Published in final edited form as:

Urol Clin North Am. 2018 August ; 45(3): 311–330. doi:10.1016/j.ucl.2018.03.013.

Imaging of Solid Renal Masses

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Abstract

The increase in serendipitous detection of solid renal masses on imaging has not resulted in a reduction in mortality from renal cell carcinoma. Consequently, efforts for improved lesion characterization have been pursued and incorporated into management algorithms for distinguishing clinically significant tumors from those with favorable histology or benign conditions. Although diagnostic imaging strategies have evolved for optimized lesion detection, distinction between benign tumors and both indolent and aggressive malignant neoplasms remain an important diagnostic challenge. Recent advances in cross-sectional imaging have expanded the role of these tests in the non-invasive characterization of solid renal tumors. This article reviews the current role of cross-sectional imaging in the characterization of benign and malignant solid renal masses.

Keywords

Renal cell carcinoma; Lymphoma; Angyomiolipoma; Renal oncocytoma; Ultrasonography; X-ray computed tomography; MR imaging; Image-guided biopsy

Introduction

The incidence of renal cancer increased from 7.1 to 10.8 cases per 100,000 patients between 1983 and 2002, with most primary tumors initially diagnosed as incidental small renal masses (ie, measuring < 4 cm) on imaging studies performed for other clinical reasons.(1) Paradoxically, this increase in diagnosis has not been associated with better clinical outcomes, with a reported increase in mortality from 1.5 to 6.5 deaths per 100,000 patients within the same time interval.(1) Furthermore, most incidentally detected tumors either grow

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slowly(2) or do not show detectable growth over time.(3, 4) Therefore, cost-effective strategies are necessary to identify clinically significant renal masses that could evolve into life-threatening disease, while avoiding the unnecessary morbidity and financial costs associated with overtreatment of benign or more indolent malignant conditions.

The first step in the workup of incidentally found renal lesions is to differentiate benign cysts from solid masses.(5, 6) Solid renal masses contain little or no fluid, and are composed predominantly of vascularized tissue (i.e., elements enhancing with the administration of exogenous contrast agents).(6) Despite their lower prevalence compared with cystic lesions, up to 90% of solid masses are malignant.(7–9) The risk of malignancy is influenced by size, occurring in approximately 50% for lesions smaller than 1 cm and more than 90% for masses greater than or equal to 7 cm.(7)

Solid malignant masses most frequently encountered in clinical practice are renal cell carcinoma (RCC), urothelial carcinoma, lymphoma, and metastasis, whereas the most frequently encountered benign solid renal masses are angiomyolipoma (AML), oncocytoma, and inflammatory pseudotumors or pseudolesions. This article provides a comprehensive imaging approach to common malignant and benign solid renal masses on state-of-the-art ultrasonography (US), computed tomography (CT), and multiparametric MR imaging, proposing strategies to differentiate benign from malignant lesions, and to distinguish RCC subtypes.

Malignant Lesions

Cancer arising in the kidney and renal pelvis accounts for 5% of all malignancies in men and 3% of malignancies in women.(10) RCC is more common among men (1.6:1, M:F). Patients with localized disease have a reported 93% 5-year survival, whereas this rate decreases to 66% and 12% for those with regional and distant metastasis, respectively.(10)

Renal cell carcinoma—The World Health Organization classification subdivides RCC into different histologic groups,(11) with clear cell RCC (ccRCC) accounting for 70% to 75%, papillary RCC (pRCC) for 10% to 21%, and chromophobe RCC (chrRCC) for 5% of all RCC cases.(11, 12) Survival heavily depends on staging, histologic grade (ie, Furhman/International Society of Urological Pathology), presence of sarcomatoid features, and necrosis. In addition, ccRCC is associated with worse prognosis than pRCC and chrRCC. (11, 13) Different histopathologic subtypes have distinct features on imaging studies and these are discussed later.

Urothelial carcinoma—Urothelial carcinoma originates from the epithelium of calyces and renal pelvis and may comprise up to 15% of all renal tumors.(14) Median age at diagnosis is more than 60 years, with an approximately 2:1 M/F ratio, and hematuria is the most frequent symptom at presentation.(14, 15) Synchronous and metachronous involvement of the urinary tract may occur in 24% and 11% of patients with renal urothelial carcinoma, respectively.(15) Differentiation of upper-tract urothelial carcinoma from RCC and other solid renal masses is simpler during earlier stages, when the presentation is characterized by wall thickening of the urothelial tract or filling defects in the collecting

system. Infiltrative masses in the renal sinus or parenchyma are features of advanced disease, in which distinction from aggressive forms of RCC is difficult.(16)

Lymphoma—Lymphomatous involvement of the kidneys is most frequently the result of secondary spread of non-Hodgkin disease, with prevalence at autopsy reaching 50% in this population.(17) Renal lymphoma may present as multiple masses, solitary lesions simulating RCC, retroperitoneal/perirenal disease, and infiltrative renal disease. A pattern of multiple renal masses is encountered in up to 60% of the patients, typically ranging from 1 to 3 cm, with homogeneous attenuation (CT) or signal intensity (MR imaging), and low-level postcontrast enhancement compared with background parenchyma (Figure 1).(18) Contiguous involvement of the kidneys by bulky retroperitoneal disease is another common presentation of lymphoma on imaging.(18) Solitary lesions occur in 10% to 20% of the patients, and although differentiation from ccRCC may be possible because of the characteristic homogeneous signal/attenuation and low-grade enhancement of lymphoma, biopsy may be needed to discriminate from non-ccRCC subtypes, especially papillary tumors.

Metastases—The reported prevalence of metastatic disease to the kidneys in oncological patients differs depending on the method of assessment, varying from 20% on autopsy studies to less than 1% in clinicopathologic studies.(19) Commonly, the primary tumor is already known or diagnosed at the same time as the renal lesion, with more than half of the cases occurring in patients older than 60 years.(19) The most common primary sites are lung, breast, female genital tract, head and neck, colon, and prostate. Bilateral or multiple masses are found in 23% and 30% of the patients, respectively.(19) Renal metastases occur more commonly at the junction of the renal cortex and medulla, often showing ill-defined borders and low-level enhancement, except in the case of hypervascular primary tumors (eg, RCC, thyroid, choriocarcinoma). These features may help to suggest the diagnosis, and differ from the most common well-defined appearance of cortical-based RCCs, although a definitive diagnosis may require a biopsy.

Benign Lesions

The reported prevalence of benign histology is 13% to 16% of all surgically resected renal masses.(7, 9) The likelihood of benign histology in small solid renal masses is influenced by size, with a prevalence of up to 40% in lesions less than 1 cm in diameter.(20) AMLs and oncocytomas comprise most of the benign solid masses, representing 44% and 35%, respectively.(9)

Angiomyolipoma—AMLs are benign neoplasms, consisting of aberrant blood vessels, smooth muscle, and mature adipose tissue,(21) representing 2% to 6% of all resected tumors in surgical series.(22, 23) Most of these neoplasms are found incidentally on imaging (eg, 0.1%–0.2% of US examinations), with a female preponderance (1:2, M/F).(24) AMLs can occur sporadically or in association with genetic syndromes. AML prevalence in patients with tuberous sclerosis vary from 55% to 90%, and in patients with lymphangioleiomyomatosis from 30% to 50%.(21) Larger AMLs may cause symptoms and

spontaneous hemorrhage (Wunderlich syndrome), a life-threatening complication in larger tumors.(25)

The detection of fatty tissue (i.e., adipocytes) by CT or MR imaging is regarded as the most specific feature for this diagnosis, although many pathologically proven AMLs do not show fatty tissue on imaging, causing a diagnostic challenge.(26) The diagnosis of classic and AML with minimal or absent fat is discussed later.

Oncocytoma—Oncocytomas are relatively uncommon cortical tumors (approximately 7% of renal masses in surgical series) composed of oncocytes (polygonal or round cells, with moderate to abundant granular cytoplasm) surrounded by thin capillaries and stroma.(27) Patients are usually asymptomatic, being more frequently men (1.2:1, M/F), with a mean age of 65 years at diagnosis. Intratumoral hemorrhage and central scars are present in 20% and 33% of all oncocytomas, respectively, and multifocality may occur in 13% of the patients. (27) Although oncocytomas are classified as benign tumors,(11) case reports have described malignant potential.(28) Similarly, aggressive local behavior may manifest with intravascular extension into branches of the renal vein(29) and invasion of the perinephric fat, the latter occurring in up to 7% of all oncocytomas (Figure 2).(30)

Inflammatory conditions and pseudotumors—A variety of non-neoplastic conditions may mimic solid renal masses. Developmental renal pseudotumors (e.g., prominent columns of Bertin, dromedary humps, persistent fetal lobulations) are easily differentiated from true renal masses by the delineation of normal renal parenchyma imaging features in the suspicious region (e.g., on multiphasic dynamic contrast-enhanced imaging). However, other conditions such as infectious, inflammatory, and granulomatous diseases (e.g., pyelonephritis/abscess, xanthogranulomatous pyelonephritis) may pose a significant diagnostic challenge.(31) Interpretation of the imaging findings in the appropriate clinical context is crucial, because focal or multifocal pyelonephritis is usually accompanied by characteristic symptoms, such as chills, fever, flank pain, and pyuria. US-Doppler and contrast-enhanced CT or MR may show single or multiple hypoperfused wedge-shaped areas, extending from the papilla to the cortex. Perirenal inflammatory changes are common. (32) Xanthogranulomatous pyelonephritis can also present as renal masses in patients with flank pain and fever, and is more commonly observed in middle-aged women with urinary stones, infection (most common by *Escherichia coli* and *Proteus*), and/or congenital anomalies.(33, 34) This disease is characterized by destruction of the normal renal architecture, enlarged kidney, contracted pelvis, staghorn calculus, and perinephric inflammatory changes.(32)

Imaging techniques

Ultrasonography—US is generally the first line imaging modality for patients with suspected renal disease given its lower cost, wide availability, and lack of ionizing radiation. There is no current role for RCC screening with US in the general population. The prevalence of incidental renal masses in asymptomatic individuals undergoing US is about 0.4%, with half of the cases resulting in RCC.(35) US is indicated in the evaluation of upper urinary tract symptoms and in the workup of indeterminate renal masses (American College

of Radiology [ACR] Appropriateness Criteria rating 8).(36) It has been favored over non-enhanced MR imaging and CT in patients with contraindications to intravenous contrast, with lower sensitivity in the detection of small lesions compared with contrast-enhanced CT. (37–39) US is not indicated to stage renal cancer (ACR Appropriateness Criteria rating 3). (40)

Characterization of cystic renal lesions is most frequently straightforward on US, although the appearance of complex cystic masses and solid lesions may overlap. Simple renal cysts are anechoic structures with positive through-transmission and refraction along the sidewalls, showing sharp and smooth walls.(41) Cysts with hemorrhagic or protein contents may harbor internal echoes or debris. Harmonic imaging can minimize reverberation artifacts related to so-called dirty echoes, facilitating the distinction of cysts from solid masses.(42, 43) As with other imaging techniques, the detection of blood flow on Doppler, or lesion enhancement after intravenous contrast injection, represent unequivocal evidence of a solid mass.(44)

Computed Tomography—The most commonly used method to evaluate indeterminate renal masses is contrast-enhanced CT (ACR Appropriateness Criteria rating 9).(36) It is also considered the method of choice to stage RCC (ACR Appropriateness Criteria rating 9),(40) with high accuracies in both early and advanced stages.(45) A CT protocol for evaluation of renal masses is proposed in Table 1.

The sensitivity of CT for small renal masses is higher than 90%,(37) approaching 100% for lesions larger than 2 cm.(38) An advantage of CT compared with US and MR imaging is the ability to characterize lesions in Hounsfield units (HU), a quantitative standardized x-ray attenuation scale. Differences of at least 10 HU between precontrast and postcontrast CT images have been historically proposed as cutoff values to differentiate solid masses from renal cysts.(46, 47) More conservative values, such as 15 to 20 HU, have been used in clinical practice to account for volume averaging artifacts and misregistration among acquisitions.(48) Similarly, enhancement of adjacent renal parenchyma may cause pseudo-enhancement (i.e. increased HU on contrast-enhanced images) in renal cysts due to x-ray beam hardening.(49) A practical approach is to consider a 20 HU difference between pre- and post-contrast CT images as unequivocal evidence of enhancement and a difference between 10 and 20 HU is equivocal for enhancement. The average attenuation of renal lesions larger than 1 cm on nonenhanced CT scans is also useful in their characterization: values less than 20 HU or more than 70 HU (i.e. homogenous) are associated with simple and hemorrhagic cysts, respectively.(50)

The last decade witnessed the emergence of multi-energy CT as a promising technique to evaluate renal masses, with increased specificity in the detection of postcontrast enhancement (i.e. reducing the effect of pseudo-enhancement), and the potential role to reduce radiation dose.(51)

MR Imaging—MR imaging is indicated in the evaluation of indeterminate renal masses and staging of renal cancer (ACR Appropriateness Criteria rating 8).(36) The specificity of MRI for benign lesions may be superior than that of CT.(52) MR is particularly helpful to

distinguish solid from cystic lesions when enhancement of renal masses is equivocal on CT (i.e. between 10 and 20 HU).(5) However, more recent evidence with multi-energy CT technology have shown comparable performance of both methods for differentiation of pRCC from hemorrhagic cysts.(53) MR is more accurate than conventional venography and CT in delineating vena caval tumor thrombus.(54)

Current state-of-the-art MR protocols for imaging renal masses include multiple parameters that allow a more comprehensive and systematic analysis of tumor phenotypes.(55, 56) For instance, diffusion-weighted imaging (DWI) and dynamic contrast-enhanced MR imaging can provide specific information about tumor histology.(57) As discussed later, the use of those parameters may help to differentiate benign from malignant renal masses, the RCC subtype, and predict tumor grade.

Shortcomings of MR imaging include a longer scan time, cost, and potential concerns related to the use of gadolinium-based contrast agents (GBCA). Group I GBCA (gadodiamide, gadopentatetate dimeglumine, and gadoversetamide) are currently contraindicated in dialysis, acute kidney injury, and severe or end-stage chronic kidney disease (CKD 4 or 5, i.e. estimated glomerular filtration rate $< 30 \text{ mL/min/1.73 m}^2$) (58) These GBCA have been associated with nephrogenic systemic fibrosis, which is a rare and potentially fatal fibrosing disease caused by accumulation of free gadolinium. (59) Group II GBCA (gadobenate dimeglumine, gadoteridol, gadoteric acid, and gadobutrol) are considered safe agents with few, if any, unconfounded cases of NSF,(60, 61) and can be used in patients with CKD stages 4 and 5 (eGFR $< 30 \text{ mL/min/1.73 m}^2$). Therefore, the most recent recommendations from the ACR indicate that the need to screen for renal function is optional when using class II GBCAs. More recently, the use of GBCA has also been associated with gadolinium deposition in the basal ganglia, but no harmful effects have been reported to date.(62, 63) Alternatively, non-enhanced sequences, such as arterial spin labeling (ASL), may aid in the evaluation of vascularity in renal masses without the necessity of exogenous contrast agents.(64) Perfusion levels estimated by ASL are correlated with those obtained by dynamic contrast-enhanced MR imaging, as well as with microvessel density at histology in renal tumors.(65)

An MR imaging protocol for evaluation of renal masses is provided in Table 2. Images are acquired in end expiration to improve the consistency of kidney position between scans, with the patient's arms located above the head, when possible, to avoid phase-wrap artifacts.(66)

Impact of imaging on patient management

Increased detection rates and lower intrinsic prevalence of malignancy in small renal masses challenge patient management. Mainstream treatment of renal cancer is still surgical. Nephron-sparing techniques achieve similar oncological results to radical nephrectomy in small RCC.(67, 68) However, subgroups of patients, such as the elderly, those with multiple comorbidities, and those with favorable tumor histology may benefit from conservative approaches such as active surveillance.(2, 69) Current strategies propose the use of size, histologic subtype, nuclear grade, and clinical criteria as parameters for the decision between active surveillance or surgical treatment.(70). Accordingly, the role of imaging is to

facilitate management by offering a noninvasive diagnosis of benign disease and, ideally, distinguish indolent from aggressive renal malignancies.

Diagnosis of Benign Disease—The ability to distinguish benign from malignant solid renal masses by US is limited.(71) Even the classic appearance of AML on US as hyperechoic masses is not specific, overlapping with RCC features.(72–74) However, contrast-enhanced US (CEUS) is a promising modality that can potentially add value in the characterization of renal masses. In a large cohort of patients, CEUS performed with a sensitivity of 100% and specificity of 95% in the diagnosis of malignancy among cystic and solid indeterminate renal masses.(75)

Unequivocal demonstration of bulk fat (i.e., adipocytes) by CT or MR imaging in a renal lesion is a specific finding for the diagnosis of AML.(76, 77) On unenhanced CT, determination of macroscopic fat is achieved when values less than -10 HU are present within the mass (Figure 3).(78) On MR imaging, bulk fat follows the signal intensity of subcutaneous and intra-abdominal fat on all sequences, characterized by (a) hyperintense signal on T1-weighted or T2-weighted images, with signal saturation after application of a frequency-selective fat-saturation technique; (b) high signal intensity on T1-weighted in-phase (IP) and opposed-phased (OP) imaging, with signal dropout on OP imaging at the interface of the lesion with the kidney (India-ink artifact); (c) high signal intensity on fat-only reconstructions from Dixon-based acquisitions (Figure 4).(79) Coexistence of areas of both bulk and intravoxel fat (scant amounts of fat mixed with smooth muscle and vessels), the latter manifested as intra-tumoral areas of decreased signal on OP images compared with IP images, are common in AML.(80)

Some AMLs may not show bulk fat on imaging (AML with minimal fat [mfAML]),(81) whereas signal loss on OP images is also commonly present in ccRCC given the presence of intracytoplasmic lipid-containing vacuoles.(55, 82) Therefore, in the authors' experience, the isolated presence of decreased signal on OP imaging relative to IP imaging is not useful in the differentiation of ccRCC from mfAML in small renal masses.(83) The diagnosis of mfAML should be considered for renal masses with homogeneous low signal intensity relative to renal cortex on T2-weighted images, particularly for smaller lesions found in women, in the absence of bulk fat, plus or minus minimal amount of intravoxel fat (ie, decreased signal intensity on OP imaging).(83) In contrast, the presence of intratumoral necrosis and cystic changes favors ccRCC over mfAML.(83) In addition, a simplified vascular parameter, known as arterial-to-delayed enhancement ratio, and defined as the difference in signal intensity between arterial and precontrast phase divided by the difference between delayed and precontrast phase, has been proposed to distinguish mfAML from RCC, with values greater than 1.5 favoring the first.(84) Ultimately, the combination of multiple MR imaging parameters may provide better diagnostic performances, with up to 100% sensitivity and 89% specificity for the diagnosis of mfAML (Figure 5).(85)

DWI can provide surrogate information about cellular density, and can potentially assist in the differentiation of benign and malignant lesions. A meta-analysis reported significantly lower apparent diffusion coefficients (ADCs) in RCC, with 95% confidence intervals ranging from 1.45×10^{-3} to 1.77×10^{-3} mm²/s, whereas values obtained from benign

lesions ranged between 1.92×10^{-3} and 2.28×10^{-3} mm²/s. Particularly, oncocytomas had significantly higher ADC values than malignant lesions, ranging from 1.84×10^{-3} to 2.17×10^{-3} mm²/s, whereas this was not observed for AML, with values between 1.25×10^{-3} and 1.83×10^{-3} mm²/s.(86)

The presence of a heterogeneous pattern of postcontrast enhancement known as segmental enhancement inversion (i.e. intra-tumor hyperenhancing areas on the corticomedullary phase that become hypoenhancing on the early excretory phase with other areas in the same tumor exhibiting the opposite enhancement pattern), was initially reported to have 80% sensitivity and 99% specificity to distinguish oncocytomas from RCC on CT.(87) However, a more recent study comparing oncocytomas and chrRCC did not show significant differences in the prevalence of the segmental enhancement inversion sign on MRI between these two entities.(88) A recent study by the authors confirmed segmental inversion enhancement as an independent predictor of oncocytoma. However, inter-reader agreement for this finding was only moderate ($\kappa=0.49$) leading to large variability in the sensitivity (17–83%) and specificity (91–99%) for this diagnosis.(89) Higher ASL perfusion levels were reported in oncocytomas compared with clear cell and non-clear cell subtypes of RCC,(90) although some overlap exists. A recent study reported promising results in a prospective trial using [⁹⁹Tc]-Technetium Sestamibi single proton emission computed tomography (SPECT) for the diagnosis of oncocytoma and mixed oncocytic/chromophobe tumors, which exhibit intense uptake ('hot tumors'), compared to RCC and AML not showing uptake ('cold' tumors).(91)

Characterization of Renal Cell Carcinoma Subtypes—Attempts to characterize RCCs on Doppler or CEUS have been inconsistent so far.(92) On CT, differentiation of RCC subtypes generally relies on analyses of postcontrast time-attenuation curves and lesion homogeneity. Postcontrast enhancement of ccRCC is significantly higher than that observed for pRCC and chrRCC, whereas heterogeneity is also more frequently seen in ccRCCs (Figure 6).(93–95)

Relative ratios of renal mass enhancement to enhancement of the aorta are significantly lower for pRCC than for nonpapillary histology on CT, with sensitivity and specificity of 86% and 85%, respectively, using a cutoff of 0.25.(96) Relative enhancement ratios in the renal mass compared with the renal parenchyma are also significantly higher for ccRCC than for pRCC (Figure 7).(97)

The MR imaging phenotype of papillary neoplasms is variable because these tumors evolve from solid hypoenhancing homogeneous masses with low signal intensity on T2-weighted images to more heterogeneous tumors after intra-tumoral hemorrhage. pRCC often presents as hemorrhagic cystic masses with peripheral enhancing components, contained by a well-developed tumor capsule.(55) Regardless of the MR imaging phenotype, the viable, vascularized portions of the tumor usually show homogeneous low signal intensity on T2-weighted images and low-level progressive enhancement (Figure 8).(98, 99)

Papillary tumors are further subdivided into type 1 (basophilic, usually low-grade) and type 2 (eosinophilic, usually high-grade) groups, the latter with worse prognosis.(100) Distinction between these two types by imaging is in general not possible for those tumors presenting as

localized renal masses, albeit type 2 tumors tend to be larger.(101) A subgroup of type 2 papillary RCC can present as ill-defined, invasive tumors, commonly with centripetal growth and renal vein invasion, complicated by pulmonary embolism.(102) This infiltrative phenotype is associated with worse prognosis than well-defined pRCC.(101)

Three-point time-intensity curve analyses have also shown value in RCC subtyping. ccRCC has significantly greater signal intensity change (difference between postcontrast and precontrast, divided by precontrast signal intensity) on both corticomedullary and nephrographic phases (205.6% and 247.1%, respectively) compared with pRCC (32.1% and 96.6%), whereas chrRCC has intermediate enhancement values (109.9% and 192.5%) (Figure 9). Distinction of ccRCC from pRCC was achieved with near perfect sensitivity and specificity using 84% signal intensity change as the threshold on corticomedullary acquisitions.(103) Perfusion in pRCC by ASL is also lower than perfusion levels observed for ccRCC, chrRCC, unclassified RCC, and oncocytoma.(90)

Imaging-Guided Biopsy

Percutaneous renal biopsy has been shown to help avoid surgery in up to 33% of the cases initially considered to be malignant on imaging.(104) Renal biopsy shows high sensitivity and specificity in identifying malignancy,(70, 104, 105) although the number of nondiagnostic samples may vary between 9%(70) and 29%.(104, 106) Considering only diagnostic samples, biopsy of small renal masses has shown up to 94% accuracy in defining histology,(70) with lower accuracies for determining Fuhrman grade (46%–85%).⁸¹ Severe complications are rare, occurring in less than 1%,(107) leading some clinicians/urologists to advocate the incorporation of imaging-guided biopsy into management algorithms of small renal masses.(70)

Standardized Diagnostic Algorithms

Recent attempts have been made to standardize the interpretation criteria for multiparametric MR imaging in the characterization of solid renal masses.(108–110) T2-weighted images and dynamic post-contrast series are key features of most proposed algorithms. Although DWI may aid in the differentiation of oncocytomas from RCC, its usefulness in subtyping RCCs has not been proven.(111) Exploration of quantitative capabilities of multiparametric MR could aid increasing diagnostic reproducibility.(56)

Figure 10 summarizes a diagnostic algorithm used by the authors for the characterization of solid renal masses on MR imaging. Note that in those groups indicated with an asterisk, the MR imaging findings of different histologic subtypes can overlap and even with the use of ancillary findings (eg, homogeneity, necrosis, scar) a specific diagnosis may not be possible. In a recent study using multi-parametric MRI, the authors assessed the performance of a 5-scale clear cell likelihood score (ccLS) based on this algorithm.(108) As the ccLS increased from 1 to 5, the likelihood of clear cell RCC also increased. The overall diagnostic accuracy, sensitivity, specificity, and positive and negative predictive values for clear cell histology across 7 different radiologists using ccLS of 4 and 5 was approximately 80%. Conversely, the specificity of ccLS 1 and 2 to exclude clear cell histology was 95% with a positive predictive value for other histologies of 93%.

The described algorithm could support a change in the management of small renal masses in which patients with a ccLS 4–5 would be encouraged to undergo curative intervention; patients with a ccLS 1–2 could be placed on active surveillance, especially if lesions are less than 3 cm; and patients with a ccLS of 3 would undergo a renal mass biopsy. In the authors' experience, this approach would result in a biopsy rate of only 20%, with unnecessary treatment of oncocytoma and lipid poor AML in 4.5% and 1.7% of the surgical cohort, respectively, and 4.4% of patients with ccRCC placed on active surveillance.(108) Further refinements in the algorithm may improve these results. Furthermore, additional non-invasive tests such as [⁹⁹Tc]-Technetium Sestamibi SPECT could be contemplated in patients with ccLS 3 for the diagnosis of oncocytoma and mixed oncocytic/chromophobe tumors.(91) Ultimately, the diagnostic performance of different imaging tests and/or the morbidity/complication rate associated with percutaneous biopsies will not be the only factors to be considered in the workup of small renal masses - a careful cost-benefit analysis of any proposed algorithm will be necessary.

Prediction of Histologic Grade

Tumor histologic grade has prognostic implications and therefore may affect patient management. However, the accuracy in presurgical grade prediction has been limited for imaging methods and even percutaneous biopsy. On MR imaging, multivariate models taking into consideration morphologic features of RCC showed that renal vein thrombosis and retroperitoneal collaterals were predictive of high-grade ccRCC, whereas peripheral location and homogeneous enhancement were associated with low-grade pRCC.(55) DWI may aid in the differentiation of low-grade from high-grade ccRCC, with sensitivities between 65% and 90%, specificities between 71% and 83%, and overall accuracy of 83%. (111) Focal areas of marked restricted diffusion increase the likelihood of high grade clear cell histology. (111)

Radiomics

A novel field in medical imaging commonly named "Radiomics" explores the ability of advanced image analysis to extract textural and morphologic features beyond the human perception that could reflect histologic, genomic and proteomic patterns, resulting in better diagnosis and risk stratification.(112) It has been shown that some phenotypical features of ccRCC could be associated with genomic mutations.(113) Textural features of ADC and intravoxel incoherent motion imaging can identify tumors with metastatic potential (114) and some subtypes of renal masses (115). Texture analysis applied to CT has also shown promising result in differentiation of renal tumors.(116, 117) The incorporation of quantitative imaging techniques such as Dixon MRI in multiparametric MRI protocols may provide additional information about the metabolism and aggressiveness of clear cell renal cell carcinoma.(118)

Summary

The continued evolution of imaging methods and evolving management options have bolstered the noninvasive assessment of solid renal masses. The combination of multiple parameters obtained from imaging studies offers an opportunity for evaluating the biology and ultimately the clinical significance of solid renal masses. As a result, patient

management may be positively affected with the use of cutting-edge imaging protocols, along with the development of evidence-based diagnostic algorithms that integrate these novel imaging criteria and percutaneous biopsies.

Acknowledgments

The authors thank Dr. Jeffrey A. Cadeddu, MD for reviewing this manuscript.

Disclosure: This manuscript was supported by the National Institutes of Health (grants P50CA196516, awarded to I.P.; and R01 5RO1CA154475, awarded to I.P.).

References

- Hollingsworth JM, Miller DC, Daignault S, et al. Rising incidence of small renal masses: a need to reassess treatment effect. *J Natl Cancer Inst.* 2006; 98(18):1331–4. [PubMed: 16985252]
- Chawla SN, Crispen PL, Hanlon AL, et al. The natural history of observed enhancing renal masses: meta-analysis and review of the world literature. *J Urol.* 2006; 175(2):425–31. [PubMed: 16406965]
- Kassouf W, Aprikian AG, Laplante M, et al. Natural history of renal masses followed expectantly. *J Urol.* 2004; 171(1):111–3. discussion 3. [PubMed: 14665856]
- Volpe A, Panzarella T, Rendon RA, et al. The natural history of incidentally detected small renal masses. *Cancer.* 2004; 100(4):738–45. [PubMed: 14770429]
- Israel GM, Bosniak MA. How I do it: evaluating renal masses. *Radiology.* 2005; 236(2):441–50. [PubMed: 16040900]
- Silverman SG, Israel GM, Herts BR, et al. Management of the incidental renal mass. *Radiology.* 2008; 249(1):16–31. [PubMed: 18796665]
- Frank I, Blute ML, Cheville JC, et al. Solid renal tumors: an analysis of pathological features related to tumor size. *J Urol.* 2003; 170(6 Pt 1):2217–20. [PubMed: 14634382]
- Li G, Cuilleron M, Gentil-Perret A, et al. Characteristics of image-detected solid renal masses: implication for optimal treatment. *Int J Urol.* 2004; 11(2):63–7. [PubMed: 14706008]
- Kutikov A, Fossett LK, Ramchandani P, et al. Incidence of benign pathologic findings at partial nephrectomy for solitary renal mass presumed to be renal cell carcinoma on preoperative imaging. *Urology.* 2006; 68(4):737–40. [PubMed: 17070344]
- Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin.* 2017; 67(1):7–30. [PubMed: 28055103]
- Lopez-Beltran A, Carrasco JC, Cheng L, et al. 2009 update on the classification of renal epithelial tumors in adults. *Int J Urol.* 2009; 16(5):432–43. [PubMed: 19453547]
- Remzi M, Ozsoy M, Klingler HC, et al. Are small renal tumors harmless? Analysis of histopathological features according to tumors 4 cm or less in diameter. *J Urol.* 2006; 176(3):896–9. [PubMed: 16890647]
- Amin MB, Amin MB, Tamboli P, et al. Prognostic impact of histologic subtyping of adult renal epithelial neoplasms: an experience of 405 cases. *Am J Surg Pathol.* 2002; 26(3):281–91. [PubMed: 11859199]
- Guinan P, Vogelzang NJ, Randazzo R, et al. Renal pelvic cancer: a review of 611 patients treated in Illinois 1975–1985. Cancer Incidence and End Results Committee. *Urology.* 1992; 40(5):393–9. [PubMed: 1441034]
- Hall MC, Womack S, Sagalowsky AI, et al. Prognostic factors, recurrence, and survival in transitional cell carcinoma of the upper urinary tract: a 30-year experience in 252 patients. *Urology.* 1998; 52(4):594–601. [PubMed: 9763077]
- Caoili EM, Cohan RH, Inampudi P, et al. MDCT urography of upper tract urothelial neoplasms. *AJR Am J Roentgenol.* 2005; 184(6):1873–81. [PubMed: 15908545]
- Xiao JC, Walz-Mattmuller R, Ruck P, et al. Renal involvement in myeloproliferative and lymphoproliferative disorders. A study of autopsy cases. *Gen Diagn Pathol.* 1997; 142(3–4):147–53. [PubMed: 9065578]

18. Urban BA, Fishman EK. Renal lymphoma: CT patterns with emphasis on helical CT. *Radiographics*. 2000; 20(1):197–212. [PubMed: 10682781]
19. Wu AJ, Mehra R, Hafez K, et al. Metastases to the kidney: a clinicopathological study of 43 cases with an emphasis on deceptive features. *Histopathology*. 2015; 66(4):587–97. [PubMed: 25406592]
20. Johnson DC, Vukina J, Smith AB, et al. Preoperatively misclassified, surgically removed benign renal masses: a systematic review of surgical series and United States population level burden estimate. *J Urol*. 2015; 193(1):30–5. [PubMed: 25072182]
21. Flum AS, Hamoui N, Said MA, et al. Update on the Diagnosis and Management of Renal Angiomyolipoma. *J Urol*. 2016; 195(4 Pt 1):834–46. [PubMed: 26612197]
22. Fujii Y, Komai Y, Saito K, et al. Incidence of benign pathologic lesions at partial nephrectomy for presumed RCC renal masses: Japanese dual-center experience with 176 consecutive patients. *Urology*. 2008; 72(3):598–602. [PubMed: 18649929]
23. Milner J, McNeil B, Alioto J, et al. Fat poor renal angiomyolipoma: patient, computerized tomography and histological findings. *J Urol*. 2006; 176(3):905–9. [PubMed: 16890650]
24. Fujii Y, Ajima J, Oka K, et al. Benign renal tumors detected among healthy adults by abdominal ultrasonography. *Eur Urol*. 1995; 27(2):124–7. [PubMed: 7744154]
25. Chronopoulos PN, Kaisidis GN, Vaiopoulos CK, et al. Spontaneous rupture of a giant renal angiomyolipoma-Wunderlich's syndrome: Report of a case. *Int J Surg Case Rep*. 2016; 19:140–3. [PubMed: 26764888]
26. Lane BR, Aydin H, Danforth TL, et al. Clinical correlates of renal angiomyolipoma subtypes in 209 patients: classic, fat poor, tuberous sclerosis associated and epithelioid. *J Urol*. 2008; 180(3): 836–43. [PubMed: 18635231]
27. Perez-Ordenez B, Hamed G, Campbell S, et al. Renal oncocytoma: a clinicopathologic study of 70 cases. *Am J Surg Pathol*. 1997; 21(8):871–83. [PubMed: 9255250]
28. Oxley JD, Sullivan J, Mitchelmore A, et al. Metastatic renal oncocytoma. *J Clin Pathol*. 2007; 60(6):720–2. [PubMed: 17557872]
29. Hes O, Michal M, Sima R, et al. Renal oncocytoma with and without intravascular extension into the branches of renal vein have the same morphological, immunohistochemical and genetic features. *Virchows Arch*. 2008; 452(3):285–93. [PubMed: 18196270]
30. Gudbjartsson T, Hardarson S, Petursdottir V, et al. Renal oncocytoma: a clinicopathological analysis of 45 consecutive cases. *BJU Int*. 2005; 96(9):1275–9. [PubMed: 16287444]
31. Bhatt S, MacLennan G, Dogra V. Renal pseudotumors. *AJR Am J Roentgenol*. 2007; 188(5):1380–7. [PubMed: 17449786]
32. Craig WD, Wagner BJ, Travis MD. Pyelonephritis: radiologic-pathologic review. *Radiographics*. 2008; 28(1):255–77. quiz 327–8. [PubMed: 18203942]
33. Chuang CK, Lai MK, Chang PL, et al. Xanthogranulomatous pyelonephritis: experience in 36 cases. *J Urol*. 1992; 147(2):333–6. [PubMed: 1732587]
34. Osca JM, Peiro MJ, Rodrigo M, et al. Focal xanthogranulomatous pyelonephritis: partial nephrectomy as definitive treatment. *Eur Urol*. 1997; 32(3):375–9. [PubMed: 9358230]
35. Haliloglu AH, Gulpinar O, Ozden E, et al. Urinary ultrasonography in screening incidental renal cell carcinoma: is it obligatory? *Int Urol Nephrol*. 2011; 43(3):687–90. [PubMed: 20848193]
36. Heilbrun ME, Remer EM, Casalino DD, et al. ACR Appropriateness Criteria indeterminate renal mass. *J Am Coll Radiol*. 2015; 12(4):333–41. [PubMed: 25842014]
37. Warshauer DM, McCarthy SM, Street L, et al. Detection of renal masses: sensitivities and specificities of excretory urography/linear tomography, US, and CT. *Radiology*. 1988; 169(2):363–5. [PubMed: 3051112]
38. Jamis-Dow CA, Choyke PL, Jennings SB, et al. Small (< or = 3-cm) renal masses: detection with CT versus US and pathologic correlation. *Radiology*. 1996; 198(3):785–8. [PubMed: 8628872]
39. Kang SK, Kim D, Chandarana H. Contemporary imaging of the renal mass. *Curr Urol Rep*. 2011; 12(1):11–7. [PubMed: 20949339]
40. Vikram R, Beland MD, Blaufox MD, et al. ACR Appropriateness Criteria Renal Cell Carcinoma Staging. *J Am Coll Radiol*. 2016; 13(5):518–25. [PubMed: 27016804]

41. Hartman DS, Choyke PL, Hartman MS. From the RSNA refresher courses: a practical approach to the cystic renal mass. *Radiographics*. 2004; 24(Suppl 1):S101–15. [PubMed: 15486234]
42. Desser TS, Jeffrey RB. Tissue harmonic imaging techniques: physical principles and clinical applications. *Semin Ultrasound CT MR*. 2001; 22(1):1–10. [PubMed: 11300583]
43. Schmidt T, Hohl C, Haage P, et al. Diagnostic accuracy of phase-inversion tissue harmonic imaging versus fundamental B-mode sonography in the evaluation of focal lesions of the kidney. *AJR Am J Roentgenol*. 2003; 180(6):1639–47. [PubMed: 12760935]
44. Quaia E. Microbubble ultrasound contrast agents: an update. *Eur Radiol*. 2007; 17(8):1995–2008. [PubMed: 17351779]
45. Catalano C, Fraioli F, Laghi A, et al. High-resolution multidetector CT in the preoperative evaluation of patients with renal cell carcinoma. *AJR Am J Roentgenol*. 2003; 180(5):1271–7. [PubMed: 12704036]
46. Bosniak MA. The small (less than or equal to 3.0 cm) renal parenchymal tumor: detection, diagnosis, and controversies. *Radiology*. 1991; 179(2):307–17. [PubMed: 2014269]
47. Silverman SG, Lee BY, Seltzer SE, et al. Small (< or = 3 cm) renal masses: correlation of spiral CT features and pathologic findings. *AJR Am J Roentgenol*. 1994; 163(3):597–605. [PubMed: 8079852]
48. Maki DD, Birnbaum BA, Chakraborty DP, et al. Renal cyst pseudoenhancement: beam-hardening effects on CT numbers. *Radiology*. 1999; 213(2):468–72. [PubMed: 10551228]
49. Birnbaum BA, Hindman N, Lee J, et al. Renal cyst pseudoenhancement: influence of multidetector CT reconstruction algorithm and scanner type in phantom model. *Radiology*. 2007; 244(3):767–75. [PubMed: 17709828]
50. Pooler BD, Pickhardt PJ, O'Connor SD, et al. Renal cell carcinoma: attenuation values on unenhanced CT. *AJR Am J Roentgenol*. 2012; 198(5):1115–20. [PubMed: 22528901]
51. Mileto A, Nelson RC, Paulson EK, et al. Dual-Energy MDCT for Imaging the Renal Mass. *AJR Am J Roentgenol*. 2015; 204(6):W640–7. [PubMed: 25730444]
52. Kreft BP, Muller-Miny H, Sommer T, et al. Diagnostic value of MR imaging in comparison to CT in the detection and differential diagnosis of renal masses: ROC analysis. *Eur Radiol*. 1997; 7(4):542–7. [PubMed: 9204336]
53. Dilauro M, Quon M, McInnes MD, et al. Comparison of Contrast-Enhanced Multiphase Renal Protocol CT Versus MRI for Diagnosis of Papillary Renal Cell Carcinoma. *AJR Am J Roentgenol*. 2016; 206(2):319–25. [PubMed: 26797358]
54. Goldfarb DA, Novick AC, Lorig R, et al. Magnetic resonance imaging for assessment of vena caval tumor thrombi: a comparative study with venacavography and computerized tomography scanning. *J Urol*. 1990; 144(5):1100–3. discussion 3–4. [PubMed: 2231879]
55. Pedrosa I, Chou MT, Ngo L, et al. MR classification of renal masses with pathologic correlation. *Eur Radiol*. 2008; 18(2):365–75. [PubMed: 17899106]
56. Cornelis F, Tricaud E, Lasserre AS, et al. Routinely performed multiparametric magnetic resonance imaging helps to differentiate common subtypes of renal tumours. *Eur Radiol*. 2014; 24(5):1068–80. [PubMed: 24557052]
57. Pedrosa I, Alsop DC, Rofsky NM. Magnetic resonance imaging as a biomarker in renal cell carcinoma. *Cancer*. 2009; 115(10 Suppl):2334–45. [PubMed: 19402070]
58. ACR Committee on Drugs and Contrast Media. Manual on Contrast Media v10.3 2017[Available from: <https://www.acr.org/Quality-Safety/Resources/Contrast-Manual>]
59. Zhang B, Liang L, Chen W, et al. An Updated Study to Determine Association between Gadolinium-Based Contrast Agents and Nephrogenic Systemic Fibrosis. *PLoS One*. 2015; 10(6):e0129720. [PubMed: 26076348]
60. Nandwana SB, Moreno CC, Osipow MT, et al. Gadobenate Dimeglumine Administration and Nephrogenic Systemic Fibrosis: Is There a Real Risk in Patients with Impaired Renal Function? *Radiology*. 2015; 276(3):741–7. [PubMed: 25875973]
61. Soulez G, Bloomgarden DC, Rofsky NM, et al. Prospective Cohort Study of Nephrogenic Systemic Fibrosis in Patients With Stage 3–5 Chronic Kidney Disease Undergoing MRI With Injected Gadobenate Dimeglumine or Gadoteridol. *AJR Am J Roentgenol*. 2015; 205(3):469–78. [PubMed: 26295633]

62. Kanda T, Nakai Y, Hagiwara A, et al. Distribution and chemical forms of gadolinium in the brain: a review. *Br J Radiol.* 2017; 90(1079):20170115. [PubMed: 28749164]
63. FDA. FDA Drug Safety Communication: FDA identifies no harmful effects to date with brain retention of gadolinium-based contrast agents for MRIs review to continue 2017 [Available from: <https://www.fda.gov/Drugs/DrugSafety/ucm559007.htm>]
64. Pedrosa I, Rafatzand K, Robson P, et al. Arterial spin labeling MR imaging for characterisation of renal masses in patients with impaired renal function: initial experience. *Eur Radiol.* 2012; 22(2): 484–92. [PubMed: 21877173]
65. Zhang Y, Kapur P, Yuan Q, et al. Tumor Vascularity in Renal Masses: Correlation of Arterial Spin-Labeled and Dynamic Contrast-Enhanced Magnetic Resonance Imaging Assessments. *Clin Genitourin Cancer.* 2016; 14(1):e25–36. [PubMed: 26422014]
66. Khatri G, Pedrosa I. 3T MR imaging protocol for characterization of renal masses. *Appl Radiol.* 2012; 41(Suppl):22–6.
67. Butler BP, Novick AC, Miller DP, et al. Management of small unilateral renal cell carcinomas: radical versus nephron-sparing surgery. *Urology.* 1995; 45(1):34–40. discussion -1. [PubMed: 7817478]
68. Lerner SE, Hawkins CA, Blute ML, et al. Disease outcome in patients with low stage renal cell carcinoma treated with nephron sparing or radical surgery. 1996. *J Urol.* 2002; 167(2 Pt 2):884–9. discussion 9–90. [PubMed: 11905916]
69. Rosales JC, Haramis G, Moreno J, et al. Active surveillance for renal cortical neoplasms. *J Urol.* 2010; 183(5):1698–702. [PubMed: 20299038]
70. Halverson SJ, Kunju LP, Bhalla R, et al. Accuracy of determining small renal mass management with risk stratified biopsies: confirmation by final pathology. *J Urol.* 2013; 189(2):441–6. [PubMed: 23253955]
71. Harvey CJ, Alsafi A, Kuzmich S, et al. Role of US Contrast Agents in the Assessment of Indeterminate Solid and Cystic Lesions in Native and Transplant Kidneys. *Radiographics.* 2015; 35(5):1419–30. [PubMed: 26273994]
72. Yamashita Y, Takahashi M, Watanabe O, et al. Small renal cell carcinoma: pathologic and radiologic correlation. *Radiology.* 1992; 184(2):493–8. [PubMed: 1620854]
73. Forman HP, Middleton WD, Melson GL, et al. Hyperechoic renal cell carcinomas: increase in detection at US. *Radiology.* 1993; 188(2):431–4. [PubMed: 8327692]
74. Sidhar K, McGahan JP, Early HM, et al. Renal Cell Carcinomas: Sonographic Appearance Depending on Size and Histologic Type. *J Ultrasound Med.* 2016; 35(2):311–20. [PubMed: 26740493]
75. Barr RG, Peterson C, Hindi A. Evaluation of indeterminate renal masses with contrast-enhanced US: a diagnostic performance study. *Radiology.* 2014; 271(1):133–42. [PubMed: 24475802]
76. Bosniak MA, Megibow AJ, Hulnick DH, et al. CT diagnosis of renal angiomyolipoma: the importance of detecting small amounts of fat. *AJR Am J Roentgenol.* 1988; 151(3):497–501. [PubMed: 3044036]
77. Simpson E, Patel U. Diagnosis of angiomyolipoma using computed tomography-region of interest < or =–10 HU or 4 adjacent pixels < or =–10 HU are recommended as the diagnostic thresholds. *Clin Radiol.* 2006; 61(5):410–6. [PubMed: 16679114]
78. Davenport MS, Neville AM, Ellis JH, et al. Diagnosis of renal angiomyolipoma with hounsfield unit thresholds: effect of size of region of interest and nephrographic phase imaging. *Radiology.* 2011; 260(1):158–65. [PubMed: 21555349]
79. Wang Y, Li D, Haacke EM, et al. A three-point Dixon method for water and fat separation using 2D and 3D gradient-echo techniques. *J Magn Reson Imaging.* 1998; 8(3):703–10. [PubMed: 9626890]
80. Israel GM, Hindman N, Hecht E, et al. The use of opposed-phase chemical shift MRI in the diagnosis of renal angiomyolipomas. *AJR Am J Roentgenol.* 2005; 184(6):1868–72. [PubMed: 15908544]
81. Jinzaki M, Tanimoto A, Narimatsu Y, et al. Angiomyolipoma: imaging findings in lesions with minimal fat. *Radiology.* 1997; 205(2):497–502. [PubMed: 9356635]

82. Outwater EK, Bhatia M, Siegelman ES, et al. Lipid in renal clear cell carcinoma: detection on opposed-phase gradient-echo MR images. *Radiology*. 1997; 205(1):103–7. [PubMed: 9314970]
83. Hindman N, Ngo L, Genega EM, et al. Angiomyolipoma with minimal fat: can it be differentiated from clear cell renal cell carcinoma by using standard MR techniques? *Radiology*. 2012; 265(2): 468–77. [PubMed: 23012463]
84. Sasiwimonphan K, Takahashi N, Leibovich BC, et al. Small (<4 cm) Renal Mass: Differentiation of Angiomyolipoma without Visible Fat from Renal Cell Carcinoma Utilizing MR Imaging. *Radiology*. 2016; 280(2):653.
85. Schieda N, Dilauro M, Moosavi B, et al. MRI evaluation of small (<4cm) solid renal masses: multivariate modeling improves diagnostic accuracy for angiomyolipoma without visible fat compared to univariate analysis. *Eur Radiol*. 2016; 26(7):2242–51. [PubMed: 26486936]
86. Lassel EA, Rao R, Schwenke C, et al. Diffusion-weighted imaging of focal renal lesions: a meta-analysis. *Eur Radiol*. 2014; 24(1):241–9. [PubMed: 24337912]
87. Kim JI, Cho JY, Moon KC, et al. Segmental enhancement inversion at biphasic multidetector CT: characteristic finding of small renal oncocytoma. *Radiology*. 2009; 252(2):441–8. [PubMed: 19508984]
88. Rosenkrantz AB, Hindman N, Fitzgerald EF, et al. MRI features of renal oncocytoma and chromophobe renal cell carcinoma. *AJR Am J Roentgenol*. 2010; 195(6):W421–7. [PubMed: 21098174]
89. Kay FU, Canvasser NE, Xi Y, et al. Diagnostic Performance and Interreader Agreement of a Standardized MR Imaging Approach in the Prediction of Small Renal Mass Histology. *Radiology*. In press.
90. Lanzman RS, Robson PM, Sun MR, et al. Arterial spin-labeling MR imaging of renal masses: correlation with histopathologic findings. *Radiology*. 2012; 265(3):799–808. [PubMed: 23047841]
91. Gorin MA, Rowe SP, Baras AS, et al. Prospective Evaluation of (99m)Tc-sestamibi SPECT/CT for the Diagnosis of Renal Oncocytomas and Hybrid Oncocytic/Chromophobe Tumors. *Eur Urol*. 2016; 69(3):413–6. [PubMed: 26386607]
92. Tamai H, Takiguchi Y, Oka M, et al. Contrast-enhanced ultrasonography in the diagnosis of solid renal tumors. *J Ultrasound Med*. 2005; 24(12):1635–40. [PubMed: 16301719]
93. Sheir KZ, El-Azab M, Mosbah A, et al. Differentiation of renal cell carcinoma subtypes by multislice computerized tomography. *J Urol*. 2005; 174(2):451–5. discussion 5. [PubMed: 16006863]
94. Kim JK, Kim TK, Ahn HJ, et al. Differentiation of subtypes of renal cell carcinoma on helical CT scans. *AJR Am J Roentgenol*. 2002; 178(6):1499–506. [PubMed: 12034628]
95. Sureka B, Lal A, Khandelwal N, et al. Dynamic computed tomography and Doppler findings in different subtypes of renal cell carcinoma with their histopathological correlation. *J Cancer Res Ther*. 2014; 10(3):552–7. [PubMed: 25313738]
96. Herts BR, Coll DM, Novick AC, et al. Enhancement characteristics of papillary renal neoplasms revealed on triphasic helical CT of the kidneys. *AJR Am J Roentgenol*. 2002; 178(2):367–72. [PubMed: 11804895]
97. Bata P, Gyebrar J, Tarnoki DL, et al. Clear cell renal cell carcinoma and papillary renal cell carcinoma: differentiation of distinct histological types with multiphase CT. *Diagn Interv Radiol*. 2013; 19(5):387–92. [PubMed: 23864331]
98. Oliva MR, Glickman JN, Zou KH, et al. Renal cell carcinoma: t1 and t2 signal intensity characteristics of papillary and clear cell types correlated with pathology. *AJR Am J Roentgenol*. 2009; 192(6):1524–30. [PubMed: 19457814]
99. Roy C, Sauer B, Lindner V, et al. MR Imaging of papillary renal neoplasms: potential application for characterization of small renal masses. *Eur Radiol*. 2007; 17(1):193–200. [PubMed: 16758161]
100. Pignot G, Elie C, Conquy S, et al. Survival analysis of 130 patients with papillary renal cell carcinoma: prognostic utility of type 1 and type 2 subclassification. *Urology*. 2007; 69(2):230–5. [PubMed: 17275070]
101. Rosenkrantz AB, Sekhar A, Genega EM, et al. Prognostic implications of the magnetic resonance imaging appearance in papillary renal cell carcinoma. *Eur Radiol*. 2013; 23(2):579–87. [PubMed: 22903703]

102. Yamada T, Endo M, Tsuboi M, et al. Differentiation of pathologic subtypes of papillary renal cell carcinoma on CT. *AJR Am J Roentgenol.* 2008; 191(5):1559–63. [PubMed: 18941101]
103. Sun MR, Ngo L, Genega EM, et al. Renal cell carcinoma: dynamic contrast-enhanced MR imaging for differentiation of tumor subtypes—correlation with pathologic findings. *Radiology.* 2009; 250(3):793–802. [PubMed: 19244046]
104. Vasudevan A, Davies RJ, Shannon BA, et al. Incidental renal tumours: the frequency of benign lesions and the role of preoperative core biopsy. *BJU Int.* 2006; 97(5):946–9. [PubMed: 16643475]
105. Caoili EM, Bude RO, Higgins EJ, et al. Evaluation of sonographically guided percutaneous core biopsy of renal masses. *AJR Am J Roentgenol.* 2002; 179(2):373–8. [PubMed: 12130435]
106. Leveridge MJ, Finelli A, Kachura JR, et al. Outcomes of small renal mass needle core biopsy, nondiagnostic percutaneous biopsy, and the role of repeat biopsy. *Eur Urol.* 2011; 60(3):578–84. [PubMed: 21704449]
107. Wang R, Wolf JS, Wood DP, et al. Accuracy of percutaneous core biopsy in management of small renal masses. *Urology.* 2009; 73(3):586–90. discussion 90–1. [PubMed: 19118884]
108. Canvasser NE, Kay FU, Xi Y, et al. Diagnostic Accuracy of Multiparametric Magnetic Resonance Imaging to Identify Clear Cell Renal Cell Carcinoma in cT1a Renal Masses. *J Urol.* 2017
109. Lopes Vendrami C, Parada Villavicencio C, DeJulio TJ, et al. Differentiation of Solid Renal Tumors with Multiparametric MR Imaging. *Radiographics.* 2017; 37(7):2026–42. [PubMed: 29131770]
110. Cornelis F, Grenier N. Multiparametric Magnetic Resonance Imaging of Solid Renal Tumors: A Practical Algorithm. *Semin Ultrasound CT MR.* 2017; 38(1):47–58. [PubMed: 28237280]
111. Kang SK, Zhang A, Pandharipande PV, et al. DWI for Renal Mass Characterization: Systematic Review and Meta-Analysis of Diagnostic Test Performance. *AJR Am J Roentgenol.* 2015; 205(2):317–24. [PubMed: 26204281]
112. Lambin P, Rios-Velazquez E, Leijenaar R, et al. Radiomics: extracting more information from medical images using advanced feature analysis. *Eur J Cancer.* 2012; 48(4):441–6. [PubMed: 22257792]
113. Karlo CA, Di Paolo PL, Chaim J, et al. Radiogenomics of clear cell renal cell carcinoma: associations between CT imaging features and mutations. *Radiology.* 2014; 270(2):464–71. [PubMed: 24029645]
114. Kierans AS, Rusinek H, Lee A, et al. Textural differences in apparent diffusion coefficient between low- and high-stage clear cell renal cell carcinoma. *AJR Am J Roentgenol.* 2014; 203(6):W637–44. [PubMed: 25415729]
115. Gaing B, Sigmund EE, Huang WC, et al. Subtype differentiation of renal tumors using voxel-based histogram analysis of intravoxel incoherent motion parameters. *Invest Radiol.* 2015; 50(3):144–52. [PubMed: 25387050]
116. Raman SP, Chen Y, Schroeder JL, et al. CT texture analysis of renal masses: pilot study using random forest classification for prediction of pathology. *Acad Radiol.* 2014; 21(12):1587–96. [PubMed: 25239842]
117. Yu H, Scalera J, Khalid M, et al. Texture analysis as a radiomic marker for differentiating renal tumors. *Abdom Radiol (NY).* 2017; 42(10):2470–8. [PubMed: 28421244]
118. Zhang Y, Udayakumar D, Cai L, et al. Addressing metabolic heterogeneity in clear cell renal cell carcinoma with quantitative Dixon MRI. *JCI Insight.* 2017; 2(15)

Key points

- Solid renal masses include various types of malignant and benign histologic diagnosis.
- Non-invasive lesion characterization is achievable in a substantial number of cases, with the use of state-of-the-art imaging techniques and evidence-based interpretation criteria.
- Cross-sectional imaging has the potential to improve patients' outcomes by reducing the number of unnecessary biopsies and/or surgical procedures.

Figure 1.

A 69-year-old man with diffuse large B-cell of the left kidney. Coronal contrast-enhanced CT image (A) showing a solid infiltrative lesion in the perihilar region of the left kidney (arrow). Note the perinephric soft tissue component surrounding the renal capsule (white arrowheads). Coronal single-shot fast spin-echo T2-weighted MR image (B) shows low-intermediate signal intensity in the mass, with interval development of new perinephric nodules (asterisk) compared with the prior CT (A). Coronal three-dimensional (3D) fat-saturated Dixon T1-weighted MR images before (C) and after (D) administration of contrast agent show low-level enhancement of the lesion (arrows) in comparison with the renal cortex. Also note low-level homogeneous enhancement of the perirenal component (asterisks).

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Figure 2.

A 75-year-old man with oncocytoma. Coronal single-shot fast spin-echo T2-weighted MR image (A) shows a large mass in the left kidney (*white arrows*) with foci of high signal intensity in the periphery and central areas of intermediate signal intensity. Note that the central component (*asterisk*) shows avid postcontrast enhancement on the fat-saturated Dixon-based T1-weighted gradient echo acquisition during the corticomedullary phase (B). Maximum intensity projection of postcontrast T1-weighted Dixon-based acquisition (C) shows invasion of the renal hilum fat, which was confirmed after nephrectomy. From Kay FU, Pedrosa I. Imaging of Solid Renal Masses. Radiol Clin North Am 2017;55;2:243–258; with permission.

Figure 3.

A 47-year-old woman with angiomyolipoma in the left kidney. Coronal (*A*) and axial (*B*) non-contrast-enhanced CT images show an 8-cm circumscribed mass in the left upper pole (*arrows*), predominantly composed of low-attenuation elements (bulk fat), similar to that of retroperitoneal and subcutaneous fat (*asterisks*). Also note some streaks of soft tissue within the lesion, corresponding with vascular and smooth muscle components (*arrowheads*).

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Figure 4.

A 47-year-old woman with angiomyolipoma in the left kidney (same patient from previous figure). Opposed-phase (A), in-phase (B), and fat-only (C) reconstructions from an axial T1-weighted Dixon acquisition. The circumscribed mass (arrows) shows high signal intensity on all images, following the same pattern of retroperitoneal and subcutaneous fat. On opposed-phase images, note the signal dropout at the interface between the mass and the kidney (white arrowheads), also known as India-ink artifact. Signal dropout in areas within the mass (black arrowheads) indicate coexistence of fat and nonfat elements (ie, intravoxel fat).

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Figure 5.

A 40-year-old woman with minimal-fat angiomyolipoma in the left kidney. Axial gradient recalled echo (GRE) T1-weighted opposed-phase (A) and in-phase (B) MR images show a slightly hypointense circumscribed lesion in the lower pole of the left kidney (arrows), without significant signal dropout to suggest intravoxel fat. Coronal non-fat-saturated single-shot fast spin-echo T2-weighted MR image (C) shows homogeneous hypointense signal in the lesion (arrow). Dynamic contrast-enhanced fat-saturated spoiled gradient recalled (SPGR) T1-weighted MR images during corticomedullary (D) and excretory (E) phases show avid early enhancement of the lesion and subsequent washout (arrows).

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Figure 6.

A 55-year-old man with clear cell renal cell carcinoma in the right kidney. Coronal single-shot fast spin-echo T2-weighted MR image (A) shows an infiltrative mass (arrows) with heterogeneous and predominantly high signal intensity in the right upper pole. Area of signal dropout (asterisk) is identified in the T1-weighted opposed-phase image (B) compared with the IP image (C), consistent with intravoxel fat. There are also foci of high signal intensity (white arrowheads), related to hemorrhage, better seen on the precontrast fat-saturated T1-weighted SPGR acquisition (D). Postcontrast image using the same acquisition as in D, during the corticomedullary (E) phase, show heterogeneous enhancement in the mass (arrows) with areas of avid enhancement (asterisk), similar to that of normal renal cortex (black arrowhead).

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Figure 7.

A 40-year-old woman with clear cell renal cell carcinoma in the right kidney (arrows). Axial GRE T1-weighted opposed-phase (A) and in-phase (B) MR images show mild signal dropout within the mass (arrowhead), consistent with intravoxel fat. There is marked hyperintense signal on coronal single-shot fast spin-echo T2-weighted MR images (C). Note the early and avid enhancement on dynamic postcontrast images (E–F; precontrast, D), higher than that of normal renal cortex.

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Figure 8.

A 65-year-old man with multifocal papillary RCC. Coronal single-shot fast spin-echo T2-weighted MR image (A) shows 3 circumscribed lesions (arrows) with homogeneous hypointense signal in the perihilar and upper pole of the left kidney. Coronal 3D fat-saturated Dixon T1-weighted MR images before (B) and after contrast injection, during the corticomedullary (C) and nephrographic (D) phases show low-level homogeneous progressive enhancement (arrows).

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Figure 9.

A 42-year-old woman with chromophobe RCC in the left kidney (arrows). Coronal single-shot fast spin echo T2-weighted MR image (A) shows a 1.3-cm, slightly heterogeneous, predominantly hypointense lesion in the left lower pole. Fat-saturated 3D Dixon T1-weighted MR image shows moderate enhancement of the lesion on the corticomedullary (C) and nephrographic (D) phases compared with precontrast (B).

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Figure 10. Diagnostic algorithm for characterization of solid renal masses. a Enhancement during corticomedullary phase: Intense, greater than or equal to renal cortex; moderate, approximately 50% of renal cortex; mild, approximately 25% to 30% of renal cortex. b Arterial-to-delayed enhancement ratio (ADER), which is the difference in signal intensity between arterial and precontrast phase divided by the difference between delayed and precontrast phase. ADER greater than 1.5 favors minimal-fat AML, whereas less than 1.5 favors ccRCC. c ccRCC is typically heterogeneous; minimal-fat AML is typically homogeneous. d Oncocytoma (ONCO) is more commonly hypervascular (enhances similarly to renal cortex), whereas chrRCC has typically moderate enhancement (approximately 50% of renal cortex). e Oncocytoma if central scar (i.e. central initial non-enhancing area with delayed enhancement), whereas ccRCC is more likely if necrosis (i.e. non-enhancing central area) is present or if tumor is heterogeneous. Asterisks mean that ancillary findings should be used for characterization. T2WI, T2-weighted imaging. Adapted from Kay FU, Pedrosa I. Imaging of Solid Renal Masses. Radiol Clin North Am 2017;55;2;243–258; with permission.

Table 1

Multidetector contrast-enhanced computed tomography protocol for renal mass characterization

From Kay FU, Pedrosa I. Imaging of Solid Renal Masses. Radiol Clin North Am 2017;55;2;243–258; with permission.

Renal Mass Multidetector CT Protocol				
Phases	Noncontrast	Corticomedullary^a	Nephrographic	Delayed
Phase timing	–	40 s	100–120 s	5–7 min
Coverage	Kidneys	Diaphragm through kidneys	Diaphragm through kidneys	Kidneys
FOV	Whole body	Whole body	Whole body	Whole body
Reconstructions	Axial: 3 mm	Axial: 3 mm	Axial: 3 mm	Axial: 3 mm
		Coronal: 2 mm	Coronal: 2 mm	Coronal: 2 mm
		Sagittal: 2 mm	Sagittal: 2 mm	Sagittal: 2 mm

Intravenous contrast: 100 to 150 mL of low-osmolar iodinated contrast at 5 mL/s.

Abbreviation: FOV, field of view.

^aOptional.

Table 2

Contrast-enhanced 3T MR imaging protocol for renal mass characterization
 From Kay FU, Pedrosa I. Imaging of Solid Renal Masses. Radiol Clin North Am 2017;55:2;243–258; with permission.

Renal Mass MR Protocol (3T)							
Acquisition	TR (ms)	TE (ms)	Flip Angle (Degrees)	Bandwidth (Hz/Pixel)	Slice Thickness/Gap	FOV (cm)	Matrix
Coronal T2-weighted SSFSE	960	80	90	652	5/1	40 × 45	312 × 279
Axial T2-weighted fat-saturated SSFSE	920	80	90	543	5/1	40 × 30	304 × 168
Axial 2D T1-weighted GRE IP/OP	120	2.3/1.15	55	1215	5/1	40 × 38	400 × 269
Axial DWI	1060	53	90	36.5	7/1	44 × 35	144 × 115
Sagittal oblique 3D Dixon (kidneys) ^a	3.7	1.32/2.3	10	1568	3/–1.5	30 × 30	248 × 230
Coronal 3D Dixon ^b	3.8	1.7/2.1	10	1923	3/–1.5	39 × 40	260 × 223
Axial 3D Dixon	2.2	1.16/2.1	10	1852	3/–1.5	38 × 33	252 × 218

Intravenous contrast: 0.1 mmol/kg gadolinium chelate at 2 mL/s, followed by 20-mL saline flush.

Abbreviations: 2D, two dimensional; 3D, three dimensional; GRE, gradient recalled echo; IP, in phase; OP, opposed-phased; SSFSE, single-shot fast spin echo; TE, echo time; TR, repetition time.

^aPrecontrast and postcontrast (3 minutes).

^bBefore, bolus-tracking (left ventricle enhancement), early arterial (ask for 2 breath in/breath out, then hold), corticomedullary (40 seconds), nephrographic (90 seconds).