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ORIGINAL ARTICLE

Accuracy of magnetic resonance imaging to identify pseudocapsule invasion in renal tumors

Rocco Papalia[1] · Valeria Panebianco[2] · Riccardo Mastroianni[1] · Maurizio Del Monte[2] · Emanuela Altobelli[1] · Eliodoro Faiella[4] · Francesco Rosario Grasso[4] · Mariangela Bellangino[5] · Giuseppe Simone[6] · Massimo Ciccozzi[7] · Silvia Angeletti[8] · Giulia D'ovidio[2] · Carlo Catalano[2] · Michele Gallucci[3] · Roberto Mario Scarpa[1] · Giovanni Muto[9]

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Abstract

Purpose To evaluate accuracy of MRI in detecting renal tumor pseudocapsule (PC) invasion and to propose a classification based on imaging of PC status in patients with renal cell carcinoma.

Methods From January 2017 to June 2018, 58 consecutive patients with localized renal cell carcinoma were prospectively enrolled. MRI was performed preoperatively and PC was classified, according to its features, as follows: MRI-Cap 0 (absence of PC), MRI-Cap 1 (presence of a clearly identifiable PC), MRI-Cap 2 (focally interrupted PC), and MRI-Cap 3 (clearly interrupted and infiltrated PC). A 3D image reconstruction showing MRI-Cap score was provided to both surgeon and pathologist to obtain complete preoperative evaluation and to compare imaging and pathology reports. All patients underwent laparoscopic partial nephrectomy. In surgical specimens, PC was classified according to the renal tumor capsule invasion scoring system (i-Cap).

Results A concordance between MRI-Cap and i-Cap was found in 50/58 (86%) cases. ρ coefficient for each MRI-cap and iCap categories was: MRI-Cap 0: 0.89 ($p < 0.0001$), MRI-Cap1: 0.75 ($p < 0.0001$), MRI-Cap 2: 0.76 ($p < 0.0001$), and MRI-Cap3: 0.87 ($p < 0.0001$). Sensitivity, specificity, positive predictive value, negative predictive value, and AUC were: MRI-Cap 0: Se 97.87% Spec 83.3%, PPV 95.8%, NPV 90.9%, and AUC 90.9; MRI-Cap 1: Se 77% Spec 95.5%, PPV 83.3%, NPV 93.5%, and AUC 0.86; MRI-Cap 2- iCap 2: Se 88% Spec 90%, PPV 79%, NPV 95%, and AUC 0.89; MRI-Cap 3: Se 94% Spec 95%, PPV 88%, NPV 97%, and AUC 0.94.

Conclusions MRI-Cap classification is accurate in evaluating renal tumor PC features. PC features can provide an imaging-guided landmark to figure out where a minimal margin could be preferable during nephron-sparing surgery

Keywords Renal tumor pseudocapsule · Partial nephrectomy · Tumor enucleation · Renal cell carcinoma

✉ Rocco Papalia
rocco.papalia@unicampus.it

[1] Department of Urology, Campus Bio-medico University of Rome, Via Alvaro del Portillo 200, 00128 Rome, Italy

[2] Department of Radiological Sciences, Sapienza University of Rome, Rome, Italy

[3] Department of Urology, Sapienza University of Rome, Rome, Italy

[4] Department of Diagnostic and Interventional Radiology, Campus Bio-medico University of Rome, Rome, Italy

[5] Department of Urology, Ospedale Sant'Andrea, Sapienza University of Rome, Rome, Italy

[6] Department of Urology, "Regina Elena" National Cancer Institute, Rome, Italy

[7] Unit of Medical Statistics and Molecular Epidemiology, Campus Bio-medico University of Rome, Rome, Italy

[8] Unit of Clinical Laboratory Science, Campus Bio-Medico University of Rome, Rome, Italy

[9] Department of Urology, Humanitas "Gardenigo" University, Turin, Italy

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Introduction

Partial nephrectomy (PN) can be performed, either with an open, pure laparoscopic- or robot-assisted approach, based on surgeon's expertise and skills [1]. In patients who elect PN, physicians should prioritize preservation of renal function through efforts to optimize nephron mass preservation and avoidance of prolonged warm ischemia [2]. Among NSS techniques, tumor enucleation (TE) maximally preserves normal renal parenchyma and is enabled by the presence of tumor PC. This is a fibrous band of compressed renal parenchyma that separates the tumor from the adjacent healthy renal parenchyma, thus, providing a natural cleavage plane during surgery [3]. The amount of healthy renal parenchyma preserved during PN represents one important modifiable factor impacting on renal function [4]. The debate on pros and cons of TE for localized renal masses is still open. TE allows direct visualization of the tumor, the potential for zero-ischemia PN, and the potential for minimal damage to the surrounding parenchyma [5]. Furthermore, TE by improving preservation of normal parenchymal mass compared to standard PN (SPN) has the potential to optimize functional recovery after PN [6]. Nevertheless, TE on a routine basis for sporadic RCC remains controversial. Some authors remark that 20–30% of localized RCC, even small renal masses, harbor potentially aggressive features and 40–50% invade into or beyond the PC [7]. Although it was reported that TE is at least non-inferior to SPN for the treatment of malignant cT1–T2 renal tumors in regard to positive surgical margins (PSM), loco-regional recurrence, and renal recurrence rates after a minimum follow-up of 24 months, the absence of PC integrity may predict the presence of positive surgical margins or have negative prognostic implications [8–11]. In this setting, preoperative imaging able to identify PC integrity would help to keep a safe surgical margin when necessary and to improve excisional precision. While CT is the most widely used technique for evaluation of renal masses, MRI has become the preferred technique to evaluate morphological features of RCC. In particular, tumor PC can be identified on MRI as a thin linear regular hypointense band surrounding the tumor on T2- and T1-weighted images [12]. The aim of our study was to evaluate the accuracy of MRI in identifying and assessing tumor PC invasion. Moreover, we propose a standardized classification to report PC status on MRI.

Materials and methods

Patients' population

From January 2017 to June 2018, a consecutive series of 58 patients with organ-confined RCC (cT1 tumors) undergoing nephron-sparing surgery were prospectively enrolled in two referral centers. Inclusion criteria were: age ≥ 18 and evidence of renal tumor on contrast-enhanced CT imaging. Exclusion criteria were: contraindication to MRI and gross hematuria. Two patients with oncocytoma at final pathology were excluded from the analysis to focus on RCC features. All patients underwent preoperative abdominal MRI with a mean interval between imaging and surgery of ± 13.4 days (range 7–30).

MRI study protocol

MR imaging examination was performed with 3.0-T (Discovery MR750; GE Medical Systems, Milwaukee, Wis). Turbo spin-echo T2-weighted (T2W) images (TR/TE, 8000/120 ms; matrix, 320 × 224 section thickness, 2 mm; field of view, 34 cm) were obtained in axial, coronal, and sagittal planes. Diffusion-weighted (DW) images were obtained during free-breathing in the axial plane using single-shot spin-echo echoplanar sequence with chemical shift-selective fat-suppression techniques (b, 0–500–800–1000 s/mm^2; TR/TE, 7979/60 ms; matrix, 128 × 96; section thickness, 3 mm; field of view, 34 cm). T1-weighted images were obtained in axial and coronal planes and were obtained post-contrast medium injection with a fat-suppressed 3D volumetric spoiled gradient-echo sequence (TR/TE, 16.4/4.7 ms; flip angle, 15°; section thickness, 2 mm; matrix, 288 × 192) aimed at complete abdominal examination.

Imaging analysis

All images were independently evaluated by two experienced uro-radiologists. Disagreements were resolved by consensus, after further examination of images. Tumor diameter was measured in three planes and the largest value was considered as the tumor size. Tumor PC was defined as a thin linear regular hypointense band surrounding the tumor on T2- and T1-weighted images. Similarly to the invasion of PC scoring system (i-Cap), recently developed by Snarskis et al. to standardize the histopathology report of tumor PC integrity, we proposed a new classification system to standardize MRI report on PC status: MRI-Cap [13]. MRI-Cap was evaluated on both T2-WI and T1WI + T2WI, and it was defined as follows:

- MRI-Cap 0: No visible hypointense rim surrounding the tumor on T2- and T1-weighted images (Fig. 1).
- MRI-Cap 1: Presence of a clearly identifiable, continuously intact, hypointense rim surrounding the lesion on T2-weighted images (Fig. 2).
- MRI-Cap 2: Presence of a PC, which appears focally interrupted but in the absence of an obvious infiltration beyond its boundaries assessed on T2-weighted images.

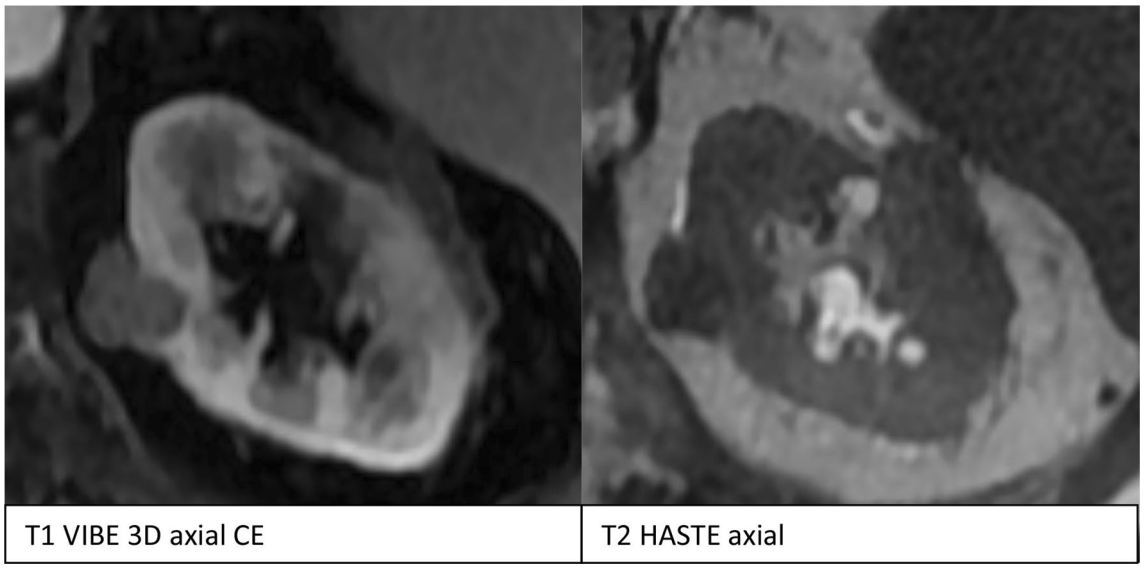

Fig. 1 Pseudocapsule category 0: no visible hypo-intense rim visible on T1 and T2 weighted images surrounding the lesion. Papillary type I RCC pT1a

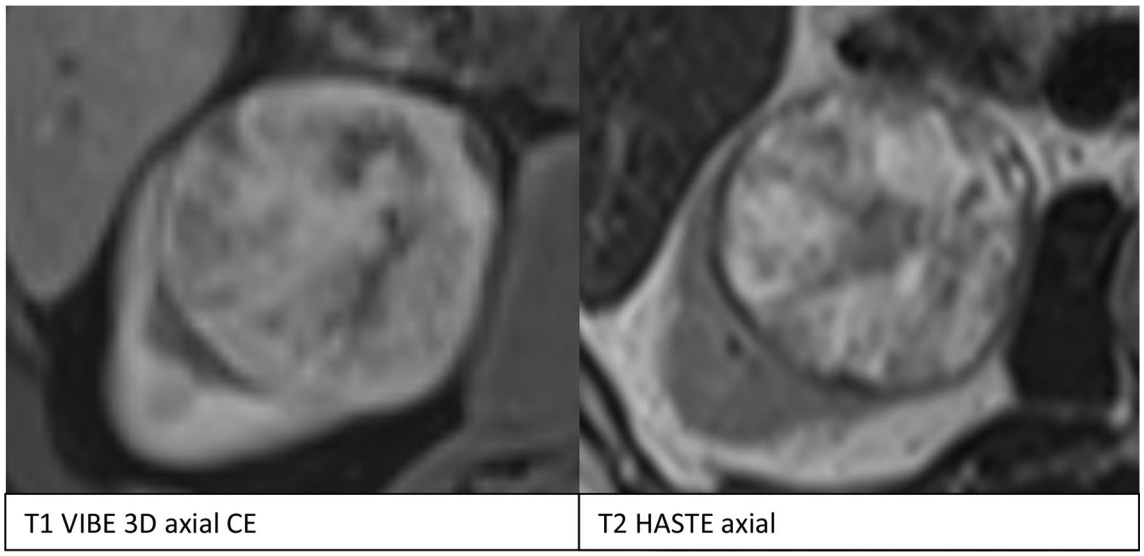

Fig. 2 Pseudocapsule category 1: presence of a clearly identifiable hypo-intense rim surrounding the lesion in T1 and T2 weighted images (pseudocapsule), which is continuously intact. Interpretation: pseudocapsule not infiltrated. ccRCC pT1a

No clear interruption visible on T1-weighted images (Fig. 3).

- MRI-Cap 3: Presence of PC which appears clearly interrupted and infiltrated assessed on both T2- and T1-weighted images (Fig. 4).

Furthermore, radiologists reported the site of possible PC infiltration. A 3D image reconstruction showing MRI-Cap score was provided to both surgeon and pathologist to achieve complete preoperative evaluation and to compare imaging and pathology reports (Fig. 5).

Surgical technique and pathological assessment

All patients underwent laparoscopic partial nephrectomy, performed by a single experienced urologist. The resection technique was in all cases started as simple enucleation (SE) and minimal margin was preserved according to PC features

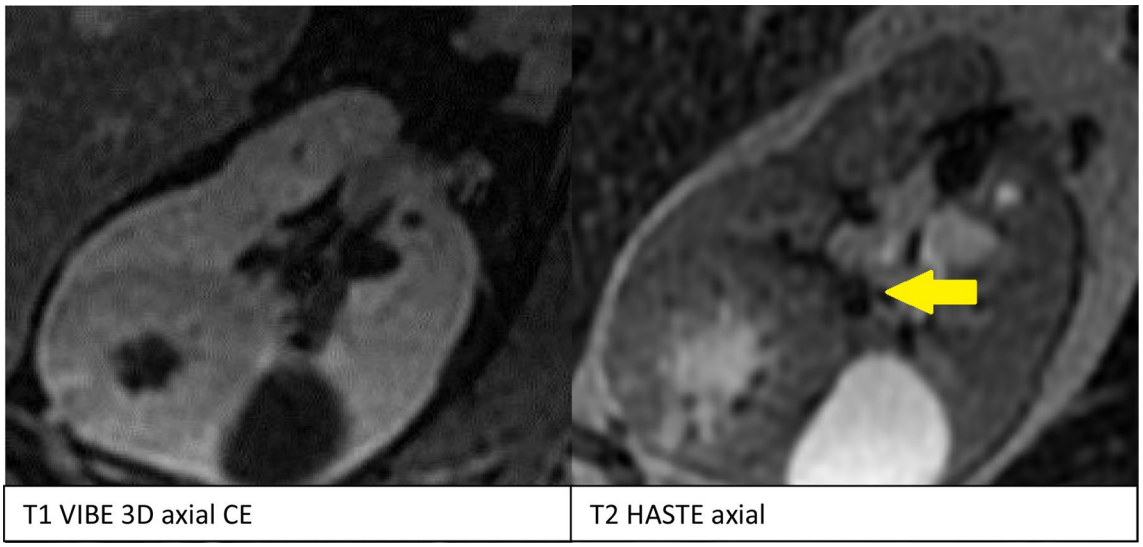

Fig. 3 Pseudocapsule category 2: presence of a pseudocapsule, which appears focally interrupted in the absence of an obvious infiltration beyond its boundaries as assessed on T2 weighted images. No clear interruption visible on T1 weighted images. Interpretation: pseudocapsule likely infiltrated. ccRCC pT1a

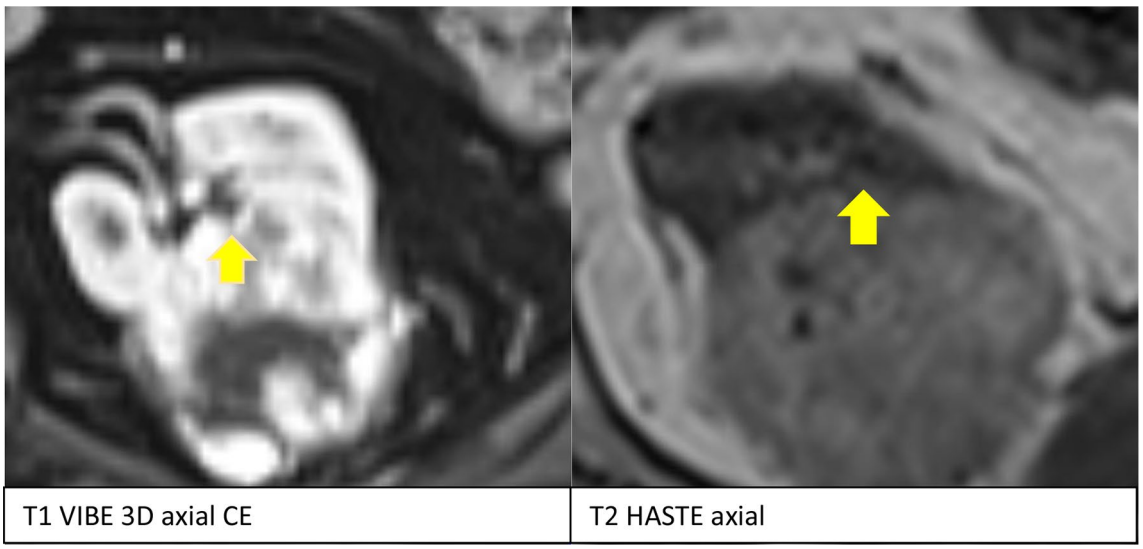

Fig. 4 Pseudocapsule category 3: presence of a pseudocapsule which is clearly interrupted and infiltrated as assessed on both T2 weighted and T1 weighted images. Interpretation: pseudocapsule definitely infiltrated. ccRCC pT1a

reported on MRI. After surgery, the specimen was properly marked to evaluate the concordance with the MR images.

The surgical specimens were fixed in 10% formalin solution, embedded in paraffin, and step-sectioned at 5 mm intervals. Slices were then stained with hematoxylin–eosin and examined by a single experienced genitourinary pathologist. When necessary, further coupes from the paraffin slices were obtained.

Tumors were staged and graded according to the TNM classification system 7th edition, and to the Fuhrman grading system, respectively [14]. Histological subtypes were assessed according to the World Health Organization 2004 classification [15]. Tumor PC was defined as a parallel band of fibrocollagenous connective tissue located at the interface between tumor and normal renal parenchyma. Mean PC thickness, PC completeness, presence and extent of PC invasion, as well as surgical margins status were reported. Pathologist used the recently introduced i-Cap score 1–3 to report PC invasion: i-Cap 1 was assigned to tumors with a completely intact PC without cancerous

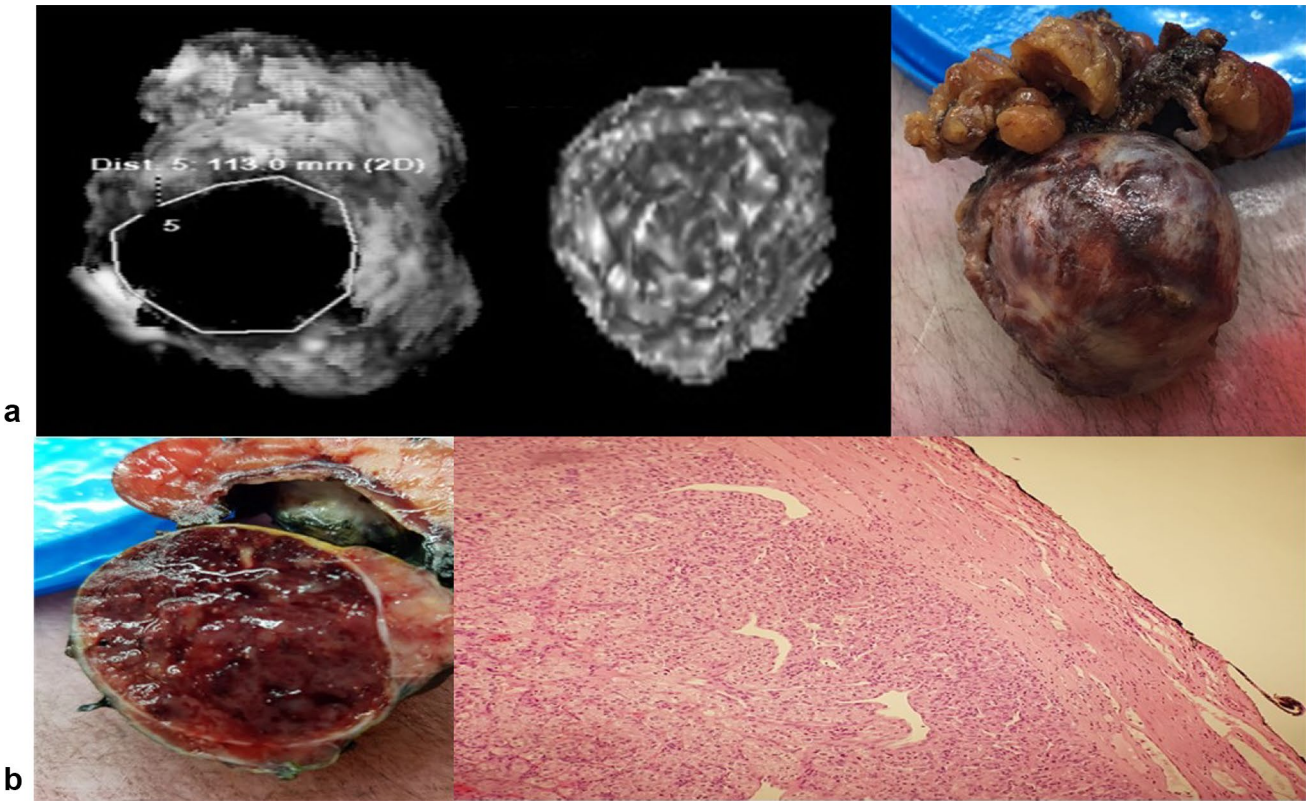

Fig. 5 MRI reconstruction showing the presence of a clearly identifiable and continuously intact PC and renal tumor specimen: **a** 3D MRI renal mass reconstruction separated from normal kidney and surgical specimen. **b** Tumor section showing peritumoral capsule confirmed on pathology

invasion; i-Cap2 was assigned to tumors showing focal absence in PC without invasion or cancerous tissue invasion partially into and yet not completely through the PC; i-Cap 3 was assigned to tumors that had completely lost PC integrity with carcinoma extending into the surrounding healthy parenchyma. In case of complete absence of PC, the pathologist referred as i-Cap 0. MRI-Cap results were compared with i-Cap to evaluate correlation between PC characteristics on images and pathology.

Statistical analysis

Preoperative MRI-Cap was compared to histology to evaluate diagnostic accuracy of MRI in identifying and differentiating intact from infiltrated and interrupted PC. Spearman's coefficient of rank correlation (ρ) and corresponding 95% confidence interval was estimated for each MRI-Cap and i-Cap categories. Sensitivity, specificity, positive predicting value (PNV), and negative predicting value (NPV) was calculated for each MRI-Cap category. Receiver-operating characteristic (ROC) curves were generated and area under the curve (AUC) was obtained. A p value of ≤ 0.05 was considered statistically significant. Statistical analysis was performed with SAS 9.4 version (SAS Institute Inc., Cary, NC, USA).

Results

Overall 58 consecutive patients (37 male and 21 female) with localized RCC were prospectively enrolled in the present study. Median age of patients was 66 years (IQR 27–77 years). Median histologic tumor diameter was 3.2 cm (IQR 1.9–5.2 cm). A cancer stage of T1a was confirmed in 51 (88%) patients, whereas T1b was present in 7 (12%) patients. 7 (12%) tumors were Fuhrman grade G1, 38 (66%) were G2, 8 (14%) were G3, and 5 (8%) were G4. Histologic subtype was clear cell in 52 (90%) cases, papillary in 4 (7%), and chromophobe in 2 (3%). In the two patients with oncocytoma excluded from the analysis, PC was absent at MRI evaluation.

A PC was identified on preoperative MRI and confirmed by pathology report in 46/58 cases (79%), while it was absent on MRI in 12/58 (21%) cases (Table 1). A concordance between MRI-Cap and i-Cap was found in 50/58 (86%) cases, whereas 8/58 (14%) lesions were misevaluated

Table 1 MRI-Cap versus i-Cap score showing concordance between preoperative MRI and final pathology evaluation of PC

MRI-Cap	i-Cap				Total
	0	1	2	3	
0	10	2	0	0	12
1	0	10	3	0	13
2	0	0	15	2	17
3	0	0	1	15	16
	10	12	19	17	58

by MRI. Sensitivity, specificity, PPV, NPV, and AUC are reported in Table 2.

Discussion

Hricak et al. first described, in 1985, the PC on MRI, appearing as a low-intensity band separating the tumor from the normal renal parenchyma or perirenal fat on both T1 and T2 sequences. T2-weighted images, however, were found to be the most sensitive for detecting the PC, interposed between the higher intensity of the tumor and normal renal parenchyma [16]. Lately, Roy et al. confirmed these findings [12]. In our series, PC was detected in 50/58 (86%) cases, confirming the high detection rate of MRI in this setting. The evaluation based on T2WI alone was consistently inferior to the T1WI + T2WI (difference between AUC = 0.139 ± 0.052, $p = 0.007$), and thus, we used the second analysis as radiologic output. Only two false-negative (FN) cases were proved after pathologic evaluation with regard to the presence of PC, not detected on MR images. The two FN patients were pT1b G3 RCC with a less than 0.2 mm PC misevaluated on MRI and identified at pathology. One MRI-Cap three patient was evaluated as i-Cap 2 at the final pathology.

MRI showed the best performance in identifying any degree of carcinoma infiltration completely through the PC and into the normal parenchyma (iCap3) with a sensitivity of 93.75%, a specificity of 95%, a PPV of 88%, an NPV of 97%, and an AUC 0.94.

Based on our results, MRI in patients with RCC should be indicated preferably when CT scan is unable to detect intact PC surrounding the entire tumor.

In fact, as reported in the previous studies, MRI was identified as the most accurate imaging modality in the detection of PC, with a sensitivity of 54–93%, whereas CT is only 10–26% [17–19].

According to emerging research, innovative and more recent sequences, such as Arterial Spin Labelling, in combination with classical T2 sequences, could further improve the detection of PC invasion [20].

This finding could be of crucial clinical importance when considering PN approach.

It has been suggested that the PC could act as an anatomic guide for the surgeon in avoiding PSM [21]. Although retrospective series suggest similar oncologic outcomes between SE and PN [22], there are still concerns about the risk of PSM associated with this procedure. However, there is evidence, suggesting that even though PSM is associated with a higher risk of recurrence, it does not appear to influence CSS [23, 24].

There is still debate on the most appropriate technique to perform PN and treatment decisions vary depending on urologist's training and individual experience. Adapting PN techniques to improve preservation of functional outcomes without undermining oncologic principles is of crucial importance. For long time, NSS comprised a minimal layer of normal-appearing parenchyma to guarantee complete tumor resection, which is a cardinal principle in the surgical management of neoplastic diseases [25, 26]. To improve functional outcomes off-clamp, minimally ischemic and selective clamping techniques have been described and simple tumor enucleation has been shown to be safe and effective [14]. Among NSS techniques, TE is the one that maximally preserves normal renal parenchyma and is enabled by the presence of tumor PC [3]

Authors pro TE underline how it guarantees equivalent oncologic control, enhanced surgical precision, possible

Table 2 ρ coefficient, sensitivity, specificity, PPV, NPV and AUC of MRI PC evaluation compared to i-Cap

	MRI-Cap 0 / i-Cap 0	MRI-Cap 1/ i-Cap 1	MRI-Cap 2 / i-Cap 2	MRI-Cap 3 / i-Cap 3	Global
ρ coefficient	0.89 (IC95% 0.83–0.94)	0.75 (IC95% 0.60–0.84)	0.76 (IC95% 0.63–0.85)	0.87 (IC95% 0.79–0.92)	0.94 (IC95% 0.90–0.96)
Sensitivity	97.8%	77%	88%	94%	
Sensibility	83.3%	95.5%	90%	95%	
PPV	95.8%	83.3%	79%	88%	
NPV	90.9%	93.5%	95%	97%	
AUC	0.91	0.86	0.89	0.94	

fewer complications, and avoidance of warm ischemia and complex renorrhaphy.

Opponents claim that, although TE can preserve more parenchyma and offer other potential advantages, for most patients with sporadic RCC, the clinical benefit is marginal. Patients more likely to benefit of TE are those with preexisting severe chronic kidney disease and solitary kidney [5].

In our experience, all PNs started always as SE to maximize healthy renal parenchyma preservation. Since a key step SE is the identification of the cleavage plane, all the procedures are mandatorily carried out under direct vision. As a consequence, the decision to include a minimum margin of healthy parenchyma was evaluated case by case intraoperatively when information about PC was not available. For the current study, minimal margin was preserved according to PC features reported on MRI.

Surgeons may apply different resection techniques along the contours of a tumor during PN. Taking into consideration that the most important factors influencing renal function are the preoperative renal function and the volume of healthy renal parenchyma that the surgeon can spare during tumor resection, imaging, and strategies that allow optimization of the modifiable factors are fundamental for PNs' outcomes.

Therefore, in this scenario, a detailed preoperative identification of PC integrity could help clinical decision-making on the most appropriate approach to PN with the aim of keeping a safe surgical margin when necessary and to improve excisional precision. An interest in evaluating peritumoral PC status has been developed since the 1940s, when early studies reported a low proportion of PC involvement by cancer [15, 27]. Lately, in the 1980s, Rocca Rossetti described the PC of renal cell carcinoma also from the ultrastructural point of view and concluded that tumors up to 7 cm in diameter had a PC often intact and that, therefore, the capsular integrity was the permitting condition of the enucleation. In fact, in case of discontinuity of the capsule, the tumor infiltration of the adjacent renal parenchyma was systematically observed. Rosenthal et Zingg first observed that PC invasion was more common in less differentiated renal tumors, suggesting a possible association with a greater risk of clinical progression [28]. More recently, studies reported a 14–33% of PC involvement [29, 30]. Minervini et al. reported the presence of a continuous, non fenestrated, layer of dense connective fibrous tissue completely surrounding the tumor in 100% of patients treated with TE in their series. They also classified PC status at the parenchymal side as: intact and free from invasion (PS−) or with signs of neoplastic infiltration within its layers, with or without invasion beyond it (PS+). PS- was reported in 66.7% of RCC, whereas, in 33.3% of cases, there were signs of infiltration within PC layers, with or without invasion beyond it (PS+). PC invasion on the parenchymal side was observed in 26.6% of tumors, of those 11 tumors (12.2% overall) had PS penetration and 13 tumors (14.4% overall) had PS penetration and invasion beyond it. PS+ was significantly associated with clinical and pathological tumor size, presence of necrosis, and pathological nuclear grade, whereas no statistically significant correlation was seen as regards tumor stage (pT1a vs pT1b) and histologic subtype (clear cell vs papillary vs chromophobe) [26].

Successively, the same group reported that there were no significant predictors of partial vs absent PC invasion. Based on these findings, they suggest that a binomial reporting system of PC invasion (complete vs partial or absent) might be of superior clinical relevance compared to i-Cap score [31].

Volpe et al. first proposed a standardized histologic definition and classification of patterns of renal tumor PC invasion (RTPI) and investigated its possible prognostic significance. They described two main patterns of RTPI: expansive (presence of tumor cells that abutted the PC which, however, remained regular, well defined, and without breaks) and infiltrative (presence of tumor cells penetrating into the PC with spikes reaching varying depth). Expansive or infiltrative RTPI were observed in 39.5% and 51.6% of cases, respectively. No statistically significant association was found between RTPI pattern and pathological size and stage, whereas a significant association was described for grade and histologic subtype (no RTPI was reported in 31.2% of chromophobe RCCs, 11.1% of papillary RCCs, and 6.4% of clear cell RCCs) [30]. At a multivariate analysis, both tumor histology and higher Fuhrman grade were associated with an increased risk of i-Cap 3 score, with papillary type and Fuhrman grade 4 carrying the highest risk (OR 3.04, 95% CI 1.52–6.09, $p=0.002$; OR 14.68, 95% CI 2.16–123.18, $p=0.007$) [13].

Indications, approaches, and techniques for PN, as well as correct reporting of outcomes, are still a matter of great debate within the urology community. The design of high-quality multi-institutional studies evaluating long-term oncologic outcomes for complex renal masses based on standardized patient selection and surgical technique report is needed to better address this issue [32].

In this context, renal mass imaging allows detailed delineation of the anatomy and vasculature and permits nephrometry scoring, and thus precise, patient-specific surgical planning [33].

Moreover, imaging can help further research to define the optimal strategy for tumor excision during PN according to the specific anatomic characteristics of each renal tumor. According to Minervini et al., resection technique might be different from resection strategy and that routine assessment of tumor excision descriptors using standardized reporting models should be mandatory in future PN series to compare the outcomes of different surgical techniques in a meaningful way [34, 35].

The knowledge of the precise location of PC infiltration, in this context, could help to insert a further tile in the mosaic of information required to plane the most appropriate surgical approach. The emerging augmented reality techniques may also enhance information about PC and, perhaps, help giving a more correct indication for TE rather than renal resection.

Based on the evidence about PC features or PC not shown on MRI, urologists could evaluate the possibility to perform renal biopsy to assess tumor histology prior to surgery. The presence of PC at MRI and the absence at histopathological analysis were never observed in our study supporting MRI reliability.

We must acknowledge some limitations of our study. First of all, a limited number of patients were enrolled. Second, images were evaluated by experienced uro-radiologists and specimens were evaluated by a single experienced uro-pathologist. Therefore, inter-observer variations and institutional biases cannot be excluded. Third, i-Cap and MRI-Cap are quality tools proposed to standardize PC status, but their clinical implication needs to be defined and confirmed by further larger multicenter studies. Notwithstanding all these limitations, to our knowledge, this is the first study that attempts to classify and grade tumor PC.

Conclusion

MRI is accurate in evaluating renal tumor PC. PC features can provide an imaging-guided landmark to figure out where and whether a minimal margin could be desirable during nephron-sparing surgery.

Author contributions Protocol/project development: RP, VP, GM, EF. Data collection or management: RM, EA, MDM, GD', FRG. Data analysis: MC, SA, MB, GS. Manuscript writing/editing: RP, RMS, CC, MG.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical standard There were de-identified data sharing agreement among institutions and informed consent was obtained from all the patients.

References

1. Lyunberg B, Albiges L, Bensalah K, et al. European Association of Urology guidelines on renal cell carcinoma. In: Presented at the EAU annual congress Copenhagen 2018. ISBN 978-94-92671-01-1
2. Campbell S, Uzzo RG, Allaf ME et al (2017) Renal mass and localized renal cancer: AUA guideline. J Urol 198:520–529
3. Di Cristofano C, Minervini A, Tuccio A et al (2009) Pathological evaluation of peritumoral pseudocapsule status after nephron sparing surgery and its prognostic implication. Arch Ital Urol Androl 81:96
4. Takagi T, Mir MC, Campbell RA et al (2014) Predictors of precision of excision and reconstruction in partial nephrectomy. J Urol 192:30
5. Gupta GN, Boris RS, Campbell SC, Zhang Z (2015) Tumor enucleation for sporadic localized kidney cancer: pro and con. J Urol. 194:623–625
6. Dong W, Gupta GN, Blackwell RH et al (2017) Functional comparison of renal tumor enucleation versus standard partial nephrectomy. Eur Urol Focus 3(4–5):437–443
7. Minervini A, Raspollini MR, Tuccio A et al (2014) Pathologic characteristics and prognostic effect of peritumoral capsule penetration in renal cell carcinoma after tumor enucleation. Urol Oncol 32:15
8. Minervini A, Campi R, Sessa F et al (2017) Positive surgical margins and local recurrence after simple enucleation and standard partial nephrectomy for malignant renal tumors: systematic review of the literature and meta-analysis of prevalence. Minerva Urol Nefrol 69:523–538
9. Cao DH, Liu LR, Fang Y et al (2017) Simple tumor enucleation may not decrease oncologic outcomes for T1 renal cell carcinoma: a systematic review and meta-analysis. Urol Oncol 35(11):661.e15–661.e21
10. Minervini A, Ficarra V, Rocco F et al (2011) Simple enucleation is equivalent to traditional partial nephrectomy for renal cell carcinoma: results of a nonrandomized, retrospective, comparative study. SATURN Project-LUNA Foundation. J Urol. 185(5):1604–1610
11. Süer E, Ergün G, Baltaci S, Bedük Y (2008) Does renal capsular invasion have any prognostic value in localized renal cell carcinoma? J Urol 180(1):68–71
12. Roy C Sr, El Ghali S, Buy X et al (2005) Significance of the pseudocapsule on MRI of renal neoplasms and its potential application for local staging: a retrospective study. AJR Am J Roentgenol 184(1):113–120
13. Snarskis C, Calaway AC, Wang L et al (2017) Standardized reporting of microscopic renal tumor margins: introduction of the renal tumor capsule invasion scoring system. J Urol 197(1):23–30
14. Beare JB, McDonald JR (1949) Involvement of the renal capsule in surgically removed hypernephroma; a gross and histopathologic study. J Urol 61:857
15. Vermooten V (1950) Indications for conservative surgery in certain renal tumors: a study based on the growth pattern of the cell carcinoma. J Urol 64:200
16. Hricak H, Demas BE, Willians RD et al (1985) Magnetic resonance imaging in the diagnosis and staging of renal and perirenal neoplasms. Radiology 154:709–715
17. Ward RD, Tanaka H, Campbell SC, Remer EM (2018) 2017 AUA renal mass and localized renal cancer guidelines: imaging implications. Radiographics 38:2021–2033
18. Yamashita Y, Honda S, Nishiharu T, Urata J, Takahashi M (1996) Detection of pseudocapsule of renal cell carcinoma with MR imaging and CT. AJR Am J Roentgenol 166(5):1151–1155
19. Takahashi S, Ueda J, Furukawa T et al (1996) Renal cell carcinoma: preoperative assessment for enucleative surgery with angiography, CT, and MRI. J Comput Assist Tomogr 20(6):863–870
20. Zhang H, Wu Y, Xue W et al (2017) Arterial spin labelling MRI for detecting pseudocapsule defects and predicting renal capsule invasion in renal cell carcinoma. Clin Radiol. 72(11):936–943

21. Longo N, Minervini A, Antonelli A et al (2014) Simple enucleation versus standard partial nephrectomy for clinical T1 renal masses: peri-operative outcomes based on a matched-pair comparison of 396 patients (RECORd project). Eur J Surg Oncol 40:762–768
22. Mukkamala A, Allam CL, Ellison JS et al (2014) Tumor enucleation vs sharp excision in minimally invasive partial nephrectomy: technical benefit without impact on functional or oncologic outcomes. Urology 83:1294–1299
23. Bensalah K, Pantuck AJ, Rioux-Leclercq N et al (2010) Positive surgical margin appears to have negligible impact on survival of renal cell carcinomas treated by nephron-sparing surgery. Eur Urol 57:466–471
24. Marszalek M, Carini M, Chlosta P et al (2012) Positive surgical margins after nephron-sparing surgery. Eur Urol 61:757–763
25. Minervini A, Di Cristofano C, Lapini A et al (2009) Histopathologic analysis of peritumoral pseudocapsule and surgical margin status after tumor enucleation for renal cell carcinoma. Eur Urol 55:1410–1418
26. Simone G, Gill IS (2015) Mottrie A et al Indications, techniques, outcomes, and limitations for minimally ischemic and off-clamp partial nephrectomy: a systematic review of the literature. Eur Urol 68(4):632–640
27. Rosenthal CL, Kraft R, Zingg EJ (1984) Organ preserving surgery in renal cell carcinoma: tumor enucleation versus partial kidney resection. Eur Urol 10:222
28. Jacob JM, Williamson SR, Gondim DD et al (2015) Characteristics of the peritumoral pseudocapsule vary predictably with histologic subtype of T1 renal neoplasms. Urology 86:956
29. Wang L, Feng J, Alvarez H et al (2015) Critical histologic appraisal of the pseudocapsule of small renal tumors. Virchows Arch 467:311
30. Volpe A, Bollito E, Bozzola C et al (2016) Classification of histologic patterns of pseudocapsular invasion in organ-confined renal cell carcinoma. Clin Genitourin Cancer 14(1):69–75
31. Minervini A, Campi R, Di Maida F et al (2018) Tumor-parenchyma interface and long-term oncologic outcomes after robotic tumor enucleation for sporadic renal cell carcinoma. Urol Oncol 36(12):527.e1–527.e11
32. Carini M, Campi R, Mari A, Minervini A (2017) Oncologic safety of robotic partial nephrectomy: setting tiles in the mosaic of evidence while designing future research projects. Eur Urol Focus. https://doi.org/10.1016/j.euf.2017.11.003
33. Klatte T, Ficarra V, Gratzke C et al (2015) A literature review of renal surgical anatomy and surgical strategies for partial nephrectomy. Eur Urol 68:980–992
34. Minervini A, Campi R, Serni S, Carini M, Satkunasivam R, Tsai S, Syan S et al (2015) Robotic unclamped "minimal-margin" partial nephrectomy: ongoing refinement of the anatomic zero-ischemia concept. Eur Urol 68:705–712
35. Minervini A, Campi R, Serni S, Carini M, Satkunasivam R, Tsai S, Syan S et al (2016) Robotic unclamped "minimal-margin" partial nephrectomy: ongoing refinement of the anatomic zero-ischemia concept. Eur Urol 70:e47–e50