

Distinguishing Benign from Malignant Adrenal Masses: Multi-Detector Row CT Protocol with 10-Minute Delay¹

Michael A. Blake, FFR (RCSI), FRCR
 Mannudeep K. Kalra, MD, DNB
 Ann T. Sweeney, MD
 Brian C. Lucey, FFR (RCSI)
 Michael M. Maher, MD
 Dushyant V. Sahani, MD
 Elkan F. Halpern, PhD
 Peter R. Mueller, MD
 Peter F. Hahn, MD, PhD
 Giles W. Boland, MD

Purpose:

To retrospectively evaluate the accuracy of precontrast attenuation, relative percentage washout (RPW), and absolute percentage washout (APW) in distinguishing benign from malignant adrenal masses at multi-detector row computed tomography (CT).

Materials and Methods:

This HIPAA-compliant retrospective study had institutional review board approval; the need for informed consent was waived. One hundred twenty-two adrenal masses were evaluated in 99 patients (51 men, 48 women; age range, 37–86 years) who had undergone CT performed according to the study protocol and who either were given a pathologic diagnosis or underwent follow-up imaging. Unenhanced images were obtained before administration of 120 mL of an intravenous contrast agent with a 75-second scan delay. Delayed images were obtained after 10 minutes. RPW and APW were computed. Receiver operating characteristic (ROC) analysis was performed to compare mean attenuation and both RPW and APW. Analysis was first performed with the exclusion of pheochromocytomas, myelolipomas, and cysts. Precontrast attenuation criteria specific for benignity or malignancy were determined, and ROC analysis of results for the entire nonpheochromocytoma group was then performed.

Results:

By using an RPW of 37.5% and excluding cysts and myelolipomas, all malignant lesions were detected with a sensitivity of 100% (17 of 17 lesions) and a specificity of 95% (90 of 95 lesions). Area under the binomial ROC curve (A_z) values were 0.912, 0.985, and 0.892 for precontrast attenuation, RPW, and APW, respectively. Precontrast attenuation of less than 0 or more than 43 HU indicated benign and malignant entities, respectively. Incorporation of these criteria into the APW analysis yielded a sensitivity of 100% (17 of 17 lesions) and a specificity of 98% (93 of 95 lesions) for a threshold washout value of 52.0%. This attenuation-corrected APW generated the greatest A_z value (ie, 0.988). Combining all the information available from the protocol yielded a sensitivity of 100% (17 of 17 lesions) and a specificity of 98% (98 of 100 lesions) for differentiating benign from malignant masses.

Conclusion:

Precontrast attenuation of less than 0 HU supercedes the washout profile in the evaluation of an individual adrenal mass. Noncalcified, nonhemorrhagic adrenal lesions with precontrast attenuation of more than 43 HU should be considered suspicious for malignancy.

¹ From the Department of Radiology, Division of Abdominal Imaging and Intervention, Massachusetts General Hospital, White 270, 55 Fruit St, Boston, MA 02114 (M.A.B., M.K.K., B.C.L., M.M.M., D.V.S., E.F.H., P.R.M., P.F.H., G.W.B.); and Department of Medicine, Division of Endocrinology, St Elizabeth's Medical Center, Boston, Mass (A.T.S.). Received September 2, 2004; revision requested October 26; revision received January 22, 2005; accepted February 24; final version accepted April 24.

Adrenal masses—both suspected and incidental—are identified at up to 5% of abdominal computed tomography (CT) examinations (1). Characterization of these masses is essential because involvement of the adrenal glands is frequently of critical importance in the staging of malignancies (2). This has prompted numerous studies of the characteristics of adrenal masses on unenhanced, dynamic, and delayed CT scans (3–12). Results of many studies have confirmed the value of the Hounsfield unit attenuation level at unenhanced CT in characterizing adrenal nodules (3–12). Approximately 30% of adenomas, however, are lipid poor and cannot be characterized on unenhanced CT scans (3,4).

Adrenal masses are commonly encountered on contrast material-enhanced CT scans when unenhanced attenuation information is not available. Knowledge of the washout characteristics of adrenal masses after intravenous contrast enhancement has improved the sensitivity and specificity of adrenal mass characterization both when the unenhanced attenuation value is known and when it is unknown (5–7). We use a dedicated adrenal multi-detector row CT protocol that permits determination of unenhanced (precontrast) attenuation and both relative percentage washout (RPW) and absolute percentage washout (APW) with a short 10-minute delay. Thus, the purpose of our study was to retrospectively evaluate the accuracy of precontrast attenuation, RPW, and APW in distinguishing benign from malignant adrenal masses.

Materials and Methods

Patients and Masses

We received approval from the institutional review board of Massachusetts General Hospital to undertake this retrospective study with waiver of informed consent. The study was compliant with the Health Insurance Portability and Accountability Act. By performing a search of electronic medical records, we identified 99 consecutive patients (51 men, 48 women; age range, 37–86

years; mean age, 66 years) who had undergone our dedicated CT protocol for evaluating adrenal masses and either had pathologic proof of diagnosis or had undergone at least a 6-month follow-up imaging examination. All adrenal mass protocol CT examinations had a specific code that enabled identification of potential patients, and we then searched their electronic medical records for imaging and pathologic inclusion criteria. Patients who undergo imaging with the dedicated CT adrenal mass protocol at Massachusetts General Hospital are clinically suspected of having an adrenal mass most commonly because a mass was detected with a previous imaging test. Patients with diffusely heterogeneous or calcified masses do not undergo this adrenal protocol. Thus, all patients included in the present study had adrenal masses that for over half of their area were relatively uniform in attenuation—attenuation that was of similar uniformity to that of a homogeneous area of the spleen.

The examinations were performed in a 34-month period, from January 2000 to October 2002. A total of 122 adrenal masses were evaluated. The 122 masses ranged in size from 0.6 to 15.0 cm and had a mean size of 1.9 cm. Seventy-seven masses were on the left side, and 45 were on the right. The masses comprised 92 adenomas, two cysts, three lymphomas, three myelolipomas, five pheochromocytomas, one schwannoma, two benign indeterminate lesions, and 14 metastases.

Pheochromocytomas were excluded from all group analyses, however, because they were apparent on the basis of clinical findings. Myelolipomas and cysts were also excluded because they can be diagnosed by their nonwashout imaging features. Therefore, 112 masses were included in the initial analysis. The pathologic nature of the lesions was confirmed for 28 lesions: 16 lesions (14 metastases and two lymphomas) were malignant and 12 lesions (six adenomas, five pheochromocytomas, and one schwannoma) were benign according to results of percutaneous biopsy, surgery, or autopsy. In the absence of direct histopathologic proof,

the diagnosis was inferred at follow-up imaging performed a minimum of 6 months (range, 6–41 months) after the initial CT examination. At follow-up imaging, interval growth was considered to be indicative of malignancy and was observed in one lesion (a metastasis), while stability was considered to be evidence of benignity and was observed in 83 lesions (78 adenomas, two cysts, and three myelolipomas) (6–8).

CT Scanning Technique

All imaging was performed with multi-detector row CT scanners with four channels (LightSpeed QX/I; GE Medical Systems, Waukesha, Wis). All patients were scanned with identical parameters, which included 140 kVp, 200–300 mA, 0.8-second gantry rotation time, 15-mm table feed per gantry rotation, 6:1 pitch (high speed mode), and a section profile of 2.5 mm (full width at half maximum) with a 2.5-mm section interval and a standard reconstruction algorithm. Initially, unenhanced images were obtained in all patients. One hundred twenty milliliters of a contrast agent with 300 mg of iodine per milliliter (Oxilan 300; Cook, Bloomington,

Published online before print

10.1148/radiol.2382041514

Radiology 2006; 238:578–585

Abbreviations:

APW = absolute percentage washout

A_z = area under binomial ROC curve

CI = confidence interval

ROC = receiver operating characteristic

RPW = relative percentage washout

SEE = standard error of estimate

Author contributions:

Guarantors of integrity of entire study, P.R.M., G.W.B.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, M.A.B., A.T.S., B.C.L., M.M.M., D.V.S., G.W.B.; clinical studies, M.A.B., M.K.K., A.T.S., B.C.L., M.M.M., D.V.S.; statistical analysis, M.A.B., M.K.K., E.F.H., P.F.H.; and manuscript editing, all authors

Address correspondence to M.A.B.

(e-mail: mblake2@partners.org).

Authors stated no financial relationship to disclose.

Ind) was administered intravenously through an antecubital vein by using a power injector at a rate of 2.5 mL/sec. Dynamic contrast-enhanced images were obtained after a 75-second scan delay (portal venous phase). Delayed images were also obtained 10 minutes after injection of the contrast agent.

Image Analysis

Average attenuation values on the precontrast, contrast-enhanced, and delayed contrast-enhanced images were recorded. A circular region of interest was placed in the center of the adrenal mass on the section on which the mass appeared largest; the region of interest covered approximately one-half to two-thirds of the mass. All images were retrospectively reviewed in consensus by two radiologists with fellowship training in abdominal imaging (M.A.B. and B.C.L., with 4 and 3 years of subspecialty experience, respectively). Images were reviewed on a digital picture archiving and communication system diagnostic workstation (Impax RS 3000 1K review station; Agfa Technical Imaging Systems, Richfield Park, NJ). A single consensus measurement was made for each mass in each imaging phase to record mean attenuation. If more than one mass was present, all measurements were made for each mass. The RPW and APW were calculated as follows: $RPW = 100 \cdot (EA - DA)/EA$ and $APW = 100 \cdot ([EA - DA]/[EA - PA])$, where EA is attenuation on contrast-enhanced scans, DA is attenuation on delayed contrast-enhanced scans, PA is precontrast attenuation, and all attenuation measurements are in Hounsfield units.

Thus, the only difference between the respective formulae is that RPW mathematically gives a 0 value to the precontrast attenuation field, whereas APW incorporates the true precontrast attenuation value. Progressive enhancement of a mass on a delayed scan (ie, when attenuation on a delayed scan was greater than attenuation on a dynamic scan) was given a washout score of 0.

Statistical Analysis

The recorded data were entered into an Excel worksheet (Microsoft, Redmond,

Wash). A threshold value of 10 HU on precontrast CT scans was chosen for distinguishing benign lesions (eg, adenomas) from indeterminate lesions (4). The lowest RPW and APW threshold values for best discriminating malignant adrenal masses were selected. By using these thresholds, sensitivities, specificities, positive predictive values, negative predictive values, positive likelihood ratios, and negative likelihood ratios were calculated.

Data were also analyzed with receiver operating characteristic (ROC) methods (Medcalc Statistical Software, Mariakerke, Belgium) (M.K.K., P.F.H., E.H.). Diagnostic accuracy was measured by using the area under the binomial ROC curve (A_z) value. The precontrast attenuation and RPW curves did not cross and were compared. The precontrast attenuation and APW curves crossed; hence, comparison of these curves for statistical difference with A_z value analysis was not valid (13). The final analysis made use of all the imaging information from the protocol; myelolipomas (which manifest at CT as macroscopic fat) and cysts (which manifest at CT as lack of enhancement and an imperceptible wall) were thus included. In addition, by examining the precontrast attenuation information available with the APW value, precontrast attenuation values that were specific for benignity or malignancy were determined. The identified caveats were introduced to this group, and ROC analysis of the resulting APW data was repeated. For this selective APW analysis, cysts and myelolipomas were excluded because they were diagnosed by using nonwashout criteria. The estimation of RPW does not require unenhanced CT scanning; therefore, attenuation correction was

not performed for RPW. An analysis of the group of patients that excluded those who had multiple adrenal lesions revealed no significant difference between that group of patients and the entire group of patients. In fact, the performance parameters in the group of patients that did not include those who had multiple lesions were slightly better; however, we present the results of analysis in the entire patient group as a more conservative and presumably more accurate set of results. We acknowledge, however, that the width of the 95% confidence intervals (CIs) may be slightly affected by clustering effects.

Results

The precontrast attenuation values of adenomas ranged from -15 to 42 HU, with a mean of 9.0 HU. Attenuation of adenomas on enhanced portal venous phase CT scans ranged from 14 to 110 HU, with a mean of 57.6 HU. Attenuation values on delayed CT scans ranged from 0 to 55 HU, with a mean of 24.0 HU. The adrenal metastases had precontrast attenuation values of 14.0–46.6 HU, enhanced attenuation values of 47.0–95.0 HU, and delayed attenuation values of 40.0–69.7 HU. The metastases had an RPW range of 0%–37.3% (mean, 15.3%) and an APW range of 0%–73% (mean, 30.8%). The washout features of the excluded myelolipomas and pheochromocytomas were individually recorded (Table).

Findings after Exclusion of Cysts and Myelolipomas

The distribution of the 112 lesions according to their precontrast attenuation and RPW values is summarized in Figures 1–3. All lesions with precontrast

Characteristics of Myelolipomas and Pheochromocytomas

Tumor Type	Precontrast Attenuation (HU)	RPW	APW
Myelolipoma	-30.0 to 20.0	25.0 to 214.0	42.3 to 90.9
Pheochromocytoma	1.8 to 42.0	15.5 to 83.3	35.9 to 88.7

Note.—There is wide variation in the ranges of attenuation and washout values for both myelolipomas and pheochromocytomas.

attenuation of 10 HU or less were adenomas. By using an RPW threshold of 37.5%, all malignant lesions were detected with a sensitivity of 100% (17 of 17 lesions; 95% CI: 77%, 100%), a specificity of 95% (90 of 95 lesions; 95% CI: 89%, 99%), a positive predictive

value of 77% (17 of 22 lesions; 95% CI: 57%, 94%), a negative predictive value of 100% (90 of 90 lesions; 95% CI: 95%, 100%), a positive likelihood ratio of 19, and a negative likelihood ratio of 0. Four adenomas had an RPW value of less than 37.5%. All of these adenomas had precontrast attenuation values of greater than 10 HU (18, 33, 38, and 33 HU). One benign schwannoma demonstrated progressive enhancement. One poorly de-enhancing lesion with a precontrast attenuation of 18 HU, an RPW of 25.0%, and an APW of 42.3% was classified as benign because of its stability over a 3-year period, although a specific diagnosis has not been rendered.

The identified precontrast parameters specific for benignity or malignancy were, respectively, an attenuation value of less than 0 HU even with an APW of less than 52.0% and an attenuation value of more than 43 HU. Use of these parameters enabled the recognition of three adenomas with attenuation values of less than 0 HU despite APW values of less than 52.0%. Two malignancies were also then recognized because they had precontrast attenuation values of greater than 43 HU although they had washout values that were above the

threshold (Fig 4). These masses represented a metastasis from small cell lung carcinoma and adrenal involvement of non-Hodgkin lymphoma. Again, benign exceptions included the schwannoma with progressive enhancement and the stable indeterminate lesion described previously. The introduction of these extreme attenuation caveats (according to which a lesion with precontrast attenuation of less than 0 HU is benign and a lesion with precontrast attenuation of greater than 43 HU is malignant) improved the performance of the APW. By using an APW of 52.0%, a sensitivity of 100% (17 of 17 lesions; 95% CI: 75%, 100%), a specificity of 98% (93 of 95 lesions; 95% CI: 90%, 99%), a positive predictive value of 89% (17 of 19 lesions; 95% CI: 58%, 96%), a negative predictive value of 100% (93 of 93 lesions; 95% CI: 95%, 100%), a positive likelihood ratio of 47.6, and a negative likelihood ratio of 0 were achieved (Fig 3).

Results of ROC analysis of the masses are outlined in Figure 5. The A_z value was 0.912 (standard error of the estimate [SEE], 0.048) for precontrast attenuation, 0.985 (SEE, 0.010) for RPW, and 0.892 (SEE, 0.033) for APW.

Figure 1

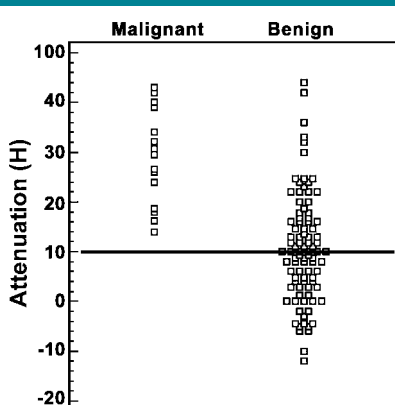


Figure 1: Scatterplot shows distribution of precontrast attenuation values—in Hounsfield units (H)—of malignant and benign adrenal lesions (excluding pheochromocytomas, cysts, and myelolipomas). All lesions with values of 10 HU or less were adenomas. Lesions with values greater than 10 HU were either lipid-poor adenomas or malignant lesions.

Figure 2

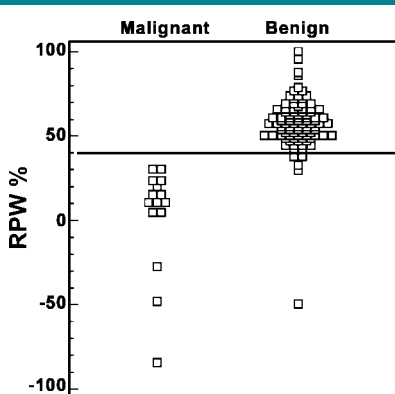


Figure 2: Scatterplot shows distribution of RPW values of malignant and benign lesions (excluding pheochromocytomas, cysts, and myelolipomas). All malignant lesions had RPW values of less than 37.5%.

Figure 3

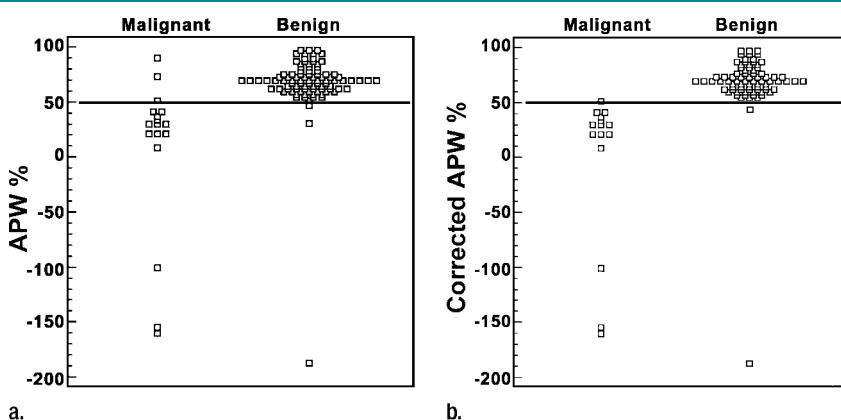


Figure 3: (a) Scatterplot shows distribution of benign and malignant lesions (excluding pheochromocytomas, cysts, and myelolipomas) at an APW threshold value of 52.0%. The majority of malignant lesions had an APW value of less than 52.0%, but there were a few exceptions. (b) Scatterplot shows distribution of benign and malignant lesions (excluding pheochromocytomas) according to attenuation-corrected APW values. This data set excluded masses with precontrast attenuation of greater than 43 HU and masses with precontrast attenuation of less than 0 HU but an APW value of less than 52.0%. All malignant lesions had an attenuation-corrected APW value of less than 52.0%.

Figure 4



Figure 4: Images in 72-year-old woman with biopsy-proved metastasis from small cell lung cancer. (a) Precontrast, (b) portal venous phase enhanced, and (c) 10-minute delayed enhanced transverse CT images of left adrenal mass (arrow) show attenuation values of 46, 95, and 59 HU, respectively; the resultant APW value is 73.1%. Despite the high APW value, use of the high precontrast attenuation value of 46 HU resulted in correct assignment of this lesion to the malignant category.

Findings after Reclassifying Lesions with Extreme Attenuation Values and Including and Excluding Cysts and Myelolipomas

The combined imaging information available from the entire protocol yielded the following parameters for 117 masses (including cysts and myelolipomas that were recognized on the basis of their imaging features): a sensitivity of 100% (17 of 17 lesions; 95% CI: 75%, 100%), a specificity of 98% (98 of 100 lesions; 95% CI: 91%, 99%), a positive predictive value of 89% (17 of 19 lesions; 95% CI: 58%, 96%), a negative predictive value of 100% (98 of 98 lesions; 95% CI: 95%, 100%), a positive likelihood ratio of 50, and a negative likelihood ratio of 0. These results were obtained by excluding lesions with precontrast attenuation of greater than 43 HU (classified as malignant lesions) and lesions with precontrast attenuation of less than 0 HU (classified as benign lesions) even when they had an APW of less than 52.0% (Fig 3b). For this data set, the ROC curve for the contribution of attenuation-corrected APW (with the exclusion of cysts and myelolipomas) is shown in Figure 6. These attenuation-correction caveats were data driven and chosen retrospectively. The resulting A_z value, 0.988 (SEE, 0.00), was greater than those obtained by using precontrast or RPW criteria (Fig 7).

Discussion

Characterizing adrenal masses is important because the nature of the mass may

Figure 5

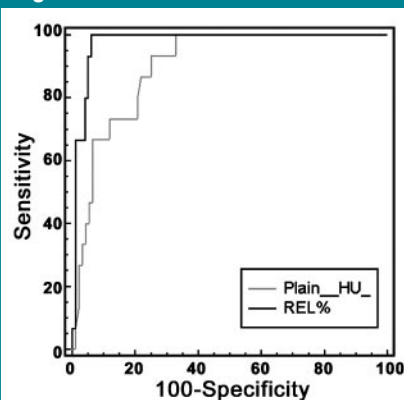


Figure 5: ROC curves for performance of pre-contrast attenuation (*Plain_HU*) and RPW (*REL%*) in enabling differentiation of benign from malignant adrenal lesions (excluding pheochromocytomas, cysts, and myelolipomas). The A_z value for precontrast attenuation was 0.912 (SEE, 0.048); that for RPW was 0.985 (SEE, 0.010).

have a profound effect on patient care. Accurate characterization is important for identifying both malignant lesions and benign adenomas because it would obviate both percutaneous biopsy and repeated interval follow-up imaging. Imaging algorithms for assessing adrenal masses in which CT plays the predominant role have been proposed (14–16). Magnetic resonance (MR) imaging and positron emission tomography (PET), however, may also be useful in the imaging evaluation of adrenal masses (17–

Figure 6

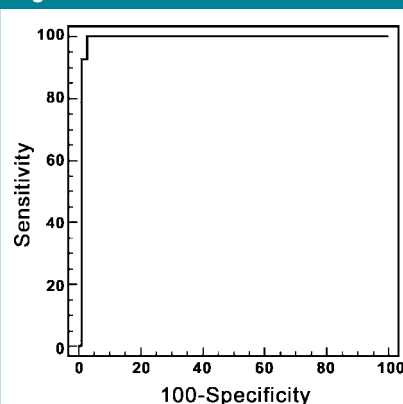


Figure 6: ROC curve for performance of attenuation-corrected APW in enabling differentiation of benign from malignant adrenal lesions (excluding pheochromocytomas, cysts, and myelolipomas). Masses with precontrast attenuation of greater than 43 HU and masses with negative attenuation but an APW value of less than 52.0% were excluded from this data set. At 0.988, the A_z value for the performance of attenuation-corrected APW was greater than that for precontrast attenuation and RPW.

20). Chemical shift MR imaging may enable characterization of additional adenomas when results of CT densitometry are indeterminate (17,18). The results of some studies (19,20), although still preliminary, suggest that PET performed with fluorine 18 fluorodeoxyglucose is highly accurate in enabling differentiation of benign from malignant

lesions. If these results are corroborated in future studies, PET could become part of the routine imaging evaluation of adrenal masses or play a role when CT results are equivocal or borderline.

The most important distinction in classifying adrenal masses is distinguishing malignant from benign lesions, although previous authors have focused on achieving a high specificity for adenomas (3–12). The majority of benign adrenal lesions are adenomas. In choosing the threshold values for distinguishing between benign and malignant lesions, we believe the recognition of malignancy is paramount even at the cost of subjecting some patients with benign lesions to biopsy. It is widely considered to be better to biopsy a few benign lesions than to miss any malignant lesion.

As expected, the optimal RPW and APW threshold values with the 10-minute delay used in our study were slightly lower than those with a 15-minute delay because there was less time for de-enhancement to occur. Caoili et al (8) recommend the use of 40% RPW and 60% APW thresholds with a 15-minute protocol. Our 10-minute delay protocol yielded lower threshold values of 37.5% and 52.0%, respectively. Keeping the same 40% and 60% thresholds for the 10-minute protocol as for the 15-minute protocol has some merit

because these thresholds preserve the desired 100% success in the detection of malignancy. The 10-minute delay protocol, however, is a more convenient method of adrenal mass characterization because it has the inherent advantage of a shorter examination time. This time advantage assumes even more importance with multi-detector row CT technology, which permits dramatic increases in patient throughput (21).

The advent of multi-detector-row CT has generally improved the imaging of adrenal lesions by facilitating faster image acquisition, allowing the acquisition of thinner sections in less time, and reducing respiratory misregistration. In addition, the acquisition of a volumetric data set enables thinner reconstructions, thus reducing the effect of partial volume averaging. However, Heneghan et al (22) have described the potential diagnostic pitfall of pseudoenhancement at helical CT. Pseudoenhancement refers to an artifactual increase in attenuation after contrast material administration and is thought to result from an inadequate correction for beam hardening in the CT reconstruction algorithm. Despite these concerns, the results of our study with multi-detector row CT attenuation values validate the results of earlier adrenal imaging research performed by using older technology.

On the basis of the results of our study, it is clear that some new additional diagnostic criteria should be followed for optimal performance. Any lesion with precontrast attenuation of greater than 43 HU should be regarded with suspicion (ie, considered malignant), regardless of its washout profile. In our study, two malignant lesions had APW values of greater than 52.0%, but both had precontrast attenuation values of greater than 43 HU, whereas none of the benign lesions had precontrast attenuation values of greater than 43 HU. Exceptions to this greater than 43 HU precontrast attenuation rule could include high-density masses caused by calcification or hemorrhage, which can usually be recognized by their imaging features; these masses were not encountered in our study.

As regards the washout parameters, the APW of an adrenal mass may at first seem to be a more accurate calculation of de-enhancement because the precontrast attenuation value is included in the calculation of APW. The APW value may therefore yield a more accurate reflection of the washout characteristics, given that the average attenuation of most adenomas on unenhanced CT will not be zero, as is the mathematical consequence of using the formula for RPW. Two lipid-poor adenomas did not reach the RPW threshold and were only diag-

Figure 7



Figure 7: Images in 54-year-old man with biopsy-proved left adrenal adenoma. (a) Precontrast, (b) portal venous phase enhanced, and (c) 10-minute delayed enhanced transverse CT images of left adrenal mass (arrow) show attenuation values of 42, 72, and 51 HU, respectively; the resultant RPW and APW values are 29.2% and 70.0%, respectively. Despite the high precontrast attenuation and poor RPW values, the marked APW value indicates that this lesion should be assigned to the benign category.

nosed with the APW value. However, RPW performed substantially better than APW when the described precontrast attenuation caveats were not followed. These caveats are necessary because some low-density adenomas do not reach the thresholds of washout and some high-density metastases demonstrate substantial washout. In all cases, precontrast attenuation of less than 0 HU should supersede both RPW and APW in importance. Three adenomas with precontrast attenuation of less than 0 HU had APW values that were less than the threshold value, and two malignancies with precontrast attenuation of greater than 43 HU demonstrated marked contrast material washout. Combining these parameters with the incorporated caveats yields a powerful diagnostic protocol. We acknowledge, however, that the value of these proposed attenuation criteria will need to be confirmed in future studies.

Our study had other limitations. This was a retrospective review of data in a relatively limited number of patients. However, it is the largest series that we are aware of in which a triple-phase multi-detector row CT adrenal mass protocol was evaluated. The majority of the adrenal masses were not pathologically proved and required imaging follow-up for characterization. This has been an accepted method of classifying benign and malignant lesions in previous studies (6–8). There was some clustering of lesions near the threshold values, and increasing the washout thresholds, as discussed above, may result in a more generous safety net for detecting malignancy at the cost of the performance of a few more biopsies that yield benign results. No adrenal carcinomas were seen among the 122 masses studied, so it remains uncertain whether use of this protocol will enable recognition of these rare but usually large tumors.

Our exclusion of pheochromocytomas is reasonable on practical grounds because our patients were clinically suspected of having a pheochromocytoma before imaging. In addition, contrast material is deliberately not always used in the evaluation of pheochromocytomas

because there are theoretical concerns that administering iodinated contrast material to a patient with pheochromocytoma could trigger a hypertensive crisis. However, results of studies addressing this issue are reassuring about the use of nonionic contrast media (23,24). We also realize that pheochromocytomas can sometimes be encountered unexpectedly and can indeed play a confusing role. Pheochromocytomas may be of sufficiently low attenuation to be mistaken for adenomas and can also show contrast material washout profiles that mimic those of adenomas (Table) (25). Pathologists have even observed macroscopic fat within pheochromocytomas (26). This capacity of pheochromocytoma to mimic an adenoma at CT should certainly be borne in mind when one is evaluating an adrenal mass with imaging studies.

Bae and colleagues (27) have reported the intriguing use of histogram analysis in the diagnosis of adrenal adenoma. The results of their study expand the use of attenuation measurements, but their analysis did not reach the level of performance of combined adrenal mass protocols such as the one we are reporting. We did not perform this type of histogram analysis and we await further reports about this method with interest.

In conclusion, our results with a 10-minute-delay multi-detector row CT protocol clarify attenuation and washout criteria that help optimize differentiation between benign and malignant adrenal masses. We now follow these principles and caveats. First, we now know that a precontrast attenuation value of less than 0 HU supersedes the washout profile in the evaluation of an individual adrenal mass. Second, all noncalcified, nonhemorrhagic adrenal lesions with precontrast attenuation of greater than 43 HU should be considered suspicious for malignancy. Third, after these extreme attenuation caveats have been incorporated, the APW value should be calculated when possible because it is a truer measure of de-enhancement. Fourth, the inconsistent behavior of pheochromocytomas should be kept in mind when one is assessing

an adrenal mass at CT, especially in the correct clinical setting. Finally, we believe that our study results confirm the diagnostic value of this short 10-minute-delay adrenal mass protocol in distinguishing benign from malignant adrenal masses with the attendant benefits of current CT technology.

References

1. Dunnick NR, Korobkin M. Imaging of adrenal incidentalomas: current status. *AJR Am J Roentgenol* 2002;179:559–568.
2. Macari M, Rofsky NM, Naidich DP, Megibow AJ. Non-small cell lung carcinoma: usefulness of unenhanced helical CT of the adrenal glands in an unmonitored environment. *Radiology* 1998;209:807–812.
3. Korobkin M, Brodeur FJ, Yutzy GG, et al. Differentiation of adrenal adenomas from nonadenomas using CT attenuation values. *AJR Am J Roentgenol* 1996;166:531–536.
4. Boland GW, Lee MJ, Gazelle SG, et al. Characterization of adrenal masses using unenhanced CT: an analysis of the CT literature. *AJR Am J Roentgenol* 1998;171:201–204.
5. Boland GW, Hahn PF, Peña C, Mueller PR. Adrenal masses: characterization with delayed contrast-enhanced CT. *Radiology* 1997;202:693–696.
6. Peña CS, Boland GW, Hahn PF, Lee MJ, Mueller PR. Characterization of indeterminate (lipid-poor) adrenal masses: use of washout characteristics at contrast-enhanced CT. *Radiology* 2000;217:798–802.
7. Caoili EM, Korobkin M, Francis IR, Cohan RH, Dunnick NR. Delayed enhanced CT of lipid-poor adrenal adenomas. *AJR Am J Roentgenol* 2000;175:1411–1415.
8. Caoili EM, Korobkin M, Francis IR, et al. Adrenal masses: characterization with combined unenhanced and delayed enhanced CT. *Radiology* 2002;222:629–633.
9. Korobkin M, Brodeur FJ, Francis IR, et al. Delayed enhanced CT for differentiation of benign from malignant masses. *Radiology* 1996;200:737–742.
10. Korobkin M, Brodeur FJ, Francis IR, et al. CT time-attenuation washout curves of adrenal adenomas and non-adenomas. *AJR Am J Roentgenol* 1998;170:747–752.
11. Szolar DH, Kammerhuber FH. Adrenal adenomas and nonadenomas: assessment of washout at delayed contrast-enhanced CT. *Radiology* 1998;207:369–375.
12. Szolar DH, Kammerhuber F. Quantitative CT evaluation of adrenal gland masses: a

- step forward in the differentiation between adenomas and nonadenomas? *Radiology* 1997;202:517–522.
13. Mann FA, Hildebolt CF, Wilson AJ. Statistical analysis with receiver operating characteristic curves. *Radiology* 1992;184:37–38.
 14. Lockhart ME, Smith JK, Kenney PJ. Imaging of adrenal masses. *Eur J Radiol* 2002;41:95–112.
 15. Mayo-Smith WW, Boland GW, Noto RB, Lee MJ. State-of-the-art adrenal imaging. *RadioGraphics* 2001;21:995–1012.
 16. 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 Am J Roentgenol* 1995;165:1453–1459.
 17. Tsushima Y, Ishizaka H, Matsumoto M. Adrenal masses: differentiation with chemical shift, fast low-angle shot MR imaging. *Radiology* 1993;186:705–709.
 18. 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.
 19. Boland GW, Goldberg MA, Lee MJ, et al. Indeterminate adrenal mass in patients with cancer: evaluation at PET with 2-[F-18]-fluoro-2-deoxy-D-glucose. *Radiology* 1995;194:131–134.
 20. Maurea S, Mainolfi C, Bazzicalupo L. Imaging of adrenal tumors using FDG-PET: comparison of benign and malignant lesions. *AJR Am J Roentgenol* 1999;173:25–29.
 21. Jhaveri KS, Saini S, Levine LA, et al. Effect of multislice CT technology on scanner productivity. *AJR Am J Roentgenol* 2001;177:769–772.
 22. Heneghan JP, Spielmann AL, Sheafor DH, Kliever MA, DeLong DM, Nelson RC. Pseudoenhancement of simple renal cysts: a comparison of single and multidetector helical CT. *J Comput Assist Tomogr* 2002;26:90–94.
 23. Raisanen J, Shapiro B, Glazer GM, Desai S, Sisson JC. Plasma catecholamines in pheochromocytoma: effect of urographic contrast media. *AJR Am J Roentgenol* 1984;143:43–46.
 24. Mukherjee JJ, Peppercorn PD, Reznick RH, et al. Pheochromocytoma: effect of nonionic contrast medium in CT on circulating catecholamine levels. *Radiology* 1997;202:227–231.
 25. Blake MA, Krishnamoorthy S, Boland GW, et al. Low-density pheochromocytoma on CT: a mimicker of adrenal adenoma. *AJR Am J Roentgenol* 2003;181:1663–1668.
 26. Ramsay JA, Asa SL, van Nostrand AW, Hassaram ST, de Harven EP. Lipid degeneration in pheochromocytomas mimicking adrenal cortical tumors. *Am J Surg Pathol* 1987;11:480–486.
 27. Bae KT, Fuangtharnthip P, Prasad SR, Joe BN, Heiken JP. Adrenal mass assessment: CT characterization with histogram analysis method. *Radiology* 2003;228:735–742.