

Usefulness of Positron Emission Tomography for Characterization of the Indeterminate Adrenal Tumor

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Abstract

Incidental adrenal masses are common, with most representing benign, nonfunctional cortical adenomas. The diagnostic approach should consist of a biochemical evaluation for hormonal hypersecretion, as well as an assessment of the risk of malignancy (primary adrenal cancer vs metastasis from another site). The size and appearance of the adrenal tumor on imaging studies are critical to management decisions. Computed tomography (CT) or T1 weighted chemical shift magnetic resonance imaging (MRI) can usually diagnose a cortical adenoma based on characteristics related to intracellular lipid content. However, 30% of cortical adenomas are lipid-poor, and will be classified as indeterminate on CT or MRI. Fluorodeoxyglucose-positron emission tomography (FDG-PET) is a useful method of further characterizing an indeterminate adrenal mass, particularly in an oncology patient in whom identification of an adrenal metastasis will affect disease stage and therapy. FDG-PET has been found to have a sensitivity of 93 to 100% and a specificity of 70 to 100% for the identification of an adrenal malignancy in both oncology and non-oncology patient populations. Indications for adrenalectomy include all functional adrenal tumors, known or suspected primary adrenal cancers that appear resectable, adrenal tumors > 4 cm, and isolated adrenal metastases.

Keywords: Adrenal tumor, PET, incidentaloma.

ASSESSMENT OF THE ADRENAL INCIDENTALOMA

Incidentally discovered adrenal tumors are common, occurring in approximately 4% of patients undergoing an imaging study for another reason and in up to 8.7% of autopsy studies.^{1,2} The differential diagnosis of an adrenal incidentaloma includes benign or malignant, functional or nonfunctional, primary adrenal tumors or metastases. Most incidentalomas are benign, nonfunctional cortical adenomas, even in patients with a known extraadrenal malignancy.³ Other benign adrenal masses include hemorrhage, cysts, infectious or inflammatory lesions, myelolipomas, ganglioneuromas, and angiomyolipomas. Adrenalectomy is indicated for all functional adrenal tumors and for known or suspected primary adrenal cancers that appear resectable. Adrenalectomy is also recommended for nonfunctional tumors that are larger than 3 to 4 cm, tumors that are growing in size, or isolated metastases in the setting of adequate treatment of the primary site.

The evaluation and management of a patient with an incidentally discovered adrenal tumor requires answering the following two questions:

1. Is the tumor functional; i.e. does it elaborate hormones of the adrenal cortex or medulla in an unregulated and potentially harmful fashion?
2. Could it be cancer?

All adrenal tumors must be evaluated for hormonal hypersecretion. Biochemical evaluation involves testing for

pheochromocytomas, cortisol-producing tumors, and in a patient with hypertension, aldosterone-producing tumors.⁴ Testing for virilizing or feminizing tumors is not routinely done unless patients have signs or symptoms associated with excess production of these hormones. The identification of pheochromocytomas and cortisol-producing tumors is particularly important since biopsy or manipulation of an unsuspected pheochromocytoma may lead to hemodynamic instability and death.^{5,6} Resection of an unrecognized cortisol-secreting tumor may lead to a potentially fatal postoperative Addisonian crisis. Adrenal tumors that elaborate virilizing or feminizing hormones or multiple hormones are more likely to be malignant.

In addition to the number and type of hormones elaborated, the risk of malignancy is also based on tumor size, imaging characteristics, and whether the patient has a known extraadrenal malignancy. Features suggestive of malignancy include margin irregularity, invasion into adjacent organs or blood vessels, local or regional lymphadenopathy, growth over time, lesion heterogeneity, and hemorrhage or necrosis.⁷ In addition, other characteristics specific to particular imaging modalities have been described, and are discussed in detail below. The identification of an adrenal metastasis in an oncology patient is particularly important because it usually affects the disease stage and therapy. Tumors that most commonly metastasize to the adrenal gland are lung cancer, melanoma, and breast

cancer.^{8,9} While most adrenal tumors can be diagnosed based on routine biochemical work-up and computed tomography (CT) or magnetic resonance imaging (MRI), additional imaging, testing, or surgery is sometimes necessary to definitively characterize the lesion. This paper will review the features of standard cross-sectional imaging and discuss the utility of positron emission tomography (PET) scanning for adrenal neoplasms.

CROSS-SECTIONAL IMAGING

CT and MRI are both used to evaluate adrenal lesions based on their water and lipid content. CT is the most common initial imaging test used to evaluate an adrenal tumor, and is the most common study on which adrenal incidentalomas are discovered. Benign cortical adenomas have low Hounsfield unit (HU) values on noncontrast CT due to their high intracellular lipid content. Different threshold values of HU have been evaluated in various studies, with lower threshold values having higher specificity but lower sensitivity for the identification of a benign lesion, and higher threshold values having higher sensitivity but lower specificity. A large, pooled analysis of 10 studies evaluating a total of 495 adrenal lesions found a threshold value of 10 HU to have 98% specificity and 71% sensitivity for the identification of a benign adrenal lesion, and is in common use at the present time.¹⁰ The reason for the relatively low sensitivity of this criterion is that approximately 30% of all adrenal adenomas are lipid-poor, and thus will have HU >10 on noncontrast CT.¹¹ Lesions that have >10 HU measured on noncontrast CT are considered indeterminate and require further investigation.

Researchers have sought to improve the diagnostic capability of CT by observing the enhancement pattern of an adrenal tumor to intravenous contrast, and measuring the percent washout of the contrast. Different studies have looked at different criteria, but, in general, greater than 50 to 60% washout of contrast at 5 to 15 minutes after enhancement is predictive of a benign adenoma with a sensitivity of 88 to 100% and specificity of 92 to 100%.¹²⁻¹⁵ Of note, such a delayed contrast-enhanced technique is not routinely done for the scan on which an adrenal tumor is incidentally discovered. However, this type of scan can sometimes identify a lipid-poor adenoma, since the washout features of cortical adenomas seem to be independent of lipid content and lipid-poor adenomas demonstrate the same washout pattern as lipid-rich adenomas.¹⁴

MRI is also frequently used to evaluate adrenal tumors. The technique of T1-weighted chemical shift MRI, also

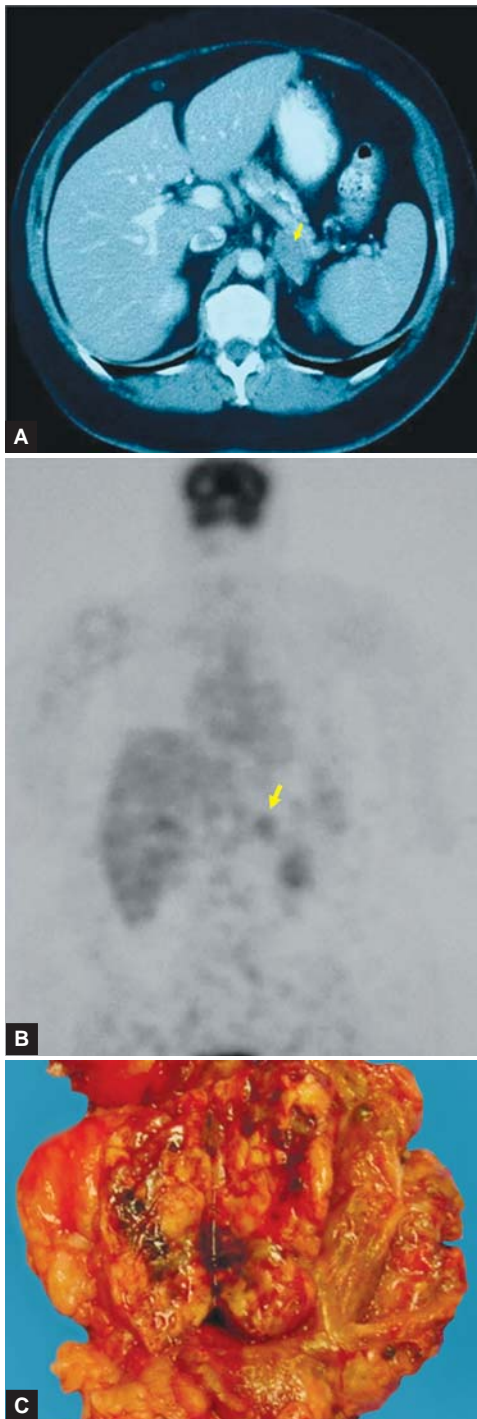
known as opposed phase imaging, has been found to be the most useful, and detects intracellular lipid by comparing in-phase and out-of-phase spin-echo or gradient-echo sequences. The high lipid content of benign cortical adenomas causes signal loss on chemical shift MRI.¹⁶ Rarely, adrenocortical carcinomas, or metastases from liposarcoma, hepatocellular carcinoma, or renal cell carcinoma may also exhibit this pattern.²³ Both qualitative and quantitative methods have been used to describe the degree of signal loss on the out-of-phase images. These include comparing the signal loss of the adrenal mass with the signal loss of the spleen, liver, or muscle, and calculating a signal intensity index using the formula $[\text{Signal intensity (in-phase)} - \text{Signal intensity (out-of-phase)}] / [\text{Signal intensity (in-phase)}] \times 100\%$.¹⁷⁻¹⁹ Multiple studies have been done evaluating both qualitative and quantitative methods, with both methods yielding acceptable results for the identification of a benign cortical adenoma.^{19,20}

PET SCANNING

When cross-sectional imaging is indeterminate for the characterization of an adrenal tumor, fluorodeoxyglucose positron emission tomography (FDG-PET) may yield additional useful information. PET scanning, which is widely used in the field of oncology, has been studied for its usefulness in characterizing an indeterminate adrenal tumor as either benign or malignant based on its glucose metabolism. The chief advantage of PET is that it provides a noninvasive option for the evaluation of these tumors as well as the entire body for metastatic disease. Patients with widespread metastatic disease are generally treated with systemic therapy, whereas patients with a solitary adrenal metastasis may be candidates for adrenalectomy. Figures 1A to C show a CT scan, PET scan, and pathologic specimen of a patient who underwent laparoscopic left adrenalectomy for a solitary melanoma metastasis.

A variety of isotopes have been used for PET scanning; ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) is the isotope most commonly used for the evaluation of the indeterminate adrenal tumor. PET scanning using FDG is based on the premise that malignant lesions have increased glucose metabolism. A fasting patient is injected with FDG and images are acquired about 1 hour later. More recently, PET/CT scanners have been used to correlate the functional imaging information obtained from the PET scan with a precise anatomic location identified by CT, and fused images are possible.

Both qualitative and quantitative methods have been used to define a PET positive adrenal tumor, and the optimal approach is still under debate. Qualitative methods are based



Figs 1A to C: (A) Computed tomography (B) ^{18}F -fluorodeoxyglucose positron emission tomography (C) Pathologic specimen from a 69 year old woman with a history of an extremity melanoma resected 12 years prior who underwent laparoscopic left adrenalectomy for an isolated melanoma metastasis

on a visual assessment of the FDG uptake of the tumor compared to either background or an adjacent organ, most commonly the liver. Quantitative methods depend on defining a region of interest (ROI) and measuring a

standardized uptake value (SUV) or calculating a standardized uptake ratio. Critics of quantitative methods contend that SUV measurements are variable due to the placement, size, and shape of the ROIs, partial volume effects, and other factors including patient body habitus, plasma glucose concentration, image noise, and image reconstruction methods.^{21,22} Different studies have used different methods for defining an adrenal tumor as PET positive, making comparisons between studies difficult (Table 1).

Qualitative assessment of FDG uptake is straightforward, and involves a visual assessment of the FDG uptake in the adrenal tumor as less than, equal to, or greater than liver or background. Some studies use the criterion of adrenal uptake either equal to or greater than liver to define a PET positive adrenal tumor,²³ while other studies use the more restrictive criterion of adrenal uptake greater than liver.²⁴⁻²⁶ This can be further expanded to express moderately or markedly increased uptake.^{25,26} The sensitivity and specificity of this approach is similar regardless of whether the patient has a known extraadrenal malignancy or not, and ranges from 86 to 100% and 75 to 100%, respectively (Table 1).^{8,23-27}

Quantitative assessment of FDG uptake involves measuring either a mean or maximal SUV from a region of interest drawn over the lesion, or calculating a standardized uptake ratio (SUR). Studies evaluating threshold SUVs for the distinction of a benign from a malignant adrenal tumor usually generate receiver operating characteristic (ROC) curves to identify the threshold values with the best sensitivity and specificity; thus, these threshold SUVs vary from study to study.^{23,25,26} In addition to evaluating the absolute value of the SUV of an adrenal tumor, a ratio can be calculated between the adrenal SUV and liver SUV. A SUR of >1 was found to have 100% sensitivity and 97% specificity for the identification of a malignant adrenal tumor in patients with a known extraadrenal malignancy in one large study evaluating 165 adrenal tumors,²⁵ while a SUR of 1.45 was deemed as the appropriate cutoff in another study evaluating patients with no prior history of cancer.²⁸ Interestingly, while this ratio is quantitative, the comparison of adrenal to liver SUV is reminiscent of the qualitative comparison of FDG uptake in these organs by visual assessment. Overall, quantitative methods in both oncology patients and those without a prior history of cancer yield similar sensitivities of 95 to 100% and specificities of 70 to 100% for the characterization of an adrenal mass as malignant (Table 1).^{8,11,24-26,28}

Regardless of whether a qualitative or quantitative method is used to characterize adrenal masses on PET scan,

Table 1: Results of large series of adrenal tumors evaluated by ¹⁸F-fluorodeoxyglucose positron emission tomography (¹⁸F-FDG PET)

Reference	Patient population	N	Benign	Malignant	Qualitative* vs quantitative analysis	Definition of PET positive	Sensitivity	Specificity
Yun 2001 ²³	Oncology	50	32	18	Qualitative	Adrenal uptake equal to or greater than liver	100%	94%
Jana 2006 ²⁴	Oncology	80	50	30	Qualitative	Adrenal uptake greater than liver	93%	96%
Metser 2006 ¹¹	Oncology (all but 8)	175	107	68	SUV _{max} † SUV _{avg} ‡ SUV of adrenal tumor	SUV _{max} >3.4 SUV _{avg} >3.1 SUV >3.1	95% 95% 98.5%	86% 90% 92%
Boland 2009 ²⁵	Oncology	165	139	26	Qualitative	Adrenal uptake greater than liver	100%	97%
					Average of 2 SUV _{max} of adrenal tumor	Adrenal SUV >2.31	100%	94%
					Adrenal SUV _{max} compared to liver SUV _{max}	Ratio of adrenal to liver SUV >1	100%	97%
Tessonnier 2008 ²⁶	No prior history of cancer	41	29	12	Qualitative	Adrenal uptake markedly greater than liver	86%	75%
					Adrenal SUV _{max} compared to liver SUV _{max}	Ratio of adrenal to liver SUV >1.8	100%	100%
Groussin 2009 ²⁸	No prior history of cancer	77¶	43	22	SUV _{max}	SUV _{max} >3.4	100%	70%
					Adrenal SUV _{max} compared to liver SUV _{max}	Ratio of adrenal to liver SUV > 1.45	100%	88%
Maurea 2001 ²⁷	Mixed oncology and non-oncology population	54	36	18	Qualitative	Adrenal uptake greater than background	100%	100%
Han 2007 ⁸	Mixed oncology and non-oncology population	105	41	64	Qualitative	Adrenal uptake equal to or greater than liver	94%	83%
					SUV _{max}	No cutoff specified		

*Qualitative analysis: adrenal uptake of ¹⁸F-FDG visually compared to liver or background uptake

† Maximum standardized uptake value (SUV) of the adrenal tumor

‡ Average SUV of the adrenal tumor

¶ 12 tumors were nonadrenocortical lesions and not included in the final analysis

it appears to be useful, and appears to improve the diagnostic accuracy over CT alone. By combining the noncontrast CT data with the PET data, the sensitivity and specificity for the diagnosis of a malignant adrenal mass in a patient with a known extraadrenal malignancy increases to 100% and 98 and 99%, respectively.^{11,25}

As with any test, there will be false positive and false negative results when using PET scanning to evaluate an adrenal tumor for malignancy (Table 2). The most common benign adrenal tumor that can be PET positive is a

pheochromocytoma.^{23,29} Other benign adrenal masses that can be PET positive include some adrenal adenomas (both functional and nonfunctional), adrenal hemorrhage, inflammatory lesions, infectious lesions, oncocytomas, and myelolipomas with hypermetabolic adenomatous and hematopoietic elements.^{8,25,30-34}

Causes of false negative PET results, i.e. malignant tumors that are incorrectly classified as benign, include small tumors and necrotic tumors, as well as non-FDG avid metastases such as those from renal cell carcinoma or

Table 2: Causes of false positive and false negative ^{18}F -fluorodeoxyglucose positron emission tomography (^{18}F -FDG PET) scan results in the evaluation of an adrenal mass for malignancy

Causes of false positive adrenal masses on PET (benign lesions that take up ^{18}F -FDG):

- Pheochromocytomas
- Some adenomas, particularly those that are functional
- Adrenocortical oncocytomas
- Adrenal hemorrhage
- Myelolipomas with hypermetabolic adenomatous and hematopoietic elements
- Inflammatory lesions
- Infectious lesions

Causes of false negative adrenal masses on PET (malignant lesions that show less intense ^{18}F -FDG uptake than most malignant lesions):

- Small tumors
- Necrotic tumors
- Metastases from neuroendocrine tumors
- Metastases from renal cell carcinoma

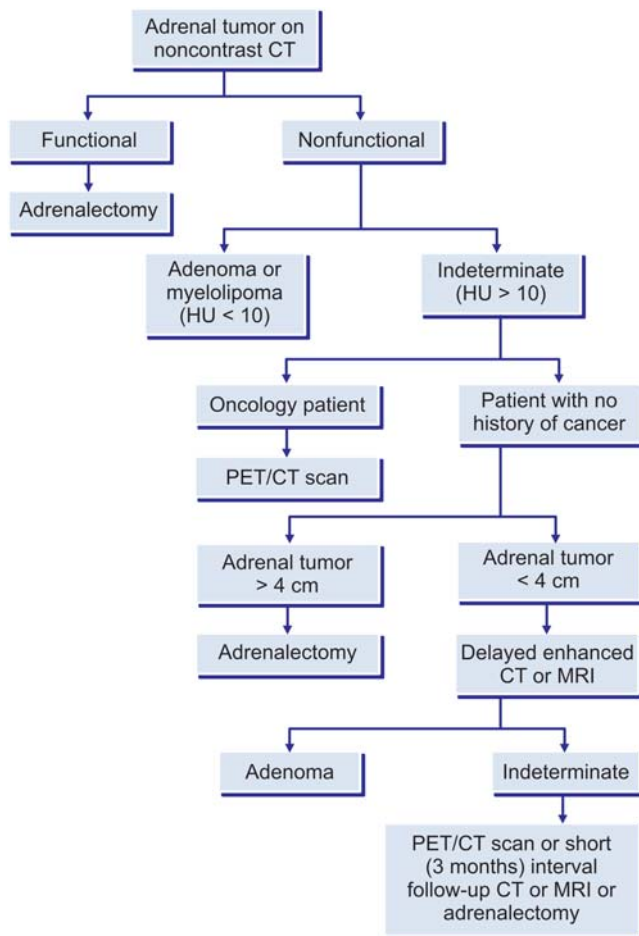


Fig. 2: Algorithm for the evaluation of an incidentally discovered adrenal tumor incorporating ^{18}F -fluorodeoxyglucose positron emission tomography (PET)

neuroendocrine tumors.^{11,23,35} Small tumors are thought to be at risk for underestimation of the calculated SUV due to partial volume effects, thus leading to false negative results.³⁵

CONCLUSION

In summary, PET scanning with FDG is a useful adjunct to the noninvasive evaluation of a patient with an incidentally discovered adrenal tumor. In Figure 2 we propose an algorithm for the evaluation of adrenal incidentaloma. The initial evaluation begins with biochemical testing and non-contrast CT. Patients with functional tumors, or overt or suspected adrenal malignancy should be referred for surgical resection. If the adrenal tumor is nonfunctional and indeterminate (noncontrast HU >10), then the next step depends on whether the patient has a known extraadrenal malignancy. In oncology patients, an FDG-PET scan is a reasonable next step, with the advantages of providing a noninvasive option for these patients with the ability to image the entire body and identify potential other sites of metastatic disease. In a patient with no prior history of cancer, the management of the adrenal tumor depends on its size and imaging characteristics; recent clinical practice guidelines advocate adrenalectomy for tumors > 4 cm.⁴ Tumors < 4 cm should be evaluated by MRI or delayed enhanced CT with measurement of percent washout of IV contrast. These techniques may be able to identify a lipid-poor cortical adenoma. If these tests are nondiagnostic, the next step should be tailored to physician and patient preference, and can include FDG-PET, short (3 months) interval follow-up CT or MRI, or adrenalectomy. Other than for diagnosing a metastasis to the adrenal gland, we do not advocate percutaneous biopsy because the results are rarely useful and the technique may be associated with substantial morbidity or mortality in the case of pheochromocytoma. FDG-PET is a good noninvasive option, and a negative scan has been shown to be highly suggestive of a benign lesion with good sensitivity and specificity.

REFERENCES

1. Bovio S, Cataldi A, Reimondo G, et al. Prevalence of adrenal incidentaloma in a contemporary computerized tomography series. *Journal of endocrinological investigation*. Apr 2006;29(4):298-302.
2. Hedeland H, Ostberg G, Hokfelt B. On the prevalence of adrenocortical adenomas in an autopsy material in relation to hypertension and diabetes. *Acta medica Scandinavica*. Sep 1968;184(3):211-14.
3. Song JH, Chaudhry FS, Mayo-Smith WW. The incidental adrenal mass on CT: prevalence of adrenal disease in 1,049 consecutive adrenal masses in patients with no known malignancy. *Ajr* May 2008;190(5):1163-68.
4. Zeiger MA, Thompson GB, Duh QY, et al. The American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons medical guidelines for the management of adrenal incidentalomas. *Endocr Pract* Jul-Aug 2009;15(Suppl 1):1-20.
5. Sutton MG, Sheps SG, Lie JT. Prevalence of clinically unsuspected pheochromocytoma. Review of a 50-year autopsy series. *Mayo Clin Proc* Jun 1981;56(6):354-60.
6. Kloos RT, Gross MD, Francis IR, Korobkin M, Shapiro B. Incidentally discovered adrenal masses. *Endocr Rev* Aug 1995;16(4):460-84.
7. Sturgeon C, Kebebew E. Laparoscopic adrenalectomy for malignancy. *Surg Clin North Am*. Jun 2004;84(3):755-74.
8. Han SJ, Kim TS, Jeon SW, et al. Analysis of adrenal masses by 18F-FDG positron emission tomography scanning. *International journal of clinical practice*. May 2007;61(5):802-09.
9. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma; analysis of 1000 autopsied cases. *Cancer* Jan 1950;3(1):74-85.
10. Boland GW, Lee MJ, Gazelle GS, Halpern EF, McNicholas MM, Mueller PR. Characterization of adrenal masses using unenhanced CT: An analysis of the CT literature. *Ajr* Jul 1998;171(1):201-04.
11. Metser U, Miller E, Lerman H, Lievshitz G, Avital S, Even-Sapir E. 18F-FDG PET/CT in the evaluation of adrenal masses. *J Nucl Med* Jan 2006;47(1):32-37.
12. Szolar DH, Kammerhuber FH. Adrenal adenomas and nonadenomas: Assessment of washout at delayed contrast-enhanced CT. *Radiology*. May 1998;207(2):369-75.
13. Korobkin M, Brodeur FJ, Francis IR, Quint LE, Dunnick NR, Lundy F. CT time-attenuation washout curves of adrenal adenomas and nonadenomas. *Ajr* Mar 1998;170(3):747-52.
14. Pena CS, Boland GW, Hahn PF, Lee MJ, Mueller PR. Characterization of indeterminate (lipid-poor) adrenal masses: Use of washout characteristics at contrast-enhanced CT. *Radiology*. Dec 2000;217(3):798-802.
15. Caoili EM, Korobkin M, Francis IR, et al. Adrenal masses: characterization with combined unenhanced and delayed enhanced CT. *Radiology*. Mar 2002;222(3):629-33.
16. Mitchell DG, Crovello M, Matteucci T, Petersen RO, Miettinen MM. Benign adrenocortical masses: Diagnosis with chemical shift MR imaging. *Radiology*. Nov 1992;185(2):345-51.
17. Tsushima Y, Ishizaka H, Matsumoto M. Adrenal masses: Differentiation with chemical shift, fast low-angle shot MR imaging. *Radiology*. Mar 1993;186(3):705-09.
18. Outwater EK, Siegelman ES, Radecki PD, Piccoli CW, Mitchell DG. Distinction between benign and malignant adrenal masses: Value of T1-weighted chemical-shift MR imaging. *Ajr*. Sep 1995;165(3):579-83.
19. Fujiyoshi F, Nakajo M, Fukukura Y, Tsuchimochi S. Characterization of adrenal tumors by chemical shift fast low-angle shot MR imaging: Comparison of four methods of quantitative evaluation. *Ajr* Jun 2003;180(6):1649-57.
20. Korobkin M, Lombardi TJ, Aisen AM, et al. Characterization of adrenal masses with chemical shift and gadolinium-enhanced MR imaging. *Radiology*. Nov 1995;197(2):411-18.
21. Boellaard R, Krak NC, Hoekstra OS, Lammertsma AA. Effects of noise, image resolution, and ROI definition on the accuracy of standard uptake values: A simulation study. *J Nucl Med*. Sep 2004;45(9):1519-27.
22. Thie JA. Understanding the standardized uptake value, its methods, and implications for usage. *J Nucl Med* Sep 2004;45(9):1431-34.
23. Yun M, Kim W, Alnafisi N, Lacorte L, Jang S, Alavi A. 18F-FDG PET in characterizing adrenal lesions detected on CT or MRI. *J Nucl Med*. Dec 2001;42(12):1795-99.
24. Jana S, Zhang T, Milstein DM, Isasi CR, Blaufox MD. FDG-PET and CT characterization of adrenal lesions in cancer patients. *European journal of nuclear medicine and molecular imaging*. Jan 2006;33(1):29-35.
25. Boland GW, Blake MA, Holalkere NS, Hahn PF. PET/CT for the characterization of adrenal masses in patients with cancer: Qualitative versus quantitative accuracy in 150 consecutive patients. *Ajr*. Apr 2009;192(4):956-62.
26. Tessonnier L, Sebag F, Palazzo FF, et al. Does 18F-FDG PET/CT add diagnostic accuracy in incidentally identified non-secreting adrenal tumours? *European journal of nuclear medicine and molecular imaging*. Nov 2008;35(11):2018-25.
27. Maurea S, Klain M, Mainolfi C, Ziviello M, Salvatore M. The diagnostic role of radionuclide imaging in evaluation of patients with nonhypersecreting adrenal masses. *J Nucl Med*. Jun 2001;42(6):884-92.
28. Groussin L, Bonardel G, Silvera S, et al. 18F-Fluoro-deoxyglucose positron emission tomography for the diagnosis of adrenocortical tumors: A prospective study in 77 operated patients. *The Journal of clinical endocrinology and metabolism*. May 2009;94(5):1713-22.
29. Shulkin BL, Thompson NW, Shapiro B, Francis IR, Sisson JC. Pheochromocytomas: Imaging with 2-[fluorine-18]fluoro-2-deoxy-D-glucose PET. *Radiology*. Jul 1999;212(1):35-41.
30. Caoili EM, Korobkin M, Brown RK, Mackie G, Shulkin BL. Differentiating adrenal adenomas from nonadenomas using (18)F-FDG PET/CT: Quantitative and qualitative evaluation. *Academic radiology*. Apr 2007;14(4):468-75.
31. Elaini AB, Shetty SK, Chapman VM, et al. Improved detection and characterization of adrenal disease with PET-CT. *Radiographics*. May-Jun 2007;27(3):755-67.
32. Shimizu A, Oriuchi N, Tsushima Y, Higuchi T, Aoki J, Endo K. High [18F] 2-fluoro-2-deoxy-D-glucose (FDG) uptake of adrenocortical adenoma showing subclinical Cushing's syndrome. *Annals of nuclear medicine*. Jul 2003;17(5):403-06.
33. Ludwig V, Rice MH, Martin WH, Kelley MC, Delbeke D. 2-Deoxy-2-[18F]fluoro-D-glucose positron emission tomography uptake in a giant adrenal myelolipoma. *Mol Imaging Biol*. Oct 2002;4(5):355-58.
34. Kim DJ, Chung JJ, Ryu YH, Hong SW, Yu JS, Kim JH. Adrenocortical oncocytoma displaying intense activity on 18F-FDG-PET: A case report and a literature review. *Annals of nuclear medicine*. Nov 2008;22(9):821-24.
35. Kumar R, Xiu Y, Yu JQ, et al. 18F-FDG PET in evaluation of adrenal lesions in patients with lung cancer. *J Nucl Med*. Dec 2004;45(12):2058-62.