Incidental Non-secreting Adrenal Masses in Cancer Patients: Intra-individual Comparison of ^{18}F-Fluorodeoxyglucose Positron Emission Tomography/ Computed Tomography with Computed Tomography and Shift Magnetic Resonance Imaging

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The ability of integrated ^{18}F-fluoro-deoxyglucose positron emission tomography and computed tomography (FDG PET/CT) to distinguish between benign and malignant incidental non-secreting adrenal masses was evaluated in cancer patients. Results were compared with those of CT and shift magnetic resonance imaging (MRI). A total of 1832 cancer patients who had undergone FDG PET/CT scans were retrospectively evaluated. Visual interpretation, tumour maximum standardized uptake value (SUV_{max}), liver SUV_{max} and tumour/liver SUV_{max} ratios were correlated with the findings of CT, shift MRI and final diagnosis (based on biopsy or clinical/radiological follow-up). A total of 109 adrenal masses were found: 49 were malignant and 60 were benign on final diagnosis. A tumour/liver SUV_{max} ratio threshold of 1.0 was more accurate in differentiating the tumour type than tumour SUV_{max} or visual interpretation alone. Diagnostic accuracy of CT and shift MRI (92 – 97%) was similar to that for FDG PET/CT (94 – 97%). In conclusion, FDG PET/CT accurately characterizes adrenal tumours, with excellent sensitivity and specificity. Use of 1.0 as the threshold for the tumour/liver SUV_{max} ratio seems to be promising for distinguishing benign from malignant adrenal masses in cancer patients.

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FDG PET/CT in cancer patients with incidental adrenal masses

Introduction

An adrenal 'incidentaloma' is an unsuspected and asymptomatic mass usually detected on computed tomography (CT) obtained for other purposes. In patients with no history of malignancy, most adrenal 'incidentalomas' are benign non-secreting tumours.[1,2] For patients with a known history of malignancy, however, the rate of metastatic tumour is 25 – 72% depending on the size and type of the primary lesion; for example, bronchogenic and renal carcinomas and melanomas have a relatively high rate of adrenal metastases compared with other epithelial malignancies.[3 – 5]

Unenhanced CT attenuation and enhancement washout on CT has become the gold standard for characterizing lipid-rich adrenal adenomas, but this imaging modality cannot help to differentiate lipid-poor adenomas from non-adenomas.[6 – 8] Better results can be expected when chemical shift magnetic resonance imaging (MRI) is used.[9] Haider *et al.*[10] reported that chemical shift MRI had a high sensitivity (89%) for adenomas measuring 10 – 30 Hounsfield Units (HU), whereas other quantitative methods, including adrenal-to-muscle ratio and adrenal-to-liver ratio, had considerable overlap between adenomas and metastatic tumours.

In many studies, patients with known malignancies are grouped with low-risk patients, with the implication that imaging work-up is necessary in both groups to confirm the benign diagnosis.[8 – 10] This uncertainty is reflected in clinical practice: some radiologists routinely recommend dedicated adrenal CT or MRI, whereas others make the presumptive diagnosis of adenoma for an incidentally discovered adrenal lesion.

Dramatic advances in adrenal imaging have made an important impact on the management of these patients. Despite the optimal use of the best available imaging technology, CT and MRI alone or in combination fail to characterize some adrenal lesions.[9,10] The options in such cases are varying degrees of intervention, ranging from fine-needle aspiration cytology or biopsy to surgery, depending on the size of the lesion.[11]

Initial studies using ^{18}F-fluorodeoxyglucose positron emission tomography (FDG PET) have shown promising results in differentiating benign and malignant adrenal tumours.[12 – 15] Apart from the study by Metser *et al.*,[14] the majority of these studies have involved limited data on adrenal tumours in non-cancer patients where conventional imaging has been unhelpful. Most of the reported PET studies describe the difficulty in drawing a region of interest (ROI) for standardized uptake value (SUV) measurement, particularly in FDG-negative lesions. This problem can be overcome by using image fusion with CT scans.

The purpose of the present study was to evaluate the value of FDG PET combined with CT (FDG PET/CT) in predicting the benign or malignant nature of non-secreting adrenal tumours in cancer patients.

Patients and methods

PATIENTS

Cancer patients with no biochemical evidence of adrenal hypersecretion who had undergone FDG PET/CT between 2004 and 2007 at the PET Centre, Katharinen Hospital, Stuttgart were retrospectively evaluated. Patients with prostate carcinoma and neuroendocrine tumours who had undergone ^{11}C-choline PET/CT and ^{68}Ga-tetra-azacyclododecane tetra-acetic acid PET, respectively, were excluded from the study.

In the majority of patients, chemotherapy

had already been started prior to FDG PET/CT. Patients with positive FDG PET/CT were referred for surgical treatment or followed up with conventional imaging (CT or MRI) for a minimum of 6 months. The decision to operate was taken according to the size of the tumour, patient preference, patient age and comorbidities. The final diagnosis of whether the adrenal masses found were benign or malignant was based on biopsy/histological confirmation, when available, or on CT/MRI follow-up.

As this was a retrospective evaluation involving patients who underwent routine treatment and diagnosis of their cancer, the study did not require ethical approval or patient informed consent.

PET AND CT

All patients fasted for at least 6 h before PET/CT examination. After ensuring a normal peripheral blood glucose level (49 – 211 mg/dl), patients received an intravenous injection of 0.2 mCi/kg 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG) and then rested for approximately 60 – 120 min before undergoing a PET/CT scan. Image acquisition was performed using an integrated PET/CT device (GE Discovery LS system, which combines GE Advance NXi PET and GE Lightspeed® Plus Multislice CT scanners; GE Healthcare, Pittsburgh, PA, USA). The CT was performed from the head to the pelvic floor using a standardized protocol (120 kV, 80 mA, slice thickness 5 mm). Contrast PET/CT or CT studies were performed in patients found to have adrenal masses in order to determine the delayed enhancement of the adrenals. The PET images were acquired using the three-dimensional mode for the same scanning range as the CT images. The acquisition time for PET was 4 min per bed position and five or six continuous positions were scanned.

Data reconstruction and analysis

Image datasets were reconstructed iteratively using an ordered subset expectation maximization algorithm and corrected with measured attenuation correction. The CT, PET and PET/CT infusion images of axial, sagittal and coronal images were obtained through a post-processing procedure.

For data analysis and processing, a semi-automatic quantification of the ROI was applied. The chosen ROI was large enough to cover more than half of the adrenal mass but avoided peripheral areas so as to avoid partial volume effects. A large ROI was also drawn on a homogeneous liver region (segment VIII). Activity counts in the ROIs were normalized to injected doses per kilogram of patient body weight and the maximum SUV (SUV_{max}) was calculated. Maximum diameter and unenhanced attenuation were assessed on co-registered CT images. The ratio of tumour SUV_{max} to liver SUV_{max} was calculated.

Visual image evaluation

For visual image evaluation all FDG PET/CT scans were independently interpreted by two experienced nuclear medicine physicians. The physicians were blinded to the reports of other imaging studies, including nuclear and conventional morphological imaging. They individually graded each adrenal tumour as being probably benign or malignant; equivocal tumours were classified as probably malignant. A qualitative comparison of adrenal FDG uptake with liver FDG uptake was also undertaken: the FDG PET/CT image was considered positive if FDG uptake in the adrenal tumour appeared markedly higher than that of the liver, and negative if it appeared less, equal or slightly higher than that of the liver.

ADRENAL MRI

A variety of equipment was used to perform

MRI, including a 1.5 Tesla (T) Signa Echospeed Excite HD scanner (GE Healthcare) and a 1.5 T Sonata scanner (Siemens Medical Solutions, Erlangen, Germany). A phased-array torso coil was used whenever possible. Axial T1-weighted in-phase and opposed-phase breath-hold images were obtained with a two-dimensional gradient-refocused echo sequence using the following parameters: TR range 150 – 193 ms; in-phase TE range, 4.4 – 7.5 ms; opposed-phase TE range 2.2 – 3.7 ms. Additional parameters were a flip angle of 70 – 90°, a field of view of 350 – 360 mm, a matrix of $127 – 192 \times 256$, a slice thickness of 5 – 6 mm, an intersection gap of 0 – 1 mm, and one signal acquisition. All studies included some type of T2-weighted sequence of variable technique.

The presence of an adenoma was diagnosed using the standard imaging criteria of an attenuation coefficient of ≤ 10 HU on unenhanced CT and absolute contrast washout of ≥ 52% at 10 min or 60% at 15 min on adrenal CT,[16 – 18] and signal cancellation based on subjective analysis of signal dropout on opposed-phased imaging on chemical shift MRI. Chemical shift imaging relies on the different resonance frequency rates of protons in fat and water molecules. Fat protons are more shielded than water protons, experience less external magnetic field and, therefore, resonate at a slower frequency. The net effect of this physical phenomenon is that there is cancellation of the signal between lipid and water protons within a voxel. Thus, tissues containing lipid and water have signal loss (i.e. appear darker) on out-of-phase images.[19]

STATISTICAL ANALYSIS

Data were summarized by calculating proportions for categorical variables and means ± SD for continuous variables. To evaluate the diagnostic performance of CT, shift MRI and PET, the sensitivity (proportion of true positives among all lesions confirmed as malignant), specificity (proportion of true negatives among all non-malignant lesions), positive prognostic value (proportion of true positives among all lesions confirmed as true and false positive) and negative prognostic value (proportion of true negatives among all lesions confirmed as true and false negative) were calculated. All statistical analyses were performed using Stata software, version 7.0 (StataCorp, College Station, TX, USA). A *P*-value < 0.05 was considered to be statistically significant.

Results

PATIENT DISPOSITION AND CHARACTERISTICS

A total of 1832 cancer patients who had undergone investigation using FDG PET/CT between 2004 and 2007 were retrospectively evaluated. Of these, 1112 were female and 720 were male; the mean ± SD age was 55 ± 4 years. Diagnoses included ear, nose and throat tumours ($n = 421$), non-small cell lung cancer (NSCLC) ($n = 384$), melanoma ($n = 333$), colonic carcinoma ($n = 214$), ovarian carcinoma ($n = 186$), breast carcinoma ($n = 151$), thyroid carcinoma ($n = 56$), urothelial carcinoma of the bladder ($n = 26$), hepatocellular carcinoma (HCC) ($n = 8$), non-Hodgkin's lymphoma ($n = 36$) and gastrointestinal stromal tumour (GIST) ($n = 17$). Incidental adrenal masses were found in 109 (6%) of the 1832 cancer patients. Of these, 71 had contrast FDG PET/CT studies and 38 had contrast CT studies to determine the delayed enhancement of the adrenals. On final evaluation, 49 of the masses were malignant and 60 were benign. Nine of the 60 benign adrenal masses were initially

classified as unclear on all imaging protocols and needed further follow-up. Biopsy (*n* = 42) (Fig. 1) or histology (*n* = 19) were available in 61 (56%) of the 109 adrenal masses. Of these, 46 were malignant and 15 were benign (Table 1). Sixteen of the 46 patients with malignant adrenal masses had further metastatic lesions. In the 48 cases of adrenal masses with no biopsy or histology available, 36 tumours were classified as benign on the basis of the absence of change in imaging features (size and tumour tissue component) during follow-up (mean ± SD follow-up period 14.1 ± 9 months, range 6 – 29 months). A further 12 tumours were classified as malignant on the basis of typical characteristics such as spiculae and further metastatic lesions.
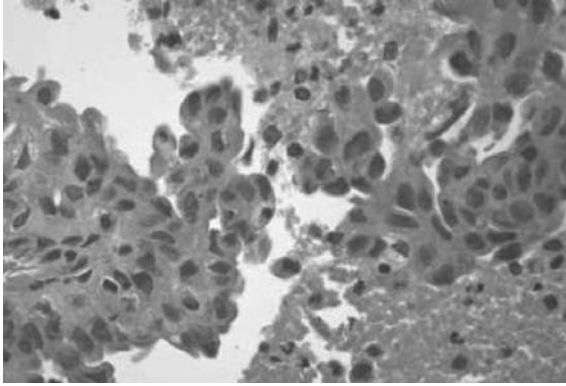

FIGURE 1: Cytological specimen consistent with a metastatic lesion of non-small cell lung cancer in the left adrenal gland (cell block from fine-needle aspirate fixed in formalin and stained with haematoxylin and eosin, original magnification ×100)

TABLE 1:
Diagnoses of the 61 biopsy/histologically proven incidental non-secreting adrenal masses

Diagnosis	No. of cases
Benign	15
Adenoma	6
Cystic mass with calcification	1
Cystic mass with granulomatous chronic inflammation	2
Haematoma	2
Ganglioneuroma	2
Schwannoma	1
Cavernous angioma	1
Malignant metastases from	46
Non-small cell lung cancer	13
Breast, colonic or ovarian carcinoma	9
Melanoma	7
Urothelial carcinoma of the bladder	6
Hepatocellular carcinoma	5
Non-Hodgkin's lymphoma	3
Gastrointestinal stromal tumour	3

CT ALONE

Applying the generally accepted recommendations of Caoili *et al*.[17,18] for the diagnosis of a lipid-poor adenoma to a mass with a non-enhanced CT number > 10 HU led to false negative results in five patients, with metastatic lesions from melanoma (*n* = 2), NSCLC (*n* = 1), colonic carcinoma (*n* = 1)

and GIST (*n* = 1). Better results were obtained when contrast-enhanced CT was used. Adenomas enhance rapidly with intravenous contrast media but the washout of the agent is also rapid. Metastases also enhance vigorously with contrast material, but the washout of the agent is more prolonged than with adenomas (Fig. 2). Applying these
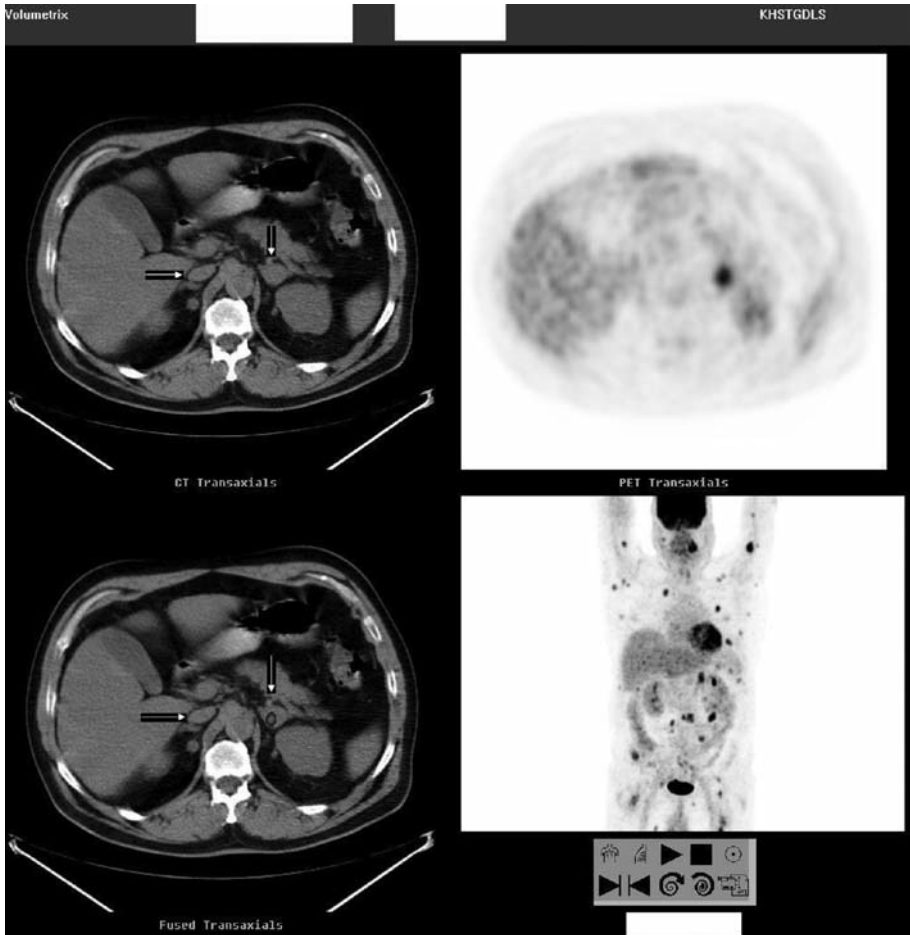

FIGURE 2: Computed tomography (CT) and ^{18}F-fluorodeoxyglucose positron emission tomography (FDG PET)/CT findings in a 61-year old male patient with widespread non-small cell lung cancer metastases. With CT alone, lipid-poor adenoma could not be sufficiently differentiated from metastases in either of the two adrenal masses present. With FDG PET/CT, the final diagnosis was lipid-poor adenoma of the right adrenal gland and metastasis of the left adrenal gland (arrows)

characterizations to the above-mentioned patients with melanoma and NSCLC correctly identified the metastases. Further improvement was possible with tumours unchanged in size for ≥ 6 months at follow-up CT performed at 6 – 12 months (mean 8 ± 4 months) after the delayed enhanced CT scan. A correct CT diagnosis of malignancy was confirmed if a mass doubled or more in volume within 6 months in a patient with a history of previous or present extra-adrenal malignancy. Equivocal results were found in six patients with infected or inflamed cystic masses. Overall, the sensitivity, specificity, positive predictive value and negative predictive value of CT were 95% (103/108 lesions), 94% (104/110 lesions), 94% (103/109 lesions) and 95% (104/109 lesions), respectively.

SHIFT MRI

In adrenal masses that did not contain lipid, the absence of significant signal loss on out-of-phase images correctly indicated adrenal metastases in 41 patients, whereas false positive results were seen in eight patients with lipid-poor adenomas that showed internal degeneration and areas of absorption and vascularization on histological examination. Equivocal results (declared as false positive) were seen in three patients with hepatocellular carcinoma, because adenoma could not be sufficiently differentiated from a metastatic lesion (Fig. 3). Overall, the sensitivity, specificity, positive predictive value and negative predictive value of shift MRI were 97% (101/104 lesions), 92% (106/114 lesions), 92% (101/109 lesions) and 97% (106/109 lesions), respectively.

FDG PET/CT

Six false positive results were found in patients with infected or inflamed cystic masses, of which two had a histological appearance of a thin rim of cortical and medullary adrenal tissue with superimposed granulomatous chronic inflammation. The infectious nature of the process was manifested by scattered intracellular and
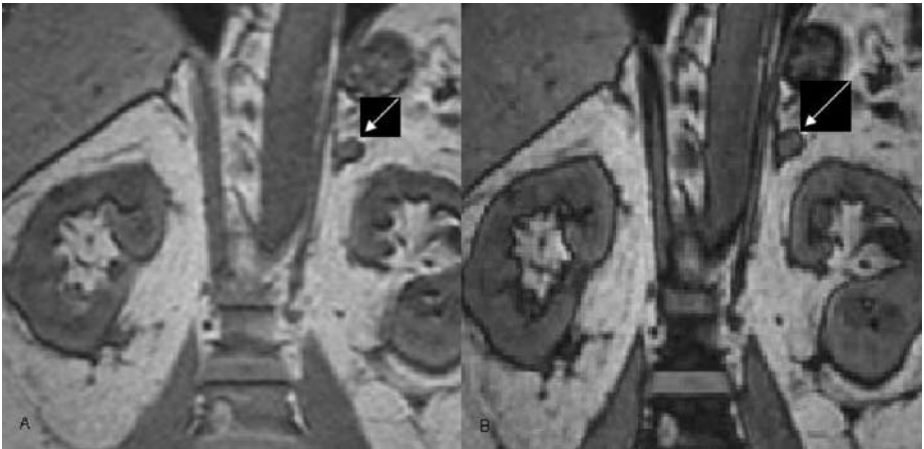

FIGURE 3: Lipid-poor adenoma misdiagnosed as non-adenoma using chemical shift magnetic resonance imaging in a patient with hepatocellular carcinoma. The adrenal mass (arrows) shows no visual signal intensity loss between (A) the in-phase image and (B) the opposed-phase image

extracellular _Leishmania amastigotes_ in one patient and _Blastomyces_ in the other (Fig. 4). Unclear results were found in two biopsy-proven adenomas and one that was histologically-proven. Tumour size in these three patients was 15 – 20 mm, and the tumour/liver SUV_{max} ratio was 1.00 – 1.05. Based on visual analysis, six of the 51 benign lesions were falsely classified as positive. In these cases, the tumour/liver SUV_{max} ratio was between 1.71 and 1.95 and the SUV_{max} was between 3.6 and 4.4. Both
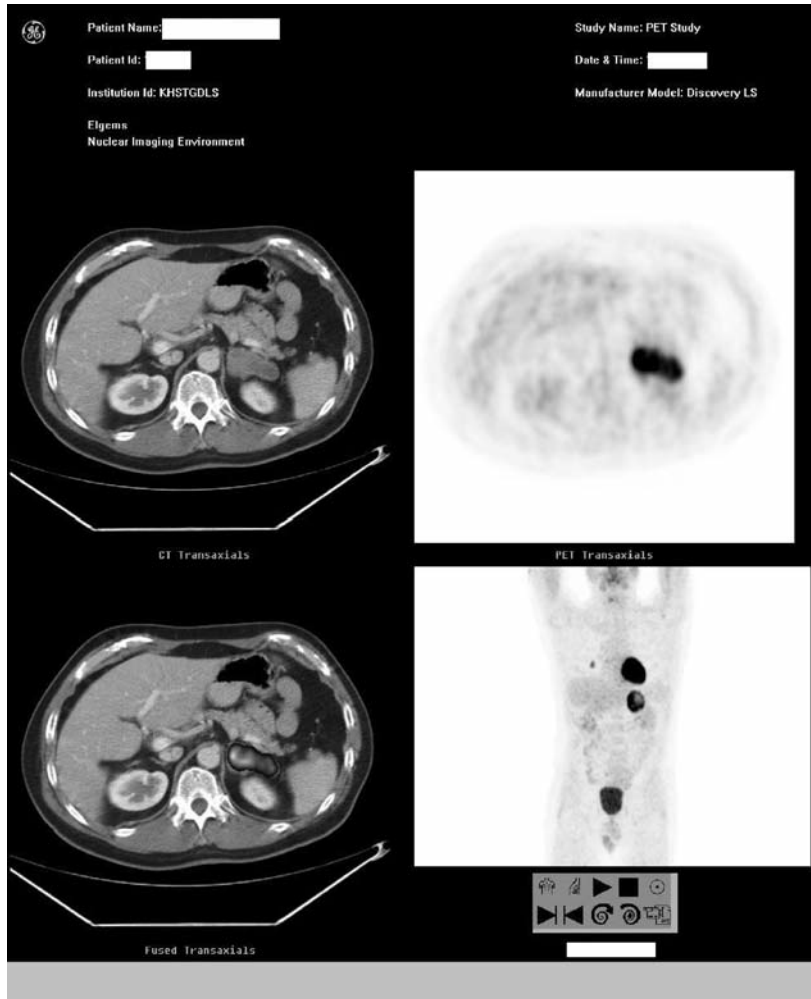

FIGURE 4: False positive result found with ^{18}F-fluorodeoxyglucose positron emission tomography (FDG PET) in a 55-year old male with intracellular and extracellular _Leishmania amastigotes_ cyst infection of the left adrenal gland. Transaxial computed tomography (CT) and fused FDG PET/CT images show abnormal FDG uptake on the left (maximum standardized uptake value [SUV_{max}] = 14.3) in a 56 mm soft-tissue attenuation adrenal mass (34 HU) misdiagnosed as carcinoma. The tumour/liver SUV_{max} ratio was 5.1. There was lateral hypometabolism corresponding with necrosis

physicians were in agreement in all cases. Overall, the sensitivity, specificity, positive predictive value and negative predictive value of PET were 97% (103/106 lesions), 94% (106/112 lesions), 94% (103/109 lesions) and 97% (106/109 lesions), respectively.

QUANTITATIVE ANALYSIS

Tumour characteristics are summarized in Table 2. The mean size was 47 mm for all tumours. Benign tumours had a significantly smaller size ($P = 0.001$), a significantly lower tumour SUV_{max} ($P < 0.001$), a significantly lower tumour/liver SUV_{max} ratio ($P < 0.001$), a significantly lower CT density ($P = 0.005$) and a significantly higher shift MRI lipid mass density ($P = 0.001$) compared with malignant tumours. In patients with no history of liver disease, the tumour/liver SUV_{max} ratio was the most accurate parameter for distinguishing the nature of the tumour: when the tumour/liver SUV_{max} ratio was 1.0, the sensitivity and specificity reached 100%. The maximal benign ratio was 0.95, whilst the minimal malignant ratio was 1.15. Overlap was observed in three patients with adenoma and a ratio of 1.00 – 1.05 (see previous section entitled FDG PET/CT). There was no significant difference between the evaluations of the two physicians: the mean differences for tumour SUV_{max}, liver SUV_{max} and tumour/liver SUV_{max} ratio were 0.06, 0.10 and 0.05, respectively.

Discussion

The adrenal gland is a common site of disease and detection of adrenal masses has increased with the increased use of cross-sectional imaging. Radiology and nuclear medicine imaging are playing a critical role, not only in the detection of adrenal abnormalities but also in characterizing them as benign or malignant. Thin-collimation CT has become the study of choice for the evaluation of tumour size and intracellular lipid content by measuring the attenuation coefficient on non-contrast-enhanced CT. Difficulties are encountered when applying standard recommendations for the differentiation of benign and malignant adrenal masses.[17,18] In the present study, at an attenuation threshold of 10 HU, the sensitivity reached 95%, with a specificity of 94%. An increase in specificity could be achieved when adrenal size, shape, and especially change in lesion size over a

TABLE 2:
Features in incidental non-secreting adrenal masses in cancer patients ($n = 109$)

Feature	Benign		Malignant		Statistical significance
	Median	Range	Median	Range	
Maximum diameter (mm)	34	15 – 98	59	19 – 155	$P = 0.001$
Unenhanced CT density (HU)	23	−5 – 61	36	21 – 45	$P = 0.005$
Shift MRI lipid mass density (SI)	31	1 – 59	−6	−13 – −1	$P = 0.001$
Tumour SUV_{max}	2.29	1.2 – 5.22	12.2	1.06 – 24	$P < 0.001$
Liver SUV_{max}	2.1	1.51 – 3.9	2.29	0.1 – 3.9	NS
Tumour/liver SUV_{max} ratio	0.7	0.5 – 0.9	6	1.0 – 56	$P < 0.001$

CT, computed tomography; HU, Hounsfield Units; MRI, magnetic resonance imaging; SI, degree of signal intensity decrease on out-of-phase magnetic resonance images; SUV_{max}, maximum standardized uptake value; NS, not statistically significant ($P > 0.05$).

longer time period (up to 3 – 5 months) were taken into account. A possible explanation for this is that up to 30% of adenomas do not contain sufficient lipid to have low attenuation on CT.[18,20] Adenomas are a heterogeneous population: approximately 70% of them have intracellular lipid, but 30% do not. Thus, although non-enhanced CT can be used to identify 70% of adenomas, it does not allow the 30% that do not contain lipid to be reliably differentiated from metastases. Although an attenuation value of ≤ 10 HU on non-enhanced CT is diagnostic of an adenoma, an attenuation value of > 10 HU is not diagnostic of a metastasis.

The use of shift MRI to differentiate adenomas from metastases relies on physiological differences in perfusion. In the present study, however, false positive results were seen with shift MRI in eight patients with lipid-poor adenomas that showed internal degeneration and areas of absorption and vascularization on histological examination. Equivocal results (declared as false positive) were seen in three patients with HCC. As with non-enhanced CT, intracellular lipid content still plays a crucial role in the differentiation of benign from malignant adrenal masses; in adrenal masses with low lipid content, the signal loss on out-of-phase images was not strong enough to allow for specific evaluation, as occurred in the eight patients with lipid-poor adenomas in the present study. An increase in specificity comparable to other studies could be achieved by using a wider attenuation coefficient range of 10 – 30 HU. This problem in lipid-poor masses has also been reported by Haider _et al._[10] Unfortunately, they had insufficient data to perform a comparison between dual-echo and non-dual-echo chemical shift MRI sequences. The reason for equivocal results in lipid-poor masses may also be related, in

part, to the use of older MRI technologies that do not allow for dual-echo single breath-hold acquisition.

One surprise of the present study was that, although both CT and shift MRI exhibited typical technical limitations, the diagnostic accuracy of 92 – 97% was of a similar range to that for FDG PET/CT (94 – 97%). For CT and shift MRI, technical limitations were found in patients with lipid-poor adenomas and those with small metastases, since differentiation between these lesions was often unsatisfactory, whereas for FDG PET/CT limitations were evident in six cancer patients with inflamed cystic adrenal masses but not in those with lipid-poor adenomas or metastases.

In the present study, for FDG PET/CT the best correlation with histological evaluation was found using a tumour/liver SUV_{max} ratio cut-off of 1.0 (mean ± SD 1.0 ± 0.10). This is in contrast to published findings in which a cut-off value of 1.8 was reported.[13] The finding that tumour SUV_{max} alone appeared to be less accurate than visual analysis is, however, consistent with that previous study.[18] In the present study, the minimal malignant SUV_{max} (1.06) was lower than the minimal benign SUV_{max} (1.2), highlighting the limitations of tumour SUV_{max}.

A speculative explanation for the differences seen compared with other studies[13] might be that they are due to the kinetics of FDG and to angiogenesis of the adrenal glands. FDG is transported into cells via the facilitated glucose transporters; currently 14 facilitated glucose transporters have been identified (solute carrier family 2 [SLC2]A1 to SLC2A14 [_Homo sapiens_]).[21] Changes in glucose transporters are directly modulated by alterations in vascular endothelial growth factor (VEGF), which is a key element of tumour angiogenesis,[22] as well as by the impact of hypoxia on

angiogenesis.[23] Various drug treatments may also modulate FDG uptake. The effect of imatinib on gene expression and FDG PET results in imatinib-sensitive and -resistant cell lines was evaluated by Trent *et al.*[24]; there was an inverse correlation between FDG uptake and the expression of insulin-like growth factor binding protein-3 (IGFBP-3). Patients who responded to treatment and who had decreased FDG uptake following therapy had enhanced expression of IGFBP-3.[24] It is known from other studies that IGFBP-3 directly induces apoptosis.[25] As a consequence, FDG uptake in tumour cells is a strong marker of tumour viability. Thus, the uptake of FDG in tumour cells predominantly depends on a variety of molecular and genetic changes. Therapeutic treatment and its antiproliferative effect on angiogenesis seem to be of particular importance. Recently, Ishimoto *et al.*[26] demonstrated that angiotensin II was localized predominantly in the periphery of the adrenal gland. Angiotensin I stabilizes whereas angiotensin II destabilizes blood vessels, increasing responsiveness to angiogenic stimuli such as VEGF-A and fibroblast growth factor-2. Chemo-therapeutic drugs, such as docetaxel, chronically administered at a low dose using a frequent schedule (metronomic dosing) in patients with prostate cancer, can cause potent antiangiogenic effects by targeting the endothelial cells of newly growing blood vessels in the tumour, as well as in other cell populations such as the periphery of the adrenal glands.[27] This may be a possible reason why, in previous studies,[13] a tumour/liver SUV_{max} ratio cut-off of 1.8 in patients with no history of malignancy gave similar results to the present study involving tumour patients receiving chemotherapy and a significantly lower tumour/liver SUV_{max} ratio cut-off of 1.0.

The major limitation of the present study was that this was a retrospective study that included patients with a variety of different malignancies and therapy regimens. Further studies are needed using greater numbers of patients with the same type of malignancy and therapy. In addition, the number of patients with available biopsy or histological findings was low.

We conclude that FDG PET/CT can accurately characterize adrenal tumours, with excellent sensitivity and specificity. The use of 1.0 as the threshold for the tumour/liver SUV_{max} ratio seems to be promising for distinguishing benign from malignant adrenal masses in cancer patients. The present study also demonstrated that, although different imaging modalities may have a similar morphological and molecular basis, they can give different imaging results. Further studies are needed to evaluate whether these findings hold true in larger patient populations and whether they can be applied to healthy patients who are not undergoing chemotherapy.

Conflicts of interest

The authors had no conflicts of interest to declare in relation to this article.

References

1 Dunnick NR, Korobkin M: Imaging of adrenal incidentalomas: current status. *AJR Am J Roentgenol* 2002; **179:** 559 – 568.

2 Abrams HL, Spiro R, Goldstein N: Metastases in carcinoma; analysis of 1000 autopsied cases.

Cancer 1950; **3**: 74 – 85.

3   Bernardino ME, Walther MM, Phillips VM, *et al*: CT-guided adrenal biopsy: accuracy, safety, and indications. *AJR Am J Roentgenol* 1985; **144**: 67 – 69.

4   Francis IR, Smid A, Gross MD, *et al*: Adrenal masses in oncologic patients: functional and morphologic evaluation. *Radiology* 1988; **166**: 353 – 356.

5   McGahan JP: Adrenal gland: MR imaging. *Radiology* 1988; **166**: 284 – 285.

6   Lee MJ, Hahn PF, Papanicolaou N, *et al*: Benign and malignant adrenal masses: CT distinction with attenuation coefficients, size, and observer analysis. *Radiology* 1991; **179**: 415 – 418.

7   Korobkin M, Lombardi TJ, Aisen AM, *et al*: Characterization of adrenal masses with chemical shift and gadolinium-enhanced MR imaging. *Radiology* 1995; **197**: 411 – 418.

8   Boland GW, Lee MJ, Gazelle GS, *et al*: Characterization of adrenal masses using unenhanced CT: an analysis of the CT literature. *AJR Am J Roentgenol* 1998; **171**: 201 – 204.

9   Israel GM, Korobkin M, Wang C, *et al*: Comparison of unenhanced CT and chemical shift MRI in evaluating lipid-rich adrenal adenomas. *AJR Am J Roentgenol* 2004; **183**: 215 – 219.

10 Haider MA, Ghai S, Jhaveri K, *et al*: Chemical shift MR imaging of hyperattenuating (>10 HU) adrenal masses: does it still have a role? *Radiology* 2004; **231**: 711 – 716.

11 Lumachi F, Borsato S, Tregnaghi A, *et al*: High risk of malignancy in patients with incidentally discovered adrenal masses: accuracy of adrenal imaging and image-guided fine-needle aspiration cytology. *Tumori* 2007; **93**: 269 – 274.

12 Jana S, Zhang T, Milstein DM, *et al*: FDG-PET and CT characterization of adrenal lesions in cancer patients. *Eur J Nucl Med Mol Imaging* 2006; **33**: 29 – 35.

13 Tessonnier L, Sebag F, Palazzo F, *et al*: Does ^{18}F-FDG PET/CT add diagnostic accuracy in incidentally identified non-secreting adrenal tumours? *Eur J Nucl Med Mol Imaging* 2008; **35**: 2018 – 2025.

14 Metser U, Miller E, Lerman H, *et al*: ^{18}F-FDG PET/CT in the evaluation of adrenal masses. *J Nucl Med* 2006; **47**: 32 – 37.

15 Groussin L, Bonardel G, Silvéra S, *et al*: ^{18}F-Fluorodeoxyglucose positron emission tomography for the diagnosis of adrenocortical tumors: a prospective study in 77 operated patients. *J Clin Endocrinol Metab* 2009; **94**: 1713 – 1722.

16 Blake MA, Kalra MK, Sweeney AT, *et al*: Distinguishing benign from malignant adrenal masses: multi-detector row CT protocol with 10-minute delay. *Radiology* 2006; **238**: 578 – 585.

17 Caoili EM, Korobkin M, Francis IR, *et al*: Adrenal masses: characterization with combined unenhanced and delayed enhanced CT. *Radiology* 2002; **222**: 629 – 633.

18 Caoili EM, Korobkin M, Francis IR, *et al*: Delayed enhanced CT of lipid-poor adrenal adenomas. *AJR Am J Roentgenol* 2000; **175**: 1411 – 1415.

19 Korobkin M, Giordano TJ, Brodeur FJ, *et al*: Adrenal adenomas: relationship between histologic lipid and CT and MR findings. *Radiology* 1996; **200**: 743 – 747.

20 Peña CS, Boland GW, Hahn PF, *et al*: Characterization of indeterminate (lipid-poor) adrenal masses: use of washout characteristics at contrast-enhanced CT. *Radiology* 2000; **217**: 798 – 802.

21 Eyre TA, Ducluzeau F, Sheddon TP, *et al*: The HUGO Gene Nomenclature Database, 2006 updates. *Nucleic Acids Res* 2006; **34(database issue)**: D319 – D321.

22 Pedersen MW, Holm S, Lund EL, *et al*: Coregulation of glucose uptake and vascular endothelial growth factor (VEGF) in two small-cell lung cancer (SCLC) sublines *in vivo* and *in vitro*. *Neoplasia* 2001; **3**: 80 – 87.

23 Airley RE, Mobasheri A: Hypoxic regulation of glucose transport, anaerobic metabolism and angiogenesis in cancer: novel pathways and targets for anticancer therapeutics. *Chemotherapy* 2007; **53**: 233 – 256.

24 Trent JC, Ramdas L, Dupart J, *et al*: Early effects of imatinib mesylate on the expression of insulin-like growth factor binding protein-3 and positron emission tomography in patients with gastrointestinal stromal tumor. *Cancer* 2006; **107**: 1898 – 1908.

25 Bhattacharyya N, Pechhold K, Shahjee H, *et al*: Nonsecreted insulin-like growth factor binding protein-3 (IGFBP-3) can induce apoptosis in human prostate cancer cells by IGF-independent mechanisms without being concentrated in the nucleus. *J Biol Chem* 2006; **281**: 24588 – 24601.

26 Ishimoto H, Minegishi K, Higuchi T, *et al*: The periphery of the human fetal adrenal gland is a site of angiogenesis: zonal differential expression and regulation of angiogenic factors. *J Clin Endocrinol Metab* 2008; **93**: 2402 – 2408.

27 Benelli R, Monteghirfo S, Balbi C, *et al*: Novel antivascular efficacy of metronomic docetaxel therapy in prostate cancer: hnRNP K as a player. *Int J Cancer* 2009; **124**: 2989 – 2996.

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