The Role of Imaging in the Management of Renal Masses

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ABSTRACT
The widespread availability of cross-sectional imaging is responsible for the increased detection of small, usually asymptomatic renal masses. More than 50% of renal cell carcinomas (RCCs) represent incidental findings on noninvasive imaging. Multimodality imaging, including conventional US, contrast-enhanced US (CEUS), multiparametric CT and MRI (mpMRI) is essential in diagnosing and characterizing renal masses, but also provides information regarding its prognosis, therapeutic management, and follow-up. In this review, the imaging data for renal masses that urologists require for accurate treatment planning will be discussed. The roles of US, CEUS, CT and mpMRI in the detection and characterization of renal masses, RCC staging and follow-up of treated or untreated local RCCs will be presented. The role of percutaneous image-guided ablation in the management of RCC will also be reviewed.

Keywords: Renal neoplasm, Renal cell carcinoma, Multimodal imaging, Minimally invasive treatment

1. Introduction

The wide availability of cross-sectional imaging plays an important role in improving the detection of small, usually asymptomatic renal masses [1, 2, 3, 4, 5, 6, 7]. Most renal masses are benign cysts. However, renal cell carcinoma (RCC) is often detected incidentally, and the patient's prognosis is better in these cases [8, 9, 10, 11]. Accurate noninvasive characterization of renal masses is important to ensure appropriate treatment planning [1, 2, 3, 4, 5, 6, 7].

The first step when detecting a renal mass is to differentiate between a benign cyst and a solid mass. Most cystic renal masses are benign, and when malignant, they are often indolent. The Bosniak classification of cystic renal lesions was recently updated [12, 13]. Although validation is required, a major modification incorporates cystic masses detected on MRI or US, establishing a definition for previously unclear imaging terms and allowing for a greater reduction in the proportion of renal cystic masses [12, 13].

Although their incidence is lower compared to cystic masses, up to 90% of solid renal tumors are malignant, and RCC accounts for 90% of renal malignancies [2],[3]. The most common benign solid renal masses are angiomyolipoma (AML) and renal oncocytoma [2, 3, 4, 5, 6, 7]. Visible lean AML (fat-poor AML) accounts for about 5% of AML [2, 3, 4, 5, 6, 7].

The prognosis of RCC is mainly related to tumor stage, histologic subtype, and nuclear grade [2, 3, 4]. Preoperative RCC staging and anatomic information are essential to guide treatment decisions [14, 15]. The histologic classification of RCC is also important, given the prognostic and therapeutic implications of the histologic subtypes of RCC. Clear cell RCC, papillary RCC and chromophobic RCC are the most common histologic subtypes of RCC [16]. RCC assessment represents another important prognostic factor. The four-tier WHO/ISUP (International Society of Urological Pathology) scoring system has replaced the traditional Fuhrman scoring system [17].

Surgery, including radical nephrectomy or partial nephrectomy is the recommended treatment for localized RCC [2,18]. The elderly and patients with comorbidities and incidental small renal masses have low RCC-specific mortality and significant competing cause mortality, therefore ablative techniques and active surveillance may represent alternative treatment options [2,18,19, 20]. Active surveillance defined as early monitoring of tumor size by serial imaging, with delayed intervention provided for tumors that show clinical progression during follow-up, is a safe management option, not compromising oncological outcome [2, 18, 21, 22].

Imaging is essential in the diagnosis and characterization of renal masses, providing valuable information regarding staging, prognosis, therapeutic management, and follow-up [7, 8, 9, 23, 24, 25]. US can easily characterize most incidental renal masses as simple cysts, but cannot always differentiate between benign and malignant solid renal tumors [26]. Contrast-enhanced ultrasonography (CEUS) has emerged as a valuable adjunct tool, useful in the differential diagnosis between solid renal masses and pseudotumors, and between complex renal cysts and solid renal tumors [26, 27, 28, 29]. CT is the gold standard for characterization of renal masses and for staging RCC [14, 30]. Multiparametric MRI (mpMRI) is a useful adjuvant tool in the armamentarium diagnosis of renal masses [31, 32].

In this review, we comment on the role of multimodality imaging, including US, CEUS, CT and mpMRI in the management of renal masses. In particular, the role of imaging modalities in the characterization of cystic renal masses, differentiation between the histologic phenotype of RCC and common benign renal tumors, assessment of RCC, staging of RCCs and follow-up of treated or untreated local RCCs were reviewed. The role of minimally invasive, image-guided RCC curative management is discussed. A urologist's perspective on the requirements regarding radiological reports of renal masses is presented.

2. What urologists expect from radiologists

Despite the reported excellent sensitivity and specificity for cross-sectional imaging in detecting, occasionally, small (<2cm) renal masses, usually endophytic renal tumors may be missed [33]. Potential implications for the treating urologist may exist, if the radiological report misses the diagnosis.

The probability of a renal mass becoming malignant is inversely proportional to its size. As more than 50% of newly diagnosed renal masses are less than 3cm in size, it is clear that the urologist wants to confirm the histology of the mass, before deciding on treatment. Unfortunately, histologic characterization based on imaging criteria alone is not always possible. Understandably, this is a difficult task, as even renal tumor biopsy can be nondiagnostic in up to 8% of cases, in centers of excellence [33]. Fat-poor AML, small papillary RCC, and renal oncocytoma pose diagnostic challenges for radiologists and pathologists.

Imaging is cardinal for staging RCC. Table 1 shows theRCC classification system *Tumor-Node-Metastatic* (TNM)[2, 15]. The upper border of the inferior vena cava neoplastic thrombus guides the operation, as a thrombus reaching the thorax and heart requires a cardiothoracic surgeon and special anesthetic requirements. Precise mapping of regional lymph node extension will help the surgeon remove palpable lymph nodes. Removal of the ipsilateral adrenal gland is possible if imaging implies invasion by a neighboring tumor. The number, size, and location of distant metastases will predict the technical feasibility of metastasectomy and help decide whether or not to proceed with cytoreductive nephrectomy [2].

Table 1. TNM RCC classification system [15]

T - Primary Tumor
TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
T1 Tumor ≤ 7 cm in greatest diameter, limited to the kidney
T1a Tumor ≤ 4 cm
T1b Tumor > 4 cm but ≤ 7 cm
T2 Tumor > 7 cm in greatest diameter, limited to the kidney
T2a Tumor > 7 cm but ≤ 10 cm
T2b Tumor > 10 cm, limited to the kidney
T3 Tumor extends into major veins or perinephric tissues, but not to the ipsilateral adrenal gland and not beyond Gerota's fascia
T3a Tumor grossly extends into the renal vein or its segmental (muscle-containing) branches, or invades perirenal and/or renal sinus fat, but not beyond Gerota's fascia
T3b Tumor grossly extends into inferior vena cava below diaphragm
T3c Tumor grossly extends into inferior vena cava above the diaphragm or invades the wall of the vena cava
T4 Tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)
N - Regional Lymph Nodes
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in regional lymph node(s)
M - Distant Metastasis
M0 No distant metastasis
M1 Distant metastasis

Although a tumor size of 4 cm is an acceptable limit for partial nephrectomy, other factors may allow partial resection of a larger tumor or dictate radical removal of a smaller tumor. Therefore, information regarding the relationship of the tumor to the collecting system, its surroundings to the renal hilus and the endophytic or exophytic nature of the tumor, may determine the difficulty of performing a partial nephrectomy. Imaging plays an important role in providing the above information, predicting the impending difficulties of the operation.

Various nephrometric scores (RENAL, Padua, c-index) have been used to measure this expected difficulty [34]. RENAL nephrometry score, assigning tumors to a score depending on points collected from (R)adius tumor, (E)xophytic/endophytic nature, (N)earness to the collecting system or sinuses, (A)interior (a)/posterior(p) descriptor, and (L)location relative to the polar line. Various publications have confirmed the correlation of KIDNEY nephrometry scores with surgical decision making, surgical complications, postoperative functional outcome, histological factors such as stage, grade, and cancer-specific survival rate [34].

During a partial nephrectomy, the kidney tumor must be identified and resected. This requires removal of perinephric fat, which can be tedious at times. Imaging can predict this difficulty by measuring perinephric fat thickness, particularly medial and posterior perinephric fat, and reporting perinephric fat stranding [35]. Equally important is the position of the kidneys in relation to the thoracic cage, especially for open surgery. Information regarding the vascular anatomy, and in particular, the origin, number, division, and course of the renal arteries and veins is also important [36].

Imaging provides the urologist with much of the information needed for treatment planning, therefore, radiology reports are invaluable and should be provided, preferably in a structured format (Table 2) [36].

Table 2. Recommended CT report templates for preoperative assessment of solid renal masses, suspected or proven to represent RCC [36]

Kidney unit with tumor
Nephrometry score
- Tumor radius (cm)
- Exophytic > 50%, Exophytic < 50%, Endophytic
- Distance to the collecting system [> 7, 4-7, < 4] (mm)
- Location: Anterior/Posterior (A/P/X)
- Location regarding to the Polar lines (above/below/cross/ between)
- Extension into renal vein

Extrarenal structures adjacent to the lesion (distance to the nearest anatomic structure and renal hilar vasculature)
Perinephric fat stranding
Amount of perinephric visceral fat [scant/abundant]
Extension of tumor into perirenal fat, pararenal fascia, adrenal gland
Kidney location [standard, high, low, ectopic]
Kidney size
Collecting system [standard, duplicated]
Vessels
- distance of main renal artery origin to the first branch and to the renal hilum
- accessory renal arteries
- length from inferior vena cava to right renal hilum
- length from aortic edge to the left hilum
- accessory renal veins

Parenchymal variant anatomy [standard, dromendary humb, fetal lobulation, column of Bertin, renal cleft, congenital fusion/rotation]
Benign pathology [cysts, stones/calcifications, scars, AML]
Contralateral kidney
Kidney size
Enhancement [normal, delayed]
Pathology [cysts, stones/calcifications, scars, AML]
Other
Regional lymphadenopathy [location, size, correlation with large vessels]
Distant metastases

3. Ultrasonography/Contrast-Enhanced Ultrasonography

Ultrasonography is the first-line imaging modality for investigation of suspected renal disease [26, 27, 28, 29]. US can reliably differentiate between cystic and solid renal lesions and can characterize complex minimally renal cysts [28]. US is recommended for the assessment of homogeneous indeterminate, hyperdense renal masses, incidentally found on CT, measuring 20-70HU on unenhanced images or more than 20HU on contrast-enhanced single-phase images [6]. These lesions often represent benign hemorrhagic/proteinaceous cysts and can be safely characterized by US, with reported sensitivity and specificity of 81.8% and 92.9%, respectively [27]. US also remains the primary imaging modality for the early detection and evaluation of solid renal tumors [28]. However, this technique is not always able to accurately differentiate between benign and malignant solid renal tumors [26,28,29].

CEUS with its lack of nephrotoxicity, absence of ionizing radiation, and ability to evaluate the pattern of enhancement, can accurately characterize many renal lesions, without the need for CT or MRI [26, 27, 28, 29]. The main renal applications include differentiation between solid and pseudotumor renal tumors, characterization of complex cystic renal masses, characterization of indeterminate renal masses and follow-up of non-surgically treated renal masses [29].

After injection of the ultrasound contrast agent, the renal arteries and main branches were elevated first, followed rapidly by the segmental, interlobar, arcuate and interlobular arteries. Subsequently, complete cortical enhancement was seen (cortical phase, 15-30 s), followed by medullary enhancement (parenchymal phase, in which the cortex and medulla increased homogeneously, 25 s-4 min). Since the ultrasound contrast agent is not excreted by the kidneys, no excretory phase is obtained [37, 38, 39, 40, 41].

CEUS is highly recommended to differentiate between renal and pseudotumor tumors (prominent Bertin column, dromedary or splenic hump, persistent fetal lobulation and adjacent areas of renal parenchyma with cortical scarring, showing compensatory hypertrophy), not characterized by conventional US, with an accuracy of up to 95% [26, 29]. The criterion for diagnosing a pseudotumor is the demonstration of the same pattern of enhancement as the surrounding parenchyma in all phases (Fig. 1) [26, 29, 41]. In contrast, enhancement of most solid renal tumors differs from that of the surrounding renal parenchyma, with differences in the degree or distribution of enhancement in at least one phase of

contrast enhancement [29, 41, 42]. Solid renal tumors do not show a specific perfusion pattern, therefore their accurate characterization by CEUS is often impossible [23, 40, 41, 43, 44, 45, 46].

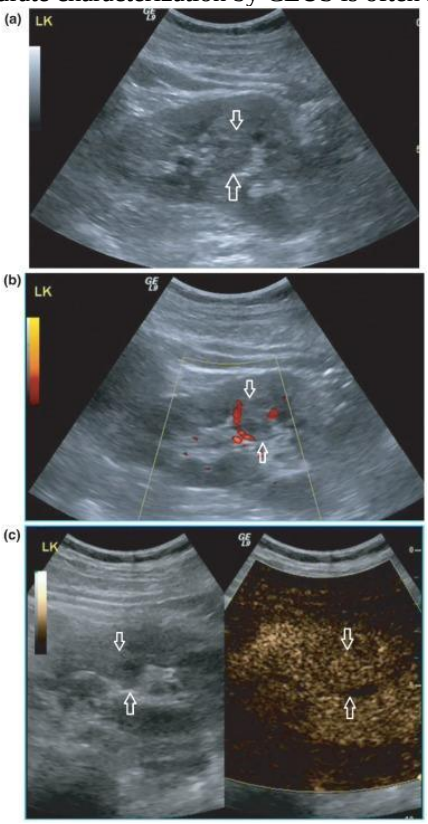

Figure 1. Sagittal (a) grayscale and (b) power Doppler images depicting a solid left renal lesion (arrows) in the interpolar region, mainly isoechoic, when compared to normal renal parenchyma. The mass seems to replace the surrounding blood vessels. After injection of ultrasound contrast agent (c) the lesion (arrow) shows the same enhancement as the remaining renal parenchyma, a finding indicating the presence of a renal pseudotumor. (Source: Dr. DD. Kokkinos).

CEUS can be used to characterize complex cystic renal masses, with accuracy comparable to CT and MRI and reports a concordance rate between the three imaging techniques of approximately 90% (Fig. 2) [26, 29, 47, 48, 49, 50, 51]. In addition, CEUS has been reported to be more sensitive than CT in demonstrating minimal wall and/or septal enhancement and solid, increasing components in complex cystic renal masses [26, 29, 51, 52]. CEUS is also recommended for non-surgical follow-up of complex cystic kidney lesions [26, 29, 53].

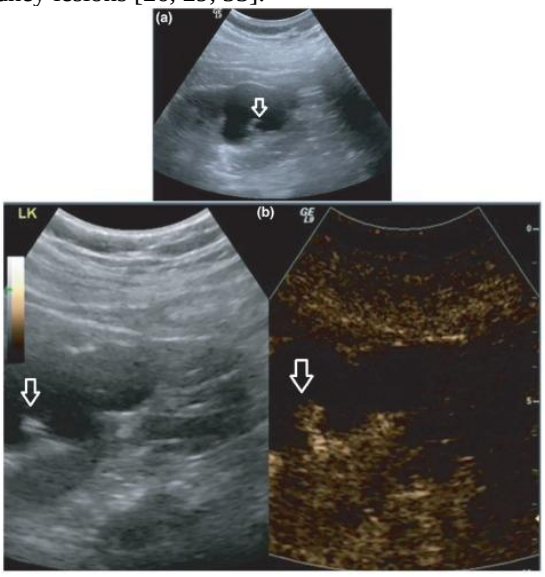

Figure 2(a) US Grayscale image showing a cystic lesion of the right kidney with irregular internal septal thickening (arrows). (b) The contrast-enhanced US display shows an increase in this section (arrows); therefore, the lesion was characterized as Bosniak class III. (Source: Dr. DD. Kokkinos).

CEUS has an important role in the characterization of indeterminate renal lesions, including avascular renal masses, without the typical US findings of simple cysts, complex renal cysts and masses with equivocal CT enhancement or indeterminate CT findings [6,26,27,28,29 ,54, 55, 56]. In a retrospective study, CEUS had a sensitivity of 100%, specificity of 95%, a positive predictive value (PPV) of 94.7%, and a negative predictive value (NPV) of 100% in the characterization of an indeterminate renal mass [55]. Follow-up CEUS is also recommended in this case [29].
CEUS can highlight renal vein invasion by RCC on initial evaluation, as arterial thrombus vascularity distinguishes soft thrombus from neoplastic, with sensitivity, specificity, PPV, NPV and accuracy reported of 83%, 96%, 71%, 98% and 94%, respectively. respectively [14, 27, 29, 57]. Finally, CEUS is helpful in post-ablation RCC follow-up, enabling detection of intralesional enhancement, indicative of residual or recurrent tumor, with sensitivity, specificity, PPV, NPV, and overall accuracy of 96.6%, 100%, 100%, 95.8 %, and 98.1%, respectively [18, 29, 58].

Table 3 main clinical indications for Color Doppler US and CEUS.

Clinical indications	**Color Doppler US Finding**	**Contrast-enhanced US Finding**
The differential diagnosis between solid kidney tumor and pseudotumor	may be non-specific	Renal tumor vasculature differs from normal parenchyma, at least in one phase post contrast/pseudotumor increases parallel to renal parenchyma in all phases
Characterization of solid kidney tumors	Often nonspecific Color Doppler has limitations in assessing neoplastic invasion of renal veins in RCC	Often nonspecific increased neoplastic renal vein thrombus/soft thrombus shows lack of enhancement
The difference between cystic and solid renal masses is a	limitation in assessing the possibility of perfusion in echogenic cysts	solid hypovascular renal tumors are increased, even slightly / debris not superior to CT/MRI in diagnosing cystic RCC
Characterization of complex cystic renal mass	limitations in assessing possible perfusion of septa and/or cyst nodules	depicting increased wall/septum and/or n odule accuracy equal to or higher than CT for the classification of cystic lesions of kidney, according to the criteria of Bosniak
RCC post-ablation	no role	to confirm the results of the treatment of the same accuracy with CT / MRI post-ablation area that enhances the contrast is considered tumor residual or recurrent

Nevertheless , the widespread use of CEUS in daily practice is questionable. Continuing training, experience, revising the Bosniak classification, additional research to include CEUS in clinical urology guidelines and new technologies, such as, fusion imaging can improve the diagnostic accuracy of the technique, ensure its safety, and confirm its role in the management of renal masses [59, 60, 61, 62].

4.Computed Tomography

Contrast-enhanced CT (CECT) represents the gold standard imaging technique for the detection and characterization of renal masses [1, 2, 3, 4, 5, 6, 7,23, 24, 25, 30, 63, 64, 65]. The renal CT protocol consists of an unenhanced phase, combined with one or more contrast phases, namely a corticomedullary phase (40−70sec), a nephrographic phase (100−120sec) and a delay-excretory phase (7−10min) [66].

The nephrographic phase is optimal for detection of RCC, as tumor contrast clearance becomes visible, against the homogeneously increasing renal parenchyma [30, 67, 68]. The corticomedullary phase can be helpful in subtypes of RCC, as clear cell RCC increases rapidly in this phase [66].
CECT is the modality of choice for evaluation of cystic renal masses [12, 13, 69, 70, 71, 72]. Table 4 shows the CT characteristics of a renal cystic mass based on the recent Bosniak classification [12, 13]. A homogeneous renal mass measured between -10HU and +20HU on unenhanced CT corresponds to a simple benign cyst, without the need for additional imaging. Homogeneous hyperdense lesion measuring more than 70HU on non-contrast CT, suggesting a benign hemorrhagic cyst or protein cyst [6]. Lesions, either homogeneous or inhomogeneous in the range of 20-70HU, are considered indeterminate and require further evaluation [6]. The most commonly used method to characterize indeterminate renal masses, including cystic and solid renal lesions, is CECT [5,6]. Increasing solid renal tumors or increasing components in the cystic renal mass (Fig. 3) are highly suggestive of malignancy [65]. A difference of at least 10HU between unenhanced and CECT has been proposed to differentiate renal cysts from solid masses [6]. However, more conservative values, such as 15-20HU are often used to calculate mean partial volume artifacts [73].

Table 4. Classification of Bosniak Cystic Renal Mass, Version 2019 [12,13].

Category	CT	Findings MRI Findings
I	cystic mass well-defined, homogeneous, watery density (-10 to +20 HU), smooth, thin walls (≤ 2mm) that may enlarge, absence of septa and/or calcification	of the well-defined cystic mass, homogeneous , hyperintense T2 signal, similar to cerebrospinal fluid, smooth, thin-walled (≤2mm) that may enlarge, absence of septa and/or calcification
	well-defined mass, smooth, thin-walled (≤2mm)	well-defined mass, smooth, thin wall (≤ 2mm)
	cystic mass, few (1-3) thin septa (≤ 2mm); walls and septa may increase; calcification of any type	of cystic mass, few (1-3) thin (≤ 2mm) contrast-enhancing septa or other non-enhancing septa; may contain calcifications of any kind
	hyperdense homogeneous mass (≥ 70HU) on homogeneous unenhanced CT	, very hyperintense T2 signal, similar to cerebrospinal fluid
	homogeneous nonenhancing mass > 20HU on CT renal mass protocol; may havecalcification	homogeneous, highly hyperintense fat suppression T1 signal, equal to or 2.5 times higher than normal renal parenchyma
II	homogeneous mass -10 to +20HU on non-enhanced CT homogeneous mass 21-30HU on portal phase CT homogeneous hypodense mass , too small to be characterized	
	cystic mass, smooth, minimal (3mm) thickening of walls and/or septa, or many (≥ 4) fine, thin increasing septa	of cystic mass, smooth, minimal (3mm) thickening of walls and/or septa, or multiple (≥ 4) smooth, thin increasing septa
IIF		cystic mass, T1 signal hyperintense heterogeneous fat suppression
III	cystic mass, thickened (≥ 4mm) walls and/or septa, or increased nodules: convex protrusions arising from walls and/or septa, thickened irregularly (≤ 3mm), with blunt margins	cystic mass, thickened (≥ 4mm) walls and/or septa, or increased nodules: convex protrusions arising from walls and/or septa, thickened irregularly (≤ 3mm), with margins blunt
I V	cystic mass, one or more increasing nodules: convex protrusion, arising from walls and/or septa, 4mm, with blunt edges,	cystic mass, one or more nodules increasing: convex protrusion, arising from wall and/or septa, 4mm,

or in various sizes, with pointed margins	with blunt edges, or in various sizes, with sharp edges

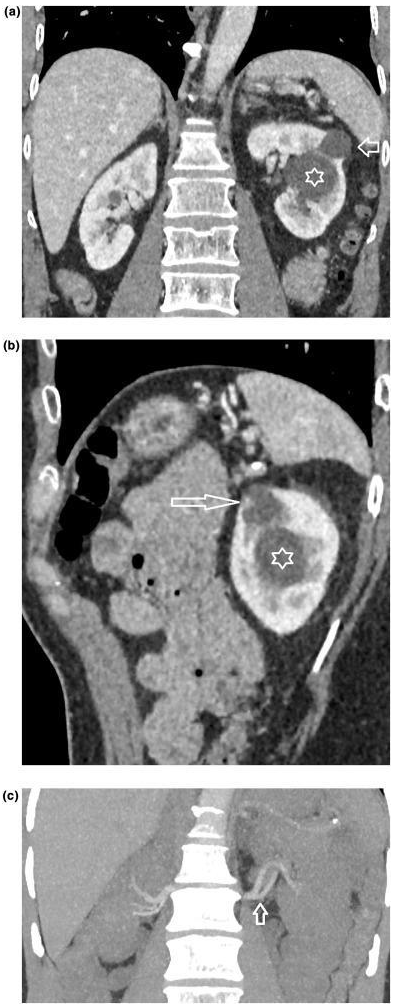

Figure 3. Clear cell RCC of left kidney. (a) Coronal and (b) sagittal contrast-enhanced CT images during the corticomedullary phase depicting a <50% exophytic left kidney cystic lesion (arrows), with a 5mm contrast-enhancing nodule (long arrow, b, Bosniak grade IV). Left simple benign renal cyst (asterisk). (c) Coronal three-dimensional maximum intensity projection reconstruction image showing the distance from the origin of the left renal artery to the first branch (arrows).

Since CT is considered the gold standard for detecting renal masses, the accuracy of the technique in detecting renal tumors is difficult, based on literature data [30,74,75]. In a small retrospective study (≤ 4cm) of indeterminate renal mass, the accuracy of CECT in predicting the diagnosis of RCC was 79.4% [74]. In addition, CT evaluation of small renal masses (≤ 1.5 cm) may be problematic, due to lesion pseudoenhancement and partial volume mean artifacts, which limit the assessment of contrast enhancement [76, 77, 78].

CT findings related to lesion homogeneity and enhancement pattern were reported to correlate with the histologic subtype of RCC [30,79, 80, 81]. The typical clear cell RCC was markedly increased in the corticomedullary phase (114±44 HU), with rapid washout in the nephrographic phase (66±24 HU) [30, 79]. Large clear cell RCCs are often heterogeneous, due to necrosis and/or cystic degeneration [79]. Papillary RCCs are usually small, homogeneous and hypovascular, with a weak increase in the corticomedullary phase, up to 20 HU [30,68]. No increase is seen in up to 25% of papillary RCC, and further evaluation with CEUS or mpMRI is suggested to verify the presence of an increasing solid tumor [30].

Chromophobe RCC and renal oncocytoma have similar histologic and imaging features [31, 32, 82, 83, 84]. Therefore, differential diagnosis is often difficult and histological exploration may be required (Fig. 4) [7, 31, 32]. Peripheral location, presence of a central stellate scar or increased spoke-wheel and inversion of segmental enhancement are common findings for both entities [7, 31, 32, 82, 83,

84, 85, 86, 87, 88]. Most fat-poor AML is hyperdense on unenhanced CT, increasing homogeneously after contrast administration [30,63]. However, differentiation between fat-poor AML and RCC with CT alone is often difficult and further evaluation by mpMRI, biopsy, or even surgical resection may be necessary [30,63,89, 90, 91].

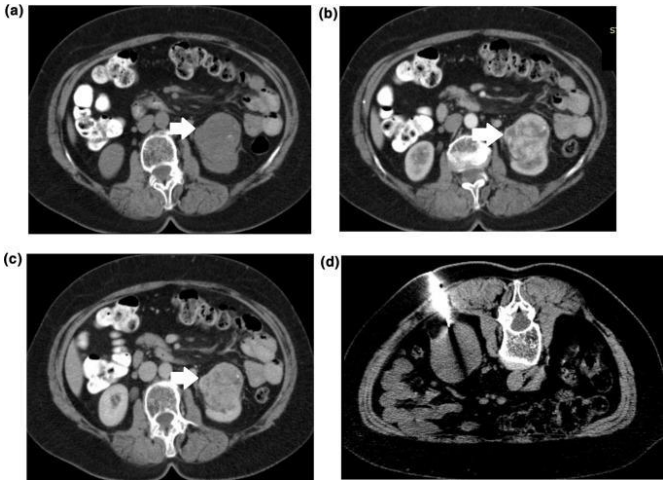

Figure 4. Clear cell RCC in women with a history of breast cancer. (a) Unenhanced axial CT shows a left renal mass (arrow). The lesion had a CT density especially similar to that of normal renal parenchyma and small calcifications. (b) In the corticomedullary phase, the lesion (arrow) shows strong and heterogeneous enhancement, with a washout effect in the nephrographic phase (c). (d) Kidney tumor biopsy revealed clear cell RCC.

Recently, dual-energy CT with contrast has been reported to improve the diagnostic performance of CT in the characterization of renal masses, with a sensitivity and specificity greater than 95% in the evaluation of renal tumors [92, 93]. New techniques, including CT perfusion, CT texture analysis and CT-based radiomics can provide important additional information in the characterization of renal masses [94, 95, 96, 97, 98, 99]

To date, multimodality imaging has not always been able to accurately characterize renal masses. found incidentally, primarily, a small renal mass (≤ 4cm) [100]. Percutaneous renal tumor biopsy has been shown to help avoid surgery in up to 33% of cases initially thought to be malignant, based on imaging [101]. Indications for renal tumor biopsy in local RCC include small renal masses, when the results may change management (Fig. 5) and masses with findings suggestive of lymphoma, metastases, infectious or inflammatory lesions [102]. Kidney tumor biopsy is also recommended prior to thermal ablation, as a separate procedure or shortly before treatment [102]. A biopsy can be performed under US or CT guidance.

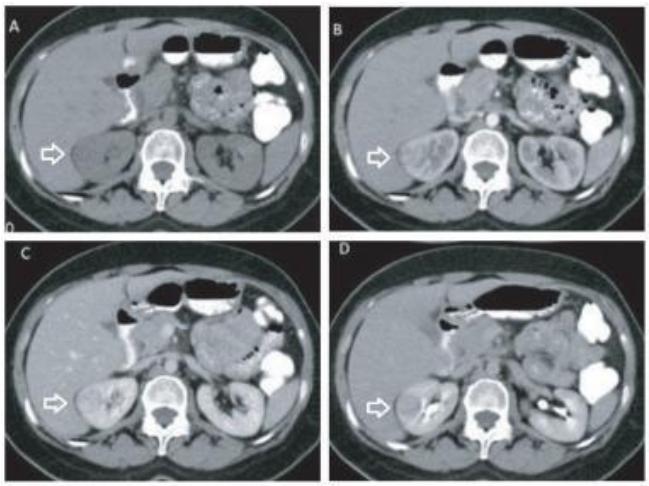

Figure 5. Incidence of kidney detected in US. (a) Unenhanced CT depicts a constricted renal mass (arrow) in the center of the right kidney. (b) An inhomogeneous pattern of enhancement (arrows) is seen in the corticomedullary phase. The lesion (arrow) has a subtle washout effect (c) in the nephrogenic

phase, becoming more intense (d) in the excretory phase. Kidney tumor biopsy showed renal oncocytoma.

CECT is widely accepted as the diagnostic modality of choice for staging RCC, with a sensitivity and specificity of up to 90% [2, 3, 4, 14, 103, 104]. The size of the RCC and the degree of local invasion determined the T stage (Table 1). Although, several studies have reported that CT often overestimates tumor size, compared to surgical specimens, the differences are minimal and clinically insignificant in most cases [105, 106]. Fatty invasion of the perinephric sinus or kidney is not always easily detected on CT [107]. Thin sections and multiplanar reforms have improved the detection of perinephric fatty infiltration, despite false positives, because inflammation, edema, vascular swelling, or fibrosis may be encountered [107, 108, 109]. CT is highly accurate in diagnosing the spread of RCC into the renal vein, with an NPV of 97% and PPV of 92% [14, 110]. CT is also effective in assessing the degree of superior inferior vena cava thrombus [111].

CT offers a high NPV in excluding involvement of adjacent organs outside of Gerota's fascia or involvement of the ipsilateral adrenal glands [14, 112, 113]. In a retrospective observational study, CT had 100% sensitivity, 95.2% specificity and 100% NPV in diagnosing adrenal gland invasion [113]. However, CT is not always able to distinguish abutments from direct invasion [14].

CT tends to overdiagnose lymph node spread, which is defined as lymph nodes with a short axis diameter greater than 1cm and abnormal lymph node architecture. However, based on size criteria, CT has 10% false negatives, whereas approximately 50% of enlarged lymph nodes prove to be benign [14,114]. Distant metastases from RCC are frequently found in the lung, bone, liver, and brain and less frequently in the thyroid, pancreas, muscle, skin, and soft tissues [14, 115]. Chest CT is useful for detecting pulmonary and mediastinal lymph node metastases and is especially recommended in large RCCs [14]. Visceral metastases tend to be hypervascular and the corticomedullary phase can help detect arterial elevation [14, 115].

Multiplanar reform and three-dimensional reconstruction are helpful in preoperative planning, providing important anatomic information, such as the position of the kidney relative to surrounding bone, tumor location and depth of extension to the kidney, relationship of the tumor to the renal collecting system, and accurate depiction of the anatomy of arteries and veins [116]. , 117] Preoperative CT also provides information about the morphology and function of the contralateral kidney. Synchronous primary tumors should be sought, as RCC can be multifocal [14].

CT is indicated for follow-up of RCC after surgery or post-ablation, in patients at moderate to high risk [18]. Basic chest and abdominal CT within three to six months after surgery is recommended, followed by imaging every six months for at least three years and annually thereafter, for two years [118].

5. Multiparametric MRI Multiparametric

MRI is a valuable complementary imaging technique for the assessment of renal masses, providing morphological and functional information [5, 6, 7, 12, 13, 14, 18, 31, 32]. MRI is especially recommended when optimal CT cannot be performed (severe allergy to iodinated CT contrast or high risk for contrast-induced nephropathy) or when radiation exposure is contraindicated (young age or pregnant women) [5, 6, 7,12, 13, 14, 18, 31, 32]. However, gadolinium-based MR agents should be administered with caution during pregnancy, only if there is a very strong clinical indication and the potential benefit justifies the potential unknown risk to the fetus [119]. When iodinated CT contrast and gadolinium-based MR agents cannot be used, MRI without iv contrast is highly recommended for renal mass characterization, RCC staging and follow-up (Fig. 6) [5, 6, 12, 13, 14, 18].

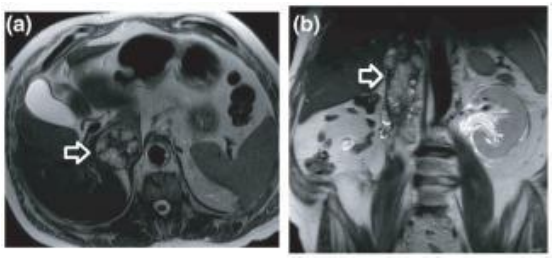

Figure 6. Unenhanced follow-up MRI in a patient with renal failure and a history of right radical nephrectomy, due to RCC. T2-weighted imaging in (a) axial and (b) coronal planes demonstrates a neoplastic thrombus (arrows) into the inferior vena cava.

The renal MRI protocol includes the following sequence: T1-weighted with deep-phase and counter-phase imaging (or the DIXON technique), T2-weighted, diffusion-weighted (DWI) imaging, dynamic contrast-enhanced and delaying, T1 post- contrast-weighted imaging [120].

Although CT and MRI have similar accuracy in characterizing cystic renal masses, mpMRI may show additional findings, such as more septa, wall and/or septal thickening and contrast enhancement, which may result in lesion enhancement (Table 4) [5,6, 12,121] , 122, 123, 124]. MRI, because of its advantages over CT, namely decreased sensitivity to calcification, increased sensitivity to enhancement and the absence of pseudoenhancement, can provide additional diagnostic information in the assessment of renal cystic masses, with abundant thick or nodular calcifications on CT, hyperdense, homogeneous non-enlarging tumor renal, larger than 3cm and heterogeneous, non-enhancing mass on CT [12,13].

CT, MRI and CEUS represent equivalent alternatives for the initial assessment of an indeterminate renal mass [6]. MRI is especially recommended for the assessment of solid renal masses with inconclusive CT findings, especially those smaller than 1.5 cm [5,6,125,126].

Multiparametric MRI features, including T2 signal, chemical shift imaging characteristics, apparent diffusion coefficient (ADC) signal, early enhancement pattern and de-enhancement aid in the characterization of solid renal tumors (Table 5) [7,31, 32, 63,127, 128, 129]. Clear cell RCCs are often large and heterogeneous, with high T2 and ADC signals, and early, strong heterogeneous increases, followed by rapid decreases (Fig. 7) [7,31, 32, 63,127, 128, 129, 130, 131 , 132]. Tumor pseudocapsules are frequently detected as a low T2 signal halo around the neoplasm (Fig. 7b) and suggest renal disease [133]. Multiparametric MRI has a sensitivity and specificity of up to 92% and 83%, respectively, in the diagnosis of clear cell RCC [32].

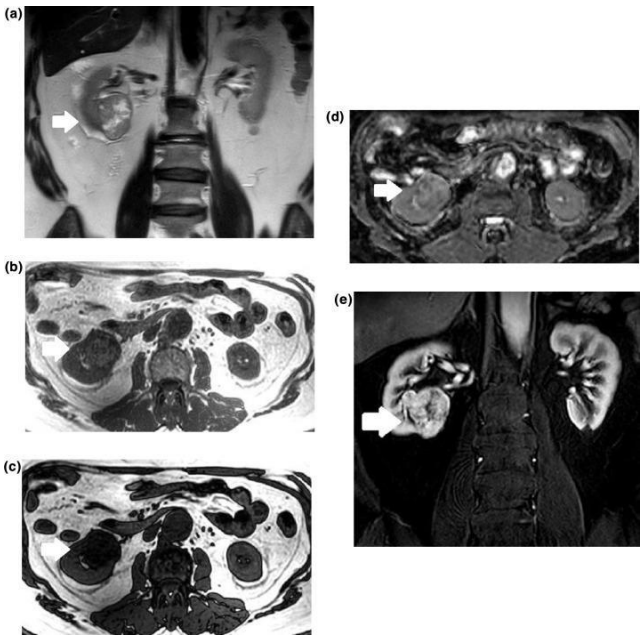

Figure 7. (a) Coronal T2-weighted image depicting a heterogeneous right lower polar renal mass (arrows), with a high T2 signal. A hyperintense central intratumoral area is seen, due to necrosis. The tumor is surrounded by a low T2 signal halo, corresponding to the pseudocapsule, in pathology. Axial images of (b) deep phase and (c) opposite phase T1 show decreased signal (arrow) on opposite imaging, due to the presence of intratumoral fat. (d) Axial ADC map (b = 600s/mm2). The mass (arrow) has a signal similar to that of the surrounding renal parenchyma. (e) Coronal-reduced dynamic contrast-enhanced image showing a strongly and heterogeneously enhanced tumor (arrow).

Papillary RCCs are often small, peripherally located, with low T2 and ADC signals and a slow, progressive increase. Intratumoral hemorrhage is frequently detected, either as a hyperintense T1 area or as a signal reduction on phase imaging, corresponding to prolonged or chronic bleeding [31,32,68,134, 135, 136, 137] . A recently published retrospective study of 109 resected small renal tumors reported a diagnostic accuracy of 81% and 91% in the characterization of clear cell RCC and papillary RCC, using mpMRI, respectively, with moderate to substantial inter-reader agreement among seven radiologists [135]. Chromophobe RCC typically have a medium to low T2 signal, low ADC when compared to clear cell RCC, and, initially, an intermediate increase, followed by a gradual decrease [31, 32, 82, 134].

Multiparametric MRI often allows the characterization of lipid-poor AML, with a sensitivity and specificity of up to 100% and 89%, respectively [31]. Fat-poor AML is characteristically small, homogeneously hypointense on T2-weighted imaging and ADC maps, with avid, baseline enhancement and rapid washout. Intratumoral fat is seldom detected, as the signal decreases on opposite-phase imaging [31,134,138]. Common mpMRI findings of renal oncocytoma include: peripheral location, moderately high T2 signal, high, strong ADC, early elevation and gradual decline [31,32, 139].

Results on the efficacy of DWI in the characterization of solid renal masses are conflicting, with significant ADC overlap among the different histologic subtypes. However, DWI can be used to predict the histologic grade of RCC, with limited diffusion often seen in high-grade clear cell RCC, when compared with low-grade tumors [140, 141, 142, 143, 144, 145].

A variety of new MRI techniques, including intravoxel incoherent motion, diffusion kurtosis, texture analysis, arterial loop labeling, MRI and radiomics dependent on blood oxygenation levels have been introduced for characterization of renal masses, evaluation of RCC aggressiveness, and assessment of treatment response, although validation is required [146 , 147, 148, 149, 150, 151]. In addition, investigation of the biochemical environment of the renal mass by additional proton MR spectroscopy can aid in lesion characterization [152].

CT and MRI represent equivalent alternatives for staging RCC, with similar diagnostic performance [14]. MRI can provide additional information in cases with uncertain CT findings, particularly when assessing perinephric fat infiltration, extension of a neoplastic thrombus into the renal vein and/or inferior vena cava, and possible invasion of the inferior vena cava wall by RCC thrombus [14,153] , 154].

Both CT and MRI perform well in postoperative or post-ablation RCC follow-up, with high accuracy in detecting local recurrence and/or distant metastases [18]. In low-risk RCC, MRI can be used as the main modality for follow-up, in the absence of radiation exposure [[2]]. When intravenous contrast is contraindicated, follow-up MRI without iv contrast is recommended (Fig. 5) [18]. CT, MRI and CEUS are usually recommended for active surveillance of local RCC [18].

6. Minimally Invasive RCC Curative Management, image-guided

Advanced RCC has a clear management pathway consisting primarily of radical nephrectomy or palliative treatment. Management of small, early-stage, asymptomatic, sporadic RCC is slightly more complex, given the unpredictable behavior of the lesions. The general consensus is to assess growth patterns with active surveillance. When treatment is considered, open or laparoscopic partial nephrectomy appears to be the standard approach, aiming to preserve as much of the healthy parenchyma as possible.

Interventional Oncology may offer another minimally invasive locoregional treatment for such patients with percutaneous image-guided ablation [19], [20, 155]. Percutaneous ablation is a form of treatment used in a number of other organs [156]. The technology initially applied for ablation of renal tumors was radiofrequency [157]. This approach is fueled by the need to treat patients who are poor surgical candidates or who have limited life expectancy for other reasons with effective minimally invasive procedures. Radiofrequency thermal effects are based on high-frequency electric currents which cause oscillations of tissue molecules and generate heat [158]. When the temperature exceeds 60 ° C, the tissue is destroyed. This technology is now established in the treatment of small renal masses, with excellent long-term results [159, 160]. Cryoablation is another established modality for the percutaneous image-guided treatment of RCC. The physical principle of cryoablation is based on the Joule-Thompson principle which describes the decrease in temperature after the rapid expansion of Argon. The lethal effect of cryoablation is based on direct cellular damage caused by osmotic cellular dehydration due to extracellular freezing and due to intracellular ice formation [161]. Percutaneous cryoablation also offers excellent long-term results in the management of small renal masses [162, 163]. Furthermore, microwave ablation was recently introduced in the treatment of percutaneous RCC and has yielded some encouraging results [164]. Microwave is based on the use of electromagnetic waves that cause continuous rotation of tissue water molecules. The uneven distribution of electric charge of water molecules causes continuous reorientation in the oscillating field; this movement increases its kinetic energy and is stored in the tissues as heat energy [164].

Minimally invasive percutaneous ablation has an important role in patients with multiple bilateral synchronous RCC, such as in von-Hippel-Lindau syndrome (VHL) [165]. Another group of patients who may benefit significantly from percutaneous ablation are patients who undergo nephrectomy and develop a new RCC or metastatic lesion in the contralateral kidney or those who develop an RCC in the single-functioning kidney [166]. For such patients, percutaneous ablation offers a valid tumor control solution, with preservation of renal function [166, 167, 168].

Although at least three ablation modalities are used for the locoregional treatment of percutaneous RCC, there is no evidence of the superiority of any of the three to date regarding complications, postprocedure renal function testing, local tumor progression, or cancer-specific survival [169, 170, 171, 172, 173].

One of the main advantages of percutaneous ablation is that the level of sedation can be individually adjusted and can be performed safely under moderate sedation, monitored anesthesia, or if needed, general anesthesia. [20,174]]. The decision to proceed needs to be obtained through a multidisciplinary meeting. The interventional radiologist should consult with the patient prior to the procedure, to discuss the risks and benefits of the procedure, anesthetic options and to assess the patient's fitness. Anticoagulation should be discontinued, according to standard percutaneous procedures and in the case of Warfarin, bridging with heparin is necessary [175].

Imaging guidance can be performed with a variety of modalities including US, CT, MRI, PET, CT-fluoroscopy, or cone-beam CT. Decisions regarding imaging guidelines should take into account patient factors, availability, cost, radiation dose, and operator preferences. A navigation system has also been developed, which offers more accurate needle placement and can also predict the area of ablation [176] (Fig. 8). The patient will usually be admitted to the hospital on the day of the procedure, will be transferred to the post procedure ward for overnight observation and discharged the next morning, aiming for a stay of less than 24 hours in the hospital. While the patient is in the CT room, premedication with 1000mg of intravenous Paracetamol is given and then, conscious sedation is given with 1−4mg of Midazolam and 50-200 micrograms of Fentanyl, just prior to ablation [20, 174].

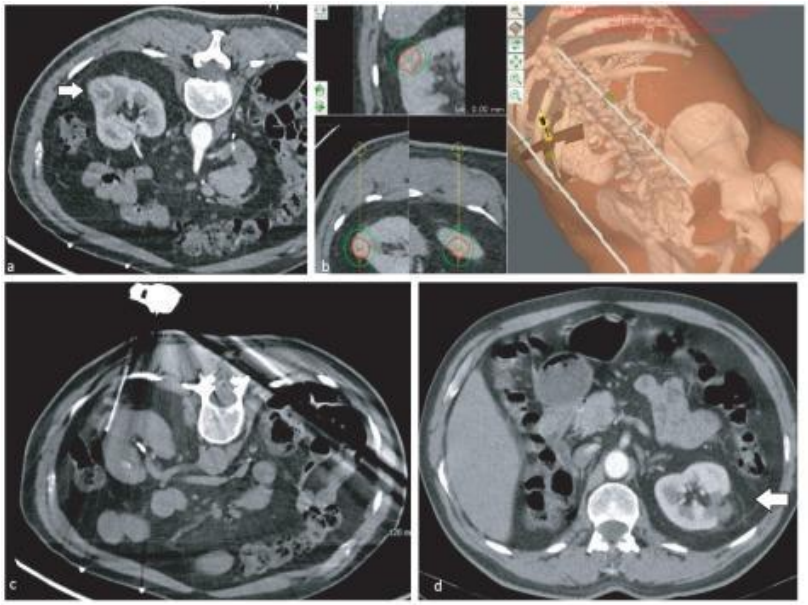

Figure 8. CT-guided percutaneous ablation of a small endophytic left renal tumor in a male previously diagnosed with clear cell RCC of the contralateral kidney, treated by radical nephrectomy. Five years later, he showed a new primary left kidney mass of 1.7 cm. Kidney tumor biopsy confirmed clear cell RCC of the left kidney. After the Multidisciplinary Team Meeting, the decision to proceed with lesion ablation was made. (a) CT scan with axial contrast in the corticomedullary phase confirming the position of the small left renal endophytic lesion (arrow). (b) A CT-guided navigation system (CAS-OneÒIR, CASCINATION AG, Bern, Switzerland) was used to target the tumor and predict the area of ablation (green circle). Navigation is helpful in such cases, as the lesions are difficult to target, due to their small size and endophytic growth. (c) RFA electrodes are inserted, and ablation is performed for 12 minutes. (d) Follow-up contrast-enhanced CT in the corticomedullary phase six months later confirmed satisfactory ablation of the area, with lack of enhancement and the presence of a “halo” sign (arrow). Satisfactory results were also confirmed in five years of follow-up, with preservation of renal function.

A biopsy of the renal lesion should be performed, prior to ablation in all cases. Usually this is obtained before any discussion in the Multidisciplinary Team Meeting (MDT) for sporadic lesions. For patients with VHL or patients with known contralateral tumors, no biopsy is required prior to MDT discussion and the lesion is biopsied before ablation in the same session. In such cases, the biopsy should be performed via a coaxial system that will also be used as an access electrode, as post-biopsy bleeding may limit delineation of the lesion boundaries [177].

In cases of proximity to the bowel, hydro dissection with a non-ionic solution should be considered, via a thin needle, to replace the bowel and to isolate the lesion [178].

Follow-up with three-phase CT is required four weeks after ablation, to assess whether there is any residual enhancing tissue. In case of incomplete ablation of the lesion, a second session is required as soon as possible. If the results of ablation are satisfactory, with no lesion enhancement, then follow-up with three-phase CT at six and 12 months is required, and annually thereafter, for a total of five years [179, 180, 181].

Ablation offers excellent long-term oncological outcomes in the treatment of locoregional RCC and should be offered to any patient with tumors up to 4cm in diameter. More specifically, the reported primary efficacy for the treatment of T1a tumors ranged from 94.4–98.2%, with secondary efficacy ranging from 98.5%–99.1% [159, 162, 182].

7. Conclusion

Renal masses are increasingly being detected in asymptomatic individuals, as an incidental finding on cross-sectional imaging. Multimodality imaging, including US, CEUS, CECT and mpMRI plays an important role in the detection and characterization of renal masses, staging of RCCs and follow-up of surgically treated or untreated RCCs. Conventional US often represents the first-line imaging tool for the assessment of renal pathology. This technique can accurately characterize simple renal cysts and minimally complex cysts. CEUS has emerged as a powerful adjunct tool for the characterization of renal masses. Well-established applications of CEUS include differentiation between solid and pseudotumor renal tumors, characterization of complex cysts and indeterminate renal lesions and follow-up of renal masses not treated surgically. CT is the examination of choice for assessment of an indeterminate renal mass, RCC staging and follow-up, in moderate and high risk patients. Multiparametric MRI is a useful adjunct in the management of renal masses, particularly when indicated when optimal CT cannot be performed (history of allergy or renal insufficiency) or when ionizing radiation is contraindicated (young age or pregnancy). This technique can provide additional useful information in the characterization of solid and cystic renal tumors, particularly small renal masses. MRI is also recommended for follow-up of low-risk RCC.

Percutaneous image-guided ablation is an effective therapy for localized RCC, with acceptable outcomes. Main indications include management of small renal masses (≤ 4cm), multiple RCCs (eg, in VHL syndrome) and RCCs in solitary kidneys.

A structured template, including a nephrometric score and associated additional CT or MRI findings for reporting solid renal masses, greatly assists clinicians in planning appropriate treatment.

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