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Imaging characterization of non-hypersecreting adrenal masses: comparison between MR and radionuclide techniques

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Aim. **In patients with non-hypersecreting adrenal masses, tumor characterization is clinically relevant to establish the appropriate treatment planning. The aim of this study was to comparatively characterize such adrenal lesions using MR and radionuclide techniques.**

Methods. **Thirty patients with non-hypersecreting unilateral adrenal tumors underwent both MR and adrenal scintigraphy. MR was performed using SE T1- (pre- and post-gadolinium DTPA) and T2-weighted images as well as in- and out-phase chemical-shift imaging (CSI). MR qualitative and quantitative (signal intensity ratios) evaluation was performed. Radionuclide studies consisted of iodine-131 nor-cholesterol (n=20), iodine-131 MIBG (n=15) and fluorine-18 FDG PET (n=11) scans. Histology (n=16), biopsy (n=3) or clinical-imaging follow-up (n=11) demomstrated 13 adenomas, 3 cysts, 2 myelolipomas, 4 pheochromocytomas (pheos), 4 carcinomas, 1 sarcoma and 3 metastases. Comparative imaging analysis was focused on adenomas, pheos and malignant tumors.**

Results. **Qualitative MR evaluation showed: signal T2-hyperintensity in 46% of adenomas and in 100% of pheos and malignant tumours, no gadolinium enhancement in 92% of adenomas and definite signal intensity loss on CSI in 100% of such tumour lesions, gadolinium enhancement in 100% of pheos and in 63% of malignancies and no absolute change of signal intensity on CSI in 100% of both pheos and malignancies. Quantitative MR analysis demonstrated: significantly higher signal T2-hyperintensity of pheos compared to adenomas and malignancies as well as significantly higher enhancement after gadolinium in pheos compared to adenomas and malignancies ($p<0.03$). Radionuclide studies showed significantly increased nor-cholesterol uptake only in adenomas (n=13), significant MIBG accumulation only in pheos (n=4) and FDG activity only in malignant adrenal lesions (n=8).**

Conclusion. **MR techniques may provide some presumptive criteria to characterize non-hypersecreting adrenal masses, such as no gadolinium enhancement and definite signal intensity loss on CSI in adenomas or quantitatively measured T2-hyperintensity and gadolinium enhancement in pheos. On the other hand, radionuclide modalities offer more specific findings in this setting since nor-cholesterol and MIBG scans are respectively able to reveal benign tumours such as adenoma and pheochromocytoma, while FDG imaging allows identification of malignant adrenal lesions. Adrenal scintigraphy is recommended in those patients, when MR images are uncertain or inconclusive.**

KEY WORDS: Glands - Neoplasms - Magnetic resonance imaging - Radiopharmaceutics.

The high resolution of anatomic imaging techniques such as computed tomography (CT) and magnetic resonance (MR), used in patients with suspected abdominal diseases, frequently results in detection of unexpected adrenal masses.[1, 2] In this set-

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ting, the main clinical question consists of differential diagnosis between benign and malignant adrenal lesions in order to select appropriate treatment.[2] As initial diagnostic approach, clinical and laboratory assessment of cortical and medullary adrenal function allow the identification of hypersecreting adrenal lesions and, hence, characterization of these tumours.[3] A tumour mass, however, may not cause adrenal hyperfunction since it may be non-hypersecreting or secretes non-active products. In such conditions, lesion typing remains uncertain. CT and MR accurately provide anatomic details of adrenal tumours as well as presumptive criteria for diagnosis.[4] In particular, adrenal adenomas may be suggested by CT on the basis of low attenuation coefficient on un-enhanced images and/or early as well as rapid washout on enhanced scans.[5] Similarly, MR is able to characterize adenomas using chemical-shift sequence or pheochromocytomas showing clearly increased signal intensity on T2-weighted images and significant enhancement after gadolinium administration.[6]

In patients with non-hypersecreting adrenal masses, radionuclide adrenal imaging performed with specifically labelled radiopharmaceuticals which target elements of adrenal function provide specific metabolic information for diagnosis, thus, complementing morphological imaging modalities.[7, 8] In particular, a diagnostic role of molecular imaging has been identified in the management of patients with non-hypersecreting adrenal masses.[9] In this regard, several radiotracers which display unique biological behaviour may be used in nuclear medicine for adrenal lesion evaluation. These include tracers labelled with single photon emitters [7, 10] such as radio-iodine labelled nor-cholesterol and meta-iodobenzylguanidine (MIBG) and gallium-67 citrate.[11] Alternatively there are agents labelled with positron emitters such as hydroxy-ephedrine,[12] deoxy-glucose [13-15] and metomidate.[16] Finally, radiolabeled somatostatin analogs have been proposed to identify somatostatin receptors in malignant adrenal tumours.[17]

In this study, we compared the results of MR imaging techniques and those of radionuclide studies in patients with non-hypersecreting adrenal masses in order to evaluate imaging criteria for accurately performing non-invasive preoperative tumour characterization and, hence, to differentiate benign from malignant lesions.

Materials and methods

Patient population

Thirty patients (10 male and 20 female, mean age 51±13 years) with non-hypersecreting unilateral adrenal masses (tumour size=4.6±3.0 cm) detected on ultrasound and/or CT studies underwent both MR imaging and adrenal scintigraphy using appropriate radiopharmaceuticals. The selection criteria for patient enrollment consisted of the presence of non-hypersecreting adrenal tumours discovered in subjects who had diagnostic evaluation of non-adrenal disorders: abdominal pain (n=7), abdominal trauma (n=3), biliary tract stone disease (n=3), renal cysts (n=4), anuria (n=3) or during the staging (n=5) or follow-up (n=5) for malignant tumours. No patient showed signs and/or symptoms of adrenal hyper-secretion. A total of 46 adrenal radionuclide studies was analyzed consisting of iodine-131 nor-cholesterol scintigraphy (n=20), iodine-131 MIBG imaging (n=15) and fluorine-18 deoxyglucose (FDG) positron emission tomography (PET) (n=11). Histology (n=16), biopsy (n=3) or 2-years clinical-imaging follow-up (n=11) were used as standard of reference demonstrating a total of 22 benign adrenal lesions, of which 13 were adenomas, 3 were cysts, 2 were myelolipomas and 4 were pheochromocytomas (pheos), as well as a total of 8 malignant tumours, of which 4 were carcinomas, 1 was a sarcoma and 3 had metastases. Informed consent, as required by the Institutional Clinical Research Sub-panel on Human Studies at our Institute, was obtained in all patients.

Laboratory analysis

In all patients, the evaluation of adrenal function consisted of screening tests for excess of mineralcorticoid, glucocorticoid, androgen and catecholamine secretion. In particular, measurement of plasma aldosterone levels and renin activity in clinostatic as well as orthostatic posture was performed. Plasma cortisol and corticotropin levels were measured at 8:00 a.m. and 11:00 p.m. and a 24-hour urine assay for free cortisol was performed. Measurements of serum dehydroepiandrosterone sulfate, 17-hydroxyprogesterone, androstenedione, testosterone and electrolyte levels were included. An overnight low-dose dexamethasone (DS) suppression test (1 mg orally at 11:00 p.m. and measurement of serum cortisol level at 8:00 a.m. the following morning) was also performed. For the evaluation of medullary

adrenal function, plasma catecholamine levels, 24-hour urinary excretions of catecholamines and their metabolites, vanillylmandelic acid and metanephrine, were measured. Hormonal values were determined by radioimmunoassay or immunoradiometric assay methods using commercially available kits. Urinary catecholamine, vanillylmandelic acid and metanephrine levels were measured by high-performance liquid chromatography. Sodium and potassium levels were assessed by flame photometry with lithium as an internal standard.

Magnetic resonance

MR imaging studies were performed with a 1.5 Tesla superconducting magnet scanner (Magnetom, Siemens, Erlangen, Germany). A spin echo technique was used to obtain 5 mm contiguous 3-dimensional sections of the abdomen. T1-weighted images (TR/TE=600/15 ms) and T2-weighted images (TR/TE= 2000/15-90 ms) were obtained. T1-weighted images were also acquired after the intravenous administration of gadolinium-DTPA (0.2 ml/kg of weight body, Magnevist, Schering). MR imaging studies were also integrated using chemical-shift (CS) sequence acquiring in-phase and out-of-phase images (TR/TE=100/6-4 ms).

Nor-cholesterol imaging

Before nor-cholesterol injection, thyroid iodine uptake was blocked with a saturated solution of potassium iodide (200 mg per day orally, starting the day before tracer administration and continuing for 8 days). Iodine-131 nor-cholesterol (37 MBq, CIS Bio International, Cedex, France) was injected intravenously. Adrenal scintigraphy was performed 5 (early) and 7 (delayed) days after tracer injection using a large field of view γ camera (Orbiter, Siemens, Erlangen, Germany) with a high-energy collimator and a 20% window centered at 364 Kev. Early and delayed posterior abdominal views were acquired. A mild laxative (bisacodyl) was given (10 mg) twice daily beginning 2 days before the 1st day of imaging to reduce interfering colonic iodine-131 activity. When required, norcholesterol adrenal scintigraphy was also performed with a concomitant DS suppression test. For this, 1 mg of DS was administered 4 times daily for 7 days prior to nor-cholesterol and for 5 days after tracer injection.

MIBG imaging

Before MIBG injection, thyroid iodine uptake was blocked with a saturated solution of potassium iodide (200 mg per day orally, starting before tracer administration and continuing for 8 days). Iodine-131 MIBG (37 MBq, Amersham Sorin, Saluggia, Italy) was administered intravenously. Posterior abdominal spot views were obtained at 24, 48 and 72 hours after tracer injection using a large field of view γ camera (Orbiter, Siemens, Erlangen, Germany) with a high-energy collimator and a 20% window centered at 364 Kev.

Fluorine-18 FDG PET

PET imaging was performed using a whole-body PET EXACT 47 scanner (Siemens, Erlangen, Germany). Patients were studied in fasting conditions for at least 4-6 hours before FDG injection. Patients were positioned on the PET gantry using a rectilinear scan computerized program localized on the superior abdomen. Before injection of ^{18}F FDG, abdomen transmission scan using a rod source of Ge-67 for the attenuation correction of the corresponding emission scans was performed for 20 minutes. Thereafter, patients were intravenously injected with 370 MBq of ^{18}F FDG. Abdomen emission imaging was acquired between 30 and 45 minutes after FDG administration. Images were reconstructed using filtered backprojection smoothed with a Hann filter with a cutoff frequency of 0.4 cycles/pixels by SUN Workstation System (Siemens, Erlangen, Germany) generating three-dimensional PET scans as axial, coronal and sagittal views.

Data analysis

Adrenal function, either cortical and medullary, was considered normal when the corresponding hormone values were in the normal range. The anatomic characteristics of adrenal tumours were assessed on MR images; in particular, tumour size was measured as maximal diameter in centimeters and the characteristics of lesion margins (regular or irregular) were assessed. Comparative evaluation of MR and radionuclide imaging findings was focused in adenomas, pheos and malignant adrenal lesions, both primary tumours and metastases; the remaining adrenal lesions, represented by cysts or myelolipoma, were not considered for the comparative imag-

TABLE I.—*Qualitative MR and radionuclide imaging results of patient population.*

#	Lesion	Site	Size°	MR T2*	MR Gd^	MR CSI"	nor-Chol	MIBG	FDG
1	Adenoma	L	3.5	Hyperintense	No	Yes	+	—	na
2	Adenoma	L	3.0	Isointense	No	Yes	+	—	na
3	Adenoma	L	2.5	Isointense	No	Yes	+	—	na
4	Adenoma	R	6.0	Hyperintense	Yes	Yes	+	—	na
5	Adenoma	L	3.0	Hyperintense	No	Yes	+	na	na
6	Adenoma	R	2.5	Isointense	No	Yes	+	na	na
7	Adenoma	L	2.0	Hyperintense	No	Yes	+	na	na
8	Adenoma	L	2.5	Isointense	No	Yes	+	—	na
9	Adenoma	R	3.0	Hyperintense	No	Yes	+	na	na
10	Adenoma	L	3.0	Isointense	No	Yes	+	—	—
11	Adenoma	R	2.0	Hypointense	No	Yes	+	—	—
12	Adenoma	R	2.0	Hypointense	No	Yes	+	na	na
13	Adenoma	L	2.5	Hyperintense	No	Yes	+	na	na
14	Pheochromocytoma	L	5.0	Hyperintense	Yes	No	-	+	na
15	Pheochromocytoma	R	3.5	Hyperintense	Yes	No	na	+	na
16	Pheochromocytoma	L	2.5	Hyperintense	Yes	No	na	+	na
17	Pheochromocytoma	L	5.5	Hyperintense	Yes	No	na	+	na
18	Carcinoma	R	12.0	Hyperintense	Yes	No	na	—	—
19	Carcinoma	L	6.5	Hyperintense	No	No	na	na	—
20	Carcinoma	L	10.0	Hyperintense	No	No	na	—	—
21	Carcinoma	R	5.0	Hyperintense	Yes	No	—	na	—
22	Sarcoma	L	13.0	Hyperintense	Yes	No	na	na	—
23	Lung metastasis	L	2.0	Hyperintense	No	No	—	na	—
24	Lung metastasis	R	5.0	Hyperintense	Yes	No	na	na	—
25	Melanoma metastasis	R	4.5	Hyperintense	Yes	No	na	na	—
26	Cyst	L	5.5	Hyperintense	No	No	na	—	na
27	Cyst	L	5.0	Hyperintense	No	No	—	—	na
28	Cyst	L	5.0	Hyperintense	No	No	—	na	na
29	Myelolipoma	R	11.0	Hyperintense	No	Yes	—	na	na
30	Myelolipoma	R	4.0	Hyperintense	No	Yes	—	na	—

°: maximal diameter in centimeters; *: lesion signal intensity compared to liver signal intensity; ^: enhancement after gadolinium administration; ": signal intensity loss; nor-Chol: nor-cholesterol; MIBG: metaiodobenzylguanidine; FDG: fluorine-deoxy-glucose; L: left; R: right; +: increased tracer uptake by adrenal lesion (scan positive); —: no tracer uptake by adrenal lesion (scan negative); na: not available.

ing analysis. The results of histology after surgery, adrenal biopsy or 2-years clinical-imaging follow-up were considered the standards of references; in particular, this latter criterion was used in 11 cases of non-hypersecreting cortical adenomas, ranging as maximal diameter between 2.0 and 3.0 cm, which were not surgically removed for the small tumor size.

MR images were evaluated using both qualitative and quantitative analysis. Signal intensity of adrenal lesions was qualitatively assessed on T2-weighted images in terms of hypo-, iso- or hyperintensity compared to that of liver tissue; furthermore, lesion enhancement on T1-weighted images after gadolinium administration (yes or no) as well as signal intensity loss on out-phase CS images (yes or no) were also analyzed, as previously described.[4, 6] Signal intensity of adrenal lesions was quantitatively assessed on T2-weighted images as well as on T1-weighted images after gadolinium in terms of signal intensity ratios (SIRs) using region of interest analysis. SIRs consisted of ratios between absolute signal intensity of adrenal lesion and that of liver, fat and muscle tissues as well as that of image background. This comparative analysis was performed among adenomas, pheos and malignant adrenal tumors using the Student's "t" test for unpaired data. Data were expressed as mean±1SD. Probability values <0.05 were considered significant.

Radionuclide studies were qualitatively evaluated independently without knowledge of clinical and pathologic findings. In particular, the presence of

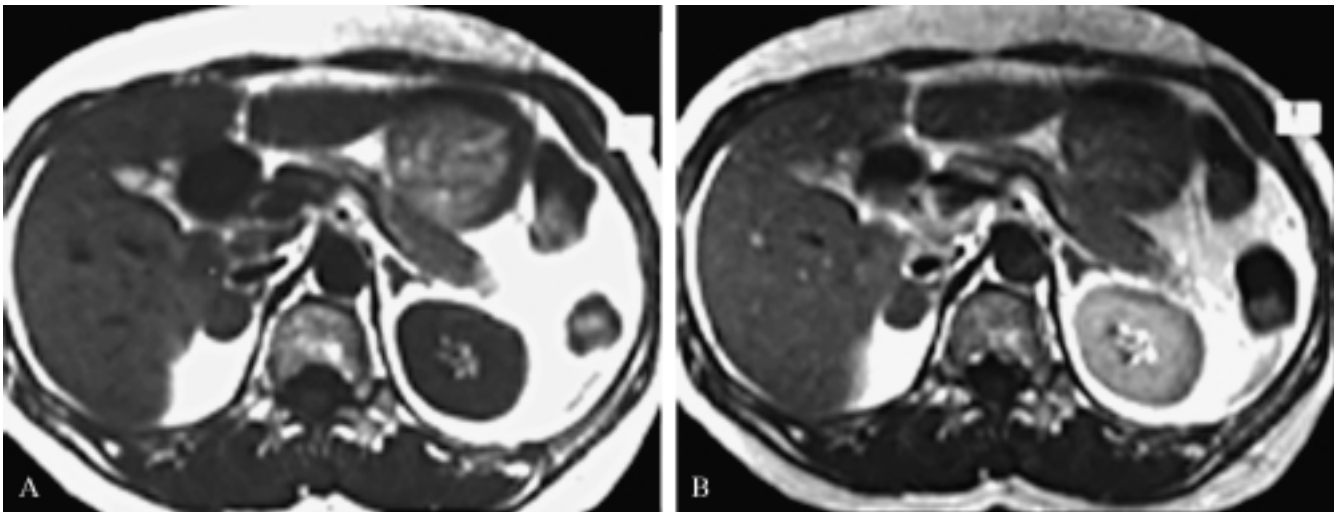

Figure 1.—A 42-year-old woman with a small (2 cm) right adrenal adenoma. A) Abdominal T1-weighted axial MR imaging shows a right adrenal mass with low signal intensity. B) Abdominal T1-weighted axial MR imaging after gadolinium administration shows no lesion enhancement.

abnormally increased uptake of nor-cholesterol, MIBG or FDG was analyzed in the adrenal regions when a tumour lesion was detected. The intensity of tumour uptake was qualitatively evaluated on a high-resolution display by 2 independent and experienced nuclear medicine physicians. In case of disagreement, final interpretation was determined by consensus reading. Adrenal activity was considered abnormal when tracer uptake was greater than initial blood pool and surrounding background activity and when no similar uptake was observed on the contralateral side.

Results

In all patients, laboratory evaluation of both cortical and medullary adrenal function, confirmed normal levels of the corresponding hormones. The results of qualitative MR imaging and radionuclide scans are illustrated in Table I.

MR qualitative analysis

In patients with adrenal adenomas, the evaluation of T2-weighted images demonstrated signal hyperintensity in 46% of cases; no significant lesion enhancement after gadolinium administration occurred in the majority (92%) of these tumors (Figure 1); finally, signal intensity loss on out-phase CS images was observed in all cases (100%), (Figure 2). In patients with pheos, the evaluation of T2-weighted images demonstrated signal hyperintensity in all cases (100%) and similarly significant lesion enhancement occurred after gadolinium administration in all cases (100%), (Figure 3); no CS signal intensity change from in-phase to out-phase imaging occurred in pheos. In patients with adrenal malignant tumors, the evaluation of T2-weighted images demonstrated signal hyperintensity in all cases (100%); significant lesion enhancement after gadolinium administration occurred in the majority (63%) of these tumors. Signal intensity loss on out-phase CS images in these tumours was not observed.

MR quantitative analysis

The results of quantitative evaluation of SIRs on T2-weighted MR images are reported in Table II; in particular, signal hyperintensity of pheos was significantly higher compared to that of adenomas and malignant tumors, while no differences were observed between these latter adrenal lesions. The results of quantitative evaluation of SIRs on T1-weighted MR images performed after gadolinium administration are reported in Table III; in particular, signal intensity after gadolinium was significantly higher in pheos compared to that of adenomas and malignant tumors,

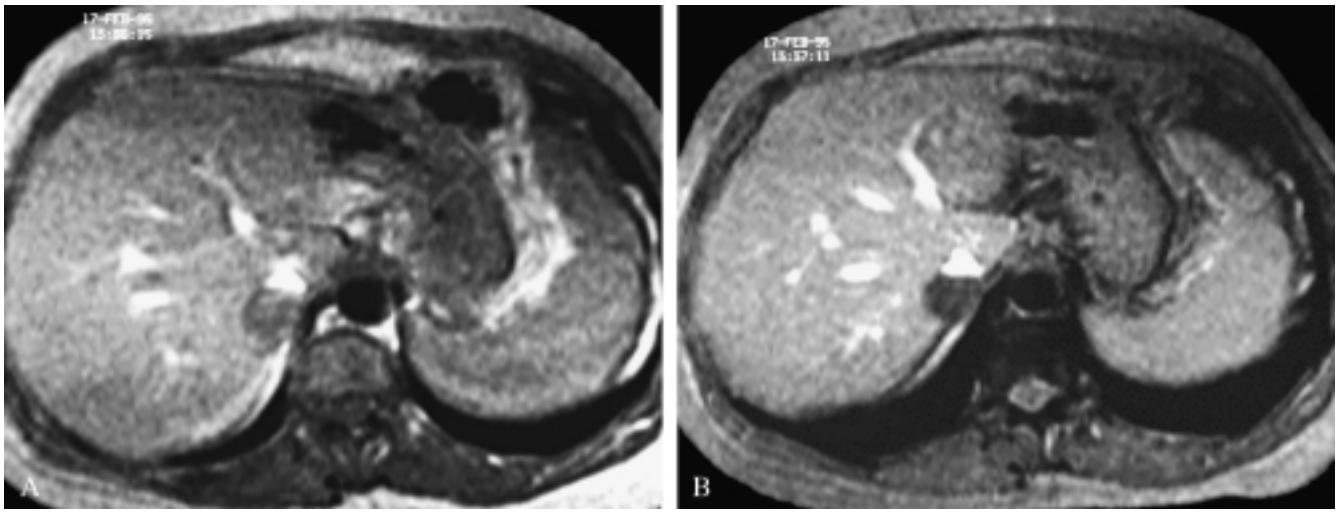

Figure 2.—A 37-year-old man with a small (2 cm) right adrenal adenoma. A) Abdominal T1 in-phase chemical-shift MR imaging shows lesion low signal intensity. B) Abdominal T1 out-phase chemical-shift MR imaging clearly shows loss of lesion signal intensity compared to in-phase acquisition.

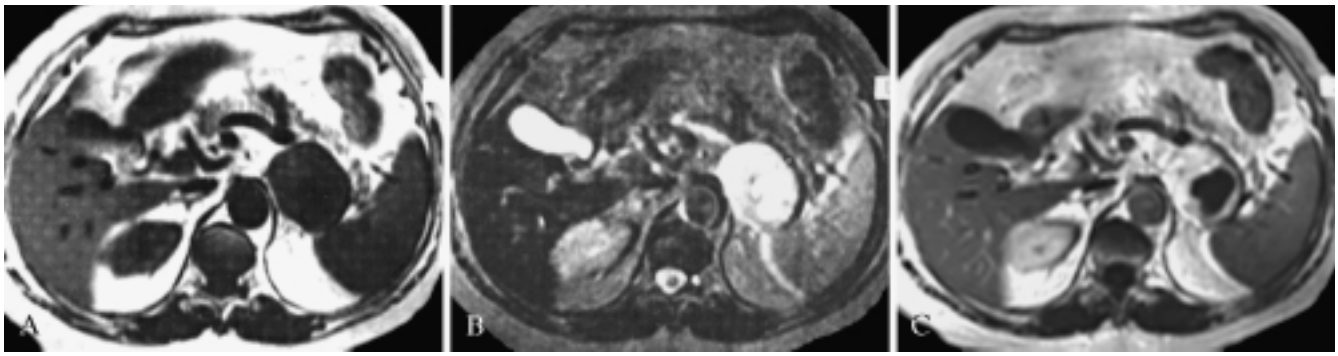

Figure 3.—A 29-year-old man with a large (5.5 cm) left adrenal pheochromocytoma. A) Abdominal T1-weighted axial MR imaging shows a left adrenal mass with low signal intensity. B) Abdominal T2-weighted axial MR imaging shows a left adrenal mass with high signal intensity. C) Abdominal T1-weighted axial MR imaging after gadolinium administration shows significant, but inhomogeneous lesion enhancement.

while no differences were observed between different types of adrenal tumours.

Radionuclide imaging

The results of qualitative evaluation of nuclear studies showed abnormally increased nor-cholesterol uptake in 100% of cases with adenomas (Figure 4) and, similarly, abnormal MIBG activity in 100% of pheos (Figure 5) as well as increased FDG uptake in 100% of malignant adrenal tumors (Figure 6); in particular, no false positive or negative findings were observed in all series of radionuclide studies.

Discussion

The data on imaging of asymptomatic non-hypersecreting adrenal masses has recently increased since the wide use of highly sensitive diagnostic techniques such as CT and MRI for the evaluation of the abdomen. In patients with these non-secreting tumours, the main role of imaging is not just to identify the presence of the tumour but to help characterise its type in a non-invasive way. This will help to ensure appropriate treatment. It is of particular importance to differentiate between benign and malignant lesions. CT and MR studies offer accurate anatomic details of any adren-

TABLE II.—*Quantitative analysis of T2-weighted MR images.*

SIRs	Adenoma	Pheo	Malignancies
Lesion/liver	1.9±1.0	3.4±1.0*°	2.7±0.8
Lesion/fat	0.75±0.3	1.7±0.5*°	1.1±0.5
Lesion/muscle	3.5±2.	7.8±3.5*°	4.1±2.2
Lesion/background	9.1±5.8	32±20*°	13±7.0

SIRs: signal intensity ratios; Pheo: pheochromocytoma; p<0.001 *vs* adenoma; °p<0.03 *vs* malignancies.

TABLE III.—*Quantitative analysis of T1-weighted gadolinium MR images.*

SIRs	Adenoma	Pheo	Malignancies
Lesion/liver	1.0±0.25	1.4±0.28*°	1.0±0.2
Lesion/fat	0.62±0.16	0.92±0.21*°	0.5±0.1
Lesion/muscle	2.0±0.5	2.6±0.35*°	1.8±0.6
Lesion/background	16±12	35±31*°	23±13

SIRs: signal intensity ratios; Pheo: pheochromocytoma; p<0.001 *vs* adenoma; °p<0.03 *vs* malignancies.

al tumour and will give an initial analysis of lesion characterization.[5, 6, 18, 19] In particular, adrenal adenomas may be suggested by CT on the basis of low attenuation coefficient on un-enhanced images and/or early as well as rapid washout on enhanced scans. Similarly, MR is able to characterize adenomas using dynamic-gadolinium or chemical-shift sequences. Pheos also show specific MR features such as clearly increased signal intensity on T2-weighted images and significant enhancement after gadolinium administration. Since gadolinium-enhanced MR imaging shows a considerable overlap in the characteristics of benign and malignant masses, its clinical applicability is limited in distinguishing adenomatous from non-adenomatous adrenal lesions. Conversely, chemical-shift acquisition using the basis of fat content of a lesion can determine adenomas from malignant lesions. It is well known that adenomas contain a large amount of cytoplasmatic lipid in contrast to adrenal metastases which contain little or none. In the majority of adenomas, the MR pattern seen consists of a reduction of signal intensity on out-of-phase scan compared with in-phase images, whereas in malignant lesions signal intensity remains unchanged. However, some adenomas may contain insufficient lipid to result in loss of signal on out-of-phase scan as well as malignant primary and secondary adrenal tumors may have lipid component showing loss of signal intensity on chemical-shift imaging and therefore this may reduce the sensitivity of this technique. Despite the effectiveness, this overlap in MRI appearances and tumour type mean that there remains a need for complementary functional imaging.

Radionuclide modalities using specific tracers such as nor-cholesterol, MIBG and FDG may provide *in vivo* tissue characterization of adrenal tumours being able

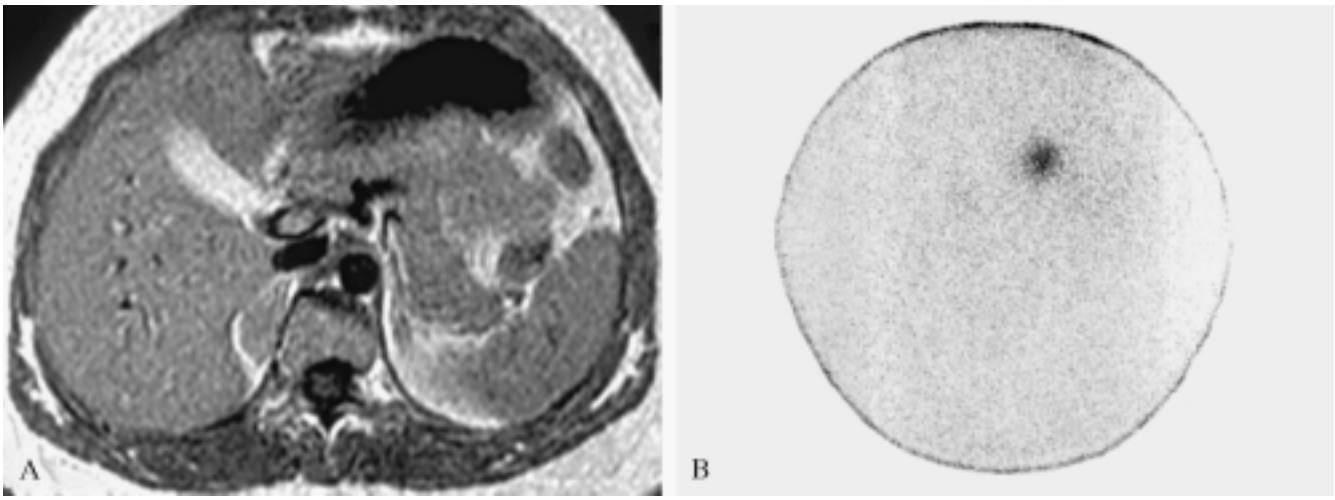

Figure 4.—A 22-year-old woman with a 2.5 cm right adrenal adenoma. A) Abdominal T1-weighted axial MR imaging after gadolinium administration shows a right adrenal mass. B) Abdominal posterior view of iodine-131 nor-cholesterol delayed imaging shows a round area of increased and exclusive tracer uptake in the right adrenal bed corresponding to the mass; no activity was observed in the contralateral side.

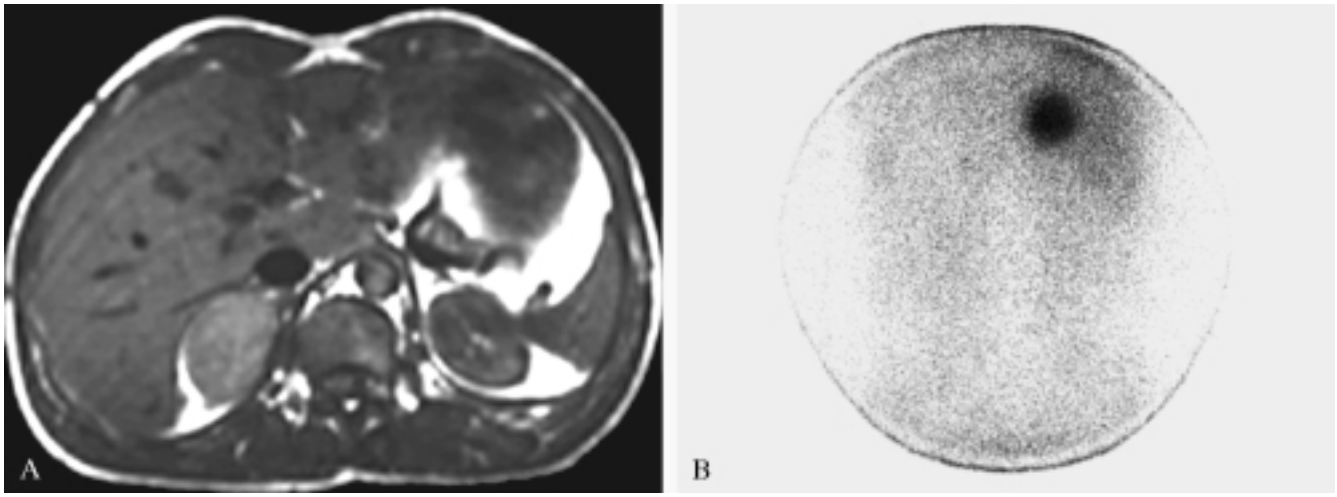

Figure 5.—A 32-year-old man with a 3 cm right adrenal pheochromocytoma. A) Abdominal T1-weighted axial MR scan shows a round right adrenal mass. B) Abdominal posterior view of MIBG imaging shows a round area of intense and exclusive tracer uptake in the right adrenal bed; no activity was observed in the contralateral side.

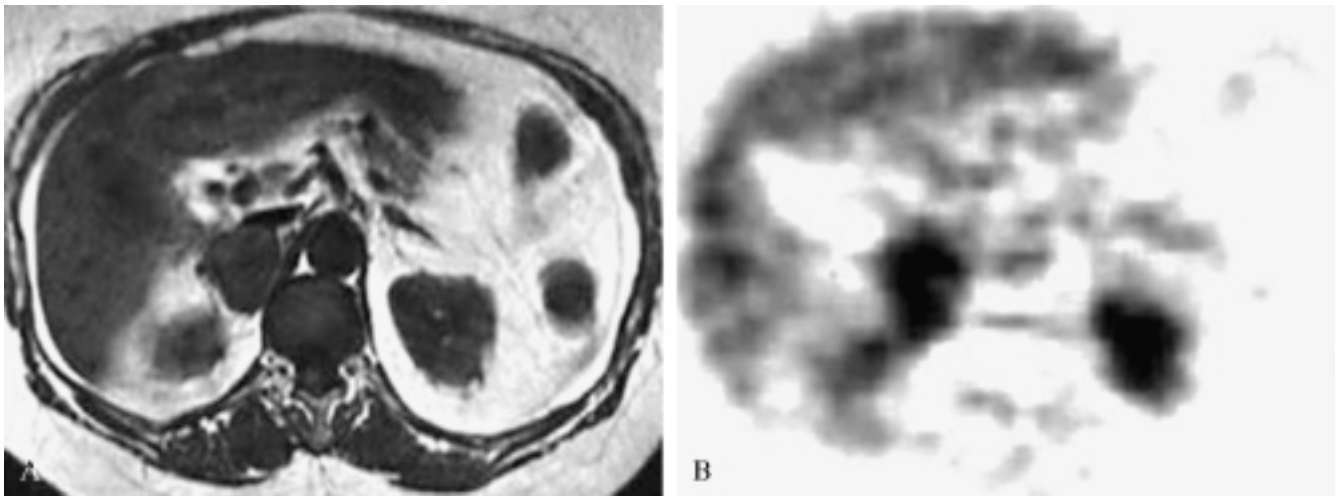

Figure 6.—A 44-year-old woman with a 4.5 cm right adrenal metastasis by melanoma. A) Abdominal T1-weighted axial MR scan shows a large right adrenal mass. B) Uncorrected abdominal FDG PET scan shows intense tracer uptake by the right adrenal lesion; diffuse physiologic activity is detectable in the liver and normal focal uptake is present in the upper pole of the right kidney as well as in the left kidney.

to differentiate between benign and malignant abnormalities. Since these agents have no relation to each other and are taken up by individual parts of adrenals on the basis of entirely separate mechanism, they are able to differentiate different types of tumours.[7, 12-15] In particular, radiolabeled nor-cholesterol scintigraphy allows the characterization of functioning, but not hypersecretory, benign cortical adenomas; similarly, MIBG imaging has been demonstrated to be useful to identify non-hypersecreting pheos [20, 21] and fluoro-18 FDG using PET scanning has been shown to be able to recognize malignant adrenal tumours on the basis of increased glucose metabolism.[13-15]

In the present study, we compared the results of MR techniques and those of radionuclide studies in a group of patients with non-hypersecreting adrenal masses in order to evaluate imaging criteria for accurately performing tumour characterization. On the

basis of our analysis, MR qualitative patterns to identify adrenal adenomas consisted of no lesion enhancement after gadolinium or, mainly, signal intensity loss on out-phase CS imaging; this latter criterion is more appropriate since no gadolinium enhancement occurs also in other benign adrenal tumours.[6, 18, 22] Conversely, the comparative evaluation of T1-T2 signal intensity changes demonstrated in our experience inhomogeneous findings not allowing definite adenoma characterization since on T2 images 54% of these lesions were hypo- or iso-intense and the other 46% showed hyperintensity. For pheos, T2 signal hyperintensity and significant gadolinium enhancement were characteristicly occurring in all cases; likewise, in adrenal malignancies signal hyperintensity was found in all cases, while gadolinium enhancement occurred only in 63% of these tumours. These observations suggest that T2 signal hyperintensity is not accurate in differentiating adrenal masses, as previously reported by our group.[22] Since CS is not able to identify pheos or adrenal malignancies, other methodological approaches may be needed. For this purpose, the results of MR quantitative analysis showed that the degree of T2 signal hyperintensity and of lesion enhancement after gadolinium were significantly higher in pheos compared to those of adenomas and malignant tumours but these latter lesions were not distinguished according to these quantitative criteria. These findings confirm the data of previous investigations [4, 6, 7] suggesting that, although the availability of several technical methods, MR imaging provide only some presumptive criteria for tissue characterization in patients with non-hypersecreting adrenal masses. In particular, signal intensity loss on out-phase CS sequence seems to be the best marker for adenomas and the quantitative assessment of T2 or T1-gadolinium signal intensity allows to better characterize pheos, while no specific MR criteria for adrenal malignancies are available.

In our series, the results of radionuclide studies were more homogeneous compared to those of MR imaging in terms of adrenal tumour characterization selectively showing nor-cholesterol uptake in adenomas, increased MIBG activity in pheo and abnormal FDG accumulation in, both primary and metastatic, adrenal malignancies. Although only a limited group of radionuclide scans were available, the 3 different radiotracers we used were able to identify different types of adrenal masses. In fact, nor-cholesterol uptake occurred in 100% of adenomas, MIBG concentration was found in 100% of pheo, FDG accumulation was observed in 100% of malignancies, with no collection of false negative or positive results. Therefore, according to our experience [10, 15, 23] and that of others,[7, 13, 14, 21] radionuclide imaging using specific radiocompounds offers specific non-invasive tissue characterization in patients with non-hypersecreting adrenal masses. In this regard, the selection of the appropriate radioagent to be used depends on the clinical patient history but it may be limited if appropriate radiopharmaceuticals and nuclear equipment are not available. Because benign adenomas are the most common cause of non-hypersecreting adrenal tumors, labeled nor-cholesterol should be the 1st choice for patients with no history of cancer disease. In case of a normal nor-cholesterol scan, MIBG should be used to confirm or rule out the presence of non-hypersecreting pheo. If MIBG is also normal, FDG PET may be considered when the clinical suspicion of malignancy is high. Conversely, when neoplastic patients are evaluated, FDG PET should be initially performed followed, if normal, by nor-cholesterol and, in sequence, MIBG studies.

Nuclear studies are not routinely used in the diagnostic protocols for managing patients with non-hypersecreting adrenal masses as well as are infrequently considered for clinical decision making in such field.[24, 25] Although combinations of anatomic criteria by CT and MR are currently used to identify malignancy or benignancy without resorting to radionuclide imaging studies, on the basis of recent experiences a diagnostic role of molecular imaging has been proposed in this setting which may effect patient management.[9] In fact, a radionuclide diagnosis of non-hypersecreting adenoma by nor-cholesterol requests surgical treatment only if large tumour size occurs, otherwise clinical and imaging follow-up is appropriate; similarly, nuclear characterization of pheochromocytoma by MIBG allows to correctly plan surgery with adequate patient preparation, and, finally, early identification of adrenal malignancy by FDG PET may determine timely tumour resection with possible favourable patient prognosis.

Conclusions

In conclusion, in patients with non-hypersecreting adrenal masses MR imaging may provide some presumptive criteria to characterize tumour lesions; no

gadolinium enhancement and definite signal intensity loss on CSI suggest adenomas, while quantitatively measured T2-hyperintensity and/or gadolinium enhancement are able to identify pheos. Conversely, radionuclide techniques offer more specific findings since nor-cholesterol and MIBG uptake occur only in benign lesions such adenoma and pheos, respectively, and FDG accumulation detects adrenal malignancies. Therefore, multi-agents adrenal scintigraphy is strongly recommended in the diagnostic protocol of patients with non-hypersecreting adrenal masses, particularly when MR findings are uncertain and inconclusive.

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