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**Pseudocapsule of Small Renal Cell Tumors: CT Imaging Spectrum and
Correlated Histopathological Features**

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ABSTRACT

Purpose: To systematically analyze histopathologic features of pseudocapsule in
small renal cell tumor (diameter \leq 4cm), assess the integrity of pseudocapsules by

Computed Tomography (CT), and provide theoretical basis for the safety of nephron sparing surgery.

Materials and Methods: The pathological data of 116 patients who underwent surgery with clear cell renal cell carcinoma admitted from May 2010 to October 2017 were retrospectively analyzed. All patients underwent a CT scan of the abdomen including an unenhanced and three-phase (arterial, nephrographic and excretory) post contrast series. Thorough gross examination and histological sections were used to determine the integrity of the pseudocapsule by two uropathologists. The consistency between pathological findings and CT imaging were evaluated by Kappa consistency test.

Results: The mean diameter of tumor was 3.0cm, range (2.6 ± 0.8) cm. On CT the pseudocapsule can present with one of the three following features: 1) A regular and distinct halo; 2) lobulated clear margins; 3) blurred margins. On histopathology, complete pseudocapsule was found in 85 tumors, incomplete pseudocapsule in 25 and no pseudocapsule was found in 6 tumors; CT scan findings demonstrated a regular halo in 82 tumors, lobulated clear margins in 26 and blurred margins in 8 tumors (Kappa=0.833, P=0.000).

Conclusions: Most small renal cell tumors have an obvious pseudocapsule. Preoperative determination of the pseudocapsule's integrity is particularly important. CT scan can reliably evaluate the tumor margins and demonstrate the pseudocapsule when present. The imaging results are well correlated with the pathologic findings.

Key words: pseudocapsule; small renal carcinoma; pathology; CT; surgery

Purpose

Renal cell carcinoma is the most common malignant tumor of the kidney in adults.⁽¹⁾ It accounts for 3% of all adult malignancies and the incidence of the young is increasing.^(2,3) In recent years, with the development and widespread use of imaging diagnostic technology, detection rate of early asymptomatic small renal masses (SRMs) is significantly improved, therefore, the incidence of early stage

renal cell carcinoma increased steadily year by year .⁽⁴⁻⁶⁾ Clear cell renal cell carcinoma(ccRCC) is the most common histological subtype. Most renal cancer is low degree of malignancy and grows slowly,⁽⁷⁾and squeezes the renal parenchyma or surrounding tissue to form the pseudocapsule, which is the protective response of the body to limit the growth and proliferation of tumor. It was initially described in the early 1900s and was commonly identified in ccRCC. However, high degree of malignant tumors are invasive with no obvious pseudocapsule.

For patients with small renal cell carcinoma, under the premise of no distant metastasis, partial nephrectomy is the general choice.⁽⁸⁾ Nephron sparing surgery(NSS) maximizes the preservation of renal function, it has shown oncological efficacy and favorable outcomes in carefully selected patients with T1a tumors, also offers an equally effective form of local control as well as 5- year disease-specific survival rates.⁽⁹⁾ The integrity of the pseudocapsule determines the safety and feasibility of partial nephrectomy. Additional, regardless of the presence or absence of pseudocapsule, there is no difference in surgical approach. Hence, preoperative determination of pseudocapsule integrity is particularly important. As far as we know, the literature on preoperative judgments of pseudocapsule integrity is less reported in English to date. Therefore, we evaluate the integrity of the pseudo-capsule by computer tomography (CT), and systematically analyze the histopathological characteristics of the pseudo-capsule of renal cell tumor (diameter ≤ 4 cm) to provide a theoretical basis for the safety of NSS.

Materials and Methods

Study Population A retrospective study was conducted to value the relationships between CT imaging spectrum and histopathological features of 116 patients who underwent NSS in our hospital with clear cell of renal cell carcinoma admitted from May 2000 to October 2016. All patients had received preoperative CT examination included unenhanced and three-phase (arterial, portal, and nephrographic-excretory) contrast-enhanced and signed informed consent. The study included 116 patients (65 men, 51 women; mean age, 56 years; range, 33–78 years). Based on the tumor growth pattern, small renal cell carcinoma is divided into single nodular type, infiltration type

(nodular boundary uncertainty) and multi-nodular fusion. All tumors were single nodular and less than 4 in diameter. 114 of the 116 patients had no symptoms and were referred because of a small renal mass found incidentally at physical examination. A renal tumor was detected at CT examination in 12 patients. No patient had distant metastases. Only 2 cases were referred with clinical symptoms which is slight pain.

Procedures

Thorough gross examination of the pseudocapsule including pseudocapsular invasion and completeness of PC was performed by the uropathologist. If the pseudocapsules existed, but some were infiltrated, it is defined as incomplete pseudocapsule. We striped the pseudocapsule completely to do pathological sections. Entire sections including the tumor-PC-parenchyma interface and representative sections from the largest plane of the tumor were submitted. All specimens were step-sectioned at 5-mm intervals, entirely embedded in paraffin blocks, stained with hematoxylin and eosin. Tumor grade was according to the Fuhrman criteria.

All CT examinations were performed using a 64-MDCT scanner. Unenhanced scans and contrast-enhanced scans were reconstructed at 3-mm intervals. The margins of the tumor were recorded and classified on the CT. CT and pathological findings were compared by case analysis.

Sample size

Based on our pilot data, the sample size was estimated on a power of 80 % at the 5 % significance level. It has been suggested that at least 22 patients per group were required.

Statistical analysis

SPSS Statistics 20.0 was used for statistical analysis. The pathological results as gold standard, using Kappa test analysis to judge consistency with the CT detecting results. Kappa coefficient >0.7 and <0.4 indicates a high or low consistency between the two results respectively; $P < .05$ was considered statistically significant.

Results

The mean diameter of tumor was 3.0cm, range (2.6 ± 0.8) cm. Pathological results showed 7 cases were of Fuhrman I grade, 39 cases were of grade I - II, 55 cases were of grade II, 12 cases were of grade II-III, 3 cases were of grade III and 0 cases were of grade IV among the 116 cases of clear cell carcinoma. Integrated pseudocapsule (figure 1) were found in 85 (73.3%) tumors with the thickness ranged from 0.2 to 1 mm, 25 (21.6%) without integrated pseudocapsule (figure 2) and 6 (5.2%) cases had no obvious pseudocapsule (figure 3). Tumor infiltrated while not penetrated into the pseudocapsule were found in 16 cases (13.8%), penetrated into the pseudocapsule were found in 7 cases (6.0%). The pathological components of pseudocapsule include compressed renal parenchyma, hyperplastic fibers, and inflammatory cells.

In MDCT, The presence of pseudocapsule on CT had three kinds. 82 (70.7%) cases of RCC were confirmed with a regular halo surrounding a renal neoplasm (figure 4). 26 (22.4%) had clear margin but not continuous or lobulated (figure 5), 8 (6.70%) were found presenting blurred margin (figure 6) surrounding the tumor. The pathological results as gold standard, The sensitivity, specificity, positive predictive value and negative predictive value of CT detecting pseudocapsule was 97.3% (107/110), 83.3% (5/6), 99.1% (107/108), 62.5% (5/8), respectively, and the consistency between CT and pathological results were high by Kappa test analysis which Kappa value was 0.833 (table 1).

The presence of a regular and distinct halo surrounding a renal neoplasm presented the completeness of pseudocapsule. Clear margin but not continuous or lobulated was regarded as incomplete capsule while blur margin presented no capsule.

Discussion

At present, small renal cancer is well differentiated, the clinical stage is low, the natural growth rate is slow and the prognosis is better. Nephron sparing surgery (NSS) is safe and reliable in the treatment of small renal cell carcinoma, with a low rate of recurrence and mortality. ^(10, 11) A meta-analysis confirms that NSS can reduce the incidence of postoperative chronic kidney disease relative to radical nephrectomy 61%, 19% reduction in mortality.

RCCs usually have no true histologic capsule but are surrounded by pseudocapsule.⁽¹²⁾ Pseudocapsule is an important feature which is helpful to evaluate the differentiation of renal cell carcinoma.⁽¹³⁾ Pseudocapsule formation is the result of tumor growth, which causes compression, ischemia, and necrosis of the adjacent renal parenchyma.⁽¹⁴⁾ This is a protective response that the body limits the growth and spread of the tumor. In early stage of small and low-grade RCCs, the presence of pseudocapsule is often seen,⁽¹⁵⁾ which is a good indicator of renal cancer prognosis.⁽⁶⁾ Complete pseudocapsule predicts higher degree of differentiation and the lesion is still early; the other hand, the incomplete pseudocapsule herald higher diffusion and metastasis rate.⁽¹⁶⁾ Joseph M et al. found clear cell RCC exhibits the most consistent PC, a complete PC was found in 77% of 60 cases with T1 stage clear cell tumors.⁽¹⁷⁾ NSS can only be performed if the tumor is confined to the renal parenchyma and there is a significant pseudocapsule around it.⁽¹⁸⁾ Wei Xi et al. findings suggest that pseudocapsule status is of good prognostic implications in RCC and lack of pseudocapsule certainly had remarkable adverse impact on patient outcome.⁽¹⁹⁾ Thus, we discuss the judgment of its completeness preoperatively to ensure pathology margin postoperative.

There are different reports about detecting pseudocapsules in small kidneys, such as ultrasound and MRI and CT. Hricak et al.⁽²⁰⁾ reported that a pseudocapsule was observed on MRI firstly in 1985, both of which showed a low signal band between tumor and normal renal parenchyma in both T1WI and T2WI. Yamashita et al. showed that T2WI is the most sensitive through different sequences of MR pseudocapsules display study.⁽¹⁵⁾ Moreover, MRI has been reported to be more reliable imaging modality, the accuracy ranging from 74% to 93%,the sensitivity was 87.5% and the specificity was 80.8%,respectively.Preoperative MRI showed complete pseudocapsule around the tumor which suggesting the feasibility of enucleation. Ultrasound has a higher veracity up to 89.29% in diagnosis of small renal cell cancer,it can detecte more than 1cm mass. Conventional ultrasound in detecting RCC pseudocapsules can manifest as two types of echogenicity: hypoechoic halo or slightly hyperechoic bands around the tumor. Ultrasound contrast showed enhanced

echo around the tumor and enhancing time is longer, the sensitivity was 85.7%, much higher than conventional ultrasound. ⁽¹³⁾

There are few studies on the performance of RCC pseudocapsules by CT. Yamashita et al. ⁽¹⁵⁾ studied 52 cases of renal cell carcinoma and compared the ability of detecting pseudocapsules between enhanced CT and MRI, they concluded the MRI T2-weighted image showing the most accurate. Tsili et al. ⁽²¹⁾ retrospectively studied 29 histologically proven RCCs which examinations were performed with a 16-MDCT scanner preoperatively. They finally concluded that multiphase MDCT with multiplanar reformations had satisfactory results in detecting renal pseudocapsule in RCC and imaging in the portal and nephrographic phases with coronal and sagittal reformations proved more accurate.

In our studies, among 116 cases, integrated pseudocapsule were found in 85 (73.3%) tumors with the thickness ranged from 0.2 to 0.8 mm, 25(21.6%) without integrated pseudocapsule and 6(5.2%) cases had no obvious pseudocapsule. Wang et al. concluded clear cell renal carcinomas showed the thickest pseudocapsule (average 0.23 mm) among 178 renal tumors. ⁽²²⁾ This is similar to our findings. In MDCT, The presence of pseudocapsule on CT had three kinds. 82(70.7%) cases of RCC were confirmed with a regular halo surrounding a renal neoplasm. 26(22.4%) had clear margin but not continuous or lobulated, 8 (6.70%) were found presenting blurred margin surrounding the tumor. The consistency between CT and pathological results were high by Kappa test analysis. This provides a certain basis for determining the integrity of the pseudocapsule by CT preoperatively.

The current study has a number of limitations: (1) the study design is retrospective; (2) This study was conducted at a single institution; (3) The number of samples is relative small remains a significant limitation; (4) There are some limitations on the determination of tumor margin on CT.

Conclusion

Most small renal tumors have obvious pseudocapsule, CT can demonstrate pseudocapsule of tumor margin, and is well correlated with the pathologic findings in ccRCC. This provide theoretical basis for the safety of nephron sparing surgery.

Further studies are necessary needed to verify the Accuracy of detecting pseudocapsules.

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Not applicable

Conflict of interest

The authors declare that they have no competing interests.

Ethics Approval and Consent to Participate

These study protocols were approved by the medical ethics committee of the Second Hospital of Tianjin Medical University, Tianjin Institute of Urology.

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Table1 Compare of CT scan and pathological results

CT scan(n)	Pathological results(n)		Total	Kappa coefficient	P-value
	Positive	Negative			
Positive	107	1	108	0.833	.000
Negative	3	5	8		
Total	110	6	116		

Kappa test analysis

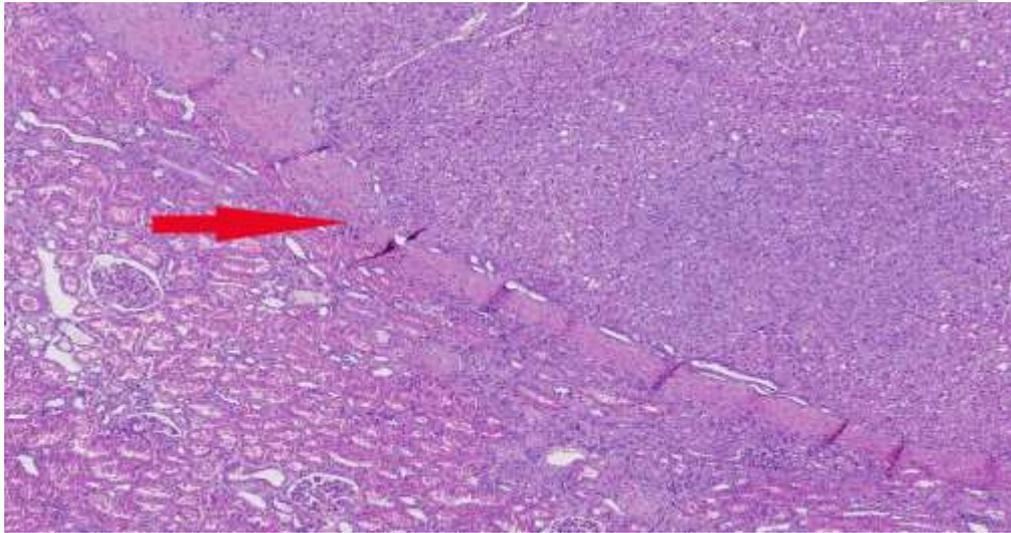


Figure 1: Microscopically, integrated pseudocapsule of ccRcc. The pathological components of pseudocapsule include compressed renal parenchyma, hyperplastic fibers, and inflammatory cells. (hematoxylin and eosin staining, $\times 40$).

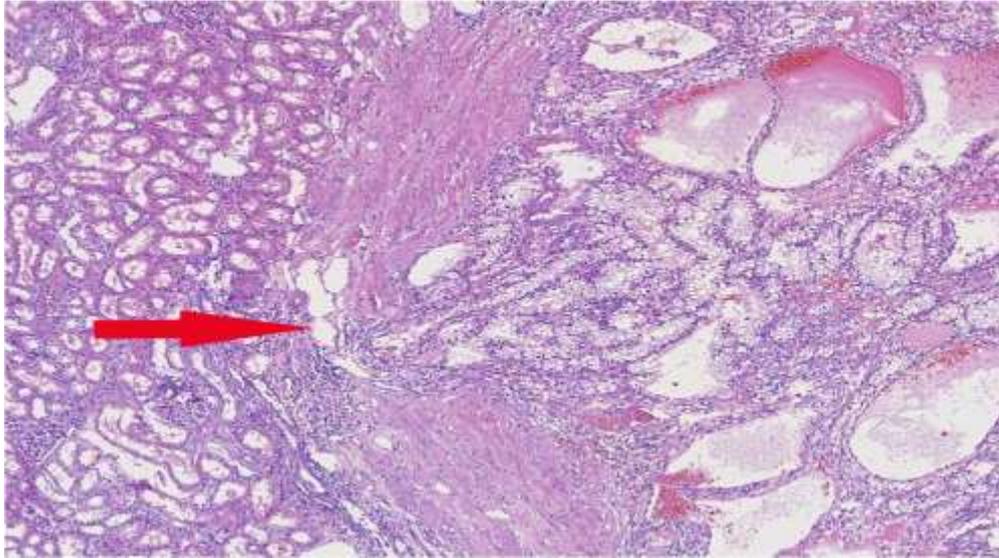


Figure 2: Microscopically, incomplete pseudocapsule of ccRcc. Tumor infiltrated and penetrated into the pseudocapsule resulting in pseudocapsule discontinuity (hematoxylin and eosin staining, $\times 100$).

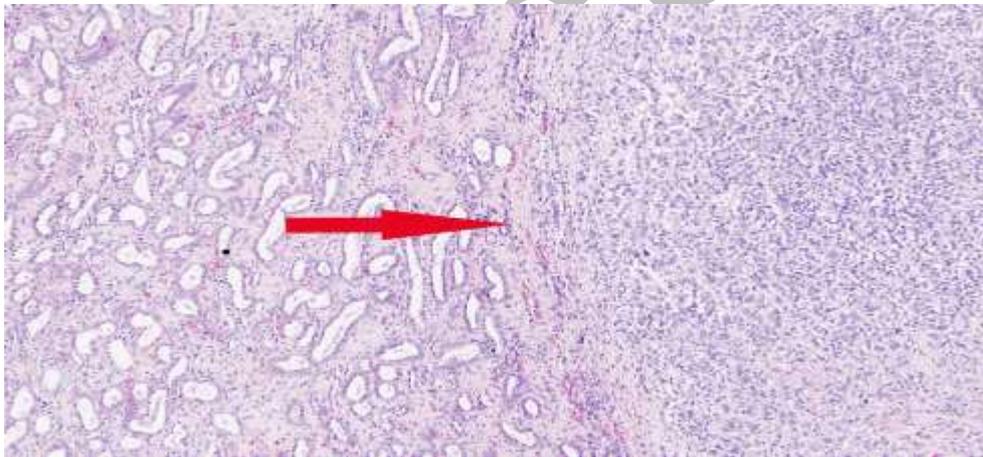


Figure 3: Microscopically, no pseudocapsule of ccRcc. The neoplastic cells directly interfaced with normal renal parenchyma without any fibrous band (hematoxylin and eosin staining, $\times 100$).

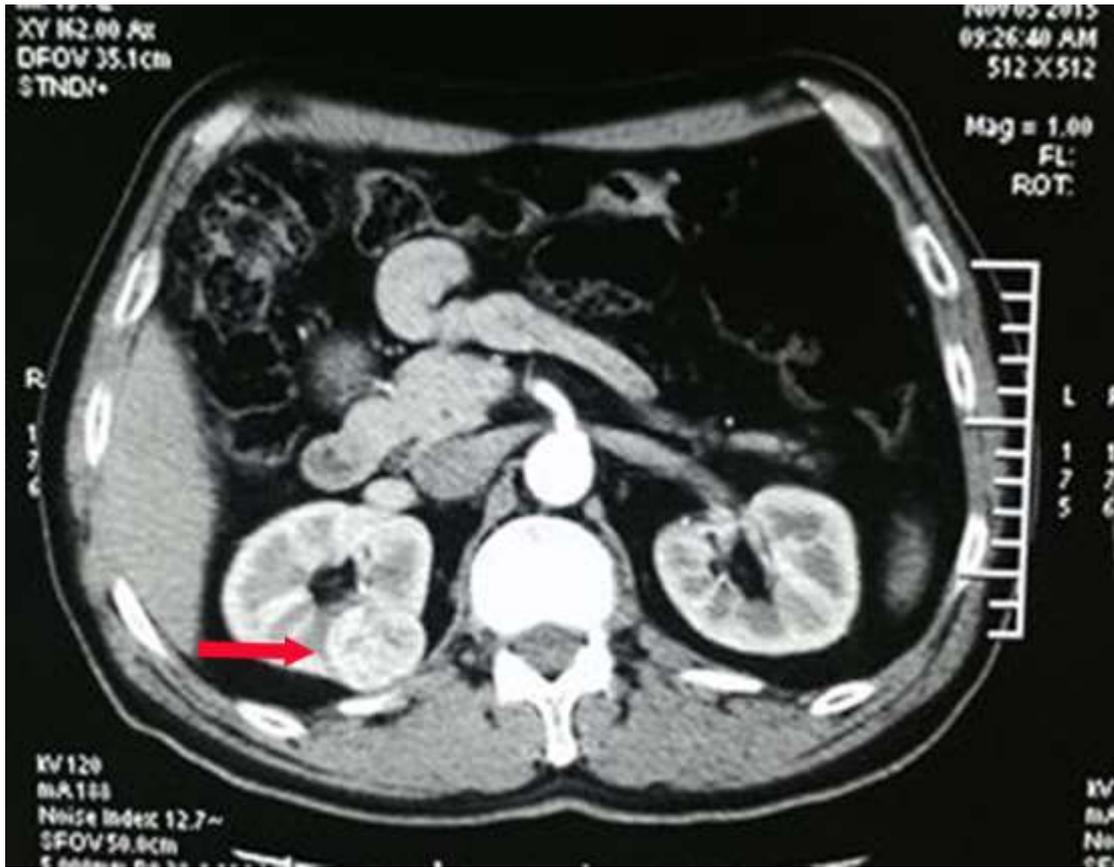


Figure 4: Abdominal CT shows a regular halo surrounding a renal neoplasm.



Figure 5: Abdominal CT shows the renal mass had clear margin but not continuous or lobulated.



Figure 6:Abdominal CT shows blurred margin surrounding the tumor.