Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Gajraj H, Young AE. Adrenal incidentaloma. *Br J Surg* 1993; 80(4):422-426	Review/Other-Dx	N/A	To determine a policy for adrenal incidentaloma in patients without known malignancy.	No results stated in abstract.	4
2. Herrera MF, Grant CS, van Heerden JA, Sheedy PF, Ilstrup DM. Incidentally discovered adrenal tumors: an institutional perspective. *Surgery* 1991; 110(6):1014-1021.	Review/Other-Dx	342 patients	To investigate the effect of size of incidental adrenal masses in patients without known malignancy.	Studies to evaluate biochemical hyperfunction were performed in 172 patients (50%), 2 of whom were found to have cortisol-producing tumors and 5 pheochromocytomas. Histologic proof of diagnosis was obtained in 55 patients at the time of adrenalectomy. Malignancy was discovered in five patients (four primary and one metastatic), the smallest malignant tumor measuring 5 cm. In the 287 patients without histologic diagnoses, a minimum of 1 year of clinical follow-up was obtained in 251 (88%), including repeat CT scan in 156 (54%). None of these patients had clinical or biochemical adrenal abnormalitie. Authors suggest biochemical screening and surgical excision for all lesions >4 cm. Follow-up CT should be performed at 3 months in lesions <4 cm.	4
3. Song JH, Chaudhry FS, Mayo-Smith WW. The incidental adrenal mass on CT: prevalence of adrenal disease in 1,049 consecutive adrenal masses in patients with no known malignancy. *AJR* 2008; 190(5):1163-1168.	Review/Other-Dx	973 patients; 1,049 adrenal masses	Retrospective study to determine the nature and prevalence of adrenal lesions identified on CT in patients with no known malignancy.	1049 adrenal masses were characterized with the following methods: histopathology (n = 12), imaging characterization (n = 909), imaging follow-up (n = 87), and clinical follow-up (n = 41). There were 788 adenomas constituting 75% of all lesions. There were 68 myelolipomas (6%), 47 hematomas (4%), and 13 cysts (1%). Three pheochromocytomas (0.3%) and one cortisol-producing adenoma (0.1%) were found incidentally. One hundred twenty-eight lesions (12%) were presumed to be benign by imaging or clinical stability. No malignant adrenal masses were found, even among the 14 patients who later developed malignancy elsewhere.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
4. Bernardino ME, Walther MM, Phillips VM, et al. CT-guided adrenal biopsy: accuracy, safety, and indications. *AJR* 1985; 144(1):67-69.	Observational-Dx	53 patients; 58 needle biopsies	To review the accuracy of CT-guided adrenal biopsy performed in a mixed population.	44 (83%) of 53 had correct tissue diagnosis at initial biopsy. 17% of samples were insufficient for diagnosis. Accurate diagnosis was obtained in 48 (90.6%) when both first and second biopsy attempts were combined. 46% of lesions were malignant. 11.3% had complications, mainly bleeding. Authors conclude that procedure is accurate and safe alternative to surgical biopsy.	4
5. Francis IR, Smid A, Gross MD, Shapiro B, Naylor B, Glazer GM. Adrenal masses in oncologic patients: functional and morphologic evaluation. *Radiology* 1988; 166(2):353-356.	Observational-Dx	28 patients	Prospective study to investigate the role of NP-59 scintigraphy in the evaluation of unilateral adrenal masses detected by CT in the oncologic patient with normal adrenal function.	In 14 of the 28 patients, there was increased uptake of the NP-59 on the side of the adrenal mass detected at CT (concordant uptake). Thirteen of the 14 masses with concordant uptake were greater than 2 cm in diameter, and one was 1.5 cm; all were found to be adenomas. In 11 of 28 patients there was decreased uptake on the side of the mass detected at CT (discordant uptake). None of these 11 masses were adenomas; nine were metastases and two were adrenal cysts. Uptake was indeterminate (symmetric) in three patients, two of whom had adrenal adenomas and one an adrenal metastasis; each mass with indeterminate uptake was less than 2 cm in diameter.	3
6. McGahan JP. Adrenal gland: MR imaging. *Radiology* 1988; 166(1 Pt 1):284-285.	Review/Other-Dx	N/A	Comment on an article by Chang et al on MRI of the adrenal gland.	In this article, Chang et al found that intensity ratios of adrenal masses to liver were not statistically significant in distinguishing benign and malignant adrenal lesions. However, the mass/fat intensity ratio was statistically significant in separating benign and malignant adrenal lesions. In this study, all lesions with a mass/fat intensity ratio >0.8 were malignant and all adrenal masses with a ratio <0.6 were benign (adenomas). 8 of the masses were indeterminate.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
7. Oliver TW, Jr., Bernardino ME, Miller JI, Mansour K, Greene D, Davis WA. Isolated adrenal masses in nonsmall-cell bronchogenic carcinoma. *Radiology* 1984; 153(1):217-218.	Review/Other-Dx	330 patients	Combined retrospective-prospective study to determine the incidence of benign vs malignant isolated adrenal lesions in patients undergoing CT staging for nonsmall-cell bronchogenic carcinoma.	32 had adrenal masses. 8/32 masses were metastases, 17 were adenomas, and 7 did not undergo biopsy. In patients with nonsmall-cell bronchogenic carcinoma, an isolated adrenal mass is more likely benign than metastatic, and biopsy is advocated prior to withholding potentially curative surgery. CT has become useful in staging of patients with bronchogenic carcinoma.	4
8. Candel AG, Gattuso P, Reyes CV, Prinz RA, Castelli MJ. Fine-needle aspiration biopsy of adrenal masses in patients with extraadrenal malignancy. *Surgery* 1993; 114(6):1132-1136; discussion 1136-1137.	Review/Other-Dx	36 patients	To investigate the effect of size of incidental adrenal masses on fine-needle outcome in patients with known malignancies.	Using 3 cm as a dividing value, 87% of masses <3 cm were benign and more than 95% of lesions >3 cm were malignant in patients with known malignancies. Authors conclude that there is a significant correlation between the size of an adrenal nodule and the presence of metastases.	4
9. Angeli A, Osella G, Ali A, Terzolo M. Adrenal incidentaloma: an overview of clinical and epidemiological data from the National Italian Study Group. *Horm Res* 1997; 47(4-6):279-283.	Review/Other-Dx	887 patients	To perform a multicentric retrospective analysis of adrenal masses incidentally discovered (adrenal incidentalomas).	Majority of patients were in the 5th and 6th decade and females were predominantly affected. The frequency of adrenocortical cancer was 12% among operated patients (316 cases). The tumor diameter was highly correlated with the risk of malignancy, as well as the CT characteristics such as density, shape and margins. The frequency of pheochromocytoma was 10% among operated patients. The occurrence of incidentally discovered adrenocortical carcinomas and pheochromocytomas is not rare. Evaluation of the mass size and CT characteristics are simple and effective methods to differentiate malignant lesions. Biochemical screening for pheochromocytoma is mandatory before surgery.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
10. Lee MJ, Hahn PF, Papanicolaou N, et al. Benign and malignant adrenal masses: CT distinction with attenuation coefficients, size, and observer analysis. *Radiology* 1991; 179(2):415-418.	Observation-Dx	55 patients: 66 adrenal masses; 3 observers	Retrospective blinded study to investigate the role of CT attenuation coefficients in differentiating benign and malignant lesions in a mixed population.	The mean CT attenuation coefficient for benign adrenal masses was -2.2 HU +/- 16.0 and was significantly different from the mean for malignant lesions (28.9 HU +/- 10.6). The area under the ROC curve for CT attenuation coefficients (0.91 +/- 0.04) was significantly larger than that for lesion size (0.84 +/- 0.05) or best observer interpretation (0.84 +/- 0.05). A threshold CT attenuation value of 0 HU had a sensitivity-to-specificity ratio of 47%:100% for characterizing benign adrenal masses, whereas a threshold attenuation of 10 HU had a ratio of 79%:96%.	2
11. van Erkel AR, van Gils AP, Lequin M, Kruitwagen C, Bloem JL, Falke TH. CT and MR distinction of adenomas and nonadenomas of the adrenal gland. *J Comput Assist Tomogr* 1994; 18(3):432-438.	Observational-Dx	37 patients; 44 adrenal masses	To determine which of these: size, CT attenuation values, MRI SI ratios on T1- and T2-weighted sequences, calculated T2 relaxation times, or T2 relaxation time ratios provide better distinction of adenomas and non-adenomas of the adrenal gland.	Using a threshold of 15 HU they found no malignancies although there were some cysts. The optimal size threshold was 3.1 cm but it did not discriminate all lesions (93%). Attenuation values on non-contrast-enhanced CT are recommended in discriminating adrenal adenomas from non-adenomas.	3
12. Ho LM, Paulson EK, Brady MJ, Wong TZ, Schindera ST. Lipid-poor adenomas on unenhanced CT: does histogram analysis increase sensitivity compared with a mean attenuation threshold? *AJR* 2008; 191(1):234-238.	Observational-Dx	104 patients; 132 adrenal nodules	To compare histogram analysis with mean attenuation threshold to determine the value of CT histogram analysis for further characterization of lipid-poor adenomas on unenhanced CT.	Unenhanced CT mean attenuation threshold <10 histogram yielded a sensitivity of 68% and specificity of 100% for the diagnosis of an adenoma. Unenhanced CT threshold >10% negative pixels yielded a sensitivity of 84% and specificity of 100% for the diagnosis of an adenoma. Authors conclude that CT histogram analysis is superior to mean CT attenuation analysis for the evaluation of adrenal nodules and may help decrease referrals for additional imaging or biopsy.	3
13. Remer EM, Motta-Ramirez GA, Shepardson LB, Hamrahian AH, Herts BR. CT histogram analysis in pathologically proven adrenal masses. *AJR* 2006; 187(1):191-196.	Observational-Dx	187 patients: 208 adenomas; 2 observers	Retrospective review to evaluate if a CT histogram analysis method can distinguish adrenal adenomas from metastases, pheochromocytomas and adrenal cortical carcinomas. Compared adenomas on unenhanced CT with enhanced CT.	Specificity for a 10% negative pixel threshold was approximately 88% for unenhanced CT scans and 99% for enhanced CT scans, with sensitivities of 71% and 12%, respectively. Although the specificity for adenoma diagnosis on enhanced CT is high using a histogram analysis method with a 10% negative threshold, low sensitivity limits clinical usefulness.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
14. Barry MK, van Heerden JA, Farley DR, Grant CS, Thompson GB, Ilstrup DM. Can adrenal incidentalomas be safely observed? *World J Surg* 1998; 22(6):599-603; discussion 603-594.	Review/Other-Dx	231 patients	To determine the clinical outcome of a well-defined population of patients with incidentalomas followed without operative intervention.	Most adrenal tumors were unilateral (right 113; left 98); 20 were bilateral. Mean tumor size was 2 cm (range 1-6 cm). In 9 (4%) patients the tumor was ≥4 cm. Follow-up [mean 7 years; range 1 month (patient died) to 11.7 years] was complete in 224 (97%) patients. 91 (39%) patients had one or more additional CT scans performed during the follow-up period, with only 4 patients demonstrating a >1 cm increase in the size of the adrenal mass. Surgical excision of these 4 lesions identified benign pathology. 81 (35%) patients died of conditions unrelated to adrenal pathology. No patient developed subsequent adrenal hyperfunction or adrenal malignancy. Conservative management of adrenal incidentalomas considered benign or nonfunctioning at diagnosis is appropriate. Additional information provided by repeat CT scanning appears to confer limited benefit. This study does not support laparoscopic removal of small, nonfunctional adrenal tumors, as has been suggested.	4
15. Young WF, Jr. Clinical practice. The incidentally discovered adrenal mass. *N Engl J Med* 2007; 356(6):601-610.	Review/Other-Dx	N/A	Review article that presents recommendations for the evaluation of patients with adrenal incidentalomas. A patient is described in a vignette.	A thorough history should be obtained and a physical examination performed to assess the evidence of adrenal hormone excess for the patient presented in the vignette.	4
16. Schteingart DE, Doherty GM, Gauger PG, et al. Management of patients with adrenal cancer: recommendations of an international consensus conference. *Endocr Relat Cancer* 2005; 12(3):667-680.	Review/Other-Dx	N/A	Consensus conference to examine management of patients with adrenal cancer.	In addition to setting up guidelines in specific areas of the diagnosis and treatment of adrenal cancer, the conference recommended and initiated the planning of an international prospective trial for treatment of patients with adrenal cancer in stages III and IV.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
17. Kutikov A, Mallin K, Canter D, Wong YN, Uzzo RG. Effects of increased cross-sectional imaging on the diagnosis and prognosis of adrenocortical carcinoma: analysis of the national cancer database. *J Urol* 2011; 186(3):805-810.	Review/Other-Dx	4,275 patients	To assess whether incidental screening due to imaging performed for other purposes has resulted in earlier detection or better outcomes in patients with adrenocortical carcinoma.	Median survival for 4,275 patients was 24 months. Localized adrenocortical carcinoma accounted for 43.9% of cases. No stage migration was noted with time. No statistical trends were noted in tumor size changes during the years in patients who underwent surgery for localized disease (P=0.32). No improvement was observed in 5-year survival during the period (P>0.1). Better risk stratification of patients with adrenal incidentaloma, while improving treatment efficacy for those with proven adrenocortical carcinoma, is an essential clinical and epidemiological task.	4
18. Pantalone KM, Gopan T, Remer EM, et al. Change in adrenal mass size as a predictor of a malignant tumor. *Endocr Pract* 2010; 16(4):577-587.	Observational-Dx	136 adrenalectomies or biopsies in 132 patients	Retrospective study to assess the value of adrenal mass absolute growth, growth rate, and percentage growth rate on serial imaging for distinguishing benign from malignant adrenal masses.	There were 111 benign (81.6%) and 25 malignant (18.4%) adrenal masses. With use of ROC curve analysis, all 3 aforementioned growth measures showed similar levels of discrimination for the entire study group as well as for the subgroups with 3 to 12 months of follow-up (n=75 masses) and noncontrast CT HU >10 or not reported (n=111 masses). After adjustment for other factors, the 3 growth measures remained statistically significant predictors of a malignant tumor. The absolute growth cutoff value of 0.8 cm had the highest sum of sensitivity and specificity of 72% and 81.1%, respectively. Change in adrenal mass size should be used in conjunction with other imaging and clinical characteristics when surgical resection is being considered.	2
19. Caplan RH, Strutt PJ, Wickus GG. Subclinical hormone secretion by incidentally discovered adrenal masses. *Arch Surg* 1994; 129(3):291-296.	Review/Other-Dx	26 patients	Review radiologic reports to determine the frequency of subclinical hormone secretion in incidentally discovered adrenal masses in patients without a history of tumor.	One patient had unrecognized primary aldosteronism, 2 had elevated free catecholamine excretion, and 3 (12%) had subclinical Cushing's syndrome. Authors conclude that subclinical hormone secretion, especially cortisol secretion, is common in patients with incidentally discovered adrenal masses and therefore surgeons/anesthesiologists must be aware that adrenal may develop in patients with incidentally discovered adrenal masses.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
20. Reincke M, Nieke J, Krestin GP, Saeger W, Allolio B, Winkelmann W. Preclinical Cushing's syndrome in adrenal "incidentalomas": comparison with adrenal Cushing's syndrome. *J Clin Endocrinol Metab* 1992; 75(3):826-832.	Review/Other-Dx	68 patients	Prospective study to determine the frequency of subclinical hormone secretion in incidentally discovered adrenal masses in patients without a history of tumor.	12% of incidentalomas showed cortisol secretion with dexamethasone suppression test consistent with adrenal cortical hyperfunction.	4
21. Grumbach MM, Biller BM, Braunstein GD, et al. Management of the clinically inapparent adrenal mass ("incidentaloma"). *Ann Intern Med* 2003; 138(5):424-429.	Review/Other-Dx	N/A	A panel was convened to address the causes, prevalence, and natural history of clinically inapparent adrenal masses, or "incidentalomas"; the appropriate evaluation and treatment of such masses; and directions for future research.	The panel recommended a 1-mg dexamethasone suppression test and measurement of plasma-free metanephrines for all patients with an adrenal incidentaloma; additional measurement of serum potassium and plasma aldosterone concentration-plasma renin activity ratio for patients with hypertension; and surgery for patients with biochemical evidence of pheochromocytoma, patients with tumors >6 cm, and patients with tumors >4 cm who also meet other criteria. The panel also advocated a multidisciplinary approach to managing adrenal incidentalomas.	4
22. Zeiger MA, Thompson GB, Duh QY, et al. American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons Medical Guidelines for the Management of Adrenal Incidentalomas: executive summary of recommendations. *Endocr Pract* 2009; 15(5):450-453.	Review/Other-Dx	N/A	American Association of Clinical Endocrinologists and American Association of Endocrine Surgeons Medical Guidelines for the Management of Adrenal Incidentalomas: executive summary of recommendations.	N/A	4
23. Bulow B, Ahren B. Adrenal incidentaloma--experience of a standardized diagnostic programme in the Swedish prospective study. *J Intern Med* 2002; 252(3):239-246.	Review/Other-Dx	381 patients	Prospective multicenter study to report a 5-year experience of a diagnostic program for adrenal incidentaloma. Emphasis on hormonally active and malignant lesions.	5% of 381 cases had benign hyper secreting tumors and about 4% had malignant tumors. The results of the biochemical diagnostic tests used had a high compatibility with the histological diagnosis found at operation in the patients with hyper secreting tumors. Tumor size, male gender and high age were predictive for the risk of a malignant tumor.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
24. Muth A, Hammarstedt L, Hellstrom M, Sigurjonsdottir HA, Almqvist E, Wangberg B. Cohort study of patients with adrenal lesions discovered incidentally. *Br J Surg* 2011; 98(10):1383-1391.	Review/Other-Dx	226 patients	Prospective cohort study to examine the incidence, clinical features and natural history of incidentally discovered adrenal mass lesions (adrenal incidentaloma) in an unselected population undergoing radiological examination.	Mean follow-up was 19 months. After baseline evaluation, 14 patients had surgery owing to primary hyperaldosteronism (3), catecholamine-producing tumor (1), tumor size (6), size and indication of subclinical hypercortisolism (3) and metastasis (1). No hypersecreting lesions were confirmed during follow-up; one patient underwent adrenalectomy for a suspected phaeochromocytoma (adrenocortical adenoma at histopathology). No primary adrenal malignancy was found. In this prospective cohort study 6·6% of patients with an adrenal incidentaloma had surgery and benign hormone-producing tumors were verified in 3.1 %. Repeat CT and hormone evaluation after 2 years did not increase the sensitivity for diagnosis of malignant or hormone-producing tumors.	4
25. Baguet JP, Hammer L, Mazzuco TL, et al. Circumstances of discovery of phaeochromocytoma: a retrospective study of 41 consecutive patients. *Eur J Endocrinol* 2004; 150(5):681-686.	Review/Other-Dx	41 consecutive patients	Retrospective study to determine circumstances of discovery of pheochromocytomas.	The association of headaches and palpitations with sweating was found in 24% of cases (10/41). Blood pressure anomalies led to the discovery of phaeochromocytoma in 51% of cases (21/41) and 59% (24/41) of all the patients suffered from hypertension. Tumor was in almost half the cases (20/41); the tumor was discovered by an imaging method (US, CT scan or MRI) which had been performed for reasons unrelated to a blood pressure abnormality.	4
26. Motta-Ramirez GA, Remer EM, Herts BR, Gill IS, Hamrahian AH. Comparison of CT findings in symptomatic and incidentally discovered pheochromocytomas. *AJR* 2005; 185(3):684-688.	Review/Other-Dx	33 patients	Retrospective study to determine incidence of incidental pheochromocytomas, see if there are differences between incidental and symptomatic pheochromocytomas.	57.6% of the pheochromocytomas were incidental. None of the pheochromocytomas had attenuation values of <10 HU on unenhanced CT scans. No imaging appearance differences between incidental and symptomatic pheochromocytomas.	4
27. Singer AA, Obuchowski NA, Einstein DM, Paushter DM. Metastasis or adenoma? Computed tomographic evaluation of the adrenal mass. *Cleve Clin J Med* 1994; 61(3):200-205.	Observational-Dx	24 adrenal masses	To investigate the role of CT attenuation coefficients in differentiating benign and malignant lesions in patients with known malignancy.	Using a threshold of 0 HU 33:100 sensitivity/specificity ratio was seen. With 10 HU same ratio was 58:92. Size threshold of 2.5 cm produced ratio of 58:100. Authors conclude that benign adenomas can be identified by measuring the size and attenuation of adrenal masses.	3

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
28. Stadler A, Schima W, Prager G, et al. CT density measurements for characterization of adrenal tumors ex vivo: variability among three CT scanners. *AJR* 2004; 182(3):671-675.	Review/Other-Dx	7 patients	Assess the variability of CT attenuation values for adrenal tumors with different scanning protocols and CT scanners to determine whether the establishment of a scanner-independent threshold for differentiation between adenomas and non-adenomas was possible.	CT density measurements varied by 2-4 HU depending on the manufacturer. This should be considered when setting absolute threshold values for CT density.	4
29. Boland GW, Lee MJ, Gazelle GS, Halpern EF, McNicholas MM, Mueller PR. Characterization of adrenal masses using unenhanced CT: an analysis of the CT literature. *AJR* 1998; 171(1):201-204.	Review/Other-Dx	10 CT reports; 495 adrenal lesions (272 benign, 223 malignant)	Analysis of CT reports to determine optimal threshold value for separating benign from malignant lesions in adrenal masses.	Sensitivity for characterizing a lesion as benign ranged from 47% at a threshold of 2 HU to 88% at a threshold of 20 HU. Specificity varied from 100% at a threshold of 2 HU to 84% at a threshold of 20 HU. Attempt to be certain that a lesion is benign may lead to an unacceptably low sensitivity for characterization. Choice of threshold is dependent on patient population and the cost-benefit approach to patient care.	4
30. Bae KT, Fuangtharnthip P, Prasad SR, Joe BN, Heiken JP. Adrenal masses: CT characterization with histogram analysis method. *Radiology* 2003; 228(3):735-742.	Review/Other-Dx	193 patients; 223 adenomas	Retrospective study to determine whether a histogram analysis method is more accurate than region of interest measurements for determining adenomas on nonenhanced CT.	Negative pixels were present in all 74 unenhanced adenomas with mean attenuation of 10 HU or less and in 14 of 16 unenhanced adenomas with mean attenuation above 10 HU. Of 184 enhanced adenomas, only 20 had mean attenuation of 10 HU or less, but 97 contained negative pixels (77 of these 97 masses had mean attenuation above 10 HU). Increase in percentage negative pixels was highly correlated with decrease in mean attenuation of both unenhanced and enhanced adenomas. None of the adrenal metastases had mean attenuation of 10 HU or less or contained negative pixels.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
31. Halefoglu AM, Bas N, Yasar A, Basak M. Differentiation of adrenal adenomas from nonadenomas using CT histogram analysis method: a prospective study. *Eur J Radiol* 2010; 73(3):643-651.	Observational-Dx	94 patients with 113 adrenal masses	To prospectively evaluate the effectiveness of CT histogram analysis method in the differentiation of benign and malignant adrenal masses.	Sensitivity was 90.9% for the 10% negative pixel percentage threshold compared to 77.2% sensitivity for ≤ 10 HU mean attenuation threshold for unenhanced CT. Both methods gave 100% specificity for the diagnosis of adenoma. The authors also obtained a 37.9% sensitivity for 5% negative pixel threshold and a slightly lower sensitivity of 28.8% for 10% negative pixel threshold compared to the 12.1% sensitivity of ≤10 HU mean attenuation threshold while maintaining 100% specificity for contrast-enhanced CT. The CT histogram analysis is a simple and easily applicable method which provides higher sensitivity than the commonly used 10 HU threshold mean attenuation method of unenhanced CT and can replace it for the diagnosis of an adenoma. But with contrast-enhanced CT, although 100% specificity is being maintained, the sensitivities obtained are very poor for each method and is therefore likely to limit CT histogram analysis to be used as a clinically useful adjunct in the diagnosis of adenoma.	3
32. Korobkin M, Brodeur FJ, Francis IR, Quint LE, Dunnick NR, Londy F. CT time-attenuation washout curves of adrenal adenomas and nonadenomas. *AJR* 1998; 170(3):747-752.	Observational-Dx	66 patients: 52 adrenal adenomas; 24 non-adenomas	To determine if delayed washout CT improved differentiation of benign and malignant adrenal lesions.	The mean percentage of enhancement washout for adrenal adenomas was 51% at 5 min and 70% at 15 min, compared with 8% and 20%, respectively, for nonadenomas. The sensitivity and specificity for the diagnosis of adenoma were both 96% at a threshold attenuation value of 37 H on the 15-min delayed enhanced scan.	3
33. Korobkin M, Francis IR. Imaging of adrenal masses. *Urol Clin North Am* 1997; 24(3):603-622.	Review/Other-Dx	N/A	Review clinical features and imaging findings of patients with known or suspected adrenal masses.	In patients with hyperfunctioning adrenal syndrome, CT is useful. In patients with a non-hyperfunctioning adrenal mass, chemical shift MRI and CT densitometry are now replacing percutaneous adrenal biopsy or serial follow-up CT as methods to establish a specific diagnosis.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
34. Caoili EM, Korobkin M, Francis IR, Cohan RH, Dunnick NR. Delayed enhanced CT of lipid-poor adrenal adenomas. *AJR* 2000; 175(5):1411-1415.	Review/Other-Dx	18 lipid-poor adenomas; 56 lipid-rich adenomas; 40 adrenal non-adenomas	Compared the delayed contrast-enhanced CT features of lipid-poor adenomas with those of lipid-rich adenomas and adrenal non-adenomas to determine whether there were differences in the washout features between these groups of lesions.	A single mean attenuation value cannot differentiate lipid-poor adenomas from adrenal non-adenomas. Lipid-poor adenomas show enhancement and enhancement washout features similar to lipid-rich adenomas and can be distinguished from non-adenomas on the basis of a percentage washout threshold value of 60% and a relative percentage washout of 40%.	4
35. Kebapci M, Kaya T, Gurbuz E, Adapinar B, Kebapci N, Demirustu C. Differentiation of adrenal adenomas (lipid rich and lipid poor) from nonadenomas by use of washout characteristics on delayed enhanced CT. *Abdom Imaging* 2003; 28(5):709-715.	Observational-Dx	65 patients; 77 adrenal masses	Describe non-enhanced, early contrast-enhanced and delayed contrast-enhanced CT features and contrast washout characteristics of adrenal adenomas (lipid rich and lipid poor) and non-adenomas to determine the role of these methods in distinguishing one type from the other.	The absolute or relative percentage washout of contrast material on delayed contrast-enhanced CT is highly specific for differentiation of lipid-poor and lipid-rich adrenal adenomas from adrenal non-adenomas.	3
36. Szolar DH, Kammerhuber FH. Adrenal adenomas and nonadenomas: assessment of washout at delayed contrast-enhanced CT. *Radiology* 1998; 207(2):369-375.	Observational-Dx	122 patients; 135 adrenal masses	To measure the changes in wash-in and washout of contrast material on contrast material-enhanced CT scans in patients with adrenal adenomas and nonadenomas.	Delayed enhanced CT at 10 minutes (sensitivity 92%; specificity 95%) and 30 minutes (sensitivity 97%; specificity 100%) was more accurate for differentiation of adenomas and non-adenomas than unenhanced CT (sensitivity 82%; specificity 95%). Authors conclude that adrenal adenomas show greater washout of contrast material than adrenal non-adenomas. Recommends combining percentage change in washout of contrast material to absolute CT attenuation values in differentiation of adrenal adenomas and non-adenomas.	2
37. Caoili EM, Korobkin M, Francis IR, et al. Adrenal masses: characterization with combined unenhanced and delayed enhanced CT. *Radiology* 2002; 222(3):629-633.	Observational-Dx	116 patients; 166 adrenal masses	To assess accuracy of dedicated CT adrenal protocol with unenhanced and delayed washout attenuation values.	The final diagnosis was adenoma in 127 masses and non-adenoma in 39. Masses measuring more than 10 HU on unenhanced CT scans were confirmed at biopsy (n = 28) or were examined for stability or change in size at follow-up CT performed at a minimum interval of 6 months (n = 33). Thirty-six (92%) of 39 non-adenomas and 124 (98%) of 127 adenomas were correctly characterized. The sensitivity and specificity of this protocol were 98% and 92%, respectively. This protocol correctly characterized 160 (96%) of 166 masses.	3

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Choyke PL. From needles to numbers: can noninvasive imaging distinguish benign and malignant adrenal lesions? *World J Urol* 1998; 16(1):29-34.	Review/Other-Dx	N/A	Review to determine role of non-invasive imaging in differentiating benign and malignant adrenal lesions.	CT densitometry with or without contrast media and chemical shift MRI have adequate sensitivity (50%-90%) and excellent specificity (>95%) for adrenal adenomas.	4
39. Szolar DH, Korobkin M, Reittner P, et al. Adrenocortical carcinomas and adrenal pheochromocytomas: mass and enhancement loss evaluation at delayed contrast-enhanced CT. *Radiology* 2005; 234(2):479-485.	Observational-Dx	67 patients (11 with adrenocortical carcinoma, 17 with pheochromocytoma, 23 with adrenal adenoma, 16 with metastasis to adrenal gland)	To retrospectively measure the adrenal gland attenuation and the percentage loss of adrenal gland enhancement at delayed contrast medium-enhanced CT in patients with adrenocortical carcinomas and pheochromocytomas and to compare these data with those in patients with adenomas and metastases.	At optimal threshold values of 50% for absolute percentage of enhancement loss and 40% for relative percentage of enhancement loss at 10 minutes, both the sensitivity and the specificity for the diagnosis of adenoma were 100% when adenomas were compared with carcinomas, pheochromocytomas, and metastases. The enhancement loss in adrenocortical carcinomas and pheochromocytomas is similar to that in adrenal metastases but significantly less than that in adrenal adenomas. The percentage change in contrast material washout is a useful addition to absolute CT attenuation values in differentiating adrenal adenomas from adrenocortical carcinomas and pheochromocytomas.	2
40. Leroy-Willig A, Bittoun J, Luton JP, et al. In vivo MR spectroscopic imaging of the adrenal glands: distinction between adenomas and carcinomas larger than 15 mm based on lipid content. *AJR* 1989; 153(4):771-773.	Review/Other-Dx	20 patients; 22 adrenal tumors	To investigate the role of chemical shift MRI in differentiating benign and malignant adrenal masses in a mixed population.	Lipid percentage was higher for adenomas (n=15) than for metastatic (n=7). One adenoma had a lipid percentage overlapping with malignant (96% correct). In vivo MR spectroscopic imaging of adrenal tumors is useful.	4
41. Mitchell DG, Crovello M, Matteucci T, Petersen RO, Miettinen MM. Benign adrenocortical masses: diagnosis with chemical shift MR imaging. *Radiology* 1992; 185(2):345-351.	Observational-Dx	31 patients; 45 adrenal masses	To investigate the role of chemical shift MRI in differentiating benign and malignant adrenal masses in a mixed population.	Both myelolipomas and 26/27 benign cortical masses showed a loss of SI on at least one chemical shift image. Opposed-phase images were slightly more sensitive than fat-suppressed images in depicting lipid within benign cortical masses. All masses had higher SI than that of the liver on standard T2-weighted MR images. Chemical shift MRI can demonstrate lipid within benign adrenocortical masses and thus increase specificity, potentially obviating biopsy and aggressive follow-up.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Tsushima Y, Ishizaka H, Matsumoto M. Adrenal masses: differentiation with chemical shift, fast low-angle shot MR imaging. *Radiology* 1993; 186(3):705-709.	Observational-Dx	46 patients; 53 adenomas	Prospective study to investigate the role of chemical shift MRI in differentiating benign and malignant adrenal masses in a mixed population.	The signal-intensity indexes of adrenal masses ([SI on IP - SI on OP]/[SI on IP x 100]), where IP = in-phase image and OP = out-of-phase image, were calculated. All adenomas had SI indexes >5%, while SI indexes of metastatic tumors and pheochromocytomas were <5%, with accuracy of 100%. Chemical shift MRI was superior to the calculated T2.	3
43. Mayo-Smith WW, Lee MJ, McNicholas MM, Hahn PF, Boland GW, Saini S. Characterization of adrenal masses (< 5 cm) by use of chemical shift MR imaging: observer performance versus quantitative measures. *AJR* 1995; 165(1):91-95.	Observational-Dx	43 patients: 46 adrenal lesions; 3 observers	To evaluate the ability of chemical shift MRI to differentiate <5 cm adrenal adenomas from metastases and to compare subjective interpretation with several different quantitative measures.	Mean SI was significantly different between adenomas and metastases on out-of-phase images (64 vs 98) (P<.0005) but not in-phase images (130 vs 122) (P=.47). The adrenal-spleen ratio discriminated between adenomas and metastases better than did the adrenal-liver ratio, the adrenal-muscle ratio, or the SI index. No significant difference in interpretation among the three observers was evident (areas under the ROC curves, 0.93, 0.95, and 0.96). The performance of the observers was comparable to the results obtained with the adrenal-spleen ratio measurement (area under the ROC curve, 0.97).	3
44. McNicholas MM, Lee MJ, Mayo-Smith WW, Hahn PF, Boland GW, Mueller PR. An imaging algorithm for the differential diagnosis of adrenal adenomas and metastases. *AJR* 1995; 165(6):1453-1459.	Review/Other-Dx	33 patients; 37 adrenal masses	Prospective study to develop an algorithm using CT and chemical-shift MRI for the characterization of adrenal masses in patients with a primary cancer and no other evidence of metastatic disease.	Lesions ≤0 H may be benign and further work-up is not required. Lesions with density >20 H may be malignant and should be biopsied when the result will influence management. Study recommends chemical-shift MRI for CT-indeterminate lesions. An adrenal-spleen ratio threshold of 70 indicates a benign lesion, and no further workup is required in these patients. Lesions with adrenal-spleen ratio >70 should have a biopsy performed, depending on the clinical situation.	4

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Outwater EK, Siegelman ES, Radecki PD, Piccoli CW, Mitchell DG. Distinction between benign and malignant adrenal masses: value of T1-weighted chemical-shift MR imaging. *AJR* 1995; 165(3):579-583.	Observational-Dx	50 patients: 58 adrenal; masses; 3 observers	Blinded study to determine value of T1-weighted chemical-shift MRI for distinction between benign and malignant adrenal masses.	The 3 readers had mean sensitivity of 87%, specificity of 92%, and PPV of 95% for diagnosis of benign lesion. At the highest (definite) confidence of a benign lesion, the mean PPV was 99%, with lower sensitivity (54%). Areas under ROC curves for the 3 radiologists were .98 (95% CI: .94-1.00), .96 (CI: .91-1.00), and .95 (CI: .89-1.00). Inter-observer variation for the diagnosis of a benign mass was low (kappa = .79). Authors conclude that chemical-shift imaging using breath-hold opposed-phase T1-weighted MRI is a reliable and reproducible technique for the diagnosis of most benign adrenal masses at the highest threshold of confidence.	2
46. Fujiyoshi F, Nakajo M, Fukukura Y, Tsuchimochi S. Characterization of adrenal tumors by chemical shift fast low-angle shot MR imaging: comparison of four methods of quantitative evaluation. *AJR* 2003; 180(6):1649-1657.	Observational-Dx	88 patients; 102 adrenal masses	Retrospective study to compare and assess 4 quantitative methods of distinguishing adenomas from malignant adrenal lesions using chemical shift fast low-angle shot MRI.	The SI index was the best method of distinguishing benign and malignant lesions. In this study 100% were identified correctly using a SI index of 11.2% to 16.5%.	3
47. Shinozaki K, Yoshimitsu K, Honda H, et al. Metastatic adrenal tumor from clear-cell renal cell carcinoma: a pitfall of chemical shift MR imaging. *Abdom Imaging* 2001; 26(4):439-442.	Review/Other-Dx	1 patient	A case of adrenal metastasis from clear-cell renal cell carcinoma in which presence of a small amount of fat was shown on chemical shift gradient-echo MRI is presented.	Radiologists should be aware that signal loss of the adrenal tumor on out-of-phase gradient-echo images does not always suggest the diagnosis of benign adenoma, particularly in patients with a history of renal cell carcinoma.	4
48. Sydow BD, Rosen MA, Siegelman ES. Intracellular lipid within metastatic hepatocellular carcinoma of the adrenal gland: a potential diagnostic pitfall of chemical shift imaging of the adrenal gland. *AJR* 2006; 187(5):W550-551.	Review/Other-Dx	1 patient	A case is presented of a 48-year-old man with a history of hepatitis C, hepatic cirrhosis, and hepatocellular carcinoma who was being treated with chemotherapy.	A baseline MRI examination revealed a 2.5 cm hepatocellular carcinoma of the right lobe and normal adrenal glands. An adrenal mass was discovered during an MR examination performed 3 months later. The adrenal mass was isointense to the spleen on both in-phase gradient-echo T1- and T2-weighted fast spin-echo images but lost signal relative to spleen on opposed-phase imaging.	4
49. Haider MA, Ghai S, Jhaveri K, Lockwood G. Chemical shift MR imaging of hyperattenuating (>10 HU) adrenal masses: does it still have a role? *Radiology* 2004; 231(3):711-716.	Observational-Dx	36 patients; 38 masses	Retrospective study to determine whether chemical shift MRI can characterize hyperattenuating adrenal masses.	89% (17/19 masses) of adrenal adenomas >10HU were detected by chemical shift MRI. Authors conclude that for some circumstances, chemical shift MRI is a reasonable second imaging test for further characterization of a hyperattenuating adrenal mass.	3

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Israel GM, Korobkin M, Wang C, Hecht EN, Krinsky GA. Comparison of unenhanced CT and chemical shift MRI in evaluating lipid-rich adrenal adenomas. *AJR* 2004; 183(1):215-219.	Observational-Dx	40 patients: 42 adrenal masses; 2 observers	Retrospective analysis to compare unenhanced CT with chemical shift MRI to determine if MRI can characterize adrenal lesions which are indeterminate by CT.	The sensitivities and specificities for diagnosing a lipid-rich adenoma using the qualitative, adrenal-to-spleen chemical shift ratio, signal-intensity index, and unenhanced CT attenuation analyses were 92% (33/36) and 17% (1/6), 100% (36/36) and 100% (6/6), 100% (36/36) and 67% (4/6), and 78% (28/36) and 83% (5/6), respectively. 8 of 13 adrenal adenomas >10 HU on unenhanced CT were characterized with chemical shift MRI.	3
51. Gabriel H, Pizzitola V, McComb EN, Wiley E, Miller FH. Adrenal lesions with heterogeneous suppression on chemical shift imaging: clinical implications. *J Magn Reson Imaging* 2004; 19(3):308-316.	Review/Other-Dx	242 patients	Retrospective study to determine the frequency and value of adrenal lesions that demonstrate heterogeneous suppression on chemical shift MRI.	Heterogeneous suppression was seen in 14% of patients. Imaging or pathologic follow-up was available for 18 of the heterogeneously suppressing lesions. 18/18 cases were benign. Therefore, heterogeneous suppression has the same significance as homogeneous suppression.	4
52. Park BK, Kim CK, Kim B, Lee JH. Comparison of delayed enhanced CT and chemical shift MR for evaluating hyperattenuating incidental adrenal masses. *Radiology* 2007; 243(3):760-765.	Observational-Dx	34 patients; 43 adrenal masses	Retrospective study to compare the accuracy of delayed enhanced CT and chemical shift MRI for characterizing hyperattenuating adrenal masses at CT, with either follow-up imaging or pathologic review as the reference standard.	Sensitivity, specificity, and accuracy for adenoma at CT were 97% (36/37), 100% (6/6), and 98% (42/43), respectively, and at MR were 86% (32/37), 50% (3/6), and 49% (21/43), respectively. CT helped confirm 5 more adenomas and 3 more metastatic tumors than did MRI. However, there was no significant difference for diagnostic accuracy between the two imaging modalities (P>.05).	2

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Halefoglu AM, Yasar A, Bas N, Ozel A, Erturk SM, Basak M. Comparison of computed tomography histogram analysis and chemical-shift magnetic resonance imaging for adrenal mass characterization. *Acta Radiol* 2009; 50(9):1071-1079.	Observational-Dx	93 patients with 109 adrenal masses	To prospectively compare CT histogram analysis and chemical-shift MRI in the characterization of adrenal masses.	On unenhanced CT examinations, all of the 67 adenomas and 21/42 metastases exhibited negative pixels. None of the metastases showed more than 10% negative pixels on CT histogram analysis. An increase in the percentage of negative pixels correlated well with a decrease in the mean CT attenuation. CT histogram analysis using a 10% negative pixel threshold gave a 91% sensitivity and 100% specificity for the diagnosis of an adenoma. On chemical-shift MRI, for an adrenal-to-spleen chemical-shift ratio of <0.71, 97% sensitivity and 100% specificity were achieved, while a 97% sensitivity and 93% specificity were obtained for an adrenal SI index of more than 16.5% for adenoma diagnosis. CT histogram analysis method using a 10% negative pixel threshold on unenhanced CT had a good sensitivity and perfect specificity for the differentiation of adrenal adenomas from non-adenomas. In spite of the good results obtained with the CT histogram analysis method, chemical-shift MRI using adrenal-to-spleen chemical-shift ratio and adrenal SI index formulas had a higher sensitivity and could help in the characterization of adrenal masses appearing indeterminate by CT histogram analysis.	3

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
54. Miller FH, Wang Y, McCarthy RJ, et al. Utility of diffusion-weighted MRI in characterization of adrenal lesions. *AJR* 2010; 194(2):W179-185.	Observational-Dx	160 adrenal lesions in 156 patients	To retrospectively evaluate the utility of ADC values for characterizing adrenal lesions and determine if DWI can distinguish lipid-rich from lipid-poor adenomas.	ADCs of adrenal malignancies (median, 1.67 x 10(-3) mm(2)/s; interquartile range, 1.41-1.84 x 10(-3) mm(2)/s) were not different compared with those of benign lesions (1.61 x 10(-3) mm(2)/s; 1.27-1.96 x 10(-3) mm(2)/s; p > 0.05). Cysts (2.93 x 10(-3) mm(2)/s; 2.70-3.09 x 10(-3) mm(2)/s) showed higher ADCs than the remaining adrenal lesions (P<0.05). The median ADCs of lipid-rich adenomas did not differ from those of lipid-poor ones (P>0.05). The CT attenuation had no negative or positive correlation with the ADCs of adrenal adenomas (r = -0.05, P=0.97). Unlike lesion size and percentage decrease in SI, the ADCs were not useful in distinguishing benign from malignant adrenal lesions. Lipid-poor adenomas could not be distinguished from lipid-rich adenomas and all other nonfatty lesions of the adrenal gland with DWI.	3
55. Tsushima Y, Takahashi-Taketomi A, Endo K. Diagnostic utility of diffusion-weighted MR imaging and apparent diffusion coefficient value for the diagnosis of adrenal tumors. *J Magn Reson Imaging* 2009; 29(1):112-117.	Observational-Dx	42 patients with 43 adrenal tumors	Retrospective study to determine the utility of DWI-MRI for the diagnosis of adrenal tumors.	There was no difference in ADC values between adenomas (1.09 +/- 0.29*10(-3) mm(2)/s; range, 0.52-1.64) and metastatic tumors (0.85 +/- 0.26*10(-3); 0.51-1.23; P=0.14). Pheochromocytomas showed the higher mean ADC value (1.59 +/- 0.34*10(-3); 1.04-1.96) compared with those of adenomas or metastatic tumors (P<0.05 and P<0.005, respectively). The mean SI index of adenomas (62.1 +/- 17.9%; 14.5-88.4) was significantly higher than those of pheochromocytomas (4.0 +/- 10.0%; -19.6-3.3; P<0.005) or metastatic tumors (-1.5 +/- 11.7%; -18.3-8.2; P<0.01). There was no correlation between ADC values and SI index. Although pheochromocytomas showed higher ADC values, we did not find that ADC value had diagnostic utility for differentiating adenomas and metastatic tumors.	3

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
56. Gillams A, Roberts CM, Shaw P, Spiro SG, Goldstraw P. The value of CT scanning and percutaneous fine needle aspiration of adrenal masses in biopsy-proven lung cancer. *Clin Radiol* 1992; 46(1):18-22.	Review/Other-Dx	16 patients had FNA	To review the accuracy of CT and percutaneous FNA of adrenal masses in biopsy-proven lung cancer.	19% of samples were insufficient. 5 patients with positive FNA died within 24 months but 2/5 with negative biopsies died with metastatic disease within 11 months. Lesions <2 cm were benign. Biopsy was necessary for diagnosis since the CT appearances of many adrenal lesions were insufficiently distinctive to exclude malignancy.	4
57. Silverman SG, Mueller PR, Pinkney LP, Koenker RM, Seltzer SE. Predictive value of image-guided adrenal biopsy: analysis of results of 101 biopsies. *Radiology* 1993; 187(3):715-718.	Observational-Dx	97 patients; 101 biopsies	To review the accuracy of biopsy performed in a mixed population.	Diagnostic samples were obtained in 86%. Biopsy had sensitivity of 93%, NPV of 91% and accuracy of 96%. Three small masses <3 cm proved to be malignant. Biopsy is an accurate procedure, however if benign tissue is not obtained then repeat biopsy or surgery is indicated. 8% complications.	3
58. Tikkakoski T, Taavitsainen M, Paivansalo M, Lahde S, Apaja-Sarkkinen M. Accuracy of adrenal biopsy guided by ultrasound and CT. *Acta Radiol* 1991; 32(5):371-374.	Observational-Dx	56 patients	To review the results of FNA of the adrenal glands guided by US or CT and determine its accuracy.	Sufficient material was obtained in 96%. Overall accuracy to differentiate benign and malignant disease was 85.7% with 2 false negatives and one false positive. No complications.	4
59. Erozen YS. Kidney and Adrenal Gland. In: Sidawy MK, Ali SZ, eds. *Fine Needle Aspiration Cytology*. 1st ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2007:299-344.	Review/Other-Dx	N/A	Book chapter.	N/A	4
60. Lack EE, Wieneke JA. Adrenal Glands. In: Bostwick DG, Cheng L, eds. *Urologic Surgical Pathology*. 2nd ed: Mosby Elsevier; 2008:952-1008.	Review/Other-Dx	N/A	Book chapter.	N/A	4
61. Paulsen SD, Nghiem HV, Korobkin M, Caoili EM, Higgins EJ. Changing role of imaging-guided percutaneous biopsy of adrenal masses: evaluation of 50 adrenal biopsies. *AJR* 2004; 182(4):1033-1037.	Review/Other-Dx	50 adrenal biopsies	Retrospective study to assess the effect of dedicated adrenal imaging with CT and MRI on the rate of percutaneous imaging-guided biopsies of adrenal masses.	Only 6/50 (12%) of adrenal biopsied were adenomas. The number of adrenal adenomas biopsied has declined markedly with the introduction of dedicated adrenal CT and MRI for adrenal adenomas. Percutaneous imaging-guided biopsy is useful in confirming the presence and nature of suspected adrenal metastases.	4
62. Lumachi F, Borsato S, Tregnaghi A, et al. CT-scan, MRI and image-guided FNA cytology of incidental adrenal masses. *Eur J Surg Oncol* 2003; 29(8):689-692.	Observational-Dx	34 consecutive patients	Prospective study to compare value of CT, MRI and FNA in patients with incidentalomas.	Sensitivity, specificity, and PPV were 66.7, 85.7, and 50.0%, for CT scan, 83.3, 92.9, and 71.4% for MRI, and 83.3, 100, and 100% ($P<0.05$) for FNA cytology, respectively. Image-guided FNA cytology was safe and definitive in many patients.	3

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
63. Hoh CK, Schiepers C, Seltzer MA, et al. PET in oncology: will it replace the other modalities? *Semin Nucl Med* 1997; 27(2):94-106.	Review/Other-Dx	N/A	Review literature over last 3 years to examine role of PET in relation to other tumor imaging modalities.	Currently, PET is used in characterizing tumor lesions, differentiating recurrent disease from treatment effects, staging tumors, evaluating the extent of disease, and monitoring therapy. In the future, PET may be used in molecular medicine and genetics.	4
64. Kumar R, Xiu Y, Yu JQ, et al. 18F-FDG PET in evaluation of adrenal lesions in patients with lung cancer. *J Nucl Med* 2004; 45(12):2058-2062.	Observational-Dx	94 patients: 113 adrenal masses; 3 observers	Retrospective study to assess the role of FDG-PET in differentiating benign from metastatic adrenal masses detected on CT or MRI scans of patients with lung cancer.	The sensitivity, specificity, and accuracy for detecting metastatic disease were 93%, 90%, and 92%, respectively. FDG-PET is an accurate, noninvasive technique for differentiating benign from metastatic adrenal lesions detected on CT or MRI in patients with lung cancer. It can be falsely negative in necrotic and hemorrhagic metastases and in small lesions (<11 mm in this series).	3
65. Kutlu CA, Pastorino U, Maisey M, Goldstraw P. Selective use of PET scan in the preoperative staging of NSCLC. *Lung Cancer* 1998; 21(3):177-184.	Observational-Dx	21 patients	To evaluate the place of PET scanning for the characterization of additional abnormalities discovered on routine, preoperative CT evaluation of patients with proven NSCLC.	Accuracy of PET in assessment of nonpulmonary lesions found on CT in operable NSCLC was 96% with sensitivity of 93% and specificity of 100%. Results show PET is useful in small cell lung cancer.	4
66. Metser U, Miller E, Lerman H, Lievshitz G, Avital S, Even-Sapir E. 18F-FDG PET/CT in the evaluation of adrenal masses. *J Nucl Med* 2006; 47(1):32-37.	Observational-Dx	150 patients; 175 adrenal masses	To evaluate the performance of FDG-PET/CT in characterizing adrenal masses in oncology patients.	For combined PET/CT data, the sensitivity, specificity, PPV, and NPV were 100%, 98%, 97%, 100%, respectively. When a cutoff SUV of 3.1 was used for this group, FDG-PET/CT correctly classified all lesions.	3
67. Yun M, Kim W, Alnafisi N, Lacorte L, Jang S, Alavi A. 18F-FDG PET in characterizing adrenal lesions detected on CT or MRI. *J Nucl Med* 2001; 42(12):1795-1799.	Observational-Dx	41 patients; 50 adrenal masses	Retrospective analysis to evaluate the ability of FDG-PET to characterize adrenal lesions in patients with proven or suspected cancers.	FDG-PET for characterization of adrenal lesions showed a sensitivity of 100%, a specificity of 94%, and an accuracy of 96%. FDG-PET has the additional advantage of evaluating the primary lesions as well as metastases, it could be cost-effective and the modality of choice for the characterization of adrenal lesions, especially in patients with malignancy.	3

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. Vikram R, Yeung HD, Macapinlac HA, Iyer RB. Utility of PET/CT in differentiating benign from malignant adrenal nodules in patients with cancer. *AJR* 2008; 191(5):1545-1551.	Observational-Dx	112 adrenal nodules in 96 patients	Retrospective study was performed to determine the sensitivity and specificity of combined PET/CT in differentiating benign from malignant adrenal nodules measuring at least 1 cm in diameter in patients with cancer.	30 adrenal lesions were malignant. 25 of the 30 malignant nodules had positive PET results. 12/82 benign nodules were PET positive with a sensitivity of 83.3% and specificity of 85.4%. Patients with 4/5 malignant nodules with negative PET results had received previous therapy. The PPV for detection of malignant lesions was 67%, and the NPV was 93%. Adrenal masses that are not FDG avid are likely to be benign with a high NPV. Especially in patients undergoing therapy, however, there is a small but statistically significant false-negative rate. A considerable proportion of benign nodules have increased FDG activity.	3
69. Minn H, Salonen A, Friberg J, et al. Imaging of adrenal incidentalomas with PET using (11)C-metomidate and (18)F-FDG. *J Nucl Med* 2004; 45(6):972-979.	Review/Other-Dx	21 patients	To examine imaging of adrenal incidentalomas with PET using (11) C-metomidate and FDG.	FDG detected 2/3 noncortical malignancies but failed to detect adrenal metastases from renal cell carcinoma. Authors conclude that (11)C-Metomidate is a promising PET tracer to identify incidentalomas of adrenocortical origin. FDG is recommended for patients with a moderate to high likelihood of neoplastic disease.	4
70. Tessonnier L, Sebag F, Palazzo FF, et al. Does 18F-FDG PET/CT add diagnostic accuracy in incidentally identified non-secreting adrenal tumours? *Eur J Nucl Med Mol Imaging* 2008; 35(11):2018-2025.	Observational-Dx	37 patients with 41 adrenal masses	To evaluate the ability of FDG-PET to distinguish benign from malignant adrenal masses when CT or MRI results had been inconclusive.	The final diagnosis was 12 malignant, 17 benign tumors, and 12 tumors classified as benign on follow-up. The visual interpretation was more accurate than SUVmax alone, tumor diameter or unenhanced density, with a sensitivity of 100% (12/12), a specificity of 86% (25/29) and a NPV of 100% (25/25). The use of 1.8 as the threshold for tumor/liver SUVmax ratio, retrospectively established, demonstrated 100% sensitivity and specificity. FDG-PET/CT accurately characterizes adrenal tumors, with an excellent sensitivity and NPVs. Thus, a negative PET may predict a benign tumor that would potentially prevent the need for surgery of adrenal tumors with inconclusive conventional imaging.	2

Incidentally Discovered Adrenal Mass
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Zettinig G, Mitterhauser M, Wadsak W, et al. Positron emission tomography imaging of adrenal masses: (18)F-fluorodeoxyglucose and the 11beta-hydroxylase tracer (11)C-metomidate. *Eur J Nucl Med Mol Imaging* 2004; 31(9):1224-1230.	Observational-Dx	16 patients	Study aimed to: Evaluate (11)C-metomidate. Point out possible advantages in comparison with FDG. Examine in vivo the expression of 11beta-hydroxylase in patients with primary aldosteronism.	(11)C-metomidate is an excellent imaging tool to distinguish adrenocortical and non-cortical lesionsThe in vivo expression of 11beta-hydroxylase is lower in Cushing's syndrome than in Conn's syndrome, and there is no suppression of the contralateral gland in primary aldosteronism. FDG is the tracer of choice for discriminating between benign and malignant lesions.	3
72. Berland LL, Silverman SG, Gore RM, et al. Managing incidental findings on abdominal CT: white paper of the ACR incidental findings committee. *J Am Coll Radiol* 2010; 7(10):754-773.	Review/Other-Dx	N/A	Recommendations from the ACR Incidental Findings Committee for managing incidental findings in the kidney, livers, adrenal glands, and pancreas.	N/A	4
73. NIH state-of-the-science statement on management of the clinically inapparent adrenal mass ("incidentaloma"). *NIH Consens State Sci Statements* 2002; 19(2):1-25.	Review/Other-Dx	N/A	To evaluate data regarding the management of clinically unapparent adrenal masses (incidentalomas).	There is insufficient data to recommend a surgical or nonsurgical for the management of patients with subclinical hyper-functioning adrenal cortical adenomas.	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

ADC = Apparent diffusion coefficient

CI = Confidence interval

CT = Computed tomography

DWI = Diffusion-weighted imaging

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

FNA = Fine-needle aspiration

HU = Hounsfield units

MRI = Magnetic resonance imaging

NPV = Negative predictive value

PET = Positron emission tomography

PPV = Positive predictive value

ROC = Receiver-operator characteristic

SI = Signal intensity

SUV = Standardized uptake value