

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:** Incidentally Discovered Adrenal Mass

**Variant 1:** No history of malignancy; mass <3 cm in diameter.

Radiologic Procedure	Rating	Comments	<a href="#">RRL*</a>
CT abdomen without contrast	8	Presumes that a noncontrast CT has not already been performed.	Med
Initial follow-up CT or MRI at 6-12 months	8	Assumes that there is no significant change on the first follow-up exam.	NS
CT abdomen with contrast	8	Indicated if noncontrast CT is indeterminate (density >10 HU) or adrenal mass is discovered on early contrast-enhanced CT.	Med
MRI abdomen without contrast	8	May be helpful when nonenhanced CT is equivocal.	None
INV biopsy adrenal gland	3	A biopsy should only be performed if there are no noninvasive options.	IP
NUC MIBG	2	Only for suspicion of pheochromocytoma.	Med
NUC iodocholesterol scan	1	This agent may be used to detect functionally active adenomas.	High
FDG-PET whole body	1		High
X-ray abdomen	1		Med
US adrenal gland	1		None
MRI abdomen with contrast	1	Promising technique, but not fully studied.	None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

An ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

**Clinical Condition:****Incidentally Discovered Adrenal Mass****Variant 2:****No history of malignancy; mass 3-5 cm in diameter. (Larger lesions should be removed.)**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL*</u></b>
CT abdomen without contrast	8	Presumes that a noncontrast CT has not already been performed.	Med
Initial follow-up CT or MRI at 3-6 months	8	Assumes that there is no significant change on the first follow-up exam.	NS
CT abdomen with contrast	8	Indicated if noncontrast CT is indeterminate (density >10 HU) or adrenal mass is discovered on early contrast-enhanced CT.	Med
MRI abdomen without contrast	8	Indicated if lesion is identified only on a contrast-enhanced CT and further characterization is required. If the lesion is indeterminate on a noncontrast CT, the MRI is unlikely to add information. Indicated if mass is discovered incidentally on MRI study.	None
INV biopsy adrenal gland	6		IP
FDG-PET whole body	6	Should be performed if CT and MRI are inconclusive. Some malignancies (including renal cancer) may not be PET avid.	High
NUC MIBG	3	Not indicated unless there are biochemical indications of pheochromocytoma.	Med
NUC iodocholesterol scan	2	For functional adenomas.	High
MRI abdomen with contrast	2		None
US adrenal gland	1		None
X-ray abdomen	1		Med
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

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**Clinical Condition:****Incidentally Discovered Adrenal Mass****Variant 3:****History of malignancy.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL*</u></b>
Initial follow-up CT or MRI at 3-6 months	8	Assumes that there is no significant change on the first follow-up exam.	NS
CT abdomen without contrast	8	Presumes that a noncontrast CT has not already been performed.	Med
INV biopsy adrenal gland	8	To confirm metastases and in cases where imaging is inconclusive.	IP
CT abdomen with contrast	8	Indicated if noncontrast CT is indeterminate (density >10 HU) or adrenal mass is discovered on early contrast-enhanced CT.	Med
MRI abdomen without contrast	8	Indicated if lesion is identified only on a contrast-enhanced CT and further characterization is required. If the lesion is indeterminate on a noncontrast CT, the MRI is unlikely to add information. Indicated if mass is discovered incidentally on MRI study.	None
FDG-PET whole body	6	Documented indications are for lung cancer, colon cancer, lymphoma, and neuroendocrine tumors; however, it is likely that adrenal metastases from other primary tumors may be detectable by FDG-PET.	High
NUC MIBG	2	Only for suspicion of pheochromocytoma.	Med
NUC iodocholesterol scan	2	For functionally active lesions.	High
MRI abdomen with contrast	2		None
US adrenal gland	1		None
X-ray abdomen	1		Med
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

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# INCIDENTALLY DISCOVERED ADRENAL MASS

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## **Summary of Literature Review**

The adrenal “incidentaloma” is an unsuspected and asymptomatic mass, usually detected on computed tomography (CT) obtained for other purposes. Incidentally discovered adrenal masses can range in size from 5 mm to over 15 cm, but the larger the lesion the more likely it is to be symptomatic. The majority of incidentalomas are benign and most often represent adenomas. The prevalence of adenomas in the general population, as summarized by Gajraj et al [1] ranges from 1%-2%, although autopsy studies have shown rates as high as 6.6%-8.7% depending on the age distribution of the patient sample. The risk of primary adrenal cortical carcinoma in this population is quite small, on the order of 0.06%; however, among patients with adrenal masses the risk is reported to be as high as 4.7% [1]. Other malignancies of the adrenal include angiosarcomas, lymphomas, and malignant pheochromocytomas. These are diminishingly rare in the general population.

Metastatic disease without a known history of primary malignancy is also unusual, occurring in about 4% of patients with incidentally discovered adrenal masses and less than 1% of the general population [1,2].

The situation is different for patients with a known history of malignancy. In this setting, the rate of metastatic disease is 25%-72% depending on size and type of primary lesion [3-5]. For instance, bronchogenic and renal carcinomas and melanoma have a relatively higher rate of adrenal metastases than other epithelial malignancies.

The guidelines suggested here only apply to masses detected incidentally during CT, ultrasound (US), or magnetic resonance imaging (MRI) evaluation. The patient is free of symptoms, although the mass may later

prove to be functional (ie, Cushing’s or Conn’s adenoma or pheochromocytoma). The appropriateness of performing additional studies to ascertain whether the mass is more likely benign or malignant is discussed herein.

## **Size**

Size is an important variable in predicting malignancy of an incidentally discovered adrenal mass. Smaller lesions, presumably because they grow more slowly, are usually benign [6]. Conversely, larger lesions, because they have already demonstrated the potential for growth, are often malignant. However, it is important to distinguish between populations with and without a history of malignancy. Herrera et al [2] studying 342 patients without a history of malignancy, found only a 1.5% rate of malignancy in the adrenal, and all malignant lesions were >5 cm. Caplan et al [7] found 3 of 23 incidental lesions to be malignant, and all were >3 cm. In contrast, in patients with a history of malignancy, Candel et al [6] found that 87% of lesions <3 cm were benign and that more than 95% of lesions >3 cm were malignant. In a similar population, Lee et al [8] found that only 79% of lesions <2.5 cm were benign. Van Erkel et al [9] in a mixed population showed that a threshold of 3.1 cm discriminated 93% of lesions. Thus, size (3-5 cm) predicts benignity much better in a population without known malignancy. Size is an important variable in a population with a known malignancy, but there is more overlap for a given threshold diameter. Overall, size is considered too unreliable to be used alone as a criterion for malignancy.

## **Endocrinologic Function**

Even though incidentally discovered adrenal masses are by definition asymptomatic, a significant proportion will show subclinical function. Caplan et al [7] found that 23% of patients who had an adrenal mass but no history of malignancy had detectable secretion of aldosterone, cortisol, or catecholamines. In a similar study Reincke et al [10] found that percentage to be 12%. Routine endocrinologic screening of patients with incidentalomas has been recommended for lesions larger than 4 cm [2]. The Swedish Cooperative Study of 388 patients with adrenal incidentalomas found that 5% of them were hypersecreting and included pheochromocytomas (70%) and functional cortical adenomas (30%) [11]. Thus, testing for subclinical hyperfunction may be warranted in selected cases. Two recent series have found a much higher percentage of pheochromocytomas discovered incidentally (29%-59%) than previously thought [12,13].

## **Computed Tomography**

CT not only detects incidentally discovered adrenal masses but also offers one of the best means of differentiating the benign from the malignant. Some

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benign lesions such as cysts and myelolipomas are readily identified by CT by their imaging features. Adrenal adenomas contain lipid to varying degrees, and this lowers their attenuation coefficient on non-contrast-enhanced CT. Lee et al [8] showed that when 0 Hounsfield units (HU) was used as a threshold value, the sensitivity for adenomas was 48% without any false positives. If the threshold was increased to 10 HU, the sensitivity was 56% with a 4% false positive rate. This has been confirmed by Singer et al [14]; however, van Erkel et al [9] found that no false positives were seen up to a threshold of 16.5 HU. Stadler et al [15] have shown that there is some variability in the density measurements on different CT scanners. A threshold value of 10 HU is generally accepted as a cutoff value for a region of interest obtained over the lesion. Bae et al [16] have demonstrated that using histograms of pixel values rather than the average value of the region of interest allows more adenomas to be identified while preserving a high specificity. If 5% or more of the pixels of a lesion are less than 0 HU, the lesion is very likely to be an adenoma. This is of particular relevance after contrast media has been given. Although sensitivity is reduced compared to nonenhanced CT, the use of histogram analysis can improve the sensitivity for adenoma from 10%-36% if >5% of pixels are negative [16].

In a more recent study by Remer et al [17] of 208 pathologically proven adrenal masses, negative pixels were seen in enhanced metastases, adrenal carcinomas, and pheochromocytomas. In addition, the authors noted that using a 5% negative pixel threshold improved specificity for adenoma diagnosis; however, the low sensitivity precluded clinical usefulness. Nonetheless, nonenhanced CT is a relatively inexpensive yet highly specific test for differentiating adenomas and some benign nonadenomas from malignant lesions, and histogram analysis may further improve its sensitivity.

Korobkin et al [18,19] have shown that delayed enhanced CT and use of washout percentages are better able to distinguish adenomas from metastases. Adenomas are not only lower in CT density but also tend to wash out faster after intravenous contrast. This may result from the increased “leakiness” of malignant vessels compared with benign lesions. Korobkin et al [18,19] showed that following a delay of 15 minutes after the administration of intravenous contrast, the sensitivity and specificity of CT could be greatly improved (sensitivity >95%, specificity >97%). Szolar et al [20] had similar results using 30-minute delay times (sensitivity 97%, specificity 100%). The accuracy of washout values was validated by Caoili et al in a study of 166 adrenal masses, accurate characterization being achieved in 96% of masses [21]. Thus, this technique is very promising and may be superior to nonenhanced CT and MRI in evaluating adrenal masses [22].

Follow-up CT has been recommended for lesions deemed to be low risk for malignancy based on their small size. The usual recommendation is that follow-up CT should be performed within 3-12 months to insure that there is no growth. However, anecdotal evidence of slow-growing metastases exists.

### **Magnetic Resonance Imaging**

MRI has until recently been insufficiently specific to be useful in this setting. Various adrenal mass-to-liver or adrenal mass-to-fat ratios and calculated T2 values were demonstrated to be inconsistent among institutions and field strengths. At their best they demonstrated a 30% overlap between adenomas and metastases [23].

Dynamic enhanced MRI depends on the differences in timing and intensity of enhancement of lesions after the intravenous administration of a gadolinium chelate bolus. Krestin et al [24] demonstrated that this method was correct 91% of the time in differentiating benign and malignant lesions. Semelka et al [25] however, using fat-suppressed T1-weighted MRI, showed that while there were differences in the mean enhancement between adenomas and metastases there was also too much overlap between the categories to make the test useful. In summary, while this technique showed initial promise, in view of mixed results in the literature it is currently not used widely to distinguish adenomas from malignant adrenal masses.

Chemical shift MRI (CSI), introduced by Leroy-Willig et al [26] in 1989, relies on differentiating lesions by their relative fat content, malignant lesions having virtually no lipid. Mitchell et al [27] showed that CSI was correct in 96% of cases, and Tsushima et al [28] showed that the technique was 100% correct when using a slight variation. Unfortunately, all of these studies were performed in a mixed population of patients with regard to the history of malignancy, so results may not be directly applicable to populations either with or without known malignancy (patient mix will greatly influence results). Moreover, while Mitchell’s technique has proven the most reliable, there is no universal agreement about technique or whether the same results will be seen at different field strengths.

Since then, several authors have shown excellent results in a relevant population using simpler CSI techniques [29-31]. Analytic methods have also varied from simple visual assessment of signal loss on out-of-phase (OOP) imaging compared to in-phase (IP) imaging to quantitative measures of signal loss. Fujiyoshi et al [32] concluded that a signal intensity index (IP-OOP/IP) was superior to other methods that normalized signal to spleen, liver, or muscle.

Haider et al [33] concluded, however, that superior results could be obtained by normalizing the signal to kidney.

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This group demonstrated substantial advantages to applying CSI imaging in cases where the CT density measurement was between 10 and 30 HU (ie, indeterminate by CT). For instance, in adenomas with densities between 10 and 30 HU, 89% of the lesions were correctly characterized by CSI. Similar results have been obtained by Israel et al [34] who concluded that up to 60% of lesions misclassified by CT density units can be correctly characterized as adenomas by chemical shift MRI. Gabriel et al [35] have demonstrated that even heterogeneous loss of signal is evidence of a benign lesion. Thus, chemical shift MRI may have better sensitivity and specificity than nonenhanced CT.

### Adrenal Biopsy

Biopsy of the incidental adrenal mass has been performed under CT guidance for over 20 years. Most studies on the efficacy of adrenal biopsy have been performed in a mixed population of patients. Biopsy samples insufficient to make a diagnosis are obtained in 4%-19% (mean = 15%) of cases [3,36-38]. When sufficient material is obtained, the accuracy of biopsy is 96%-100% for malignant lesions. Biopsy interpretation is more difficult in benign processes. Complication rates range from 8%-12% and consist of bleeding, pneumothorax, infection, and anecdotes of tumor tracking. Several deaths have been reported after an adrenal biopsy of a pheochromocytoma. Lumachi et al [39] demonstrated that when biopsy was compared to CT and MRI it had the highest combination of sensitivity and specificity (83% and 100%, respectively). Thus, biopsy is better suited to a population with a high risk of malignant lesions and is most useful when noninvasive studies are negative. The role of adrenal biopsy has evolved, and it is now performed to exclude the presence of metastases when noninvasive tests are inconclusive [40].

### Radionuclide Studies

Iodocholesterol (NP 59) scans are not in widespread use in the United States. NP 59 studies will detect any lesion with functioning adrenal tissue. Thus, hyperfunctional adenomas (Conn's and Cushing's adenomas) and many nonhyperfunctioning adenomas will bind this agent. When the CT and NP 59 scan are concordant, the lesion is benign in all cases [4]. In patients without a history of tumor, only 52% of benign lesions demonstrated this pattern in a study by Nakajo et al [41]; however, the majority of the remainder were also benign. Homogeneous uptake was seen in two adrenal cancers. Francis et al [4] studying a population of patients with a history of tumor, showed that most (82%) of lesions with discordant uptake were metastatic; 11% were indeterminate. Thus, radionuclide studies are very useful if concordant, but overlap significantly if they are discordant with the CT findings.

Metaiodobenzylguanidine (MIBG) studies are useful in patients suspected of a pheochromocytoma, but this is rarely the case in the incidentally detected adrenal mass.

Fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-labeled for positron emission tomography (PET) can be used to identify metastases in oncologic patients with various cancers [42-46]. FDG-PET is sensitive to metabolically active lesions, and metastases usually show greater uptake than benign lesions. In several studies there have been few false positives with FDG-PET, and excellent sensitivity has been achieved [42-46]. False negative scans have occurred in renal cell carcinoma metastases [47]. Specific uptake values (SUV) are typically greater than 4 for metastatic disease and less than 4 for benign lesions [48]. Thus, FDG-PET imaging is particularly promising for evaluating adrenal masses related to lung, colon, melanoma, and lymphoma but may not be the method of choice for renal cell carcinoma [47].

### Summary

For patients with no history of malignancy, most small (<3 cm) incidentally discovered adrenal masses are benign, and an extensive and costly workup is usually not justified. Endocrinologic evaluation should be considered, as subclinical hyperfunction is present in 5% of adrenal incidentalomas. If workup is deemed clinically important, unenhanced CT or chemical shift MRI is useful for effectively excluding a large number of patients from consideration for a malignancy. Follow-up with CT or MRI is another valid method of assessing the nature of the small incidentaloma. FDG-PET evaluation or adrenal biopsy should only be considered for lesions considered indeterminate by CT or MRI. For incidentalomas between 3-5 cm the following could be considered: follow-up CT, unenhanced CT, delayed enhanced CT with use of washout percentages, chemical shift MRI, an endocrinologic evaluation, FDG-PET, adrenal biopsy (if pheochromocytoma is excluded), or surgery. Follow-up CT or CSI are the most reasonable choices. Lesions larger than 5 cm should be removed due to the higher risk of malignancy.

For patients with a history of malignancy, the incidentally discovered adrenal mass is more often malignant, and thus even smaller adrenal lesions are suspect. It is important to exclude from further evaluation any patient with widespread nonadrenal metastases since, in this setting, the presence or absence of adrenal metastases is unlikely to influence the patient's outcome. The unenhanced CT, delayed enhanced CT, and chemical shift MRI are relatively inexpensive and readily available tests in this setting. If these are inconclusive, FDG-PET should be considered prior to biopsy, as a lesion with a high SUV is likely malignant. Adrenal biopsy should be reserved for cases where the noninvasive techniques are equivocal and to confirm the presence of metastases. In patients

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suspected of having a functional lesion, iodocholesterol or MIBG studies may be useful. Radiography and US have a very limited role in assessing adrenal lesions.

### Anticipated Exceptions

Patients with pheochromocytoma should not have adrenal biopsy unless properly pretreated. This diagnosis should be excluded prior to biopsy with urinary or plasma catecholamine levels. In equivocal cases a glucagon stimulation test should be done before biopsy of a potential pheochromocytoma.

### Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level*	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv
*RRL assignments are not included for some examinations. The RRL assignments for the IP (in progress) exams will be available in future releases. The RRL assignments for the NS (not specified) exams cannot be made because the RRL depends on the region of the body exposed to ionizing radiation, and the body part will vary as a function of the clinical situation.	

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