clinical evidence is emerging that the performance of ^{18}F-FDG-PET and PET/CT for the detection of Tg-positive and radioiodine-negative metastases of DTC is also improved after thyrotropin stimulation (either by hormone withdrawal or recombinant human thyrotropin administration); however, the clinical significance of this improved diagnostic performance remains uncertain.[11]

^{18}F-FDG-PET or PET/CT in DTC are also useful prognostic factors for identifying which patients with known distant metastases are at highest risk for disease-specific mortality.[12] These methods represent valuable selection tools for identifying those patients who are unlikely to respond to additional radioiodine therapy and may allow the measurement of post-treatment response following external beam irradiation, surgical resection, embolization or systemic therapy.[7,8]

There are increasing literature data about the usefulness of ^{124}I-PET and PET/CT in DTC.[13] Two aspects deserve special mention with regard to the applications of these functional imaging methods: the staging of recurrent/residual disease in DTC and the dosimetry before treatment with Iodine-131 (^{131}I). ^{124}I-PET and PET/CT provide images of higher spatial resolution and lesion contrast than either planar imaging or tomographic imaging with ^{131}I, although the impact of this improved lesion detection compared to ^{131}I imaging in patients with known or suspected metastatic DTC remains to be proven.[7] The combination of ^{18}F-FDG and ^{124}I-PET/CT allows detection of non-iodine-avid lesions and discrimination from simultaneously occurring iodine-positive lesions, thus improving restaging in recurrent DTC.[14] The pre-treatment dosimetry by using ^{124}I-PET may result in a significant alteration in the therapeutic procedure compared to standard therapy with fixed activities of ^{131}I.[13]

- PET and PET/CT in poorly differentiated and anaplastic thyroid carcinoma

PDTC and ATC show aggressive clinical behavior with high glucose metabolism and intense ^{18}F-FDG uptake. In patients with PDTC and ATC, ^{18}F-FDG-PET or PET/CT may be indicated for staging and for prognostic purposes and, in selected cases, for evaluating the efficacy of therapy.[14,15]

- PET and PET/CT in medullary thyroid carcinoma

PET imaging with different tracers is not recommended for routine initial screening of patients with a FNAB and/or serum calcitonin levels suggestive for MTC, but it may have a role in detecting suspected MTC recurrences, based on increased serum calcitonin levels post-thyroidectomy. In fact, MTC recurrences are often difficult to detect using conventional imaging and traditional scintigraphic methods.[16-18] There is increasing evidence in the literature of the beneficial

role of ^{18}F-FDG-PET and PET/CT in recurrent MTC; these methods could be very helpful in detecting MTC recurrences in those patients in whom a more aggressive disease is suspected.[17,19] To date, ^{18}F-DOPA seems to be the most useful PET tracer in detecting recurrent MTC based on rising levels of calcitonin.[20] Nevertheless, the literature focusing on the use of ^{18}F-DOPA-PET or PET/CT in the detection of recurrent MTC still remains limited.[21] Other PET tracers, such as ^{68}Ga-SMS, were also evaluated for this indication in a limited number of studies.[17] At any rate, the different PET tracers reflect different metabolic pathways and seem to show a complementary role in detecting recurrent MTC.[17,20]

- PET and PET/CT in thyroid nodules with indeterminate FNAB and thyroid incidental ^{18}F-FDG uptake

There is great interest in the role of ^{18}F-FDG-PET and PET/CT in addressing histologically non-diagnostic or inconclusive thyroid nodules at FNAB.[22,23] A recent meta-analysis reported a pooled sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 95%, 48%, 39%, 96%, and 60%, respectively. False-negative ratio of ^{18}F-FDG-PET or PET/CT in this setting is low; therefore, these methods may help to identify patients who would benefit from surgery. Conversely, a positive ^{18}F-FDG-PET result does not identify cancer because approximately 50% of these patients had benign nodules.[23] In addition, a recent prospective study demonstrated that adding ^{18}F-FDG-PET/CT findings to neck ultrasonography provides no diagnostic benefit because the sensitivity (77%) and specificity (62%) of ^{18}F-FDG-PET/CT in the presurgical evaluation of indeterminate thyroid nodules are too low to recommend its use routinely.[24] Therefore, incorporation of ^{18}F-FDG-PET or PET/CT into the initial work-up of patients with non-diagnostic or inconclusive cytology before surgery deserves further investigation.

Sometimes ^{18}F-FDG-PET and PET/CT reveal thyroid incidental uptake (TIU) of the tracer which may have a focal or a diffuse pattern. Diffuse TIU at ^{18}F-FDG-PET or PET/CT can be considered at low risk of malignancy, being more likely associated with thyroiditis or diffuse thyroid autonomy. Conversely, focal TIU at ^{18}F-FDG-PET or PET/CT can represent both benign and malignant lesions with a risk of malignancy of about 35%.[25,26] Therefore, a complete work-up including laboratory examinations, ultrasonography and FNAB should usually be obtained to exclude malignant lesions in focal TIU detected by ^{18}F-FDG-PET or PET/CT.

PET AND PET/CT IN ADRENAL DISEASES

Nuclear medicine procedures provide unique functional information in patients with adrenal diseases, which can be particularly useful both in the presence of a hyperfunctioning clinical syndrome for localizing the site of hormonal hyperproduction (i.e. enabling the differential diagnosis between unilateral and bilateral forms), and in the presence of anatomic alteration seen on morphological imaging for characterizing the adrenal lesion (i.e. distinguishing benign from malignant ones). Currently, great interest is being focused on a variety of PET tracers that target specific characteristics of adrenal gland function, allowing an accurate characterization and staging of adrenal tumors.

- Adrenal cortex

Although ^{18}F-FDG is not specific for the adrenal gland, PET and PET/CT using this tracer are able to differentiate benign masses which usually show faint ^{18}F-FDG uptake, from malignant ones which show significantly higher ^{18}F-FDG uptake, with a diagnostic accuracy of 75-100%.[27] A recent systematic review and meta-analysis revealed that most adrenal masses can be characterized as benign or malignant by using ^{18}F-FDG-PET or PET/CT with high sensitivity (97%) and specificity (91%); false positive results can occur in some benign adrenal masses, particularly adenomas.[27] ^{18}F-FDG-PET and PET/CT compare favorably with a CT washout test for the characterization of adrenal masses, so that further imaging tests are generally unnecessary.[27] Furthermore, ^{18}F-FDG-PET and PET/CT may identify extra-adrenal metastatic lesions in malignant adrenal diseases and may also be useful to evaluate tumor response to treatment.[28]

^{11}C-Metomidate is an inhibitor of ^{11}C-hydroxylase, a key enzyme in corticosteroids synthesis. PET with ^{11}C-Metomidate (or its analogues) allows identification of lesions of adrenocortical origin. Therefore, by

using this tracer, adrenal metastases and pheochromocytomas are differentiated from adrenocortical tumors.[29] However, ^{11}C-Metomidate-PET and PET/CT do not allow differentiation between benign and malignant adrenocortical lesions. Furthermore, the short half-life of ^{11}C (20 minutes) limits the use of ^{11}C-Metomidate to centers with on-site cyclotron.[29]

- *Adrenal medulla*

Recently, a wide range of PET radiopharmaceuticals, both specific and non-specific for chromaffin tumors, have emerged as an alternative method to radioiodinated metaiodobenzylguanidine (MIBG) scintigraphy, which is still the most widely used functional imaging technique for localizing pheochromocytoma.[30,31] Specific PET radiopharmaceuticals include ^{11}C-HED, ^{18}F-DOPA and ^{18}F-Dopamine, which are used for imaging purposes, and ^{124}I-MIBG, which is used especially for dosimetric estimates prior to ^{131}I-MIBG therapy; non-specific PET tracers include ^{18}F-FDG and ^{68}Ga-SMS.[30]

The catecholamine analogue ^{11}C-HED was the first positron emitter tracer specific for chromaffin tumors to be used in humans. PET with ^{11}C-HED has been applied in patients with pheochromocytoma, allowing the visualization of both primary and metastatic lesions (90% sensitivity); however, its widespread clinical use is limited by the short physical half-life of ^{11}C, requiring onsite production, and high costs.[32]

Furthermore, ^{18}F-Dopamine, a catecholamine precursor, and ^{18}F-DOPA, an amino acid that is converted by aromatic amino acid decarboxylase to dopamine, provide excellent imaging of pheochromocytomas, with higher diagnostic sensitivity than ^{18}F-FDG and $^{123/131}$I-MIBG, and high specificity.[32,33] Additional advantages of ^{18}F-DOPA and ^{18}F-Dopamine over $^{123/131}$I-MIBG are: short time of imaging, less radiation exposure, no need of thyroid blockade and of withdrawing medication (with ^{18}F-DOPA).[32,34]

^{18}F-FDG is not recommended for initial diagnosis of pheochromocytoma since it is not specific; due to its ability in identifying hypermetabolic lesions, it also depicts adrenocortical cancer and metastatic lesions. Moreover, ^{18}F-FDG has a limited sensitivity, about 70% for solitary benign or malignant pheochromocytoma; nevertheless, it may have a role as an alternative modality in MIBG-negative malignant pheochromocytomas, mainly those with SDHB mutation.[30,32,35]

In addition, ^{68}Ga-SMS are under evaluation for PET imaging in tumors originating from the adrenal medulla; the preliminary data available suggest that ^{68}Ga-SMS-PET and PET/CT may be useful in patients with pheochromocytoma/paraganglioma.[36]

Recent studies with different PET radiopharmaceuticals have shown different results in the various clinical syndromes of pheochromocytoma (sporadic versus familial forms or benign versus malignant forms), supporting the need for an individualized approach guided by the clinical and genetic phenotype. According to recent published EANM guidelines for radionuclide imaging of pheochromocytomas and paragangliomas, there is no clear advantage of PET radiopharmaceuticals over MIBG in patients with non-metastatic sporadic pheochromocytoma, due to the good sensitivity of MIBG scintigraphy in these patients.[37] A real advantage of PET radiopharmaceuticals seems to be for patients with metastatic disease, whose extent may be underestimated by MIBG scintigraphy. In these patients, different behaviors of PET radiopharmaceuticals have been reported in different clinical syndromes on the basis of specific gene mutations. In the absence of SDHB mutation or when genetic status is unknown, ^{18}F-DOPA seems to be the tracer of choice, whereas in patients with SDHB associated pheochromocytoma/paraganglioma – in whom both MIBG and ^{18}F-DOPA show disappointing results – ^{18}F-FDG is the preferred agent for localizing metastatic lesions.[35,37,38]

CONCLUSION

There is increasing evidence in the literature about the usefulness of PET/CT imaging with different tracers in thyroid and adrenal diseases. Since PET/CT is an expensive diagnostic tool which necessitates ionizing radiation exposure, cost-effectiveness studies are needed in order to define the appropriate use of this diagnostic method in various endocrine disorders.

CONFLICTS OF INTEREST:

The authors declare no conflicts of interest.

DISCLOSURES

None.

REFERENCES

1. Treglia G, Cason E, Fagioli G, 2010 Recent applications of nuclear medicine in diagnostics (first part). Ital J Med 4: 84-91.
2. Giovanella L, 2012 Positron emission tomography/computed tomography in patients treated for differentiated thyroid carcinomas. Expert Rev Endocrinol Metab 7: 35-43.
3. Chacko AM, Divgi CR, 2011 Radiopharmaceutical chemistry with iodine-124: a non-standard radiohalogen for positron emission tomography. Med Chem 7: 395-412.
4. Jager PL, Chirakal R, Marriott CJ, Brouwers AH, Koopmans KP, Gulenchyn KY, 2008 6-L-18F-fluorodihydroxyphenylalanine PET in neuroendocrine tumors: basic aspects and emerging clinical applications. J Nucl Med 49: 573-586.
5. Oberg K, 2012 Gallium-68 somatostatin receptor PET/CT: Is it time to replace (111)Indium DTPA octreotide for patients with neuroendocrine tumors? Endocrine 42: 3-4.
6. Eriksson B, Orlefors H, Oberg K, Sundin A, Bergström M, Långström B, 2005 Developments in PET for the detection of endocrine tumours. Best Pract Res Clin Endocrinol Metab 19: 311-324.
7. Abraham T, Schöder H, 2011 Thyroid cancer--indications and opportunities for positron emission tomography/computed tomography imaging. Semin Nucl Med 41: 121-138.
8. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, Haugen BR, et al, 2009 Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 19: 1167-1214.
9. Dong MJ, Liu ZF, Zhao K, et al, 2009 Value of 18F-FDG-PET/PET-CT in differentiated thyroid carcinoma with radioiodine-negative whole-body scan: a meta-analysis. Nucl Med Commun 30: 639-650.
10. Giovanella L, Ceriani L, De Palma D, Suriano S, Castellani M, Verburg FA 2012 Relationship between serum thyroglobulin and 18FDG-PET/CT in 131I-negative differentiated thyroid carcinomas. Head Neck 34: 626-631.
11. Ma C, Xie J, Lou Y, Gao Y, Zuo S, Wang X 2010 The role of TSH for 18F-FDG-PET in the diagnosis of recurrence and metastases of differentiated thyroid carcinoma with elevated thyroglobulin and negative scan: a meta-analysis. Eur J Endocrinol 163: 177-183.
12. Robbins RJ, Wan Q, Grewal RK, et al, 2006 Real-time prognosis for metastatic thyroid carcinoma based on 2-[18F]fluoro-2-deoxy-D-glucose-positron emission tomography scanning. J Clin Endocrinol Metab 91: 498-505.
13. Freudenberg LS, Jentzen W, Stahl A, Bockisch A, Rosenbaum-Krumme SJ, 2011 Clinical applications of 124I-PET/CT in patients with differentiated thyroid cancer. Eur J Nucl Med Mol Imaging 38: Suppl 1: 48-56.
14. Grabellus F, Nagarajah J, Bockisch A, Schmid KW, Sheu SY, 2012 Glucose transporter 1 expression, tumor proliferation, and iodine/glucose uptake in thyroid cancer with emphasis on poorly differentiated thyroid carcinoma. Clin Nucl Med 37: 121-127.
15. Treglia G, Annunziata S, Muoio B, Salvatori M, Ceriani L, Giovanella L, 2013 The role of fluorine-18-fluorodeoxyglucose positron emission tomography in aggressive histological subtypes of thyroid cancer: an overview. Int J Endocrinol 2013: 856189.
16. American Thyroid Association Guidelines Task Force, Kloos RT, Eng C, Evans DB, et al, 2009 Medullary thyroid cancer: management guidelines of the American Thyroid Association. Thyroid 19: 565-612.
17. Treglia G, Rufini V, Salvatori M, Giordano A, Giovanella L, 2012 PET Imaging in Recurrent Medullary Thyroid Carcinoma. Int J Mol Imaging 2012: 324686.
18. Rufini V, Treglia G, Perotti G, Leccisotti L, Calcagni ML, Rubello D, 2008 Role of PET in medullary thyroid carcinoma. Minerva Endocrinol 33: 67-73.
19. Treglia G, Villani MF, Giordano A, Rufini V, 2012 Detection rate of recurrent medullary thyroid carcinoma using fluorine-18 fluorodeoxyglucose positron emission tomography: a meta-analysis. Endocrine 42: 535-545.
20. Treglia G, Castaldi P, Villani MF, et al, 2012 Comparison of 18F-DOPA, 18F-FDG and 68Ga-somatostatin analogue PET/CT in patients with recurrent medullary thyroid carcinoma. Eur J Nucl Med Mol Imaging 39: 569-580.
21. Treglia G, Cocciolillo F, Di Nardo F, et al, 2012 Detection Rate of Recurrent Medullary Thyroid Carcinoma Using Fluorine-18 Dihydroxyphenylalanine Positron Emission Tomography: A Meta-analysis. Acad Radiol 19: 1290-1299.
22. Giovanella L, Suriano S, Maffioli M, Ceriani L, 2011 18FDG-positron emission tomography/computed tomography (PET/CT) scanning in thyroid nodules with nondiagnostic cytology. Clin Endocrinol 74: 644-648.
23. Vriens D, de Wilt JH, van der Wilt GJ, Netea-Maier RT, Oyen WJ, de Geus-Oei LF, 2011 The role of [(18) F]-2-fluoro-2-deoxy-d-glucose-positron emission tomography in thyroid nodules with indeterminate fine-needle aspiration biopsy: Systematic review and meta-analysis of the literature. Cancer 117: 4582-4594.
24. Deandreis D, Al Ghuzlan A, Auperin A, et al, 2012 Is (18) F-fluorodeoxyglucose-PET/CT useful for the presurgical characterization of thyroid nodules with indeterminate fine needle aspiration cytology? Thyroid 22: 165-172.
25. Bertagna F, Treglia G, Piccardo A, Giubbini R, 2012 Diagnostic and Clinical Significance of F-18-FDG-PET/CT Thyroid Incidentalomas. J Clin Endocrinol Metab 97: 3866-3875.
26. Treglia G, Giovanella L, Bertagna F, Di Franco D, Salva-

tori M, 2013 Prevalence and risk of malignancy of thyroid incidentalomas detected by (18)f-fluorodeoxyglucose positron-emission tomography. Thyroid 23: 124-126.
27. Boland GWL, Dwamena B, Sangwaiya MJ, et al, 2011 Characterization of adrenal masses by using FDG PET: A systematic review and meta-analysis of diagnostic test performance. Radiology 269: 117-126.
28. Deandreis D, Leboulleux S, Caramella C, Schlumberger M, Baudin E 2011 FDG PET in the management of patients with adrenal masses and adrenocortical carcinoma. Horm Cancer 2: 354-362.
29. Hahner S, Sundin A, 2011 Metomidate-based imaging of adrenal masses. Horm Cancer 2: 348-353.
30. Rufini V, Calcagni ML, Baum RP, 2006 Imaging of neuroendocrine tumors. Semin Nucl Med 36: 228-247.
31. Jacobson AF, Deng H, Lombard J, et al, 2010 ^{123}I-meta-iodobenzylguanidine scintigraphy for the detection of neuroblastoma and pheochromocytoma: results of a meta-analysis. J Clin Endocrinol Metab 95: 2596-2606.
32. Pacak K, Eisenhofer G, Goldstein DS, 2004 Functional imaging of endocrine tumors: role of positron emission tomography. Endocr Rev 25: 568-580.
33. Treglia G, Cocciolillo F, de Waure C, et al, 2012 Diagnostic performance of 18F-dihydroxyphenylalanine positron emission tomography in patients with paraganglioma: a meta-analysis. Eur J Nucl Med Mol Imaging 39: 1144-1153.
34. Rufini V, Treglia G, Castaldi P, et al, 2011 Comparison of 123I-MIBG SPECT-CT and 18F-DOPA PET-CT in the evaluation of patients with known or suspected recurrent paraganglioma. Nucl Med Commun 32: 575-582.
35. Timmers HJ, Kozupa A, Chen CC, et al, 2007 Superiority of fluorodeoxyglucose positron emission tomography to other functional imaging techniques in the evaluation of metastatic SDHB-associated pheochromocytoma and paraganglioma. J Clin Oncol 25: 2262-2269.
36. Naji M, AL-Nahhas A, 2012 ^{68}Ga-labelled peptides in the management of neuroectodermal tumours. Eur J Nucl Med Mol Imaging 39: Suppl 1: S61-67.
37. Taïeb D, Timmers HJ, Hindié E, et al, 2012 EANM 2012 guidelines for radionuclide imaging of phaeochromocytoma and paraganglioma. Eur J Nucl Med Mol Imaging 39: 1977-1995.
38. Timmers HJ, Chen CC, Carrasquillo JA, et al, 2009 Comparison of ^{18}F-fluoro-L-DOPA, ^{18}F-fluoro-deoxyglucose, and ^{18}F-fluorodopamine PET and ^{123}I-MIBG scintigraphy in the localization of pheochromocytoma and paraganglioma. J Clin Endocrinol Metab 94: 4757-4767.