The role of quadriphasic contrast enhanced computed tomography in distinguishing adrenal adenomas from nonadenomas

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**Authors:** G. Foti, N. Faccioli, W. Mantovani, R. Manfredi, R. Pozzi Mucelli; Verona/IT  
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Purpose

The purpose of this study is to retrospectively evaluate the accuracy in characterizing incidental adrenal lesions obtained by using a quadriphasic CT protocol encompassing unenhanced (UE), arterial enhanced (35-sec, AE), portal enhanced (70-sec, PE) and 5-minute delayed enhanced (5-minute, DE) CT scans.
Methods and Materials

PATIENTS POPULATION

Hundred-eighty-six consecutive patients were considered for inclusion in this study.

Inclusion criteria were: presence of at least an adrenal mass; patients undergoing quadriphasic abdominal CT.

Exclusion criteria were: incomplete CT protocol (n=52); final diagnosis of the adrenal mass not established (n=30). Therefore, our study population consisted of 87 patients (49 males, 38 females, mean age 58.4 years, range 32 to 88), presenting a total of 104 adrenal lesions (9 bilateral metastases, 8 bilateral adenomas).

The final diagnosis was achieved with percutaneous biopsy (n=11), surgery (n=19), at least 1 year imaging follow-up (n=74). Absence of size change on follow-up CT study determined the diagnosis of adenoma (lipid-poor for UE attenuation > 10 HU and lipid-rich for UE attenuation # 10HU); rapid size increase at follow-up study yielded the diagnosis of metastasis.

Patients population, inclusion and exclusion criteria and methods to achieve final diagnosis are summerized in Figure 1.

IMAGING TECHNIQUE

All the examinations were performed with a commercially available CT scanner (Brilliance 64, Philips, Eindhoven, The Netherlands) with the following imaging parameters: slice thickness 2 mm,

1:1 table pitch, 120 kVp, variable tube current depending on patient size. All patients underwent UE scan, followed by 3 enhanced scans performed with 35-seconds (AE), 80-seconds (PE), and 5-minutes delay (DE) respectively, after the intravenous administration of 1.5 ml/per kilogram of iopromide (Ultravist 370, Bayer-Schering, Germany, 370 mg of iodine per milliliter) with a power injector, at a flow rate of 3 ml/sec.

DATA ANALYSIS

All images were randomly reviewed by two experienced radiologists, unaware of clinical or pathologic data. For all lesions, location and largest diameter in the axial plane were recorded. On the section with the largest surface area, a circular or ovoid region of interest (ROI) was used to measure average CT attenuation values, including one-half to two-
thirds of the area of the mass to reduce partial volume effects. Cystic, necrotic, and calcified regions were excluded. Two measurements were obtained for each parameters in two different reading sessions (with at least 1 month delay). A single consensus measurement was obtained for each lesion in each imaging phase to record mean attenuation in Hounsfield units (HU).

The imaging phases in which the peak attenuation (PEAK, obtained by the list sum of absolute attenuation values registered at the time of AE and PE scans) was achieved were evaluated. For lesions presenting the PEAK at the time of AE and PE scan, wash-out parameters were calculated also from the PEAK as well as from AE and PE scans.

The diagnostic parameter calculated are described in table 1.

The mean amount of wash-out calculated from AE, PE and PEAK was compared.

The thresholds yielding best accuracy (assessed as correct classification rate) in differentiating adenomas from nonadenomas were retrospectively determined on the basis of receiver operator curves (ROC) analysis and corresponding sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) in distinguishing total adenomas from nonadenomas and lipid-poor adenomas from nonadenomas were calculated. Moreover, overall accuracy of the quadriphasic protocol evaluated and of other triphasic CT protocols was determined.

STATISTICAL ANALYSIS

Statistical analysis was performed by using SPSS software (version 14.0; Chicago, Ill.). Paired sample t-test (or the Wilcoxon test, when appropriate) was used to assess differences among imaging parameters calculated. Independent Student t test (or the Mann-Whitney U test, when appropriate) was applied to compare lesions subgroups. P values were considered significant when less or equal than 0.05.

Table 1: Wash-in and Wash-out Parameters Calculated.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>EQUATIONS</th>
<th>COMMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWI UE-AE</td>
<td>A35s - A0</td>
<td>Absolute wash-in</td>
</tr>
<tr>
<td>AWI UE-PE</td>
<td>A80s - A0</td>
<td>Absolute wash-in</td>
</tr>
<tr>
<td>RPWI AE-DE</td>
<td>A80s - A35s/A35s x 100</td>
<td>Relative wash-in</td>
</tr>
<tr>
<td>AWO AE-DE</td>
<td>A35s - A5m</td>
<td>Absolute wash-out</td>
</tr>
<tr>
<td>AWO PE-DE</td>
<td>A80s - A5m</td>
<td>Absolute wash-out</td>
</tr>
<tr>
<td>AWO PEAK-DE *</td>
<td>Apeak - A5m</td>
<td>Absolute wash-out</td>
</tr>
</tbody>
</table>
RPWO AE-DE \(\frac{A_{5m} - A_{35s}}{A_{35s}} \times 100\) Relative wash-out
RPWO PE-DE \(\frac{A_{5m} - A_{80s}}{A_{80s}} \times 100\) Relative wash-out
RPWO PEAK-DE * \(\frac{5m - A_{peak}}{A_{peak}} \times 100\) Relative wash-out
PEW AE-DE \(\frac{A_{35s} - A_{5m}}{A_{35s} - A_{0}} \times 100\) Relative wash-out
PEW PE-DE \(\frac{(A_{80s} - A_{5m})}{A_{80} - A_{0}} \times 100\) Relative wash-out
PEW PEAK-DE * \(\frac{(A_{peak} - A_{5})}{A_{peak} - A_{0}} \times 100\) Relative wash-out

* parameters calculated only for the subset of lesions presenting peak enhancement attenuation at the time of AE or PE scan (91/104).

\(A_{0}\) = baseline attenuation; \(A_{35s}\) = AE scan attenuation; \(A_{80s}\) = PE scan attenuation; \(A_{5m}\) = DE scan attenuation; \(A_{peak}\) = peak attenuation obtained by the list sum of AE and PE scans attenuation.
Fig. 0: Figure 1: Flowchart showing inclusion and exclusion criteria for our study.

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Results

The final diagnosis was 65 adenomas (51 lipid rich adenomas, figure 2; 14 lipid poor adenomas, figure 3) and 39 nonadenomas (33 metastases, figure 4; 5 pheochromocytomas, 1 carcinoma).

The peak enhancement was registered at the time of AE scan for 21 masses, 19 adenomas (14 lipid-rich and 5 lipid-poor adenomas) and 2 nonadenomas (both pheochromocytomas), in PE scan for 70 masses, 46 adenomas (37 lipid-rich and 9 lipid-poor adenomas), and 24 nonadenomas (20 metastases and 3 pheochromocytomas and 1 carcinoma), and at the time of DE scan in case of 13 nonadenomas (all metastases) (figures 5).

In these subset of 13 lesions, the presence of delayed peak enhancement was associated with other imaging features usually shown by malignant lesions (including UE attenuation > 11HU, DE attenuation > 32 HU, RPWO and PEW > 30%): this pattern was therefore considered as a particularly slow wash-in with lack of any measurable wash-out. As a consequence wash-out parameters from peak attenuation were not calculated for these subset of lesions.

In the subset of 91 lesions not presenting the peak attuation at the time of DE scan, the mean values of wash-out were significantly higher when calculated from PEAK (15HU for AWO, 37% for RPWO, 35% for PEW), with respect to those calculated from AE scan (3HU for AWO, 5% for RPWO, 12% for PEW, p = 0.0001) and from PE scan (12HU for AWO, 32% for RPWO, 31% for PEW, p = 0.002) (figure 6).

For this reason, the thresholds of wash-out parameters for best differentiating adenomas from nonadenomas were calculated by using the peak enhancement attenuation value.

Table 2 describes the area under the curve, 95% Confidence Interval (95 % C.I.) and statistical value, together with the best thresholds of each diagnostic parameter for diagnosing adenoma and relative efficiency values in distinguishing total adenomas from nonadenomas and lipid-poor adenomas from nonadenomas.

RPWO PEAK-DE, using 30% threshold, represented the single imaging parameter yielding the best diagnostic accuracy in distinguishing total adenomas from nonadenomas (efficiency 90%, 95 % C.I. 81.9 ; 95.3) and lipid-poor adenomas from nonadenomas (efficiency 92.5%, 95 % C.I. 79.6 ; 98.4), followed by AWO PEAK-DE (efficiency 85.7%, 95 % C.I. 76.8 ; 92.2 for separating total adenomas versus nonadenomas; efficiency 87.5%, 95 % C.I. 73.2 ; 95.8 for separating lipid-poor adenomas versus nonadenomas) and PEW PEAK-DE (efficiency 83.5%, 95 % C.I. 74.3 ; 90.5 for separating total adenomas versus nonadenomas; efficiency 85%, 95 % C.I. 72.2 ; 90.3 for separating lipid-poor adenomas versus nonadenomas).
The quadriphasic CT protocol analyzed allowed to correctly diagnose 101/104 lesions (efficiency 97.1 %, 95% C.I. 94.8 ; 99.4), with three misdiagnoses due to one lipid-poor adenoma with slow wash-out, and 2 nonadenomas with RPWO > 30 %. Overall accuracy was better.

The diagnostic accuracy of this protocol was therefore better if compared to the protocol including UE, AE and DE scans (efficiency 90.0%, 94/104 lesions correctly diagnosed; p=0.011) the triphasic protocol including UE, PE and DE scans (efficiency 96.1%, 100/104 lesions correctly diagnosed p=0.282), and that including UE, AE, PE scan (95.1%, 99/104, lesions correctly diagnosed p=0.009) (figure 7).

Table 2: Area Under The Curve, 95% Confidence Interval and Statistical Value, Best Thresholds for Diagnosing Adenoma and Relative Efficiency Values in Distinguishing Total Adenomas from Nonadenomas and Lipid-poor Adenomas from Nonadenomas of Multiple Imaging Parameters.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>AUC</th>
<th>95%CI</th>
<th>p value</th>
<th>THRESHOL</th>
<th>EFF n1</th>
<th>EFF n2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size (104) mm</td>
<td>0.94</td>
<td>(0.9;0.99)</td>
<td>0.0001</td>
<td>&lt; 30 mm</td>
<td>76.9</td>
<td>81.1</td>
</tr>
<tr>
<td>UE attenuation (104)</td>
<td>0.96</td>
<td>(0.92;0.99)</td>
<td>0.0001</td>
<td># 10 HU</td>
<td>88.5</td>
<td>77.4</td>
</tr>
<tr>
<td>DE attenuation (104)</td>
<td>0.84</td>
<td>(0.77;0.92)</td>
<td>0.0001</td>
<td>&lt; 32 HU</td>
<td>74.0</td>
<td>73.6</td>
</tr>
<tr>
<td>AWI from UE to AE (104)</td>
<td>0.78</td>
<td>(0.69;0.88)</td>
<td>0.0001</td>
<td>&gt; 20 HU</td>
<td>73.1</td>
<td>66.0</td>
</tr>
<tr>
<td>AWI from UE to PE (104)</td>
<td>0.77</td>
<td>(0.67;0.86)</td>
<td>0.0001</td>
<td>&gt; 37 HU</td>
<td>73.1</td>
<td>66.0</td>
</tr>
<tr>
<td>RPWI from AE to PE (%)†(104)</td>
<td>0.82</td>
<td>(0.73;0.90)</td>
<td>0.0001</td>
<td>&lt;0%; &gt;100%</td>
<td>78.9</td>
<td>86.8</td>
</tr>
<tr>
<td>Metric</td>
<td>Value</td>
<td>95% CI</td>
<td>p-value</td>
<td>Threshold</td>
<td>EFF</td>
<td>EFF n1</td>
</tr>
<tr>
<td>------------------------------</td>
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<td>--------------</td>
<td>---------</td>
<td>-----------</td>
<td>-----</td>
<td>--------</td>
</tr>
<tr>
<td>AWO from Peak to DE (91)</td>
<td>0.88</td>
<td>(0.79;0.98)</td>
<td>0.0001</td>
<td>&gt; 12 HU</td>
<td>85.7</td>
<td></td>
</tr>
<tr>
<td>RPWO from peak to DE (%)</td>
<td>0.95</td>
<td>(0.90;0.99)</td>
<td>0.0001</td>
<td>&gt; 30 %</td>
<td>90.0</td>
<td></td>
</tr>
<tr>
<td>PEW from Peak to DE (%)</td>
<td>0.89</td>
<td>(0.82;0.96)</td>
<td>0.0001</td>
<td>&gt; 30 %</td>
<td>83.5</td>
<td></td>
</tr>
</tbody>
</table>

* For diagnosing adenomas

† Double threshold was used to separate adenomas (RPWI < 0% or >100%) and nonadenomas (RPWI > 0% and < 100%) [20]

EFF = efficiency, considered as best correct classification rate

EFF n1 = for separating total adenomas versus nonadenomas;

EFF n2 = for separating lipid-poor adenomas versus nonadenomas

Size, UE attenuation, DE attenuation, AWI from UE to AE, AWI from UE to PE, RPWI from AE to PE were calculated for the entire dataset (104 lesions); AWO, RPWO and PEW were calculated by using the peak attenuation value only for those lesions not presenting the peak attenuation at the time of DE scan (91 lesions, excluding 13 metastases).
Fig. 0: Figure 1: Flowchart showing inclusion and exclusion criteria for our study.

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Fig. 0: Figure 2: Incidental adrenal lipid-rich adenoma in a 65 year-old male suffering from colon cancer: the lesion is hypodense on baseline scan (a), enhances in arterial enhanced (b) and portal enhanced (c) scan, with good wash-out at the time of 5-minute delayed scan (d).

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Fig. 0: Figure 3: Tiny incidental adrenal lipid-poor adenoma in left gland, in young woman with recently diagnosed lung cancer: a small oval-shaped nodule with high attenuation is recognized on baseline CT scan (a). The nodule enhances slowly from baseline to arterial enhanced scan (b), reaching the peak enhancement during portal enhanced scan (c), and exhibiting good wash-out at the time of 5-minute delayed scan (d).

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Fig. 0: Figure 4: Bilateral adrenal metastases in a 56 year-old man suffering from lung cancer: bilateral irregular shaped adrenal masses with high attenuation are recognized on baseline CT scan (a). The masses enhance slowly from baseline to arterial enhanced (b), and portal enhanced scan (c), exhibiting poor wash-out at the time of 5-minute delayed scan (d).

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Fig. 0: Figure 5: Graphic showing peak enhancement phase for adenomas and nonadenomas. AE= arterial enhanced scan; PE= portal enhanced scan; DE= 5-minute delayed enhanced scan.

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**Fig. 0:** Figure 6: Graphic showing mean values of wash-out parameters calculated from PEAK, AE and PE scans, respectively and statistical results of multiple comparisons. and incorrectly diagnosed adrenal lesions by using different CT imaging protocol according to imaging phases available.

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**Fig. 0**: Figure 7: Graphic showing correctly and incorrectly diagnosed adrenal lesions by using different CT imaging protocol according to imaging phases available. UE = unenhanced scan; AE= arterial enhanced scan; PE= portal enhanced scan; DE = 5-minute delayed enhanced scan.

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Conclusion

The quadriphasic CT protocol evaluated, thanks to the availability of two intermediate scans, was associated with a significant increase of wash-out calculated, when compared with other triphasic imaging protocol including a 5-minute delayed scan.

Yielding high overall diagnostic accuracy in distinguishing adenomas from nonadenomas, this CT imaging protocol could be used for the characterization of incidental adrenal lesions.
References


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