



Incidental Adrenal Nodules

- Adrenal nodules are found incidentally in up to 5% of CT scans
- All incidentally detected adrenal nodules need clinical evaluation and laboratory tests for hormonal secretion
- Adrenal protocol CT has a high sensitivity for differentiating between benign and malignant masses
- Nodules indeterminate after adrenal protocol CT require special attention; MRI, PET-CT, CT-guided percutaneous biopsy for suspected metastasis to the adrenal, surgery or follow-up imaging may be appropriate depending on individual patient factors

Adrenal masses are found incidentally in up to 5% of patients undergoing CT examinations with modern multidetector scanners or MRI examinations. In patients with no known cancer, the risk of malignancy is estimated to be 1 in 4,000. Although adrenal metastases are common in patients with a history of cancer, even in these patients the large majority of adrenal masses <4 cm in diameter are benign adenomas.

On the other hand, 8-10% of incidentally detected adrenal masses are functional, secreting hormones such as catecholamines, aldosterone, or cortisol. In many of these cases, there are no overt signs of endocrine disease. Some produce cortisol autonomously, causing overt or subclinical Cushing's syndrome. Approximately 10-40% of pheochromocytomas are clinically silent and they represent approximately 3% of incidentally detected adrenal masses in patients with no history of cancer. In addition, it has been estimated that 8-10% of patients with hypertension have primary hyperaldosteronism, although many of these patients have very small adrenal adenomas. Therefore, the first step in managing patients with an incidentally detected adrenal mass is to perform a clinical examination and tests for pheochromocytoma and subclinical or overt Cushing's syndrome. If the patient is hypertensive, an evaluation for primary aldosteronism should be performed as well. Consultation with an endocrinologist should be considered.

There is one exception to this rule; myelolipomas, macroscopic fat-containing masses, can be identified when first seen on CT or MR imaging and need no further diagnostic tests.

Radiological Evaluation

If the adrenal mass appears to be functional, no further diagnostic imaging is recommended, as surgery is often necessary. If it is non-functional, the first step in the



Figure 1. Axial CT demonstrating an incidental left adrenal mass in a 55 year old man undergoing unenhanced CT for urinary stone evaluation. The adrenal mass is well defined and uniform in appearance and measures 1.3 HU in attenuation as indicated by the region of interest tool and thus is most consistent with a benign adrenal adenoma.

radiologic evaluation for malignancy is to determine whether it has been imaged previously. If there are prior images and the lesion size has been stable for >6 months, it is almost certainly benign. If a non-contrast-enhanced CT scan (Figure 1) is available, this is also useful in assessing whether the lesion is likely to be a benign adenoma. Unlike metastatic malignant masses, adenomas typically have a high lipid content. If the attenuation of a uniform mass is <10 Hounsfield units (HU), it is highly unlikely to be malignant (Table 1). Signs of possible malignancy include a CT density of >43 HU, an irregular border, and necrosis.

If no prior imaging is available or there is insufficient information from the available images, the next step (Figure 2) is an adrenal protocol CT examination. This consists of three steps: a non-contrast CT (Figure 3A), followed (if necessary) by contrast-enhanced CT images taken at 60-75 seconds (Figure 3B) and at 10 minutes (Figure 3C) after the administration of contrast, using a fine collimation multi-detector CT scanner. If the adrenal mass is uniform and <10 HU on non-contrast CT, it is not necessary to perform the contrast-enhanced examinations, because these lesions are lipid rich and almost certainly benign. At 60-75 seconds after the administration of contrast agent, the enhancement is at its peak. Contrast agent washes out

of malignant tissue more slowly than normal and differences in wash out rate are measured by calculating the relative percentage washout (RPW) and absolute percentage washout (APW) of the contrast agent from data collected from the non-contrast, peak contrast-enhancement, and 10-minute delay contrast-enhanced images. After excluding pheochromocytomas, the sensitivity and specificity of adrenal protocol CT for detecting adrenal adenomas is reported to be 98% and 100%, respectively, from combined non-contrast, APW, and RPW data using a threshold of >38% for RPW and >52% for APW. However, surgery is often recommended for lesions over 4 cm, even when the radiological characteristics are benign.

Figure 2. Algorithm for Diagnostic Evaluation of Adrenal Nodules

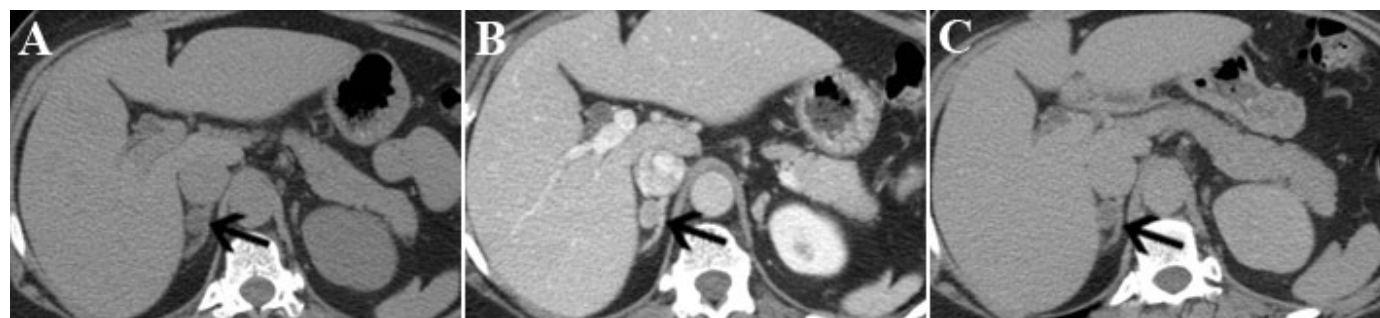
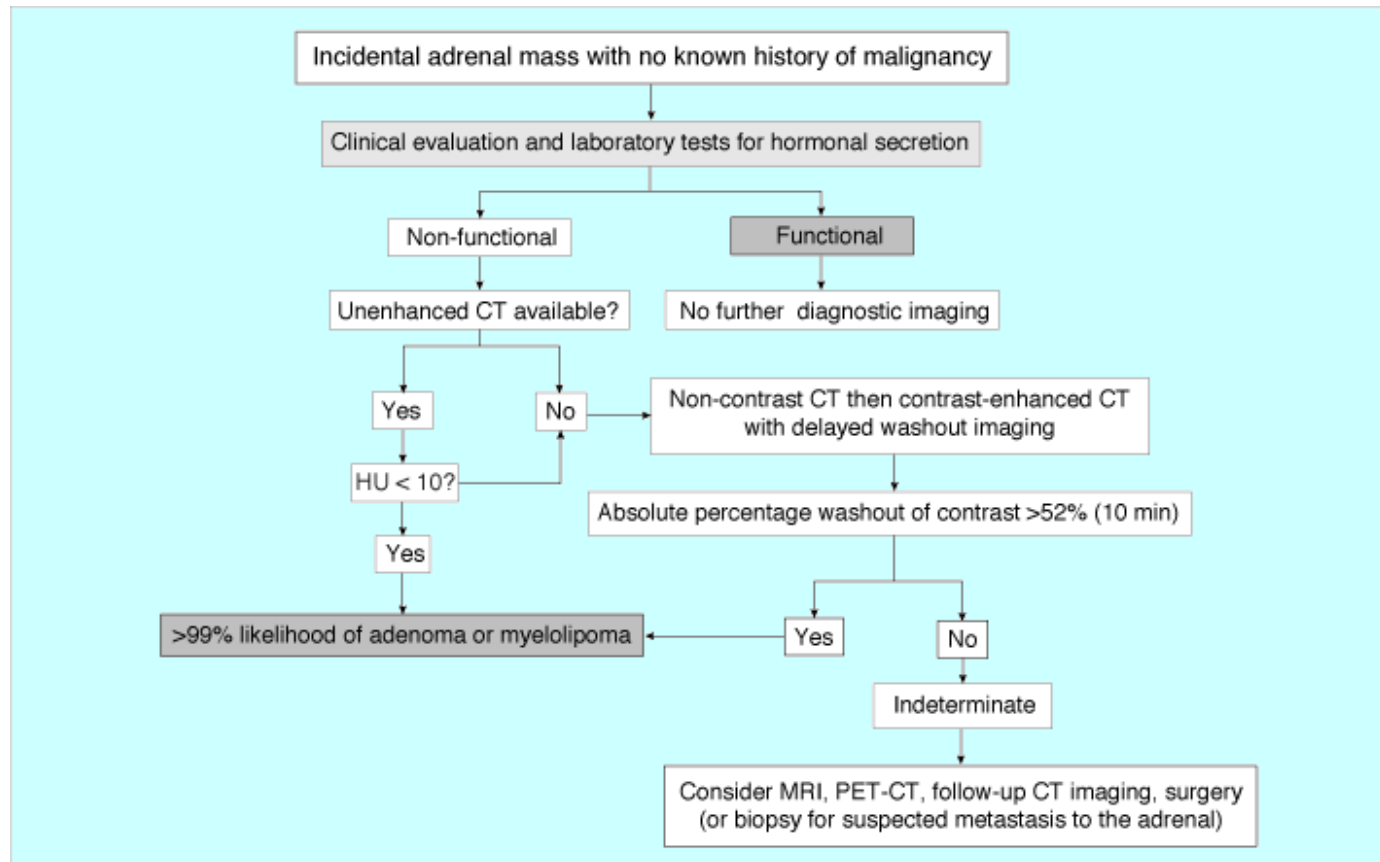


Figure 3. Axial images from an adrenal mass protocol CT scan performed to characterize an incidentally discovered right adrenal mass in a 48 year old woman. **(A)** The attenuation of the adrenal mass (arrow) in the unenhanced scan was 15 HU, which is indeterminate and could indicate a lipid-poor adenoma or a malignant lesion. **(B)** In the dynamic contrast-enhanced scan the mass (arrow) had an attenuation of 80 HU and **(C)** in the delayed washout scan, performed 10 minutes later, the mass (arrow) had an attenuation of 30 HU. The absolute adrenal washout rate was calculated to be 71.7% and the relative washout rate was 62.5%, indicating that the adrenal mass was a benign adenoma.

Table 1. Reported Accuracy of Imaging for Distinguishing Benign and Malignant Adrenal Masses

Imaging Method	Sensitivity	Specificity
Non-contrast CT (< 10 HU) ¹	85%	100%
Adrenal protocol CT ²	100%	98%
Chemical-shift MRI ¹	81-100%	94-100%
PET (maximum SUV*) ³	93-100%	80-100%
PET/CT ³	100%	98- 100%

*SUV, standard uptake values

Data from: ¹Mayo-Smith, et al, 2001; ²Blake et al, 2006a; ³Blake et al, 2006b.

Indeterminate Adrenal Nodules

Even if the adrenal protocol CT examination is indeterminate most such incidental lesions prove to be benign. The approach to the patient depends upon the clinical scenario. If the patient has a known extra-adrenal malignancy, then this nodule may represent a metastasis. A CT guided biopsy should be considered. However in the absence of known malignancy, biopsy is generally not useful, as these biopsies cannot reliably distinguish between benign adrenal adenomas and adrenocortical carcinomas. Again, excision of nodules greater than 4 cm is often recommended.

Additional tests which may be helpful include chemical shift MRI, PET-CT, or short interval repeat CT scans in 3-12 months. The MGH Adrenal Tumor Center has been recently organized as a collaboration between radiologists, endocrinologists, endocrine surgeons and pathologists. One of its goals is to review available evidence to assess the best management of patients with incidental adrenal nodules.

Like the adrenal protocol CT examination, chemical shift MR imaging exploits the differences in lipid content between adenomas and malignancies. The sensitivity of chemical shift MR varies with the CT attenuation of the mass and has been reported to be 89% for adenomas when considering masses in the range of 10-30 HU and 67% for adenomas when considering all masses with an attenuation >10 HU. The specificity is 100% across the full range of attenuations. However, in general, MR is not considered superior to adrenal protocol CT for indeterminate adrenal nodules although it may sometimes be helpful for example if only non IV contrast CT is possible or a pheochromocytoma is being considered.

Reports on the use of [¹⁸F]-fluorodeoxyglucose (FDG) PET to detect adrenal malignancy have reported sensitivities of 93-100% and specificities of 80-100%. False negative results occasionally prove to be necrotic or hemorrhagic malignancies, or lesions that are too small to be adequately imaged with PET. The use of PET-CT has the advantage of co-registering lesion morphology with metabolic data but should be reserved only for patients with high clinical suspicion of metastatic disease in the work-up of an indeterminate adrenal lesion.

CT-guided percutaneous biopsy of an indeterminate lesion should be considered if there is clinical suspicion of adrenal metastasis, specifically in the presence of a

primary malignancy. Diagnostic accuracy of this procedure for detecting adrenal metastases in oncology patients is reported to be 83-96% and it is associated with few complications. Unfortunately, as mentioned before, an adrenal biopsy cannot reliably distinguish an adrenal adenoma from an adrenocortical carcinoma.

For the small minority of cases in which no conclusive categorization has been made, follow up unenhanced CT is recommended to assess for growth. If the patient has a history of malignancy, a follow-up scan should be performed at 3 months. For those with no history of malignancy a longer interval follow-up scan at 6 months is more appropriate, although with larger (3-4 cm) lesions 3 month follow-up should be considered.

Functional Masses

It is important to identify pheochromocytomas because they may produce cardiovascular crises if the diagnosis is not made or if appropriate treatment is delayed. However, they can be clinically silent and can mimic other adrenal lesions on both CT and MR imaging. In addition, about 10% are malignant. Catecholamine metabolites in blood or urine catecholamines and their metabolites are almost always abnormal in patients with pheochromocytomas.

Although unenhanced scanning may be sufficient to detect the tumor in patients with a clinical suspicion of pheochromocytoma, CT scanning with IV contrast is not contraindicated in patients with suspected pheochromocytomas. Most pheochromocytomas have a relatively high attenuation (44±11 HU) and enhance avidly with contrast material. However, many do not fit this description. If needed, nuclear scintigraphy using ¹²³I-metabiodobenzylguanidine (MIBG) can be used to confirm pheochromocytoma; however a negative MIBG scan does not exclude a pheochromocytoma. This imaging technique has a specificity of 100% but a lower sensitivity. MIBG scans can also be used to search for a clinically suspected extra-adrenal pheochromocytoma (paraganglioma) or metastatic pheochromocytoma.

The diagnosis of primary aldosteronism is a biochemical diagnosis. Once the diagnosis is confirmed, if surgical therapy is being considered, then bilateral adrenal vein catheterization is necessary. This test is performed by vascular interventional radiologists using fluoroscopic guidance. A previously performed adrenal CT may also help the angiographer identify the location of the adrenal veins as the revised standard protocol for initial adrenal nodule evaluation now incorporates such

vascular information. With constant ACTH stimulation, blood samples are taken from each adrenal vein and peripheral vein to determine the ratio of aldosterone to cortisol compared to background. This test may be necessary even when an adrenal mass is noted, as tiny aldosteronomas may be found on the contralateral side to a non-functioning adrenal adenoma.

Scheduling

CT, MR, and nuclear medicine examinations can be ordered through ROE (<http://mghroe/>) or by telephone **617-724-XRAY (9729)** for all locations. CT and MR are performed at the main campus as well as Mass General West Imaging, Waltham and Mass General Imaging, Chelsea. PET-CT scans are performed at the MGH main campus and Mass General Imaging, Chelsea. MIBG examinations are performed at the MGH Main Campus and Mass General West Imaging, Waltham.

Appointments for an adrenal vein catheterization and sampling are made through Vascular Imaging and Intervention (Contact Physicians: Sanjeeva P. Kalva, MD, and Benjamin J. Pomerantz, MD), **617-726-8315**.

Further Information

For further questions on incidental adrenal nodules, please contact [Michael A. Blake, MRCPI, FRCR, FFR, RCSI](#), Abdominal and Interventional Radiology, **(617-726-8396)**, or [Gilbert H. Daniels, MD](#), Thyroid Unit (Endocrinology Division), Department of Medicine **(617-726-8430)**.

We would like to thank Michael A. Blake and Gilbert Daniels for their advice and assistance in preparation of this article.

References

- Barzon, L, Sonino, N, Fallo, F, *et al.* (2003) *Prevalence and natural history of adrenal incidentalomas*. Eur J Endocrinol **149**: 273-85
- Blake, MA, Holalkere, NS and Boland, GW. (2008) *Imaging techniques for adrenal lesion characterization*. Radiol Clin North Am **46**: 65-78, vi
- Blake, MA, Kalra, MK, Maher, MM, *et al.* (2004) *Pheochromocytoma: an imaging chameleon*. Radiographics **24**: S87-99
- Blake, MA, Slattery, JM, Kalra, MK, *et al.* (2006) *Adrenal lesions: characterization with fused PET/CT image in patients with proved or suspected malignancy--initial experience*. Radiology **238**: 970-7
- Grumbach, MM, Biller, BM, Braunstein, GD, *et al.* (2003) *Management of the clinically inapparent adrenal mass ("incidentaloma")*. Ann Intern Med **138**: 424-9
- Haider, MA, Ghai, S, Jhaveri, K and Lockwood, G. (2004) *Chemical shift MR imaging of hyperattenuating (>10 HU) adrenal masses: does it still have a role?* Radiology **231**: 711-716
- Song, JH, Chaudhry, FS and Mayo-Smith, WW. (2008) *The incidental adrenal mass on CT: prevalence of adrenal disease in 1,049 consecutive adrenal masses in patients with no known malignancy*. AJR Am J Roentgenol **190**: 1163-8
- White, ML, Gauger, PG, Doherty, GM, *et al.* (2008) *The role of radiologic studies in the evaluation and management of primary hyperaldosteronism*. Surgery **144**: 926-33; discussion 933

©2009 MGH Department of Radiology

Janet Cochrane Miller, D. Phil., Author
Raul N. Uppot, M.D., Editor