Renal oncocytoma: CT diagnostic criteria revisited

D Eiss (1), F Larousserie (2), A Mejean (3), M Ghouadni (1), S Merran (4), JM Correas (1) and O Hélon (1)

Abstract

Purpose. To redefine and evaluate the computed tomographic criteria for the diagnosis of renal oncocytoma (RO) for which renal sparing surgery should be preferred.

Material and method. Retrospective study of 57 patients with 69 RO. Macroscopic and histological correlation was obtained in all cases. A double blinded comparative study was made of 60 renal tumors (containing adenocarcinomas and oncocytomas) larger than 3 cm in diameter in order to evaluate the redefined CT diagnostic criteria.

Results. Among RO larger than 3 cm in diameter, 55% presented a sharply defined low attenuation scar on post-contrast scans at the tubular nephrographic phase, central or eccentric, with homogeneous attenuation throughout the remainder of the hypervascular tumor which was classified in 3 different groups. The use of our CT diagnostic criteria gave a statistically significant (p<0.05) Kappa index of inter-observer concordance of 0.71 and a specificity of 96% for the diagnosis of RO.

Conclusion. Our redefined computed tomographic criteria for the diagnosis of renal oncocytoma, eventually associated with renal biopsy, should increase the indications for renal sparing surgery for RO larger than 3 cm in diameter.

Key words: Oncocytoma. CT. Renal. Benign tumor.


Renal oncocytoma (RO) is a benign tumor composed of oncocytes. The benign nature of this tumor was established in the 1990s (1-4). Several names have been used to describe this tumor: oncocytic adenoma, oncocytoma, proximal tubular adenoma, renal cell adenoma. Before its benign nature was established, several misnomers were used to describe this lesion including oncocytic adenocarcinoma and oncocytic-cell carcinoma. According to Amin et al., misconceptions in the literature regarding renal oncocytoma would be due to confusion with chromophobe cell carcinoma, inadequate lesion sampling, or lack of standardized diagnostic criteria (5, 6).

Diagnostic difficulties during the preoperative work-up often cause patients to be treated as though they had a renal cell carcinoma of similar size (7). The purpose of this study was to retrospectively redefine the CT diagnostic criteria for renal oncocytoma allowing distinction between RO and RCC and CCC and to evaluate the diagnostic accuracy of these redefined criteria.

Material and methods

Material

A total of 57 patients were included, 26 females (46%) and 31 males (54%) for a M/F ratio of 1.2. The mean patient age was 61.7 years (range: 32 – 85 years). All patients were imaged between 1987 and 2000 either at the Hôpital Necker – Enfants Malades (Paris) or at the Fédération Mutualiste (Paris). The 57 patients had a total of 69 surgically proven oncocytomas (table I). Four (6,5%) patients had multiple oncocytomas. Oncocytomas ≤3 cm (n=36) were separated from oncocytomas >3 cm (n=33), a criteria frequently used in other reported series.

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Abbreviations

RO : Renal oncocytoma
RCC : Renal cell carcinoma – clear cell carcinoma
CCC : Chromophobe cell carcinoma
MRI : Magnetic resonance imaging
CT : Computed-tomography

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All surgically resected renal tumors during this time period at the Hôpital Necker are summarized in Table II.

A double blinded review of 60 patients with tumors >3 cm including 15 RO and 45 cancers (42 RCC and 3 CCC) was performed. The number of lesions and ratio of RO to cancers were selected to approximate the ratio seen in routine practice while maintaining a sufficient number of RO to allow analysis. The cancers were selected amongst those causing most diagnostic challenges with the imaging differential diagnosis of RO. Tumor size >3 cm was selected because we specifically wanted to redefine the CT imaging features of RO >3 cm.

Method

Most examinations were obtained on a non-helical Highlight Advantage CT scanner (GE Healthcare Milwaukee Wis). Four patients were imaged using a multidetector-row helical CT scanner (Marconi Medical System). The imaging protocol included contiguous 5 mm thick axial images of the kidneys prior to injection of contrast and following intravenous injection of contrast material during the nephrographic phase (2-4 minutes). A total of 100-150 ml of iodinated contrast material was injected at 1.5 to 3 ml per second. Early arterial and/or delayed excretory phase images were only occasionally obtained and were not specifically evaluated.

Imaging criteria

All CT examinations were first reviewed to redefine the imaging features of RO. The following criteria were recorded:
- Size, location, number.
- Pattern of enhancement.
- Presence of a central or eccentric, stellate, hypodense scar on postcontrast images (nephrographic phase) and its appearance.
- Intratumoral calcification.
- Intratumoral fat.
- Presence of features suspicious for malignancy:
  1) Renal vein invasion.
  2) Local or regional adenopathy.
  3) Perirenal fat invasion.

Double blinded review

The redefined diagnostic criteria were summarized. Two radiologists familiar with these redefined criteria reviewed the CT examinations of 60 patients with renal tumor (oncocytomas and carcinomas) >3 cm performed between 1988 and 2000.

<table>
<thead>
<tr>
<th>Table I</th>
<th>Surgical treatment of patients with solitary oncocytoma (percentage).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>T≤3 cm</td>
</tr>
<tr>
<td>Nephrectomy</td>
<td>8 (38%)</td>
</tr>
<tr>
<td>Tumorectomy</td>
<td>13 (62%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table II</th>
<th>Renal tumors (percentage) listed and excised between 1987 and 2000 at the Hôpital Necker.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TUMORS</td>
<td>≤3 cm (%)</td>
</tr>
<tr>
<td>Clear cell carcinoma</td>
<td>123 (16.8)</td>
</tr>
<tr>
<td>Tubulopapillary carcinoma</td>
<td>28 (3.8)</td>
</tr>
<tr>
<td>Chromophobe cell carcinoma</td>
<td>3 (0.45)</td>
</tr>
<tr>
<td>Oncocytomas (solitary)</td>
<td>14 (1.95)</td>
</tr>
<tr>
<td>Angiomyolipomas</td>
<td>15 (2)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>82 (11.15)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>228 (31)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table III</th>
<th>Computed tomographic features of multiple or solitary renal oncocytoma.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postcontrast appearance</td>
<td>OR≤3cm (%)</td>
</tr>
<tr>
<td>Homogeneous</td>
<td>25</td>
</tr>
<tr>
<td>Fairly homogeneous</td>
<td>3</td>
</tr>
<tr>
<td>Heterogeneous</td>
<td>4</td>
</tr>
<tr>
<td>Scar</td>
<td>3</td>
</tr>
<tr>
<td>Scar + homogeneous tumoral tissue</td>
<td>3</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>36</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table IV</th>
<th>Computed tomographic features of solitary renal oncocytoma (percentage).</th>
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</thead>
<tbody>
<tr>
<td>Postcontrast appearance</td>
<td>OR≤3cm (%)</td>
</tr>
<tr>
<td>Homogeneous (totally)</td>
<td>12/22 (54.5)</td>
</tr>
<tr>
<td>Heterogeneous</td>
<td>7/22 (31.8)</td>
</tr>
<tr>
<td>Scar</td>
<td>3/22 (13.6)</td>
</tr>
<tr>
<td>Scar + homogeneous tumoral tissue</td>
<td>3/22 (13.6)</td>
</tr>
</tbody>
</table>
All 60 patients underwent surgery. All CT examinations included at least a contrast material enhanced acquisition obtained during the nephrographic phase. The cancers included in this study were selected from all cancers operated at our institution after excluding cancers ≤3cm and cancers with evidence of local or distant metastasis. Tumors with imaging findings consistent with malignant disease were excluded in order to have a control population with lesions showing imaging features as similar as possible to our oncocytoma population and further assess the specificity of our redefined CT diagnostic criteria. Patients with multiple tumors were excluded because of the additional diagnostic challenges due to the variable appearance of these lesions in a single patient (1, 8-10).

Review of 100 CT examinations

Finally, 100 CT examinations of patients operated for renal tumor > 3 cm in size, including the 45 cases from the double blinded review, were reviewed to assess the specificity of the redefined CT diagnostic criteria.

Histopathological correlation

Macroscopic and histological tumor evaluation was obtained for all tumors. All oncocytoma slides were reviewed. The following elements were recorded:

- Macroscopy:
  - Margins, capsule, perirenal fat invasion, color, cystic/hemorrhagic change, fibrous central scar, renal vein invasion, adrenal invasion, renal pelvis invasion, calcifications.
  - Microscopy:
    - Presence of oncotypic cells, trabecular or tubular architecture, presence of edematous stroma.
  - Histochemistry.

Statistical analysis

The main statistical tool used was the interobserver variability (kappa). The degree of agreement was considered satisfactory if kappa was above 0.60, poor if kappa was between 0.60 and 0.30 and mediocre if kappa was below 0.30.

Table V

Results of the double blinded review.

<table>
<thead>
<tr>
<th>Reviewer</th>
<th>B</th>
<th>RO</th>
<th>CANCER</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>RO</td>
<td>5</td>
<td>3</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>CANCER</td>
<td>1</td>
<td>51</td>
<td></td>
<td>52</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>54</td>
<td></td>
<td>60</td>
</tr>
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</table>
The chi-2 test was used to assess the validity of the sampled population. This test estimates the probability of error when a presumed association between variables does, in fact, not exist. This test does not provide data on the direction or strength of the association.

**Results** *(tables III, IV, V, VI)*

Within the group of isolated RO larger than 3 cm in diameter, 17 (63%) showed a hypodense central or eccentric scar during the tubular nephrographic phase on postcontrast CT *(fig. 1)*. In this group, 15 (55%) oncocytomas showed homogeneous tissue surrounding the scar.

For smaller RO *(≤3cm)*, 12/22 (55%) were homogeneous at the nephrographic phase *(fig. 2)* whereas 7/22 (31%) were heterogeneous. Only 3 (13%) showed a hypodense scar on postcontrast images.

A single large RO was atypical with presence of small intratumoral calcifications and small foci of fatty tissue *(fig. 3)* related to focal bony metaplasia. Based on the imaging features recorded in our population of RO, we have classified the patterns of scars in order to improve their diagnostic value.

Three categories were observed *(fig. 4)*:
- **Type I**: Small stellate central or eccentric scar with a scar/tumor ratio ≤50% (80% of cases);
- **Type II**: Small non-stellate scar with corners included in a circle *(A)* or an ellipse *(B)* (12% of cases);
- **Type III**: Large stellate scar with scar/tumor ratio >50% (8% of cases).

Irrespective of the type, the scar was surrounded by homogeneous tumor tissue in 88% of cases and the scar appeared as a contiguous area of hypodensity on consecutive images.

Correlation with histology showed that the scar seen on CT frequently corresponded to scar tissue on macroscopic and microscopic evaluation. At macroscopy, the scar corresponded to central fibrosis, sometimes stellate in appearance. At microscopy, the scar corresponded to very edematous fibrous tissue that seemed characteristic.

**Double blinded review**

Two experienced radiologists reviewed all 60 examinations, including the 15 cases of RO. Only 8 of 15 RO showed a characteristic central scar surrounded by homogeneous tumor tissue. The 7 other RO were homogeneous or heterogeneous and had to be considered cancers by both reviewers. Both reviewers suggested the possibility of RO for tumors with hypodense scar and surrounding tumor homogeneous tissue without hypoenhancing foci to suggest necrosis.

The results for each reviewer are summarized in *table VI*.

Reviewer n°1 correctly diagnosed 5 of 8 RO for a sensitivity of 62.5% and reviewer n°2 correctly diagnosed 6 of 8 RO for a sensitivity of 75%. Reviewer n°1 correctly diagnosed 50 of 52 cancers for a
specificity of 96% and reviewer n°2 correctly diagnosed 51 of 52 cancers for a specificity of 98%. Both reviewers misdiagnosed different lesions for a total of 3 cancers incorrectly diagnosed as renal oncocytomas.

The interobserver agreement was calculated at 0.71, consistent with substantial agreement (0.60-0.80) with p value <0.05.

Discussion
Diagnostic difficulties for benign renal tumors mainly relate to RO. Angiomyolipomas are usually identified by their fatty component on CT. Excluding the rare cases of angiomyolipomas with very little or no detectable fat on CT, the differential diagnosis of a non-fat containing tumor on CT is typically limited to carcinoma versus benign oncocytoma since the latter may correspond to up to 10% of solid renal tumors (11-13).

Advances with renal mass characterization on CT combined with the increasing number of indications for partial nephrectomy have lead us to want to redefine reliable CT diagnostic criteria for RO. Until now, RO was suggested on postcontrast CT by the presence of a central hypoenhancing scar (2, 4, 12, 14-21). Because of its lack of specificity, patient management has been unaffected by the presence of this finding (18). Numerous false positive results have been due to the lack of precise definition for this CT finding in the literature. Based on our results, two subgroups of RO must be considered: Group 1 (G1) ≤3 cm and Group 2 (G2) >3cm. The most frequently observed pattern for G1 lesions (57%) is that of a hypodense mass relative to renal parenchyma versus benign oncocytoma since the latter may correspond to up to 10% of solid renal tumors (11-13).

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Large RO (>3 cm) showed in 2/3 of cases a hypodense scar-like non-enhancing region, central or eccentric in location, on postcontrast images. An important feature that we have observed is that the central scar is only significant when the surrounding tumoral tissue...
shows homogeneous enhancement except for tumor related perfusion anomalies. RCC may sometimes show central scar-like regions but these are usually surrounded by heterogeneously enhancing tumoral tissue due to local areas of necrosis.

From a sample of 100 cancers >3 cm without evidence of local or distant metastasis operated on at the Hôpital Necker diagnosed at postcontrast CT imaging at the tubular nephrographic phase, only one case showed a central scar with homogeneously enhancing surrounding tumoral tissue (fig. 5). The tumor was a CCC after review of histological material. Three additional tumors showed a central scar but the surrounding tumoral tissue was heterogeneously enhancing.

Fig. 4: Classification of large (>3cm) oncocytomas with scar
Type I: Small stellate scar with scar/tumor < 50%.
Type II A: Non stellate scar in which the corners are included in a circle.
Type II B: Non stellate scar in which the corners are included in an ellipse
Type III: Large stellate scar with scar/tumor > 50%.

Fig. 4: Classification des oncocytomes de grande taille (> 3 cm) avec cicatrice
Type I : Petite cicatrice stellaire avec cicatrice/tumeur ≤ 50 %.
Type II A : Cicatrice non stellaire dont les sommets s’inscrivent dans un cercle.
Type II B : Cicatrice non stellaire dont les sommets s’inscrivent dans une ellipse.
Type III : Grande cicatrice stellaire avec cicatrice/tumeur > 50 %.
(fig. 6). On the other hand, only 3 RO showed heterogeneous peritumoral tissue enhancement. The remaining RO >3 cm (1/3) without scar showed either heterogeneous or homogeneous enhancement in equal number. Heterogeneously enhancing RO cannot be distinguished from RCC whereas homogeneously enhancing RO cannot be distinguished from CCC. The imaging criteria were defined from evaluation of images acquired at the nephrographic phase of intravenous contrast distribution. The small number of available early arterial phase or delayed excretory phase acquisitions precluded evaluation of these phases of intravenous contrast distribution. It would be interesting to evaluate delayed enhancement of the central scar of RO.

Double blinded review
We have tried to demonstrate that renal oncocytomas may be under certain conditions differentiated from renal carcinomas. Based on the results from our study and those from the main study published to this day (18), we have redefined the CT diagnostic criteria for renal oncocytoma and have tested their validity on a group of 60 renal tumors >3 cm in diameter. We have distinguished between small and large renal tumors based on two main reasons. First, surgical management is different and the impact of diagnosis on management is less. Second, the redefined diagnostic criteria apply only to the group of larger tumors where a hypodense scar is more frequently present.

Reviewer n°1 correctly diagnosed 5 of 8 RO for a sensitivity of 62.5% and reviewer n°2 correctly diagnosed 6 of 8 RO for a sensitivity of 75%. Two RO were incorrectly diagnosed as carcinomas by both reviewers because the CT examination was indeterminate in one case and the RO was very large and atypical with foci of calcification for the other. One additional RO was misdiagnosed as carcinoma by reviewer n°1 because the tumoral tissue surrounding the scar was described as heterogeneous.

A point worth mentioning is the fact that diagnostic errors involved RO in group 3 of our proposed classification suggesting that our redefined diagnostic criteria are more specific for smaller scars with more abundant surrounding tumoral tissue. Specificity for reviewer n°1 was calculated at 96% and specificity for reviewer n°2 was calculated at 98%. Both reviewers misdiagnosed different lesions for a total of 3 cancers incorrectly diagnosed as renal oncocytomas. How can this discordance be explained?

The CT examinations for all three cases of carcinoma were difficult to interpret (the areas of heterogeneous enhancement were incorrectly attributed to vascular related).

As such, indeterminate or uncertain lesions should be considered as malignant. The interobserver agreement was calculated at 0.71, consistent with substantial agreement (0.60-0.80) with a p value <0.05. These values indicate that the redefined diagnostic criteria have a moderate sensitivity with excellent specificity. In other words, under optimal conditions, carcinomas should not be misdiagnosed as benign lesions.
Carcinomas with CT features quite similar to those of RO remain challenging. A total of 100 cases of patients with renal tumor who underwent surgery at the Hospital Necker between 1988 and 2000 were reviewed. Patients with tumors ≤3 cm in diameter and those with evidence of loco-regional (renal vein invasion or adenopathy) or distant metastases were excluded from this review.

In this group of tumors, only one CCC showed imaging features suggestive of RO; histology confirmed the presence of a fibrous scar. This suggests that it is very infrequent (<1%) for cancers >3 cm in size to have a central scar with homogeneously enhancing surrounding tumoral tissue. We believe that to suggest a diagnosis of RO in the presence of a solid renal mass with central or eccentric scar, all of the following diagnostic criteria should present:

- Hypodense scar relative to surrounding tumoral tissue during the tubular nephrographic phase.
- Stellate or polygonal shaped scar based on our proposed classification (fig. 4).
- Homogeneous surrounding tumoral tissue (excluding vascular related areas of heterogeneity).
- Absence of tumor calcification.
- Absence of intra-tumoral hemorrhage.
- Absence of loco-regional tumor (renal vein invasion or adenopathy) or distant metastasis.

Management

The optimal treatment for RO is partial nephrectomy when possible (15). Soulé et al. reported on 13 patients treated with partial nephrectomy for RO with survival rate of 100% at 45.6 mois (1). In spite of advances with renal biopsy and renal imaging, definite presurgical diagnosis is seldom achieved and the possibility of carcinoma must always be entertained (4).

Over the recent years, several publications have described the efficacy of partial nephrectomy in patients with RCC, especially in patients with solitary kidney, renal failure or bilateral multifocal carcinoma (1). The reported rate of local recurrence varied between 4 and 10% and the survival rate was identical to patients with total nephrectomy. Based on these reports, partial nephrectomy has been utilized for patients with smaller lesions or bilateral renal lesions. Arguments against this practice include the known incidence of bilateral tumor (7-11%) and the risk of incomplete tumor resection. However, the rate of local recurrence 3 to 6 years after partial nephrectomy is about 2%; this is fairly similar to the rate of contralateral recurrence after complete nephrectomy. The rate of multifocal lesions for tumors less than 3 cm in size is less than 3% (23). As a result, most authors agree that management of isolated tumors less than 3 cm in size should be conservative as long as technically feasible.

The management of isolated benign-appearing renal masses larger than 3 cm in size remains a challenge. Theoretically, conservative management with partial nephrectomy or tumorectomy with intraoperative surgical margin evaluation would seem reasonable. However, intraoperative histological diagnosis of a re-
nal tumor may not be reliable. Accurate histological diagnosis requires careful evaluation of a properly fixed specimen. In the presence of eosinophilic tumor cells, differential diagnosis between RO and carcinoma (eosinophilic variant of CCC, granular cell variant of RCC or tubulopapillary carcinoma) requires additional staining that is not available during the time of surgery: Hale’s colloidal iron stain and immunohistochemical stain with antibody panel.

Based on our results and recent reports on cytologic morphology combined with ancillary studies (24), it seems reasonable to consider that in patients with large renal tumor with CT imaging features typical for RO, CT or US guided core biopsy may be more reliable.

**Conclusion**

Because of challenges related to confident preoperative diagnosis of RO, these tumors most frequently are treated as renal carcinomas of similar size. Our results provide specific CT diagnostic criteria for RO >3 cm with classical stellate scar. The possibility of RO should only be raised in the presence of a stellate or polygonal shaped scar surrounded by homogeneously enhancing tumoral tissue in a solid renal mass at the tubular nephrographic phase of contrast distribution on CT.

The presence of calcifications, hemorrhage or heterogeneous enhancement of the tumoral tissue surrounding the scar should raise concern for carcinoma. Large homogeneous RO and small (<3 cm) RO have no specific diagnostic imaging features on CT.

These redefined CT diagnostic criteria combined with the increasing use of percutaneous core biopsy with appropriate histological evaluation including Hale’s colloidal iron stain and immunohistochemical stain, only available on fixed tissue, should increase the indications for partial nephrectomy or renal sparing surgery for RO larger than 3 cm in size.

**References**