# Localization of Pheochromocytoma: MIGB, CT, and MRI Correlation

Michael G. Velchik, Abass Alavi, Herbert Y. Kressel, and Karl Engelman

Departments of Radiology and Medicine, The Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

Nineteen patients (8 M, 11F) ranging in age from 15 - 67 yr old (mean = 39 yr) with clinically diagnosed pheochromocytomas were prospectively evaluated with <sup>131</sup>I metaiodobenzylguanidine (MIBG) scintigraphy (n=19), computed tomography (CT) (n=19), and magnetic resonance imaging (MRI) (n=17) in order to determine their relative diagnostic efficacy. Pathologic confirmation was obtained in all 19 patients: 13 intraadrenal and six extraadrenal with metastases in five (Table 1). All three imaging modalities were in agreement in 11 of 14 completed examinations (79%). MIBG and CT agreed in 16 of the 19 patients in whom both were performed (84%). MIBG/MR and CT/MR results were concordant in 12 of 14 (86%) and 13 of 14 (93%) jointly completed examinations, respectively. There was one false-negative (FN) MIBG scan, two FN CT scans, and one FN MR scan. MIBG, CT, and MRI are complementary procedures with MIBG providing more specific functional information and the latter two superior anatomic detail. MIBG scintigraphy is recommended as the initial localizing study of choice (especially for the detection of extraadrenal disease and postoperative recurrence), as a guide for CT and/or MR and specific functional confirmation of their findings. Although MRI is capable of imaging in multiple planes (without exposure to ionizing radiation or the need for i.v. contrast material) with superior contrast compared to CT, it is expensive and has poor patient cooperation. However, it may be capable of differentiating pheochromocytomas from other adrenal masses on the basis of signal characterization.

J Nucl Med 30:328-336, 1989

## P

**Theochromocytomas are catecholamine-producing** tumors of neuroectodermal origin. Although they are rare in the general population (incidence = 0.01-0.001%) (1) and an uncommon cause of hypertension ( $\ll 1\%$ ) (2-4), they are potentially lethal and are amenable to surgical cure or pharmacologic control (5,6). Once a clinical diagnosis has been established by a combination of history, physical examination, and laboratory evaluation (24-hr urinary catecholamines or metabolites), localization becomes of paramount importance to direct the surgical approach.

Previously employed abdominal radiographs (plain film, tomography, intravenous urogram) are inadequate for localization in this era of three-dimensional tomographic imaging. Angiography and venous sampling for catecholamines are invasive, technically difficult, may precipitate a hypertensive crisis, and are therefore not suitable as the initial localizing studies of choice although they are occasionally helpful in difficult or equivocal cases as a secondary procedure (7,8). Ultrasonography is noninvasive and free of ionizing radiation, but may have difficulty detecting small adrenal lesions and extraadrenal tumors obscured by bowel gas (9).

Approximately 90% of pheochromocytomas are intraadrenal in origin (7). Computed tomography (CT) and magnetic resonance imaging (MRI) have emerged as the optimal noninvasive anatomic adrenal imaging studies (10-15). CT has an accuracy of 85-95% in detecting adrenal masses with a spatial resolution approaching 1 cm (11-14). However, it is less accurate in the detection of extraadrenal tumors and lesions  $\leq 1$  cm (16-18). Furthermore, CT cannot differentiate among pheochromocytomas, adenomas, or metastases. MRI is inferior to CT with respect to resolution but has superior contrast (without the need for i.v. contrast), and can image in multiple planes (without ionizing radiation) thus resulting in comparable overall sensitivity with potentially greater specificity by virtue of its tissue signal characterization (15,19-22). Iodine-131 metaiodobenzylguanidine ([<sup>131</sup>I]MIBG) specifically localizes in ad-

Received June 6, 1988; revision accepted Oct. 11, 1988.

For reprints contact: Michael G. Velchik, Dept. of Radiology, The Hospital of the University of Pennsylvania, Philadelphia, PA 19104.

 
 TABLE 1

 Scan and Pathologic Results in 19 Patients with Pheochromocytoma

Patient no.	MIBG	СТ	MR	Location	Path	Met
1	+	+	+	Left adrenal	+	Liver
2	+	+	+'	LLQ	+	Bone
3	+	+	+	Left adrenal	+	Liver
4	+	+	+	Left adrenal	+	
5	+	+	+	Perivesical	+	LN
6	+	+	+	Left adrenal	+	
7	+	+	+	Right adrenal	+	
8	+	-	+	Right adrenal	+	
9	+	+	IC	LLQ	+	
10	+	+	IC	R & L adrenal	+	
11	+	+	+	Right adrenal	+	
12	+	-	-	Perivesical	+	
13	+	+	IC		+	Liver
14	+	+		Right adrenal	+	
15	-	+	+	Right adrenal	+	
16	+	+		Right adrenal	+	
17	+	+	+	Right adrenal	+	
18	+	+	+	LLQ	+	
19	-	-	-	Left med hyp	+	
Positive	17	16	12			
Negative	2	3	2			
Suboptimal	0	0	1'			
Incomplete	0	0	3(IC)			
Total	19	19	17		19	5
* Suboptimal.						

renergic tissues (23,24) and has proven to be safe, sensitive, and most importantly, relatively specific in the detection of pheochromocytoma (25). However, uptake has also been reported in carcinoid and medullary carcinoma of the thyroid. Several studies have independently compared two of the three imaging modalities (10,15-18). However, to the authors' knowledge, this is the first prospective study that compares all three modalities.

#### MATERIALS AND METHODS

#### **Patient Population**

Nineteen patients (8 M, 11 F) ranging in age from 15–67 yr (x = 39) with a confirmed diagnosis of pheochromocytoma were evaluated between September 1984 and August 1987. Fifteen of the 19 patients were admitted to the Clinical Research Center where they were clinically evaluated by one of the authors (KE). The remaining four patients were referred by outside clinicians and were examined as outpatients. Informed written consent was obtained in all cases. The study was approved by the Institutional Review Board, the Committee on Studies Involving Human Beings and the Radioactive Drug Research Committee of the University. Permission for the use of iodine-131 metaiodobenzylguanidine ([<sup>131</sup>I]-MIBG) was obtained from the National Center for Drugs and Biologics of the FDA.

Criteria for initial patient selection or recruitment into the study consisted of reasonable clinical grounds for the suspicion of pheochromocytoma including a medical history of hypertension (especially if paroxysmal, or resistant to medical therapy with conventional antihypertensive medications) and/or episodic "spells" (sweating, tremor, anxiety, flushing, pallor, headache, chest pain, or epigastric pain), and/or a family history of syndromes known to be associated with pheochromocytoma neurofibromatosis, multiple endocrine neoplasia (MEN 2A and 2B), Von Hipple Lindau or familial pheochromocytoma in the absence of MEN. Signs and symptoms included: hypertension (19), headache (11), sweating (9), palpitations (8), and weight loss (2) (Table 2).

The physical exam directed special emphasis toward documenting orthostatic hypotension or hypertension on multiple occasions in the supine and erect positions.

The clinical diagnosis was confirmed by elevated 24-hr urinary catecholamines (epinephrine and norepinephrine) and metabolites (normetanephrine, metanephrine, and VMA) that were obtained in all cases, usually in duplicate. Occasionally, ancillary tests such as the clonidine suppression test(n=4) or glucagon stimulation test(n=1) were employed.

#### Imaging

*MIBG.* In preparation for the scan: (a) informed written consent was obtained; (b) any potentially interfering medications (reserpine, MAO inhibitors, phenylpropanolamine, tricyclic antidepressants, etc.) were discontinued; (c) a negative pregnancy test was obtained in women of childbearing potential; (d) thyroid blockade was achieved with an iodine solution (Lugol's solution - three drops PO BID or saturated solution of potassium iodine- three drops PO qd starting 2 days prior to injection and continuing for a total of 10–14 days); and (e) bladder catheterization was performed (routinely in inpatients; optionally in outpatients) to remove [<sup>131</sup>I]MIBG normally excreted in the urine that might mask a perivesical tumor and potentially result in a false-negative diagnosis.

A whole-body scan was performed 48 (and occasionally 24 and 72) hr after the slow intravenous administration of 0.5 mCi of [ $^{131}$ I]MIBG. Images were obtained at a photopeak setting of 364 keV with a 20% window in the anterior and posterior projections for a total of 50,000 cts/image or 20 min/image on a left field-of-view gamma camera equipped with a medium-energy collimator interfaced to a DEC PD11/ 34 Digital computer (64×64 matrix;word mode). Additional projections were obtained as necessary and secondary radiopharmaceuticals [technetium diethylenetriaminepentaacetic acid ([Tc]DTPA); technetium methylene diphosphonate] were occasionally employed to aid in localization.

CT. The majority of CT scans were performed with a GE 9800 scanner (General Electric, Milwaukee, WI). All patients received oral contrast material (gastrographin) and half of the patients received i.v. contrast. Images were obtained in the transaxial plane with a slice thickness of 0.5-1.0 cm at an interval of 1-2 cm.

*MRI.* MR images were obtained with 1.5 Tesla superconducting magnet (GE) with a spin-echo pulse sequence (TR=400-600 msec; TE=20-40 msec) and (TR=2000-2500 msec; TE=60-80 msec) in order to achieve  $T_1$  and  $T_2$  weighted images, respectively. The images were formatted 2 tees in transaxial, coronal, and sagittal planes with a 1-cm slice thickness.

#### RESULTS

Iodine-131 MIBG scintigraphy and CT were both performed in all 19 patients. MRI was performed in 17

 TABLE 2

 Signs, Symptoms, Biochemical Data (Urinary Excretion)

#	Pt	Age	Sex	Symptoms	BP	E (<20 μg/24 hr)	NE (<83 µg/24 hr)	MET (0.3-1.3 mg/24 hr)	VMA (2.2-10 mg/24 hr)
1	RC	61	F	S, P	170/110	22	619	6.2	23.8
2	DD	25	Μ	H, S	190/108	518	11312	71	186
3	AF	59	Μ	S, P	134/95	75	240	38	65
4	RK	42	Μ	н	160/100	76	1845	5	36.8
5	MP	18	F	H, P	190/140	15	1488	4	—
6	WD	59	Μ	H, S, P	140/80	282	80	4.7	—
7	JR	53	F	S, P	120/70	<20	656	1.7	
8	RM	44	F	H, P	172/110	1014	3172		—
9	SA	21	F	H, S, WL	150/112	16	1857	13.6	46.2
10	TA	47	Μ	H, WL	175/105	<1	468	14	21.3
11	EΚ	67	F	S, P	210/120	37	219	4.6	
12	DL	35	Μ	н	220/110	8.8	260	2.2	
13	JD	16	Μ	H, S, P	230/130	<10	2519	5.3	32
14	NV	15	F	Р	210/140	0	584	4.6	15.6
15	EK	38	F	H, S, P	200/120	38	1260	2.4	-
16	RB	23	F	н	150/98	68	236 (954)	1.8	12.3
17	SD	35	F	S, P	200/106	253	215	3.6	15
18	PG	28	F	H, S	200/124	4	808	2.4	20.1
19	NR	59	М	S	210/110	240	16	1.3	12.6
				H = headache (11) S = sweating (9) P = palpitations (8)					
				WL = weight loss (2)					

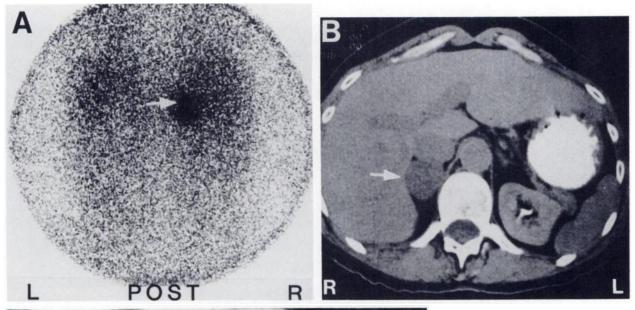
of 19 patients but was incomplete in three (due to claustrophobia) and suboptimal in one (due to patient motion). Surgical pathologic confirmation was obtained in all 19 patients (Table 1).

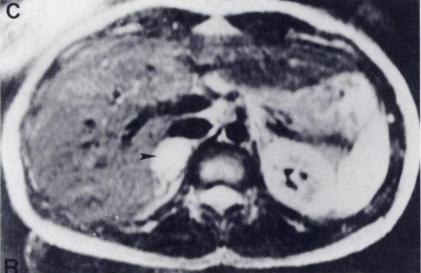
All three imaging modalities were in agreement in regard to localization in 11 of 14 completed examinations (79%) (Fig. 1). MIBG and CT agreed in 16 of the 19 patients in whom both were performed (84%). MIBG/MR and CT/MR results were concordant in 12 of 14 (86%) and 13 of 14 (93%) jointly completed examinations, respectively. There was one false-negative (FN) MIBG scan (Patient 15; Fig. 2), two FN CT scans (Patients 8 and 12; Figs. 3 and 4) and one FN MR scan (Patient 12; Fig. 4). All pheochromocytomas had a signal intensity equivalent to liver, kidney, or muscle on  $T_1$  weighted images and high signal intensity, greater than liver, kidney, and muscle on  $T_2$  weighted images.

Consider the cases in which there was disagreement. In Case 8 (Fig. 3), both MIBG and MRI correctly identified a right adrenal pheochromocytoma (proven at surgery) but CT was falsely negative due to the confluence between the lesion and the IVC. This FN might have been avoided if i.v. contrast had been employed though, in retrospect, the lesion may even be apparent without i.v. contrast. This illustrates the advantage of MRI with respect to superior image contrast (without the need for i.v. contrast) and its ability to separate normal vascular structures which are devoid of signal, from the tumors. In Case 12 (Fig. 4), MIBG scintigraphy correctly localized a perivesical pheochromocytoma (proven at surgery), but both CT and MR were falsely negative. In retrospect, the tumor is clearly identifiable on the coronal scan but was initially attributed to prostatic hypertrophy. In Case 15 (Fig. 2), CT and MRI correctly identified a right adrenal lesion but the MIBG scan was falsely negative.

### DISCUSSION

Pheochromocytomas occur with equal frequency in males and females (8M:11F in this study), in all races, most often in the 30-50 yr age range (15-67;mean=39 in this study). Approximately 90% are sporadic and 10% familial (usually intraadrenal, autosomal dominant, and bilateral), the latter being commonly associated with certain syndromes (MEN II & III, neurofibromatosis, von Hipple Lindau). In our series the majority were sporadic, however, there was one patient (Patient 10) with von Hipple Lindau syndrome. In the MEN syndromes there is a tendency toward bilateral disease and frequently a progression from diffuse medullary hyperplasia (Patient 19) to nodular medullary hyperplasia and finally overt pheochromocytoma. Although they may occur anywhere from the base of the skull to the pelvis, in the distribution of sympathetic tissue, 90% are intraadrenal in location. Approximately 10% are extraadrenal (30% in children). Prominent extraadrenal sites include the paraaortic abdominal sympathetic gan-





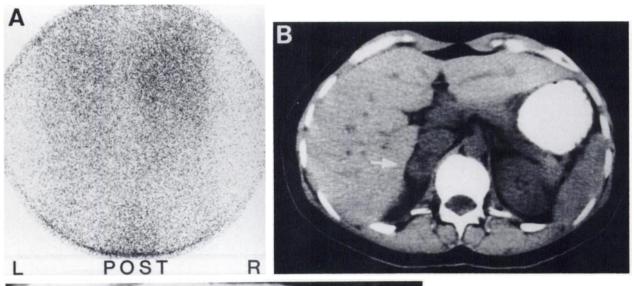
Right adrenal pheochromocytoma (Patient 7). A: MIBG. A posterior image (50k) of the abdomen obtained 48 hr after the i.v. administration of 0.5 mCi of [<sup>131</sup>I]MIBG shows an intense abnormal focus of radioactivity in the region of the right adrenal gland (arrowhead). Normal activity is present in the liver. B: CT. A transaxial image reveals a 3-cm mass in the right adrenal gland (arrowhead) corresponding to the abnormality seen by scintigraphy. C: MRI. A T<sub>2</sub> weighted (TR=2,000 msec; TE=60 msec) transverse image shows the right adrenal mass (arrowhead) to have extremely high signal intensity typical of a pheochromocytoma. Pathology. Right adrenal pheochromocytoma.

glia, at the base of the skull (glomus jugulare tumors), the carotid body, intrathoracic sympathetic ganglia, and bladder.

Although pheochromocytomas may be diagnosed clinically by means of elevated urinary catecholamine measurements in a patient with a typical history of hypertension, headache, tachycardia, and sweating (3,5,7,25-28), they still pose a significant clinical dilemma with respect to definitive surgical treatment since treatment is dependent upon accurate localization which may be difficult in some cases (29,30). Although the tumors are uncommon, they have a significant

associated morbidity due to uncontrolled hypertension and mortality since 10% are malignant. However, they are a potentially curable cause of hypertension. Surgical therapy is predicated upon accurate localization and although the majority of pheochromocytomas are intraadrenal in location, it is the uncommon extraadrenal and multiple tumors that often confound attempts at localization and hence cure.

CT has been advocated as the anatomic adrenal imaging examination of choice. It has been reported to detect 95% of all intraadrenal lesions and has an overall accuracy above 90% primarily due to its exquisite spa-



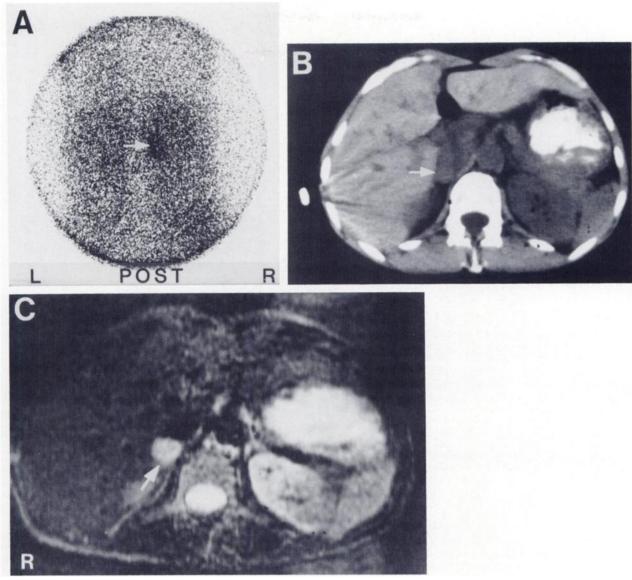


Right adrenal pheochromocytoma; FN MIBG (Patient 15). A: MIBG. A posterior image (50k) of the abdomen obtained 48 hr after the i.v. administration of 0.5 mCi of [131]MIBG is normal. Normal activity is present in the liver. B: CT. A transaxial image reveals a 2.5-cm mass in the right adrenal gland (arrowhead). C: MRI. A T<sub>2</sub> weighted (TR=2500 msec; TE=80 msec) transverse image shows the right adrenal mass (arrowhead) to have extremely high signal intensity typical of a pheochromocytoma. Pathology. Right adrenal pheochromocytoma.

tial resolution (approaching 1 cm) and its tomographic cross-sectional format. It is readily available in almost all hospitals. However, adrenal masses <2 cm in diameter and some extraadrenal lesions (Patient 12; Fig. 4) >2 cm in diameter may escape detection (12, 13, 16). Furthermore, extraadrenal disease cannot be detected if the scan is only restricted to the adrenal region and does not encompass all potential sites of occurrence from the base of the skull to the pelvis. The identification of recurrent disease in postoperative patients may be obscured by streak artifacts from surgical clips or tissue fibrosis and distorted anatomy. Most importantly it is not specific with respect to function or histology, i.e., an enlarged adrenal or adrenal mass may be due to a metastasis, nonfunctioning adenoma, or functioning cortical adenoma rather than a pheochromocytoma. CT is incapable of differentiating between cortical and medullary masses or functioning and nonfunctioning lesions. It provides purely anatomic information which

deteriorates below 2 cm. It subjects the patient to ionizing radiation and frequently requires the administration of intravenous contrast material with its associated risk of allergic reactions and potentially life-threatening hypertensive crisis in patients with pheochromocytomas. Although glucagon is no longer routinely employed due to faster scanners, it is an absolute contraindication since it may provoke a life-threatening hypertensive crisis.

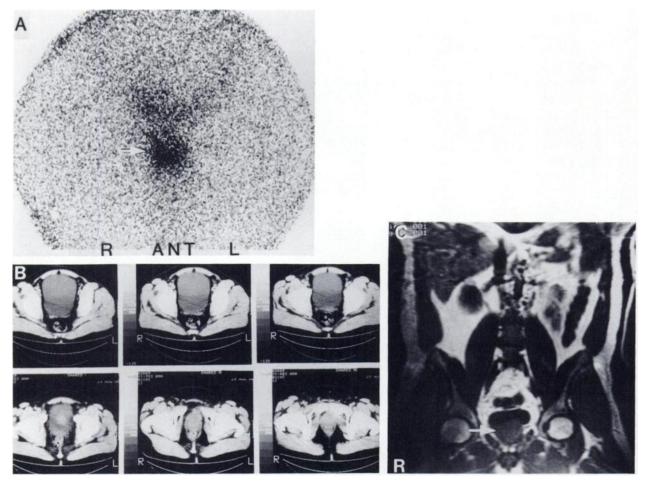
MRI is capable of imaging in multiple planes permitting accurate three-dimensional localization and has superior contrast compared to CT without the need for i.v. contrast or ionizing radiation. Furthermore, it may be able to distinguish among different histologic types of adrenal masses by virtue of signal intensity characteristics or a unique "signal signature" (10,20-22). We and others (10,15,19-22) have demonstrated that pheochromocytomas consistently have a high signal intensity on T<sub>2</sub> weighted images which may permit one to



Right adrenal pheochromocytoma; FN CT (Patient 8). A: MIBG. A posterior image (50k) of the abdomen obtained 48 hr after the IV administration of 0.5 mCi of [<sup>131</sup>]]MIBG shows an intense abnormal focus of radioactivity in the region of the right adrenal gland (arrowhead). Normal activity is present in the liver. B: CT. The transaxial image was initially interpreted as being normal due to the inability to separate the lesion from the IVC, although in retrospect after comparison with the MR image, a right adrenal lesion is seen just posterior to the IVC (arrowhead). This may have been better delineated after an i.v. contrast injection. C: MRI. A T<sub>2</sub> weighted (TR=2,500 msec; TE=80 msec) transverse image clearly differentiates the IVC (no signal due to flowing blood) from the high signal intensity of the right adrenal pheochromocytoma (arrowhead). Pathology. Right adrenal pheochromocytoma.

separate them from other histologic types of primary and secondary adrenal tumors. Glazer et al. (20) were able to distinguish between nonhyperfunctioning adrenal adenomas (which tended to be isointense or hypointense compared to the liver with TR=2 sec and TE=56 msec) and metastasis or pheochromocytomas (which tended to by hyperintense compared to liver), but they were unable to differentiate between the latter two. Other investigators have also shown considerable overlap with respect to tissue characterization by means of signal intensity (19). Reinig et al. (21) initially claimed to be able to separate pheochromocytomas, metastases, and adenomas completely by tumor/liver ratios (at TR/ SE=750/40 and 2,500/80), but later acknowledged that "a significant number of adrenal adenomas and metastases have similar signal characteristics, which do not allow them to be distinguished by MRI" (22). Although further investigation in this area seems warranted, at this time it appears that MRI has not as yet demonstrated any superiority over MIBG scintigraphy with respect to specificity.

MRI is expensive and not readily available at this



Perivesical pheochromocytoma; FN CT and MRI (Patient 12). A: MIBG. An anterior image (50k) of the pelvis obtained 48 hr after the i.v. administration of 0.5 mCi of [<sup>131</sup>]]MIBG shows an intense abnormal focus of radioactivity in the perivesical region (arrowhead). Above this, faint activity is seen in the bladder. B: CT. Multiple transverse slices through the pelvis are unremarkable. C: MRI. A T<sub>1</sub> weighted (TR=600 msec; TE=20 msec) coronal image shows a mass of intermediate signal in intensity in the region of the prostate (arrowhead) that was initially interpreted to be prostatic hypertrophy but corresponds to the abnormality seen by scintigraphy. Pathology. Perivesical pheochromocytoma.

time. There is poor patient acceptance and compliance as illustrated by the significant proportion of incomplete or suboptimal (4/19=21%) MR examinations due to claustrophobia and patient motion, respectively, both of which are exacerbated by long examination times. It should be noted that this group of patients had a significantly higher rate of suboptimal or incomplete examinations than usual (21% vs. 4%) perhaps related to the nature of their disease. As a result of the relative unavailability of MRI and its high demand, scheduling time is at a premium. In addition, scanning time is long especially if multiple pulse sequences are employed. These time constraints make it difficult to scan the entire body from the base of the skull to the pelvis. It is contraindicated in certain patients (pacemakers, postoperative patients with ferromagnetic clips or life-support equipment). Its spatial resolution is inferior to that of CT, and like CT it may have difficulty in identifying extraadrenal disease.

Iodine-131 MIBG scintigraphy is relatively specific with respect to function, and therefore complements CT and MR which both provide more detailed anatomical information. Although its spatial resolution, display of regional anatomy, and three-dimensional localization are inferior to that of CT and MR, it has superior contrast and is therefore especially well suited as the initial localizing procedure of choice. It is the most costeffective way to screen the whole body (particularly extraadrenal sites) from the base of the skull to the pelvis and may serve as a guide for CT and MR or to confirm CT and MR findings thereby lending specificity to them. It can detect residual or recurrent disease in postoperative patients where CT and MR may have difficulty due to distorted anatomy. It is devoid of problems that often confound CT and MR including allergic reactions, metallic clips, claustrophobia, etc.

However, [<sup>131</sup>I]MIBG is not readily available, requires an IND, and is expensive (\$600/2 mCi). The examination is lengthy (20 min/image  $\times$  6; optimally 48 hr postinjection). There is poor spatial resolution and definition of regional anatomy sometimes resulting in imprecise localization and often requiring an injection of a secondary radiopharmaceutical such as [99mTc] DTPA since normal anatomic landmarks are not visualized. There is a reported false-negative rate of 10% (25) although this may be improved considerably with the use of  $[^{123}I]MIBG$  (31,32). It has been speculated that false negatives may be due to the poor imaging characteristics of <sup>131</sup>I, rapid uptake and turnover of MIBG, small tumor size, previous radiotherapy, infiltration of the dose, and bladder radioactivity obscuring a perivesical lesion, etc. Although <sup>123</sup>I has superior imaging characteristics compared to <sup>131</sup>I, it is even more expensive (\$1200/dose), less readily available, and must be used the day it is shipped because of its short  $T_{1/2}$ . Perivesical lesions may be obscured by bladder radioactivity due to normal urinary excretion resulting in a potential FN diagnosis. This potential pitfall may be avoided by bladder catheterization or by obtaining delayed images. Both perivesical lesions in this series (Patients 5 and 12) were correctly detected by MIBG scintigraphy. Fortunately, perivesical tumors represent <1% of all pheochromocytomas. Finally, there is the matter of radiation exposure which is not insignificant (adrenal = 50 rad; bladder = 4 rad; whole body = 0.1rad) (1,31). Contrarily, this may be advantageous for "magic bullet" type therapy (33,34).

Several studies have found CT and MIBG scintigraphy to be complementary in the detection of pheochromocytoma (16-18). Chatal et al. (17) found an agreement of 80% for the two exams similar to our figure of 79%. The studies acknowledged the advantages of MIBG scintigraphy—ability to screen the whole body, high specificity, and the detection of extraadrenal primaries and metastases. Falke et al. (10) found MR to be superior to CT in adrenal imaging due to its greater image contrast, multiplanar imaging capabilities, and better specificity. Quint et al. (35) recently reported their results comparing all three imaging modalities which they found to be nearly equivalent, although MIBG and MRI were superior with respect to the detection of extraadrenal tumors. Our results are in agreement although their study was retrospective in nature and used MIBG scintigraphy as the gold standard.

Patient 19 deserves special comment. All three imaging modalities were negative in this patient with elevated catecholamines and metabolites who already had medullary hyperplasia documented by left adrenalectomy presumably of sporadic origin since there was no family history and no evidence of medullary carcinoma of the thyroid. Patients with medullary hyperplasia often have elevated catecholamine levels and a clinical presentation that is similar to patients with pheochromocytoma (36). MEN syndrome should be suspected in any patient with medullary hyperplasia (36). As previously stated, in the MEN syndromes there is often a histologic spectrum with progression from diffuse medullary hyperplasia to nodular hyperplasia and finally frank pheochromocytoma (37). Adrenal enlargement of varying degrees is seen by CT and MR. A spectrum of radionuclide uptake may be seen ranging from normal to mild to moderate (25). A diagnosis of medullary hyperplasia should be entertained in a patient with clinically evident (including abnormal biochemistry) pheochromocytoma but negative localizing studies.

In summary, we believe that MIBG, CT, and MR are complementary in the localization of pheochromocytoma, the former providing primarily functional information and the latter two predominantly anatomical information, each with its inherent advantages and limitations. We believe that MIBG scintigraphy is the initial localizing procedure of choice, due to its ability to screen the entire body with exquisite contrast (high target to background ratio), especially in the detection of extraadrenal disease and in postoperative sites where anatomic planes may be distorted. Thus it may act as a guide to direct CT and MR both of which have superior spatial resolution and hence depiction of anatomic detail. It can confirm CT and MR findings and lend specificity to them by virtue of its physiological mechanism of localization. CT is currently the anatomical adrenal imaging examination of choice because of its superior resolution and wide availability. However, CT will eventually be replaced by MR as its availability increases because of its multiplanar imaging capabilities, superior image contrast (without the need for i.v. contrast), lack of ionizing radiation, and potential for tissue characterization by means of signal signatures. We emphasize that these scans should be done solely for the purpose of localization after there has been biochemical confirmation of the suspected diagnosis of pheochromocytoma.

#### ACKNOWLEDGMENT

This work was partially supported by CRC NIH Grant #5 MOI RR00040.

#### REFERENCES

- McEwan AJ, Shapiro B, Sisson JC, et al. Radioiodobenzylguanidine. Semin Nucl Med 1985; XV: 132-153.
- Mayer EM, Gifford RW. Hypertension secondary to pheochromocytoma. Bull NY Acad Med 1982; 59: 139-158.
- Engelman K. Phaeochromocytoma. Clin Endocrinol Metab 1977; 6:79.

- 4. Gifford RW Jr. Evaluation of the hypertensive patient with emphasis on detecting curable causes. *Milbank Mem Fund Quarterly* 1969; 47.
- Sjoerdsma A, Engelman K, Waldmann TA, Cooperman LH, Hammond WG. Pheochromocytoma: current concepts of diagnosis and treatment combined clinical staff conference at the National Institutes of Health. Ann Intern Med 1966; 65:1302-1326.
- Engelman K, Sjoerdsma A. Chronic medical therapy for pheochromocytoma. Ann Intern Med 1964; 61:229-241.
- 7. Manger WM, Gifford RW. Pheochromocytoma. New York: Springer-Verlag, 1972: 31-37.
- 8. Harrison TS, Seaton JF, Cerny JC, et al. Localization of pheochromocytomata by caval catheterization. *Arch Surg* 1967; 95:339–343.
- 9. Bowerman RA, Silver TM, Jaffe MH, et al. Sonography of adrenal pheochromocytomas. *Am J Roentgenol* 1981; 137:1227-1231.
- Falke THM, te Strake L, Shaff MI, et al. MR imaging of the adrenals: correlation with computed tomography. J Comput Assist Tomogr 1986; 110:242-253.
- 11. Korobkin M, White EA, Kressel HY, et al. Computed tomography in the diagnosis of adrenal disease. *Am J Roentgenol* 1979; 132:231–238.
- 12. Dunnick NR, Schaner EG, Doppman JL, et al. Computed tomography in adrenal tumors. *Am J Roent*genol 1979; 132:43-46.
- Stewart BH, Bravo EL, Haaga J, et al. Localization of pheochromocytoma by computed tomography. N Engl J Med 1978; 229:460–461.
- Kerstaedt N, Sagel SS, Stanley RJ, et al. Computed tomography of the adrenal gland. *Radiology* 1978; 129:723-730.
- Moon KL Jr, Hricak H, Crooks LE, et al. Nuclear magnetic resonance imaging of the adrenal gland: a preliminary report. *Radiology* 1983; 147:155-160.
- Francis IR, Glazer GM, Shapiro B, et al. Complementary roles of CT and <sup>131</sup>I-MIBG scintigraphy in diagnosing pheochromocytoma. Am J Roentgenol 1983; 141:719-725.
- Chatal JF, Charbonnel B. Comparison of iodobenzylguanidine imaging with computed tomography in locating pheochromocytoma. J Clin Endocrinol Metab 1985; 61:769–772.
- Koizumi M, Endo K, Sakahar H, et al. Computed tomography and <sup>131</sup>I-MIBG scintigraphy in the diagnosis of pheochromocytoma. Acta Radiologica Diagnosis 1986; 27:305-309.
- Fink IJ, Reinig JW, Dwyer AJ, et al. MR imaging of pheochromocytomas. J Comput Assist Tomogr 1985; 9:454–458.
- Glazer GM, Woolsey EJ, Borrello J, et al. Adrenal tissue characterization using MR imaging. *Radiology* 1986; 158:73-79.
- 21. Reinig JW, Doppman JL, Dwyer AJ, et al. Adrenal masses differentiated by MR. *Radiology* 1986; 158:81-84.

- Reinig JW, Doppman JL, Dwyer AJ, et al. MRI of undeterminate adrenal masses. Am J Roentgenol 1986; 147:493-496.
- Wieland DM, Wu J, Brown LE, et al. Radiolabeled adrenergic neuron blocking agents: adrenomedullary imaging with [<sup>131</sup>I]iodobenzylguanidine. J Nucl Med 1980; 21:349-353.
- 24. Wieland DM, Brown LE, Tobes MC, et al. Imaging the primate adrenal medullae with <sup>123</sup>I- and <sup>131</sup>I- metaiodobenzylguanidine: concise communication. J Nucl Med 1981; 22:358-364.
- 25. Shapiro B, Copp JE, Sisson JC, et al. Iodine-131 metaiodobenzylguanidine for the locating of suspected pheochromocytoma: experience in 400 cases. J Nucl Med 1985; 26:576-585.
- Bravo EL, Tarazi RC, Cifford RW, et al. Circulating and urinary catecholamines in pheochromocytoma: diagnostic and pathophysiologic implications. N Engl J Med 1979; 301:682–686.
- 27. Cryer PE. Physiology and pathophysiology of the human sympathoadrenal neuroendocrine system. *N Engl J Med* 1980; 303:436-444.
- Frier DT, Harrison TS. Rigorous biochemical criteria for the diagnosis of pheochromocytoma. J Surg Res 1973; 14:177-180.
- Bravo EL, Gifford RW. Pheochromocytoma: diagnosis, localization and management. N Engl J Med 1984; 311:1298-1303.
- Frier DT, Eckhauser FE, Harrison TS. Pheochromocytoma: a persistently problematic and still potential lethal disease. *Arch Surg* 1980; 115:388–391.
- Lynn MD, Shapiro B, Sisson JC. Pheochromocytoma and the normal adrenal medulla: improved visualization with I-123 MIBG scintigraphy. *Radiology* 1985; 156:789-792.
- 32. Lynn MD, Shapiro B, Sisson JC, et al. Portrayal of pheochromocytoma and normal human adrenal medulla by m-[<sup>123</sup>]Iodobenzylguanidine: concise communication. J Nucl Med 1984; 25:436–440.
- Sisson JC, Shapiro B, Beierwaltes WH, et al. Radiopharmaceutical treatment of malignant pheochromocytoma. J Nucl Med 1984; 24:197-206.
- Hoefnagel CA, Voute PA, de Kraker J, et al. Radionuclide diagnosis and therapy of neural crest tumors using iodine-131 metaiodobenzylguanidine. J Nucl Med 1987; 28:308-314.
- Quint LE, Glazer GM, Francis IR, Shapiro B, Chenevert TL. Pheochromocytoma and paraganglioma: comparison of MR imaging with CT and I-131 MIBG scintigraphy. *Radiology* 1987; 165:89–93.
- Rudy FR, Robley DB, Cimorelli AJ, Hill GS, Engelman K. Adrenal medullary hyperplasia: a clinicopathologic study of four cases. *Human Pathol* 1980; 11:650–657.
- Valk TW, Frager MS, Gross MD, et al. Spectrum of pheochromocytoma in multiple endocrine neoplasia a scintigraphic portrayal using I-131-metaiodobenzylguanidine. Ann Intern Med 1981; 94:762-767.