Published in final edited form as:

Top Magn Reson Imaging. 2014 April ; 23(2): 95–115. doi:10.1097/RMR.000000000000019.

MRI Phenotype in Renal Cancer:

Is It Clinically Relevant?

Naomi Campbell, MD*, Andrew B. Rosenkrantz, MD*, and Ivan Pedrosa, MD†,‡

*Department of Radiology, Center for Biomedical Imaging, NYU Langone Medical Center, New York, NY

†Department of Radiology, UT Southwestern Medical Center, Dallas, TX

‡Advanced Imaging Research Center, UT Southwestern Medical Center, Dallas, TX

Abstract

Renal cell carcinoma (RCC) is most commonly diagnosed as an incidental finding on cross-sectional imaging and represents a significant clinical challenge. Although most patients have a surgically curable lesion at the time of diagnosis, the variability in the biologic behavior of the different histologic subtypes and tumor grade of RCC, together with the increasing array of management options, creates uncertainty for the optimal clinical approach to individual patients. State-of-the-art magnetic resonance imaging (MRI) provides a comprehensive assessment of renal lesions that includes multiple forms of tissue contrast as well as functional parameters, which in turn provides information that helps to address this dilemma. In this article, we review this evolving and increasingly comprehensive role of MRI in the detection, characterization, perioperative evaluation, and assessment of the treatment response of renal neoplasms. We emphasize the ability of the imaging “phenotype” of renal masses on MRI to help predict the histologic subtype, grade, and clinical behavior of RCC.

Keywords

renal cell carcinoma; MRI; phenotype; clear-cell renal cell carcinoma; papillary renal cell carcinoma

Renal cell carcinoma (RCC) represents a significant clinical burden, comprising 2% to 3% of adult malignancies.¹ The frequency of RCC has increased by 2% per year during the past 65 years.¹ In more than 50% of cases, RCC is diagnosed as an incidental finding,² attributable to the increased use and quality of cross-sectional imaging examinations. Although most patients have a surgically curable lesion at the time of diagnosis, the wide spectrum of biologic behavior of the various histologic subtypes of RCC creates a clinical challenge in optimal management. Such variability in prognosis, combined with expanding therapeutic options, has driven advances in medical imaging to provide potential noninvasive solutions. For instance, the noninvasive diagnosis of a renal mass as RCC is not

Reprints: Ivan Pedrosa, MD, Department of Radiology, Advanced Imaging Research Center, UT Southwestern Medical Center, 2201 Inwood Rd., 2nd Floor, Suite 202, Dallas, TX 75390-9085, (ivan.pedrosa@UTSouthwestern.edu).

The authors declare no conflict of interest.

straightforward given an overlap in appearance with fat-poor angiomyolipoma (AML) and oncocytoma. In addition, cystic RCC, as well as solid RCC with certain imaging features, may be expected to exhibit a more indolent disease course³ and thus be suitable for active surveillance. Diagnostic limitations associated with percutaneous biopsy further underscore the value of accurate characterizing of renal lesions by imaging. However, even once a decision has been made to resect a renal lesion, further decisions are required regarding the optimal surgical intervention, including suitability of the lesion for nephron-sparing surgery.^{4,5} Assessment of local staging, tumor aggressiveness, and contralateral renal function all may influence such decisions regarding the surgical procedure most likely to minimize local recurrence while preserving renal function.

Despite curative resection of the primary lesion, 20% to 30% of localized tumors will recur.¹ However, the advent of molecular targeted therapy for the treatment of metastatic RCC has heralded new hope for a disease typically unresponsive to cytotoxic chemotherapy and exhibiting limited response to the previous standard of care, cytokine therapy. These new agents are not without significant side effects and expense. Therefore, an ability to predict treatment response is of paramount importance to allow timely diversion of likely and true nonresponders into alternative treatment options, to determine appropriateness and timing of metastatectomy, and to counsel patients about prognosis. In this context, reliable noninvasive determination of histologic subtype may facilitate subtype-specific treatment decisions.

Magnetic resonance imaging (MRI) provides a comprehensive assessment of renal masses that includes multiple forms of tissue contrast as well as functional parameters. These features of MRI have led to its rapid evolution for the detection, diagnosis, staging, and assessment of aggressiveness and treatment response of RCC, in a context of the previously noted clinical demands. Advances in MRI have created a role for its use in the management of both localized disease as well as in advanced-stage disease. In this article, we review appropriate MRI protocols for renal mass imaging, the MRI features of major RCC subtypes, and the clinical application of MRI to impact the prognosis and management of RCC.

RENAL EPITHELIAL NEOPLASMS: HISTOPATHOLOGY AND ASSOCIATION WITH BIOLOGIC BEHAVIOR

Renal cortical tumors are a genetically, biologically, and histologically diverse group of neoplasms, ranging in metastatic potential from the benign oncocytoma to the relatively indolent chromophobe and less aggressive papillary subtypes to the more aggressive clear cell subtype.^{6,7} Indeed, histologic subtype of RCC has been strongly correlated with prognosis.^{8,9}

Clear cell RCC is by far the most common subtype (65%–70% of RCC diagnoses).⁹ Histopathologically, clear cell RCC contains cells with clear cytoplasm related to dissolved lipids, which grow in an acinar or solid-nested growth pattern and are enveloped in dense, arborizing vasculature.⁷ Necrosis, hemorrhage, calcification, osseous metaplasia, and cystic degeneration all may occur in this subtype.⁶ Approximately 50% to 84%^{10,11} of cases of

sporadic clear cell RCC exhibit inactivation of the Von Hippel-Lindau tumor suppressor gene on chromosome 3p, with consequent accumulation of hypoxia-inducible factor and promotion of angiogenesis via overexpression of vascular endothelial growth factor (VEGF) and platelet-derived growth factor.¹² Clear cell RCC has been shown in large series to have the highest metastatic potential and poorest survival of the major histologic subtypes.^{9,13}

Despite the overall less favorable outcome of clear cell RCC, this subtype can exhibit varying degrees of cystic change, a feature that in turn may portend a more favorable prognosis. Indeed, multilocular cystic RCC is a subtype itself of clear cell RCC that is almost entirely cystic in nature. This entity is histologically characterized as a cystic lesion lined only by a single layer of clear-to-pale cells and that contains scant papillae and a variable fibrous component, being separated from the renal cortex by a fibrous capsule and without evidence of frank solid elements. In contrast with the more typical, predominantly solid clear cell RCC, the multilocular clear cell RCC has a very indolent course and excellent progression,¹⁴ without a single reported instance in the literature of associated recurrence, distant metastasis, or tumor-related death.

Papillary RCC (pRCC) accounts for 10% to 15% of RCC.⁹ This subtype is histologically distinguished by its papillae that are composed of a fibrovascular core containing foamy macrophages. Necrosis, hemorrhage, and cystic degeneration are often present.⁶ A well-developed tumor capsule is also commonly present. The pRCC is typically diagnosed at an earlier stage and lower grade than clear cell RCC and has a significantly lower incidence of visceral metastases when compared with stage-matched cohort of clear cell tumors.^{15,16} In addition, metastatic lymphadenopathy is associated with a better outcome in pRCC than in clear cell RCC (overall survival of 65% vs 19%, respectively).¹⁵

Although pRCC is generally considered as having a better prognosis, this view is challenged by the recognition by Delahunt and Eble¹⁷ of 2 cellular subtypes of pRCC (types 1 and 2), a scheme subsequently recognized by the World Health Organization 2004 classification⁶ of renal tumors. Type 1 pRCC, which accounts for up to 73% of cases,² consists of papillae lined by a single layer of small cells with scanty clear-to-basophilic cytoplasm. Type 2 pRCC consists of papillae lined by cells that are eosinophilic and contain pseudostratified nuclei with a higher nuclear grade. Most papillary type 1 tumors are considered low-grade tumors, whereas most papillary type 2 tumors are high-grade neoplasms.¹⁸ In addition to their disparate histologic features, differing biologic behavior of type 1 and type 2 pRCCs has been described, with type 2 lesions reported to have a worse prognosis.¹⁹ For instance, at multivariate analysis, Delahunt et al²⁰ found that type 2 lesions presented at higher grade and a more advanced stage¹⁷ and that the subtype of pRCC is independently associated with survival. In addition, Pignot et al²¹ observed an overall survival and disease-free survival of type 1 pRCC of 89% and 92%, respectively, compared with values of 55% and 44%, respectively, for type 2 pRCC. Furthermore, Yamashita et al²² observed that type 2 pRCC had a significantly higher frequency of vascular invasion and presence of a high-grade component. Finally, although venous invasion is more common in the clear cell subtype, this finding, when present in the papillary subtype, has been shown to confer a very poor prognosis, with a 5-year cancer-specific survival significantly worse than that of clear cell RCC with venous thrombus.¹⁵

Despite the abovementioned data, this binary classification of pRCC may be overly simplistic and remains controversial. Not all pRCCs can be clearly classified into these 2 categories, as a substantial fraction exhibits features of both subtypes, and additional variants of pRCC, including the oncocytic pRCC, have been recognized.^{23–25} In addition, molecular and genetic studies fail to demonstrate the clear separation between these subtypes that has been described by standard histologic assessment.²⁶ Perhaps, most importantly, not all studies have confirmed the prognostic significance of the type 1 versus type 2 distinction, as many cases of type 2 pRCC will exhibit indolent behavior.^{23,27,28}

Chromophobe RCC is the third most common subtype and accounts for 6% to 11% of RCC.⁹ This subtype histologically exhibits solid sheets of cellular growth.¹⁹ A perinuclear halo is a characteristic feature, and binucleate cells are common.⁹ Necrosis and hemorrhage are uncommon.⁹ Metastatic disease is rare in this subtype and, when observed, is associated with a better prognosis than metastatic disease in either the papillary or clear cell subtypes.²⁹ Chromophobe RCC may have a higher propensity to metastasize to the liver as compared with clear cell and papillary histology.³⁰

Collecting duct tumors, also known as Bellini tumors, are located centrally in the renal medulla and account for less than 1% of RCC. These tumors portend a very poor prognosis, with most cases presenting with high-grade nuclear features and established metastatic disease.⁷ Medullary carcinoma is a particularly aggressive and fast-growing subtype of collecting duct tumors that is virtually exclusively observed in young black men with sickle cell trait.⁶

The rare mucinous tubular and spindle cell carcinoma, also located in the renal medulla, has been reported in approximately 100 cases in the literature. This entity has been reported to be generally low-grade and to exhibit indolent behavior, with extremely limited reports of metastatic potential.⁷

Sarcomatoid transformation does not represent a unique subtype but rather may occur in the setting of any of the previously noted subtypes. Although a relatively rare occurrence, reported in up to 13% of cases of RCC,^{31–33} sarcomatoid transformation represents a locally aggressive process with a high metastatic rate and a significantly worse prognosis.³⁴ Mean survival for cases of RCC with sarcomatoid transformation has been reported to be up to 24 months, although it is typically less than this.³¹ Most cases contain histologic necrosis, which is independently associated with an even poorer outcome.³⁴

Although most cases of RCC are sporadic, a number of syndromes associated with hereditary forms of RCC exist, including Von Hippel-Lindau syndrome (associated with clear cell RCC), hereditary pRCC (associated with pRCC), and Birt-Hogg-Dube (associated with oncocytomas, chromophobe RCC, and hybrid lesions composed of admixture of these 2 entities).¹⁹ Patients with a hereditary RCC syndrome tend to develop multiple, bilateral RCCs, often first observed at a younger age than cases of sporadic RCC.

The MRI findings in less common tumor subtypes such as Xp11.2 translocation RCC^{35,36} and clear cell papillary type as well as other histopathologic differentiations of RCC (eg, rhabdoid) have not been widely described. Hemorrhage, necrosis, an infiltrative appearance,

and advanced stage at presentation have been reported in small series of Xp11.2 translocation RCC.^{35,36} Clear cell papillary type is reported to be associated with end stage renal disease,³⁷ and in a small pathology series of 15 cases, all tumors were lowgrade, without lymphatic or distant metastatic disease.³⁸ Because of potential overlap in MRI findings among the most common RCC subtypes and the possibility of a less common histopathologic subtype/differentiation, biopsy remains necessary when it is desired to make a specific histopathologic diagnosis preoperatively.

Not all renal masses are malignant. Angiomyolipomas are the most common benign renal tumor and are composed of fat, smooth muscle, and dysplastic blood vessels in varying proportions. A small fraction of AMLs contain only trace amounts of lipid and have been referred to within the literature as minimal-fat AMLs, although a precise pathologic criterion for this distinction is lacking. The clinical significance of this subtype resides in the difficulty in making a presurgical diagnosis with standard imaging methods due to lack of the characteristic fat contents identified in the more classic AMLs. Oncocytomas are the second most common benign renal cortical tumor, accounting for 6% to 9% of cases.⁷ Oncocytomas, which are composed of a markedly granular eosinophilic cytoplasm,⁷ share a common cell of origin with chromophobe RCC, as both are derived from the intercalated cells of the collecting duct system. Mitotic activity and necrosis within oncocytomas are rare.

MRI PROTOCOL FOR RENAL MASS EVALUATION

Magnetic resonance imaging of renal masses may be adequately performed using either a 1.5T or 3T magnet in combination with a phased-array body coil. To characterize a renal lesion, included pulse sequences must allow for a robust assessment of tissue enhancement. Furthermore, tissue characterization, including the presence of cystic characteristics, as well as the presence of intralesional bulk and microscopic lipid contents are essential steps in the characterization of a renal mass. To this end, standard renal mass MRI protocols typically incorporate a combination of axial dual-echo in-and-opposed-phase gradient-echo T1-weighted images followed by axial and coronal T2-weighted echo-train imaging, usually with either fast/turbo spin echo or with half Fourier single-shot fast spin-echo acquisition. A form of frequency-selective fat saturation is typically applied in the axial or coronal T2-weighted images. Single-shot spin-echo echo-planar diffusion-weighted imaging (DWI) with generation of apparent diffusion coefficient (ADC) maps is also now frequently incorporated into clinical protocols; although largely based on empiric experience, DWI of the kidneys is often performed using b values of 0, 400, and 800 s/mm².³⁹ Addition of a b value of 50 s/mm² should be considered if biexponential fitting is to be used.⁴⁰ Three dimensional (3D) fat-suppressed gradient-echo T1-weighted images performed before and at multiple time points after intravenous administration of gadolinium-based contrast agent are an essential component of the renal mass evaluation. Dixon-based approaches (see below) provide a more homogenous fat suppression than spoiled gradient-echo imaging with frequency-selective fat suppression strategies. For this application, where the general goal is achieving homogenous suppression of fat signal instead of accurate fat quantification, a Dixon-based acquisition with only 2 echoes provides an optimal balance between acquisition speed and image quality. Depending on the institutional preferences, dynamic

contrast-enhanced (DCE) images can be obtained in the axial or coronal plane. The addition of precontrast and postcontrast images in other planes, including sagittal images, can be helpful in the evaluation of exophytic masses and for the confirmation of concerning features (ie, thick septae/nodules) in cystic renal masses.

The detection of bulk fat within a renal mass, indicative of an AML, has generally relied upon either signal loss within the mass when comparing similar image sets acquired both with and without fat suppression or by the observation of etching artifact along a lesion's interface with adjacent renal parenchyma on opposed-phase gradient-echo T1-weighted images.⁴¹ However, both of these imaging findings primarily allow for detection of the presence of adipose tissue (ie, "bulk fat"). Quantification of the amount of fat within an AML, not achievable with these standard sequences, can have clinical relevance given that AMLs containing a greater proportion of fat, with associated decreased vascular component, are less likely to benefit from embolization, the standard treatment to prevent hemorrhage in suitably sized lesions.^{42–44} Furthermore, an AML may contain only a tiny amount of fat that may be eccentric in location, thus potentially being missed by standard two-dimensional (2D) sequences. Both of these limitations of the standard sequences used for the detection of bulk fat are addressed via the recent emergence of multipoint Dixon sequences (Fig. 1). These sequences are based predominantly on the acquisition of multiple echoes at echo times offset from those of the standard in-phase and opposed-phase echo times and use concomitant phase information of the raw data as well as advanced reconstruction schemes to compute image sets representing the contribution of solely water and lipid protons. In addition to providing more robust fat and water separation, these sequences allow for calculation of the fat signal ratio (ratio between lipid signal and total signal), which allows for a more reliable quantification of fat content within an AML. In addition, these sequences are readily obtained using a 3D acquisition scheme, thereby providing contiguous thinner slices, which in turn may assist the detection of tiny amounts of fat within some AMLs. Indeed, 5% of lipid-rich AMLs detected using a 3D 2-point Dixon sequence are not identified using a standard 2D dual-echo T1-weighted sequences, attributable to small lesion size.⁴⁴ Although this initial study is promising, the ultimate role of the multiecho Dixon sequence in the detection and quantification of fat within renal AMLs still warrants further study.

As will be described in depth later, the ability to assess renal mass vascularity via contrast-enhanced MRI is critical for lesion characterization. The precontrast image set of the dynamic T1-weighted acquisition allows the detection of intrinsic T1 hyperintensity within renal lesions, indicative of hemorrhagic or proteinaceous content. This finding can be observed in both complex benign renal cysts as well as in RCC of various histologic subtypes. Attention must be given to achieving appropriate timing of the subsequently obtained dynamic postcontrast phases. Initially, a corticomedullary-phase image set is obtained, in which the timing of the acquisition corresponds approximately with that of the peak aortic enhancement. This phase both provides excellent assessment of arterial vascular anatomy and is also crucial for the differentiation of RCC subtypes.⁴⁵ Next, a nephrographic-phase image set is obtained, acquired approximately 1 minute after the start of the acquisition of the corticomedullary phase. Nephrographic-phase images have been established as the optimal phase for detection of renal lesions.⁴⁶ Alternatively, early and late

nephrographic phases can be obtained at 40 seconds (approximately 1 minute after the start of contrast administration) and at 90 seconds (approximately 2 minutes after the start of contrast administration), respectively, after the initiation of the corticomedullary phase.⁴⁷ Finally, an excretory-phase image set is obtained, acquired approximately 3 minutes after the start of the acquisition of the corticomedullary phase; this phase is useful for demonstrating the relationship between a renal mass and the renal collecting system⁴⁸ and possibly for further characterizing renal mass subtype in some instances. Additional imaging may be obtained during the excretory phase in different planes (eg, sagittal) and may help establish the preferred surgical approach for partial nephrectomy. At the authors' institutions, subtraction images, in which the precontrast image set is subtracted from each of the postcontrast image sets, are routinely generated and evaluated to assist in the evaluation for enhancement. Subtraction images may be particularly useful for the assessment of possible enhancement within smaller lesions or lesions with increased signal on precontrast T1-weighted images. For instance, Hecht et al⁴⁹ demonstrated that qualitative assessment of subtracted images is superior in the detection of renal mass enhancement in comparison with quantitative region-of-interest (ROI)-based assessment of the directly acquired images, with particularly strong benefit for lesions that are hyperintense on precontrast T1-weighted images. However, generation of reliable subtraction images requires adequate coregistration of the precontrast and postcontrast image sets, which can be challenging in the setting of substantial respiratory motion artifact or inconsistent respiratory effort. Assessment of the degree of ghosting artifact around the renal contour and adjacent parenchyma has been suggested as a possible means of evaluating the extent of misregistration.⁵⁰ Acquisition of the DCE sequences at end-expiration facilitates achieving a reproducible position of the diaphragm during image acquisition and thus decreases misregistration artifact on subtraction images.⁴⁷ Finally, the volumetric nature of the dynamic postcontrast acquisitions enables multiplanar reformatting, which can be of particular use in the preoperative evaluation of renal masses, for instance, in determining suitability for partial nephrectomy. Moreover, maximum intensity projection reconstruction of the corticomedullary acquisition provides angiographiclike reconstructions of the arterial vascular anatomy, which are also helpful for surgical planning.

The T2-weighted images have typically been used in the diagnosis of cystic or necrotic elements within renal masses as well as in the assessment of the degree of complexity of cystic renal lesions, for instance, by assisting the demonstration of areas of thickening, irregularity, or nodularity of the cyst wall or of internal septations.⁴⁷ More recent data have shown a key role for the T2 signal of solid renal masses in identifying the renal mass subtype as well as in characterizing the aggressiveness of certain lesions.^{51–54}

The precise role of DWI in the evaluation of renal masses has yet to be established. Studies have shown the use of DWI findings in lesion detection^{55,56} and characterization^{57,58} However, the added value of information derived from DWI compared with that obtained from DCE sequences and other standard sequences remains unclear. In the authors' experience, DWI may be most helpful in patients with contraindications to receiving gadolinium-based contrast agents, in whom this technique provides an additional mechanism of image contrast to standard T1- and T2-weighted imaging.

Although CT has historically served as the mainstay of renal mass characterization given its lower cost, wider availability, and greater level of comfort among some radiologists and surgeons, this paradigm is currently shifting in view of the multifaceted evaluation provided by MRI via the abovementioned sequences. Magnetic resonance imaging not only avoids ionizing radiation but also can provide a more comprehensive evaluation. For instance, studies have shown that MRI can detect very small enhancing elements within cystic masses,^{59,60} is more sensitive for areas of complexity within cystic lesions,⁶¹ and can detect solid low-level enhancement within renal masses that is missed by CT.²³ In addition, only MRI can reliably detect intravoxel fat. Furthermore, MRI may provide more accurate information regarding local staging, for instance, in perinephric fat and renal sinus fat invasion,⁶² with the latter in turn serving as a predictor of muscular venous branch invasion (MVBI).⁶³ Moreover, various quantitative MRI techniques, including DCE-MRI, arterial spin labeling (ASL), DWI, and intravoxel incoherent motion (IVIM), provide a far more sophisticated assessment of histologic features of renal masses that is currently not possible with CT.

MRI PHENOTYPE OF RCC

In vivo characterization of RCC is of paramount clinical importance, as management pathways in localized and metastatic diseases are subtype specific. Percutaneous core biopsies are not only invasive but also prone to sampling error and thus can be nondiagnostic in 2.5% to 22% of cases^{19,64,65}. In addition, tumor grade, most commonly evaluated by the Fuhrman nuclear grading scheme, is widely used within prognostic models for localized diseases, such as the stage, size, grade, and necrosis scheme and University of California, Los Angeles Integrated Staging System,^{66,67} although it cannot be reliably predicted by biopsy.¹⁹ However, the role of MRI as a noninvasive, reproducible, and reliable biomarker to predict such features of RCC is increasing. Later, we will discuss how the radiologist can apply findings from the various MRI sequences for these determinations.

Qualitative Morphologic Assessment

Numerous qualitative features from a standard renal mass MRI protocol have shown significant associations with particular histologic subtypes of renal masses and may allow for an accurate determination of subtype in most cases.

Clear Cell RCC—The hallmark feature of clear cell RCC on MRI is its characteristic hypervascularity, reflecting dysregulated angiogenesis.⁵² This hypervascularity is best identified on corticomedullary-phase images and may manifest as solid areas within the tumor exhibiting enhancement that is similar to or greater than that of the normal renal cortex⁴⁵ (Fig. 2). On later phases, clear cell RCC shows rapid washout of contrast, appearing hypointense to the renal cortex by the excretory phase.⁴⁵ Although this particular enhancement pattern is strongly suggestive of the clear cell subtype, it should be evaluated in the context of other lesion characteristics. For instance, clear cell RCC typically exhibits solid elements with heterogeneous signal intensity on T2-weighted images, including hyperintense elements. In addition, up to 60% of clear cell RCC contain evidence of intravoxel lipid on dual-echo gradient-echo T1-weighted images⁶⁸ (Fig. 2). Although this

finding can be rarely observed in other RCC subtypes, the combination of intravoxel lipid with tumor hypervascularity and heterogeneous T2-signal appearance with hyperintense areas is virtually diagnostic of clear cell subtype. Clear cell RCC can also exhibit varying degrees of internal necrosis, hemorrhage, and cystic change, although none of these imaging findings are specific for the clear cell subtype.

Among cases of clear cell RCC, a number of findings have been shown to be predictive of whether the lesion is of low or high Fuhrman grade. For instance, intratumoral necrosis, occurring once a lesion outgrows its blood supply, manifests in central stellate nonenhancing T2-hyperintense areas and has been significantly associated with high-grade clear cell RCC⁵² (Fig. 3). In addition, necrosis has been shown to be a significant marker of adverse prognosis, even independent of histologic grade, determined by both histopathologic analysis⁶⁹ and MRI.⁷⁰ Retro peritoneal vascular collaterals and renal vein thrombosis (Fig. 4) have also both been associated with high-grade clear cell RCC.⁵² Finally, one study reported that a predominant cystic component had a specificity of up to 94% for the prediction of low nuclear grade for clear cell RCC.⁵²

Papillary RCC—Papillary RCC is distinguished by its characteristic very low level of enhancement, exhibiting markedly lower enhancement than the renal cortex on corticomedullary-phase images with a reported mean tumor-to-cortex enhancement index of 20% (SD, $\pm 20\%$).⁴⁵ In addition, the degree of enhancement of pRCC is progressive over time, such that its internal enhancement may become more apparent to the radiologist during later phases.⁴⁵ Other typical features of pRCC include a peripheral location, circumscribed margins, and rounded contour as well as homogeneity and decreased signal of its solid elements on T2-weighted images^{52–54} (Fig. 5). Histologically, pRCC can contain hemosiderin and other chronic blood products (Fig. 6), leading to areas showing susceptibility effect on late echo dual-echo T1-weighted images. Papillary RCC may also contain prominent internal areas of hemorrhagic cystic change; such cases appear on MRI as a T1 hyperintense cystic lesion with peripheral mural nodules. The peripheral solid subelements of these masses typically demonstrate homogeneous T2 hypointensity and low-level enhancement, similar to that of entirely solid pRCC.^{47,52,71} A recent study noted enhancement on MRI using subtracted postcontrast images in histologically confirmed pRCC that did not meet criteria for enhancement on multiphase CT²³; this observation supports a particular role for MRI over CT in the assessment of this RCC subtype given the known low-level enhancement of pRCC that may create an overlapping imaging appearance with that of a complex cyst. Detection of enhancement in pRCC is particularly challenging in hemorrhagic cystic masses.

The potential difference in biologic behavior and clinical prognosis between types 1 and 2 pRCC have led to a desire to distinguish these 2 entities by imaging. To this end, Yamada et al⁷² evaluated CT features of 12 type 1 and 8 type 2 pRCCs, noting that type 2 lesions presented at a more advanced stage and more frequently had irregular margins. Nonetheless, these authors observed that the typical homogeneous low-level enhancement of pRCC could be observed in either type. More recently, Egbert et al²³ assessed 43 type 1 and 13 type 2 pRCCs. Although type 2 lesions were likewise noted on CT to be more commonly

infiltrative in morphology, overlap in imaging features was again noted, and no significant difference in MRI features could be identified between the 2 groups.

Recently, an imaging-based classification has been proposed for pRCC based on whether the lesion exhibits a focal or infiltrative morphology on MRI.⁷¹ Similar to previous reports, all 128 pRCCs in this study, types 1 and 2, exhibited the typical homogeneous hypovascular appearance associated with papillary tumors⁵² (Fig. 5). Moreover, there was no difference in the frequency of metastatic disease among focal papillary tumors, which included 65 type 1 and 54 type 2 neoplasms. In contradistinction, all 9 cases of pRCC with an infiltrative appearance on MRI represented type 2 tumors. This infiltrative appearance (Fig. 7) was found to be a significant predictor of metastatic disease, independent of subtype (1 vs 2), tumor size, or T stage, suggesting an independent use for an MR phenotype. Furthermore, renal vein thrombosis, which was present in 89% of the infiltrative lesions and in no focal lesions, was found to have the strongest association with metastatic disease of any of the variables. These findings highlight the biologic and radio-logic heterogeneity of the type 2 subgroup^{17,20} (Fig. 6) and indicate an intriguing role for MRI features (ie, infiltrative morphology and renal vein thrombus) to further stratify type 2 lesions and more accurately identify those lesions that are likely to develop metastatic disease.

Chromophobe RCC—Although conventional MRI has strong performance in the differentiation of clear cell RCC and pRCC, its performance is lower in the reliable identification of chromophobe RCC. This likely reflects the much lower frequency of chromophobe RCC as well as its less unique appearance using the described imaging methods. In particular, separate studies have observed the degree of enhancement of chromophobe RCC to be intermediate between that of the more common clear cell and papillary subtypes at multiple postcontrast phases, creating a challenge in using a qualitative assessment of lesion enhancement to reliably identify the chromophobe subtype. Indeed, the mean enhancement of chromophobe RCC during the corticomedullary phase is approximately 60% (SD, 50%).⁴⁵ Regardless, the diagnosis should be suspected in masses with intermediate enhancement during the corticomedullary phase, particularly in large masses (eg, >3 cm) with somewhat homogenous appearance and no evidence of central necrosis. It is, however, anticipated that more advanced quantitative imaging techniques will be needed to allow for the accurate prediction of this histologic subtype (Fig. 8).

Quantitative Assessment of High-Resolution DCE-MRI

Most clinical MRI protocols rely on the acquisition of high resolution, contrast-enhanced 3D data sets with limited temporal resolution (see MRI Technique above). An estimation of the degree of lesion enhancement performed in a qualitative fashion by a visual assessment of the various postcontrast acquisitions is prone to both interobserver and intraobserver variability. To reduce this variability and thereby potentially improve the accuracy of assessments based on MRI phenotype, quantitative approaches have been described. For instance, Sun et al⁴⁵ performed an ROI-based analysis on 113 RCCs evaluated by MRI, in which a small ROI was manually traced on a solid region visually showing the greatest degree of enhancement. As expected, clear cell RCC demonstrated greater enhancement than the renal cortex in the corticomedullary phase and washout in the nephrographic phase,

whereas pRCC enhanced much less than the renal cortex in both phases, although exhibiting progressive enhancement in the later phase. Further more, the difference in percentage signal intensity change between clear cell and papillary subtypes was highly significant and exhibited excellent accuracy in distinguishing these 2 subtypes using corticomedullary-phase images. No significant difference in enhancement metrics was observed between low and high-grade lesions for any subtype in this study. Subsequently, Vargas et al⁷³ used a similar small-ROI analysis on DCE-MRI in 152 renal masses, incorporating both benign and malignant tumors. Concordant with Sun et al, these authors observed a significantly higher percentage signal intensity change in clear cell RCC, compared with other RCC subtypes, on all phases. However, this approach did not allow for the differentiation of clear cell RCC and oncocytoma based on enhancement characteristics, and AMLs were noted to exhibit even higher percentage signal intensity change than clear cell RCC on the corticomedullary phase. Thus, although this study confirmed a role for the quantitative assessment of enhancement for renal mass evaluation, overlap in metrics prevented the establishment of precise threshold values.

Misregistration between phases due to respiratory or patient motion as well as subjectivity in placement of a small ROI may contribute to interobserver and intraobserver variability in the characterization of renal mass enhancement and thereby lower the performance of this method. Alternatively, Chandarana et al⁷⁴ proposed the assessment of whole-lesion (WL) enhancement including the analysis of the histogram distribution of enhancement throughout the lesion (software pending commercialization) as a potentially more robust and reproducible approach. This group evaluated 55 clear cell and 19 papillary subtypes, comparing their method with both qualitative and ROI-based quantitative approaches. The most accurate parameter for differentiation of the 2 subtypes, the third-quartile WL enhancement, had significantly greater performance than the qualitative assessment. Although WL enhancement parameters exhibited higher accuracy, sensitivity, and specificity than the ROI assessment, these differences were not statistically significant. Furthermore, despite interreader disagreement in more than 10% of cases using the qualitative assessment, there was excellent interreader agreement for the WL-enhancement histogram analysis (kappa coefficients ranging from 0.91 to 1.0). Finally, the postprocessing generally inherent in such WL analysis was greatly reduced by automated lesion registration and segmentation, thereby facilitating potential adoption of this model into clinical practice.

The value of quantification of WL tumor enhancement was also explored by Vargas et al⁷⁵ for the prediction of RCC grade. In this study, although single-slice ROIs showed no association with grade, lower WL enhancement on nephrographic and excretory phases was associated with higher tumor grade with significant associations observed between tumor grade and mean, median, top 10%, top 25%, and top 50% WL enhancement. These associations likely relate to a greater degree of necrosis in the more aggressive tumors.

High-Temporal-Resolution DCE-MRI

Dynamic contrast-enhanced-MRI with high temporal resolution entails the acquisition of 2D or 3D MRI images before, during, and after a bolus of contrast, with markedly increased temporal resolution, typically less than 5 seconds per acquired time point. This approach is

intended to provide even more exquisite detail regarding vascular and perfusional changes in renal masses.⁷⁶ Although these data may be analyzed using a semiquantitative manner, incorporating such heuristic parameters as the initial upslope, time to peak, and washout, of contrast, a truly quantitative analysis using a pharmacokinetic model can offer additional pathophysiologic information.⁷⁷ A number of such models have been proposed, with the ideal model for RCC evaluation yet to be clearly established.^{76,78} A recent study applied a generalized kinetic model and extended shutter-speed model analysis in 24 renal masses and reported 100% of accuracy in distinguishing the 3 chromophobe RCCs from the other lesions in the cohort,⁷⁹ suggesting an ability of perfusion MRI to address a clinical challenge of conventional DCE. Nonetheless, the acquisition, postprocessing, and interpretation of perfusion MRI require greater standardization and automation before its routine incorporation into clinical practice.⁸⁰

Arterial Spin Labeling

It has been suggested that factors extraneous to the renal mass itself, such as blood flow and tissue permeability, may limit the accuracy of contrast-enhanced MRI in the evaluation of lesion vascularity. ASL provides a noninvasive method of assessing vascularity that is independent of these factors and avoiding the need for contrast administration. This technique, which has been most widely applied for the evaluation of cerebral perfusion, uses the water component of blood as a natural contrast agent and magnetically “labels” incoming water protons using both radiofrequency pulses and gradient fields.^{59,81} The difference in signal between images obtained before and after such magnetic labeling provides direct information about tumor perfusion. Additional advantages of this method include applicability to patients at risk for nephrogenic systemic fibrosis⁸² and the ability to perform successive measurements of perfusion without repeating the contrast administration. The differentiation of RCC subtype would seem to be a natural application of this technique.^{81,82} For instance, Lanzman et al⁸¹ evaluated 32 renal masses using ASL. ASL demonstrated a significant difference in mean and peak tumor perfusion between RCC subtypes, with pRCC exhibiting the lowest perfusion, as expected. In addition, oncocytoma exhibited greater perfusion than any RCC subtype using ASL, suggesting a possible additive role for this technique in comparison with DCE-MRI. To date, the application of ASL has been limited by a lack of commercial availability, and its use has been essentially limited to academic centers.

Diffusion-Weighted Imaging

Diffusion-weighted imaging is an additional noninvasive technique that can capture intrinsic MRI properties of tissues for quantitative MRI lesion analysis without the administration of contrast. It is based on the principle of random Brownian motion of water molecules and is sensitive to the reduction in water motion that occurs in highly cellular tissues that have an increased density of cell membranes.⁷⁶ The role of DWI in the characterization of renal lesions is developing,^{55,56} and there is enthusiasm for the potential of the ADC as a means to offer objective characterization.

The most consistently identified association between ADC values and RCC subtype has been a significantly lower ADC in pRCC compared with other subtypes. Whereas this lower

ADC in pRCC was initially reported by Taouli et al³⁹ in a cohort of 28 RCCs, Wang et al⁵⁷ subsequently evaluated 85 RCCs at 3T and found that, using a b value of 800 s/mm², ADC values provided highly sensitive and specific differentiation of all 3 major RCC subtypes, with pRCC again being found to exhibit the lowest ADC values and clear cell RCC having the highest ADC values. However, Sandrasegaran et al⁸³ did not observe a significant difference in ADC values in the clear cell subtype.

More recently, Rosenkrantz et al⁵⁸ assessed the use of ADC values for the prediction of grade of clear cell RCC. In a cohort of 57 clear cell RCCs, ADC maps obtained using a b value of 800 s/mm² were significantly lower in high-grade compared with low-grade tumors (Fig. 3). Furthermore, incorporation of ADC values significantly improved the performance of a multivariate model that included conventional MRI features such as necrosis and perilesional fat invasion for the prediction of high-grade clear cell RCC. A separate study with 17 clear cell RCCs also observed lower ADC values in the high-grade lesions, although this was not statistically significant in this small cohort.⁸³

Intravoxel Incoherent Motion MRI

The ADC values derived from DWI are sensitive to any source of incoherent motion and thus are impacted by both capillary perfusion as well as true molecular diffusion. Le Bihan et al^{84,85} described an alternative DWI model termed IVIM MRI, which allows for separation of the relative contributions of perfusion and true diffusion to the measured signal. The perfusion contribution, labeled in this model as pseudodiffusion, is most pronounced at low b values and can be differentiated from true diffusion by acquiring images with a range of low and high b values and subsequently applying a biexponential curve fit to the acquired signal intensities.⁸⁶ This approach provides the metrics pseudodiffusivity D_p , reflecting capillary perfusion; diffusivity D_t , reflecting true diffusion; and f_p , reflecting the volume fraction of the perfusion component within the measured signal. In the initial application of IVIM in renal lesions, Chandarana et al⁴⁰ demonstrated a significantly higher f_p and lower D_t in enhancing renal masses compared with nonenhancing masses, differentiating these 2 groups with a higher accuracy than ADC values obtained using a standard monoexponential fit. This group subsequently applied the IVIM model for differentiating RCC subtypes,⁸⁶ observing that f_p had a higher accuracy than ADC or D_t for identification of the clear cell subtype. Furthermore, the combination of f_p and D_t yielded improved performance for subtype differentiation, contributing to growing evidence suggesting that separation of the differential contributions of perfusion and true diffusion effects may provide greater diagnostic use than achieved by a standard monoexponential diffusion assessment.⁸⁶

CLINICAL ROLE OF MRI IN LOCALIZED DISEASE

Avoidance of Surgery for Likely Benign Lesions

Although RCC is the most common renal neoplasm, 11% to 16% of resected masses suspected to represent RCC prove to be benign,^{87,88} with most of these composed of oncocytomas or AMLs. Traditionally, the reliable identification of oncocytomas and some AMLs by imaging has been considered very challenging, such that it is generally accepted

that many such lesions will undergo resection. However, improved understanding of the imaging appearance of these lesions raises the possibility that their recognition on imaging may allow for a subsequent confirmatory biopsy and avoidance of surgery for a benign entity.

AML With Minimal Fat—Although most AMLs contain bulk fat and can be readily diagnosed with ease on CT or MRI, it is estimated that, in 5% of cases, bulk fat is not evident on imaging. Such AMLs with minimal lipid contents are composed nearly entirely of smooth vessel and disordered vascular components. It is this small subset of AMLs that is frequently confused with RCC by imaging and prone to unnecessary surgery, thus receiving much attention recently in the literature as a possible key application for MRI.

Kim et al⁸⁹ initially reported a loss of signal intensity on opposed phase images (ie, chemical shift MRI) of more than 25% to allow the differentiation of AML from other renal masses with a sensitivity and specificity of 96% and 93%, respectively. However, only 9 of 26 of the AMLs with minimal fat in their cohort were pathologically proven. Furthermore, their non-AML cohort was composed of clear cell RCCs and a number of different renal masses, including pRCC, lymphoma, oncocytoma, and reninoma. That clear cell RCC is the subtype with the more abundant lipid content has been well documented by electron microscopy,⁹⁰ and it is rare or not typical of the other renal tumors included in this cohort to have intralesional lipid. Thus, the selection of the non-AML tumors in this study likely influenced the differences noted between the 2 cohorts.

Indeed, Hindman et al⁹¹ evaluated 20 minimal-fat AMLs and 88 clear cell RCCs and observed no difference between the 2 groups, applying a similar analysis to that of Kim et al with the dual-echo chemical-shift sequence. In this study, however, a more homogenous comparison group was selected consisting only of clear cell RCCs, the subtype known to often contain intracellular lipid and thus be most likely to mimic a minimal-fat AML on chemical shift MRI. Furthermore, all AMLs were histologically proven using strict inclusion criteria requiring less than 25% of fat content on histologic assessment. Interestingly, the combination of small lesion size (<2 cm) and decreased signal intensity on T2-weighted imaging had an excellent diagnostic accuracy of 0.98 in distinguishing minimal-fat AML from clear cell RCC (Fig. 9). Decreased T2 signal intensity has been previously reported in minimal-fat AMLs⁹² and, although in general considered nonspecific, is highly suggestive of AML when observed in combination with signal loss on opposed-phase images.

Sasiwimonphan et al⁹³ found that minimal-fat AMLs demonstrated decreased T2 signal intensity, increased T1 signal intensity, high signal loss on opposed-phase images, and high ratio in signal intensity between early and delayed postcontrast images. Although the overlap in all of these features between minimal-fat AML and RCC precluded the use of any one feature for accurately making this distinction, a multifactorial model combining these features using calculated threshold values allowed for a sensitivity of 73% and specificity of 99% in distinguishing minimal-fat AML from RCC.

The diagnosis of AML can be achieved reliably with percutaneous biopsy, even in those AMLs with minimal amounts of fatty tissue, given the extremely high specificity of certain

immunohistochemical stains (HMB45 and MelanA) for this diagnosis. Thus, when the described imaging findings of minimal-fat AML are encountered, it seems reasonable for the radiologist to raise the possibility of this diagnosis and to suggest that a biopsy be performed, so as to avoid a potentially unnecessary surgery. Currently, the authors provide this recommendation when encountering a solid renal mass exhibiting avid homogeneous enhancement and decreased T2 signal.^{94–96}

Oncocytoma—Oncocytoma represents an additional common mimic of RCC on imaging. In contrast to the reliable identification of most AMLs by the detection of bulk fat, oncocytomas lack any single unique feature to enable the identification of most instances on imaging. A study from 1984 using CT concluded that the presence of a central scar in an otherwise homogeneous renal mass was indicative of an oncocytoma⁹⁷ (Fig. 10). However, areas of necrosis that occur within RCC can mimic the presence of a central scar (Fig. 3), and scars can occur in a small fraction of RCCs⁹⁸; such this finding has subsequently been shown to be unreliable, and until recently, oncocytomas have been considered indistinguishable from RCC on imaging.⁹⁹ Furthermore, oncocytomas may mimic RCC by exhibiting locally aggressive behavior such as evidence of perirenal fat invasion at histopathology in up to 7% of patients¹⁰⁰ and even invasion of branches of the renal vein.¹⁰¹

In 2009, Kim et al¹⁰² proposed that “segmental enhancement inversion” within a renal mass on dynamic postcontrast CT can reliably identify a mass as an oncocytoma; in their study, composed of 88 RCCs and 10 oncocytomas, this finding achieved a sensitivity of 80% and specificity of 99% in this diagnosis. This finding refers to the presence within the lesion of two distinct solid regions, with the region exhibiting a greater degree of enhancement during the corticomedullary phase subsequently exhibiting a lesser degree of relative enhancement during the delayed phase and the area with lesser degree of enhancement during the corticomedullary phase demonstrating a greater degree of enhancement during the delayed phase.¹⁰² However, several subsequent studies specifically assessing the value of this finding have failed to replicate the high diagnostic performance achieved in the original study by Kim et al, and its value remains controversial.^{103–105} Given the shared cell of origin of oncocytoma and the chromophobe subtype of RCC, particularly strong overlap between these two entities is expected. Although both the central scar and the segmental enhancement inversion can be seen on MRI studies as well, these two features do not allow for differentiation between oncocytoma and chromophobe RCC on MRI.¹⁰⁶

Although the radiologist may consider suggesting a diagnosis of oncocytoma and recommending biopsy in a renal mass exhibiting a central scar or segmental enhancement inversion, the role of biopsy in this mass is less clearly established compared with that of AML. This difficulty relates to the strong overlap between oncocytoma and chromophobe RCC even on histologic, and possibly on immunohistochemical, assessment. Some centers report excellent performance in confidently diagnosing oncocytoma on biopsy using special stains, such as the Hale colloidal iron stain.¹⁰⁷ However, the reliability of this assessment depends on the expertise of the pathologist and has not been universally validated. In addition, some hybridrenal lesions may contain distinct regions of both oncocytoma and RCC within it, thereby being prone to sampling error even if the obtained tissue is confidently interpreted by the pathologist.¹⁰⁸ Given these pitfalls, we suggest that, even

when a renal mass biopsy returns a diagnosis of oncocytoma, continued imaging surveillance should be pursued to ensure continued stability.

Active Surveillance

The increasing incidental detection of renal masses has been associated with the diagnosis of a greater frequency of renal masses at a smaller size and earlier stage. Many such lesions exhibit slow growth and have very low rates of metastatic spread.¹⁰⁹ Current data are unclear whether therapeutic intervention in fact provides a survival benefit for these small incidental lesions.¹¹⁰ Therefore, active surveillance is increasingly becoming accepted as a reasonable management option. With this approach, immediate treatment is deferred while the lesion undergoes evaluation with serial imaging examinations. Any evidence of lesion progression between imaging examinations will subsequently trigger an intervention with curative attempt at the time of follow-up imaging. Historically, decisions regarding suitability of active surveillance in individual patients have been based on patient age and comorbidity, in combination with patient preferences, and have largely not been influenced by imaging features aside from lesion size alone. However, improved characterization of renal masses by MRI introduces the possibility of incorporating MRI features into this determination. Two particular groups of lesions for which MRI features may have a role in considerations of the suitability of active surveillance, small solid renal masses, which account for most newly diagnosed RCC,¹¹¹ as well as predominantly cystic renal lesions, are discussed later.

Small Solid Renal Masses—A large fraction of small solid renal masses (ie, <3 cm) exhibit indolent behavior, including slow growth or, possibly, even an absence of growth, during extended observation. Multiple studies have demonstrated the risk of metastatic disease to be essentially nonexistent in such renal masses exhibiting stability in size^{112–117} (Fig. 9). However, there traditionally has been no means of reliably predicting in advance which solid renal masses will or will not exhibit rapid growth, as standard features such as baseline lesion size or volume have been insufficient in this regard.¹¹⁸

Given that rapid growth of a solid renal mass under-going surveillance serves as the primary trigger for intervention (Fig. 10), prediction of those lesions most likely to grow at the time of diagnosis would be of significant clinical value. Dodelzon et al⁵¹ assessed associations between baseline MRI features of 47 solid renal masses undergoing active surveillance and subsequent lesion growth rate. At multivariate analysis, patient age and homogeneity on T2-weighted images were significant independent predictors of slow growth (Figs. 11, 12). Thus, it is possible that the MRI phenotype of a solid renal mass may serve as a marker to help select patients who are optimal candidates for active surveillance.

Predominantly Cystic Renal Lesions—Although up to 15% of all RCCs have been described as cystic RCC, this term does not refer to a specific RCC subtype given that a significant cystic component can be associated with any of the major RCC subtypes.¹¹⁹ Nonetheless, cystic change of RCC has been mostly strongly associated with the clear cell subtype, in which a significant cystic component can form within a solid mass or the solid component may form as a mural nodule within a cyst. Cystic RCC is thus a heterogeneous

group that encompasses a spectrum of entities. To aid in this management, predominantly cystic renal lesions are usually classified on imaging based on their degree of internal complexity by using the Bosniak cyst classification system, with this classification scheme guiding selection of a subset of cases for operative management. Specifically, cystic lesions classified as category 3 or 4 lesions have historically been considered to be at a substantially elevated risk of malignancy, thereby warranting prompt surgical intervention.

In contrast to this historical approach, most recent data indicate an overall favorable prognosis for the broad spectrum of predominantly cystic renal lesions. Jhaveri et al¹²⁰ recently evaluated 47 cystic renal masses for interval growth, local recurrence, or metastatic disease. Among cases with preoperative imaging, 73% did not show significant growth. In addition, only a single lesion was found to be high grade at pathologic assessment. No patient with localized disease at the time of diagnosis developed a local recurrence or distant metastasis during follow-up imaging. Finally, there was 100% disease-free survival during a follow-up period of 2 years. In an additional recent study, Smith et al¹²¹ evaluated outcomes after treatment in 69 Bosniak 2F and 3 lesions. Despite rates of malignancy at pathologic assessment of 25% in the category 2F lesions and of 54% in the category 3 lesions, no patients developed local recurrence or metastatic disease during follow-up after treatment. The results of these 2 studies support the indolent behavior, including very low metastatic potential, of predominantly cystic renal lesions. Thus, accurate determination of the predominantly cystic nature of an incidentally detected renal mass may assist in recognizing the favorable prognosis and potential suitability of surveillance for such lesions.

One particular group of cystic renal lesions warrants mention. Multilocular cystic RCC is classified in the World Health Organization 2004 classification of renal neoplasms as a subtype of clear cell RCC subtype that accounts for less than 3% of all RCCs.⁶ Despite the overall more aggressive behavior of clear cell RCC in general, this uncommon subset has been shown to have a highly innocuous natural history. For instance, Suzigan et al¹²² observed an absence of metastatic disease and disease specific survival of 100% at a mean follow-up of 66.1 months among 45 such cases, all found to be low grade. In addition, there has not been a single reported case within the literature of local progression or metastatic disease associated with this entity. Hindman et al¹²³ compared the CT and MRI findings of 23 cases of multilocular cystic RCC that underwent resection with pathologic findings. In this series, 7 masses were interpreted on imaging as category 2F cysts; 13, as category 3 cysts (Fig. 13); and 3, as category 4 cysts. The authors observed increasingly large fibrotic components in the higher Bosniak category lesions (ie, 60%-80% of vascularized fibrosis in the category 4 lesions) and suggested that this fibrotic component may correspond with the apparent solid enhancing elements mimicking tumor observed on imaging in the higher Bosniak category lesions. These insights may help to explain the indolent behavior of some cystic lesions that seem to exhibit a significant solid component on imaging. Nonetheless, an ability to reliably distinguish solid tumor and fibrosis within cystic renal lesions by imaging is currently lacking.

Preoperative Assessment

Local Staging—Partial nephrectomy has become the standard of care for small renal masses given improvements in surgical technique, comparable oncologic control with total nephrectomy, and avoidance of the negative impact of total nephrectomy on long-term renal function.^{4,5,124} However, preoperative evaluation of renal masses before partial nephrectomy requires an accurate assessment of the local stage of the tumor to assist surgical planning. Features to evaluate include tumor size; overall exophytic extent of the mass; location within the kidney; proximity to the renal collecting system; and potential invasion of the perinephric fat, renal sinus fat, renal vein, and renal collecting system.⁶² For example, the percentage of exophytic component in the mass is the best predictor of the need for intraoperative ultrasound at partial nephrectomy.¹²⁵ The use of MRI in the preoperative assessment of these features has been confirmed,⁶² with a negative predictive value of 100% for the detection of either collecting system or perinephric fat invasion as well as of 97% for renal sinus fat invasion.⁶² Of note, renal sinus fat invasion carries a worse prognosis^{126–128} given that RCC typically initially invades muscular venous branches of the renal vein before subsequent invasion of renal sinus fat and that the prognostic impact of MVBI is similar to that of frank renal vein invasion.¹²⁹ In a recent study of 186 renal masses evaluated by MRI, a distance between the tumor and the renal sinus fat of 0 mm had a sensitivity of 100% and a specificity of 94% for the detection of renal sinus fat invasion and 100% of sensitivity and 42% of specificity in the assessment for MVBI.⁶³

CLINICAL ROLE OF MRI IN ADVANCED DISEASE

The MRI phenotype of RCC can also add clinical value in the setting of metastatic disease, playing a complimentary role to renal mass biopsy. The role of lesion characterization by MRI in guiding the selection of both optimal surgical and medical management, as well as in the assessment of treatment response, is discussed later.

Surgical Management

Cytoreductive nephrectomy for patients with metastatic RCC represents the standard of care when technically feasible in patients with appropriate performance status.¹ This practice is supported by data from large randomized prospective trials performed in the era of cytokine therapy, demonstrating a cumulative 31% of reduction in the risk of death in patients treated with both surgery and interferon compared with those treated with interferon alone.^{130–132} This treatment approach is also supported by more recent, although relatively preliminary, data obtained after the advent of antiangiogenic molecular-targeted therapy.^{133,134} For instance, in a retrospective analysis composed of 314 patients receiving anti-VEGF therapy, 201 of whom also underwent cytoreductive therapy, Choueiri et al¹³⁴ observed improvements in overall survival in the nephrectomy group.

Most of the available evidence supporting cytoreductive nephrectomy is based upon patients with the clear cell subtype, who have been observed to account for most of the patients enrolled into the relevant clinical trials.²⁹ Accordingly, there is a lack of data supporting this approach in patients with other RCC subtypes, who in fact may fail to derive a similar therapeutic benefit from this invasive treatment. For instance, in a retrospective review of

606 patients who underwent cytoreductive nephrectomy at a single institution, Kassouf et al¹³⁵ noted that only 15% had non-clear-cell histology and that this group had a worse outcome in disease-specific survival than did the non-clear-cell group (14 vs 23 months).

Although a clinical benefit of cytoreductive nephrectomy in non-clear-cell RCC has yet to be definitively shown, this intervention is frequently applied without pathologic determination of the histologic subtype. The ability of MRI to subtype the tumor may prompt the radiologist to suggest a biopsy before potential cytoreductive nephrectomy in those lesions with MRI features suggesting a non-clear-cell histology. The resulting information may allow the surgeon to make a more informed decision regarding the appropriateness of debulking nephrectomy and potentially spare a patient who is less likely to benefit from this procedure from being exposed to its inherent morbidity.

Medical Management

There has been a recent paradigm shift in the medical management of metastatic RCC from cytokine therapy to antiangiogenic molecular-targeted therapy, facilitated by enhanced understanding of the molecular and genetic pathways that drive this disease.¹² In the dominant clear cell subtype, overexpression of VEGF and platelet-derived growth factor promotes angiogenesis, such that these receptors serve as specific target of the new agents currently in use, including the multikinase inhibitors sunitinib, pazopanib, axitinib, and sorafenib as well as the monoclonal antibody bevacizumab. Another group of antiangiogenic agents, the mammalian target of rapamycin inhibitors, such as temsirolimus and everolimus, have also shown efficacy in the medical management of metastatic RCC.¹³⁶

Similar to the situation regarding debulking nephrectomy, most of the data supporting antiangiogenic therapy for metastatic RCC are based on patients with the clear cell subtype, who likewise have comprised the bulk of the population enrolled in the relevant clinical trials.²⁹ Increasing evidence suggests that the response to this treatment depends on the histologic subtype,¹ which therefore should impact selection of the first-line agent from among the array of options. Although the National Comprehensive Cancer Network guidelines recommend sunitinib, pazopanib, or the combination of bevacizumab and interferon as first-line agents for most patients with metastatic clear cell RCC, these guidelines recommend clinical trial enrollment as the first-line option for patients with non-clear-cell subtypes given the lack of existing data regarding an optimal first-line agent.¹ As it is expected that non-clear-cell subtypes will have a weaker response to the tyrosine kinase inhibitors that serve as targeted first-line agents for clear cell RCC, temsirolimus and erlotinib have been suggested as first-line agents for patients with non-clear-cell RCC who are not enrolled in a clinical trial, although the data supporting this practice are limited. Given this dichotomy in treatment between patients with clear cell and non-clear-cell subtypes undergoing medical management for metastatic disease, a pretreatment biopsy has been suggested to help guide selection of the optimal agents.² Moreover, patients presenting with stage IV disease at diagnosis frequently exhibit large heterogeneous tumors with extensive necrosis. The MRI can play a complementary role in those cases where the results of the percutaneous biopsy are nondiagnostic or not definitive for a specific subtype.

As noted, sarcomatoid RCC does not represent a distinct RCC subtype but rather the development of undifferentiated elements, a transformation that can occur in the setting of any RCC subtype and that confers a significantly worse prognosis.^{1,19} Neither cytoreductive nephrectomy nor antiangiogenic therapy is associated with a significant survival benefit in this condition.^{137,138} However, studies with small patient cohorts have shown benefit from treatment with standard cytotoxic agents, such as combination therapy with gemcitabine and either doxorubicin or capecitabine, that are not typically used for treatment of nonsarcomatoid metastatic RCC.^{1,19,139–141}

Given the distinct difference in selection of agents for the medical management of this patient cohort, identification of sarcomatoid RCC by imaging could have a clear clinical impact. Most patients are symptomatic (89%) and have distant metastases (77%) at initial presentation.¹⁴² Sarcomatoid RCCs tend to be large (mean diameter of approximately 10 cm) and commonly have irregular or infiltrative morphology as well as necrosis, renal sinus fat invasion, and perinephric fat invasion.¹⁴³ It has been suggested that a nodular T2 hypointense hypovascular focus with decreased ADC within a clear cell RCC may suggest sarcomatoid transformation.¹⁴⁴

Assessment of Treatment Response

Conventional Imaging Features—Although initial studies of metastatic RCC treated with multikinase or mammalian target of rapamycin inhibitors demonstrated prolonged progression-free survival (PFS) and overall survival compared with interferon therapy, there was limited objective response based on the changes in tumor size defined by the response evaluation criteria in solid tumors (RECIST), challenging the role of RECIST in this setting.¹⁴⁵ Of note, many patients with stable disease by RECIST criteria exhibited prolonged survival, supporting the proposed cytostatic nature of the newer antiangiogenic agents in comparison with the cytocidal properties of more traditional chemotherapeutic agents that are generally assessed by RECIST. By targeting angiogenesis, these new agents induce necrosis,^{146,147} evident on CT as a decrease in attenuation and enhancement of metastatic lesions, thereby producing changes in vascularity before any measurable change in lesion size. Thus, RECIST is insufficient for assessing response to the new antiangiogenic therapies, in herently underestimating their clinical benefit and falsely classifying many responders as simply having a stable disease.

To address this challenge, CT-based Choi criteria have been proposed and investigated in numerous studies^{148–151}; this system has had varying success, being particularly prone to overcalling progressive disease and thereby excluding patients from potentially beneficial agents.^{148–151} Alternative CT-based schemes, including the morphology, attenuation, size, and structure (MASS) and size and attenuation on contrast-enhanced CT (SACT) criteria, have also been implemented with some success^{152,153} but may be somewhat complicated for routine clinical use. More recently, MRI-based criteria have been explored. Specifically, Kang et al¹⁵⁴ evaluated 16 patients being treated for metastatic RCC with sorafenib using both RECIST 1.0 and the authors' proposed MR-modified Choi criteria in which the determination of partial response incorporates both a decrease in tumor size as well as a decrease in enhancement. Although RECIST was not predictive of clinical outcome,

concordant with past studies, the MR-modified Choi criteria were significantly associated with median time to progression, attributed to the significant decrease in degree of enhancement in those tumors responding to treatment. A significant increase in T1 signal was noted within lesions after treatment, possibly suggesting a role for MRI over CT in assessing lesions for changes in enhancement after treatment. However, a recent study of patients with metastatic RCC undergoing antiangiogenic therapy compared RECIST 1.0, Choi criteria, tumor shrinkage of greater than 10% of decrease in the sum of the longest unidimensional diameter, and 15% or 20% of decrease in mean CT tumor density for assessing response to treatment and found that 10% of reduction in the sum of the longest unidimensional diameter on the first follow-up CT was an optimal early predictor of outcome.¹⁵⁵ Given the simplicity of such an approach and the easy implementation in clinical practice, continued research is needed to establish if other combinations of change in size and enhancement have an advantage in determining treatment response.

Dynamic Contrast-Enhanced MRI—Magnetic resonance imaging has the potential to assist in monitoring the response of metastatic RCC to antiangiogenic therapy.^{156,157} In a pilot study of the role of DCE-MRI to monitor the response of metastatic RCC to sorafenib in a small patient cohort, Flaherty et al¹⁵⁸ observed a significant decrease in the gadolinium forward exchange constant K_{trans} during treatment as well as a significant association between the percent decrease in this parameter and PFS. Interestingly, the baseline K_{trans} of the tumor before treatment was significantly associated with subsequent treatment response, suggesting an intriguing role for DCE-MRI to not only monitor but also predict therapeutic benefit. However, other studies have found conflicting results. Hahn et al¹⁵⁹ noted that the area under the curve during the initial 90 seconds after injection of gadolinium (Initial area under the curve⁹⁰) and K_{trans} were good pharmacodynamic biomarkers in patients treated with sorafenib (ie, there was a correlation between dose of the drug and changes in MRI variables), but the changes in DCE-MRI parameters after 4 weeks of sorafenib therapy were not predictive of PFS, suggesting that these biomarkers cannot be used as surrogate end points. Nevertheless, the correlation between K_{trans} and PFS was confirmed again in this study.¹⁵⁹

Arterial Spin Labeling—Similar to assessing tumor perfusion in primary renal masses, ASL allows for the assessment of tumor perfusion in metastatic sites and has the potential to serve as a biomarker of treatment response for metastatic RCC.⁵⁹ De Bazelaire et al¹⁶⁰ used ASL to identify significant decreases in tumor blood flow one month after treatment with the multikinase inhibitor vatalinib in patients exhibiting both partial response and stable disease compared with patients with subsequent progressive disease, suggesting a potential role for ASL in the early prediction of tumor response. In addition, Schor-Bardach et al¹⁶¹ used ASL to observe lower tumor blood flow at baseline in human RCC xenografts implanted into nude mice that failed to respond to treatment with sorafenib. Thus, as with DCE-MRI, ASL also seems to have potential for both predicting and monitoring response to anti-angiogenic therapy.

CONCLUSIONS

Magnetic resonance imaging has been proposed as a biomarker in RCC.⁵⁹ Testament to this designation, MRI is having an increasingly sophisticated role in the detection, characterization, perioperative evaluation, and assessment of treatment response for renal lesions. For instance, MRI allows for the differentiation between the most common RCC subtypes with a high degree of certainty and also for the prediction of tumor grade and metastatic potential. Although the benign entities of minimal-fat AML and oncocytoma mimic RCC on conventional imaging, their MRI phenotypes may allow for suggestion of the correct diagnosis by the radiologist, facilitating selection of such cases for confirmatory biopsy and potential avoidance of unnecessary surgery. Magnetic resonance imaging also has an increasingly recognized role in identifying incidental renal masses likely to have an indolent disease course and that may be optimal candidates for active surveillance. Given that the surgical and medical management of advanced disease is subtype specific, the MRI phenotype of renal masses can also impact management decisions. Finally, MRI may provide a key role in the assessment of response to emerging molecular-targeted therapies for which the traditional size-based criteria such as RECIST are proving insufficient. As MRI technology continues to advance, it is anticipated that MRI will occupy an increasingly important role in all of these aspects of the clinical management of RCC.

REFERENCES

1. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Kidney Cancer. Version 1.2013. Available at: http://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed November 4, 2013
2. Escudier B, Eisen T, Porta C, et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2012; 23(suppl 7):vii65–vii71. [PubMed: 22997456]
3. Cao Y, Paner GP, Perry KT, et al. Renal neoplasms in younger adults: analysis of 112 tumors from a single institution according to the new 2004 World Health Organization classification and 2002 American Joint Committee on Cancer Staging System. *Arch Pathol Lab Med*. 2005; 129:487–491. [PubMed: 15794671]
4. Russo P. Partial nephrectomy for renal cancer: Part I. *BJU Int*. 2010; 105:1206–1220. [PubMed: 20500566]
5. Saranchuk JW, Touijer AK, Hakimian P, et al. Partial nephrectomy for patients with a solitary kidney: the Memorial Sloan-Kettering experience. *BJU Int*. 2004; 94:1323–1328. [PubMed: 15610114]
6. Lopez-Beltran A, Scarpelli M, Montironi R, et al. 2004 WHO classification of the renal tumors of the adults. *Eur Urol*. 2006; 49:798–805. [PubMed: 16442207]
7. Tickoo SK, Gopalan A. Pathologic features of renal cortical tumors. *Urol Clin North Am*. 2008; 35:551–561. [PubMed: 18992609]
8. Amin MB, Tamboli P, Javidan J, et al. Prognostic impact of histologic subtyping of adult renal epithelial neoplasms: an experience of 405 cases. *Am J Surg Pathol*. 2002; 26:281–291. [PubMed: 11859199]
9. Cheville JC, Lohse CM, Zincke H, et al. Comparisons of outcome and prognostic features among histologic subtypes of renal cell carcinoma. *Am J Surg Pathol*. 2003; 27:612–624. [PubMed: 12717246]
10. Cohen HT, McGovern FJ. Renal-cell carcinoma. *N Engl J Med*. 2005; 353:2477–2490. [PubMed: 16339096]

11. Shinagare AB, Krajewski KM, Jagannathan JP, et al. Genitourinary imaging: part 2, role of imaging in medical management of advanced renal cell carcinoma. *AJR Am J Roentgenol.* 2012; 199:W554–W564. [PubMed: 23096199]
12. Kim W, Kaelin WG Jr. The von Hippel-Lindau tumor suppressor protein: new insights into oxygen sensing and cancer. *Curr Opin Genet Dev.* 2003; 13:55–60. [PubMed: 12573436]
13. Teloken PE, Thompson RH, Tickoo SK, et al. Prognostic impact of histological subtype on surgically treated localized renal cell carcinoma. *J Urol.* 2009; 182:2132–2136. [PubMed: 19758615]
14. Koga S, Nishikido M, Hayashi T, et al. Outcome of surgery in cystic renal cell carcinoma. *Urology.* 2000; 56:67–70. [PubMed: 10869626]
15. Margulis V, Tamboli P, Matin SF, et al. Analysis of clinicopathologic predictors of oncologic outcome provides insight into the natural history of surgically managed papillary renal cell carcinoma. *Cancer.* 2008; 112:1480–1488. [PubMed: 18240184]
16. Patard JJ, Leray E, Rioux-Leclercq N, et al. Prognostic value of histologic subtypes in renal cell carcinoma: a multicenter experience. *J Clin Oncol.* 2005; 23:2763–2771. [PubMed: 15837991]
17. Delahunt B, Eble JN. Papillary renal cell carcinoma: a clinicopathologic and immunohistochemical study of 105 tumors. *Mod Pathol.* 1997; 10:537–544. [PubMed: 9195569]
18. Amin MB, Corless CL, Renshaw AA, et al. Papillary (chromophil) renal cell carcinoma: histomorphologic characteristics and evaluation of conventional pathologic prognostic parameters in 62 cases. *Am J Surg Pathol.* 1997; 21:621–635. [PubMed: 9199639]
19. Ljungberg, B.; Bensalah, K.; Bex, S., et al. Guidelines on Renal Cell Carcinoma. Uroweb 2013. Available at: http://www.uroweb.org/gls/pdf/10_Renal_Cell_Carcinoma_LR.pdf. Accessed November 4, 2013
20. Delahunt B, Eble JN, McCredie MR, et al. Morphologic typing of papillary renal cell carcinoma: comparison of growth kinetics and patient survival in 66 cases. *Hum Pathol.* 2001; 32:590–595. [PubMed: 11431713]
21. 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; 69:230–235. [PubMed: 17275070]
22. Yamashita S, Ioritani N, Oikawa K, et al. Morphological subtyping of papillary renal cell carcinoma: clinicopathological characteristics and prognosis. *Int J Urol.* 2007; 14:679–683. [PubMed: 17681054]
23. Egbert ND, Caoili EM, Cohan RH, et al. Differentiation of papillary renal cell carcinoma subtypes on CT and MRI. *AJR Am J Roentgenol.* 2013; 201:347–355. [PubMed: 23883215]
24. Kunju LP, Wojno K, Wolf JS Jr, et al. Papillary renal cell carcinoma with oncocytic cells and nonoverlapping low grade nuclei: expanding the morphologic spectrum with emphasis on clinicopathologic, immunohistochemical and molecular features. *Hum Pathol.* 2008; 39:96–101. [PubMed: 17949780]
25. Park BH, Ro JY, Park WS, et al. Oncocytic papillary renal cell carcinoma with inverted nuclear pattern: distinct subtype with an indolent clinical course. *Pathol Int.* 2009; 59:137–146. [PubMed: 19261090]
26. Yang XJ, Tan MH, Kim HL, et al. A molecular classification of papillary renal cell carcinoma. *Cancer Res.* 2005; 65:5628–5637. [PubMed: 15994935]
27. Ku JH, Moon KC, Kwak C, et al. Is there a role of the histologic subtypes of papillary renal cell carcinoma as a prognostic factor? *Jpn J Clin Oncol.* 2009; 39:664–670. [PubMed: 19586962]
28. Gontero P, Ceratti G, Guglielmetti S, et al. Prognostic factors in a prospective series of papillary renal cell carcinoma. *BJU Int.* 2008; 102:697–702. [PubMed: 18489525]
29. Motzer RJ, Bacik J, Mariani T, et al. Treatment outcome and survival associated with metastatic renal cell carcinoma of non-clear-cell histology. *J Clin Oncol.* 2002; 20:2376–2381. [PubMed: 11981011]
30. Hoffmann NE, Gillett MD, Cheville JC, et al. Differences in organ system of distant metastasis by renal cell carcinoma subtype. *J Urol.* 2008; 179:474–477. [PubMed: 18076920]
31. de Peralta-Venturina M, Moch H, Amin M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. *Am J Surg Pathol.* 2001; 25:275–284. [PubMed: 11224597]

32. Sella A, Logothetis CJ, Ro JY, et al. Sarcomatoid renal cell carcinoma. A treatable entity. *Cancer*. 1987; 60:1313–1318. [PubMed: 2441841]
33. Tomera KM, Farrow GM, Lieber MM. Sarcomatoid renal carcinoma. *J Urol*. 1983; 130:657–659. [PubMed: 6887392]
34. Cheville JC, Lohse CM, Zincke H, et al. Sarcomatoid renal cell carcinoma: an examination of underlying histologic subtype and an analysis of associations with patient outcome. *Am J Surg Pathol*. 2004; 28:435–441. [PubMed: 15087662]
35. Dang TT, Ziv E, Weinstein S, et al. Computed tomography and magnetic resonance imaging of adult renal cell carcinoma associated with Xp11.2 translocation. *J Comput Assist Tomogr*. 2012; 36:669–674. [PubMed: 23192203]
36. Liu K, Xie P, Peng W, et al. Renal carcinomas associated with Xp11.2 translocations/TFE3 gene fusions: findings on MRI and computed tomography imaging. *J Magn Reson Imaging*. 2013
37. Lopez-Beltran A, Carrasco JC, Cheng L, et al. 2009 update on the classification of renal epithelial tumors in adults. *Int J Urol*. 2009; 16:432–443. [PubMed: 19453547]
38. Park JH, Lee C, Suh JH, et al. Clear cell papillary renal cell carcinoma: a report of 15 cases including three cases of concurrent other-type renal cell carcinomas. *Korean J Pathol*. 2012; 46:541–547. [PubMed: 23323104]
39. Taouli B, Thakur RK, Mannelli L, et al. Renal lesions: characterization with diffusion-weighted imaging versus contrast-enhanced MR imaging. *Radiology*. 2009; 251:398–407. [PubMed: 19276322]
40. Chandarana H, Lee VS, Hecht E, et al. Comparison of biexponential and monoexponential model of diffusion weighted imaging in evaluation of renal lesions: preliminary experience. *Invest Radiol*. 2011; 46:285–291. [PubMed: 21102345]
41. 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; 184:1868–1872. [PubMed: 15908544]
42. Han YM, Kim JK, Roh BS, et al. Renal angiomyolipoma: selective arterial embolization.—effectiveness and changes in angiomyogenic components in long-term follow-up. *Radiology*. 1997; 204:65–70. [PubMed: 9205224]
43. Rimon U, Duvdevani M, Garniek A, et al. Large renal angiomyolipomas: digital subtraction angiographic grading and presentation with bleeding. *Clin Radiol*. 2006; 61:520–526. [PubMed: 16713423]
44. Rosenkrantz AB, Raj S, Babb JS, et al. Comparison of 3D two-point Dixon and standard 2D dual-echo breath-hold sequences for detection and quantification of fat content in renal angiomyolipoma. *Eur J Radiol*. 2012; 81:47–51. [PubMed: 21126839]
45. 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; 250:793–802. [PubMed: 19244046]
46. Cohan RH, Sherman LS, Korobkin M, et al. Renal masses: assessment of corticomedullary-phase and nephrographic-phase CT scans. *Radiology*. 1995; 196:445–451. [PubMed: 7617859]
47. Pedrosa I, Sun MR, Spencer M, et al. MR imaging of renal masses: correlation with findings at surgery and pathologic analysis. *Radiographics*. 2008; 28:985–1003. [PubMed: 18635625]
48. Kang SK, Kim D, Chandarana H. Contemporary imaging of the renal mass. *Curr Urol Rep*. 2011; 12:11–17. [PubMed: 20949339]
49. Hecht EM, Israel GM, Krinsky GA, et al. Renal masses: quantitative analysis of enhancement with signal intensity measurements versus qualitative analysis of enhancement with image subtraction for diagnosing malignancy at MR imaging. *Radiology*. 2004; 232:373–378. [PubMed: 15215544]
50. Zhang J, Pedrosa I, Rofsky NM. MR techniques for renal imaging. *Radiol Clin North Am*. 2003; 41:877–907. [PubMed: 14521200]
51. Dodelzon K, Mussi TC, Babb JS, et al. Prediction of growth rate of solid renal masses: utility of MR imaging features—preliminary experience. *Radiology*. 2012; 262:884–893. [PubMed: 22267588]
52. Pedrosa I, Chou MT, Ngo L, et al. MR classification of renal masses with pathologic correlation. *Eur Radiol*. 2008; 18:365–375. [PubMed: 17899106]

53. 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; 17:193–200. [PubMed: 16758161]
54. Yoshimitsu K, Irie H, Tajima T, et al. MR imaging of renal cell carcinoma: its role in determining cell type. *Radiat Med.* 2004; 22:371–376. [PubMed: 15648450]
55. Manenti G, Di Roma M, Mancino S, et al. Malignant renal neoplasms: correlation between ADC values and cellularity in diffusion weighted magnetic resonance imaging at 3 T. *Radiol Med.* 2008; 113:199–213. [PubMed: 18386122]
56. Squillaci E, Manenti G, Di Stefano F, et al. Diffusion-weighted MR imaging in the evaluation of renal tumours. *J Exp Clin Cancer Res.* 2004; 23:39–45. [PubMed: 15149149]
57. Wang H, Cheng L, Zhang X, et al. Renal cell carcinoma: diffusion-weighted MR imaging for subtype differentiation at 3.0 T. *Radiology.* 2010; 257:135–143. [PubMed: 20713607]
58. Rosenkrantz AB, Niver BE, Fitzgerald EF, et al. Utility of the apparent diffusion coefficient for distinguishing clear cell renal cell carcinoma of low and high nuclear grade. *AJR Am J Roentgenol.* 2010; 195:W344–W351. [PubMed: 20966299]
59. Pedrosa I, Alsop DC, Rofsky NM. Magnetic resonance imaging as a biomarker in renal cell carcinoma. *Cancer.* 2009; 115:2334–2345. [PubMed: 19402070]
60. Adey GS, Pedrosa I, Rofsky NM, et al. Lower limits of detection using magnetic resonance imaging for solid components in cystic renal neoplasms. *Urology.* 2008; 71:47–51. [PubMed: 18242363]
61. Israel GM, Hindman N, Bosniak MA. Evaluation of cystic renal masses: comparison of CT and MR imaging by using the Bosniak classification system. *Radiology.* 2004; 231:365–371. [PubMed: 15128983]
62. Pretorius ES, Siegelman ES, Ramchandani P, et al. Renal neoplasms amenable to partial nephrectomy: MR imaging. *Radiology.* 1999; 212:28–34. [PubMed: 10405716]
63. Karlo CA, Di Paolo PL, Donati OF, et al. Renal cell carcinoma: role of MR imaging in the assessment of muscular venous branch invasion. *Radiology.* 2013; 267:454–459. [PubMed: 23418001]
64. Lebre T, Poulain JE, Molinie V, et al. Percutaneous core biopsy for renal masses: indications, accuracy and results. *J Urol.* 2007; 178:1184–1188. pt 1. [PubMed: 17698122]
65. Renshaw AA, Lee KR, Madge R, et al. Accuracy of fine needle aspiration in distinguishing subtypes of renal cell carcinoma. *Acta Cytol.* 1997; 41:987–994. [PubMed: 9250289]
66. Leibovich BC, Blute ML, Cheville JC, et al. Prediction of progression after radical nephrectomy for patients with clear cell renal cell carcinoma: a stratification tool for prospective clinical trials. *Cancer.* 2003; 97:1663–1671. [PubMed: 12655523]
67. Patard JJ, Kim HL, Lam JS, et al. Use of the University of California Los Angeles integrated staging system to predict survival in renal cell carcinoma: an international multicenter study. *J Clin Oncol.* 2004; 22:3316–3322. [PubMed: 15310775]
68. Outwater EK, Bhatia M, Siegelman ES, et al. Lipid in renal clear cell carcinoma: detection on opposed-phase gradient-echo MR images. *Radiology.* 1997; 205:103–107. [PubMed: 9314970]
69. Lam JS, Shvarts O, Said JW, et al. Clinicopathologic and molecular correlations of necrosis in the primary tumor of patients with renal cell carcinoma. *Cancer.* 2005; 103:2517–2525. [PubMed: 15880379]
70. Beddy P, Genega EM, Ngo L, et al. Tumor necrosis on magnetic resonance imaging correlates with aggressive histology and disease progression in clear cell renal cell carcinoma. *Clin Genitourin Cancer.* 2013
71. Rosenkrantz AB, Sekhar A, Genega EM, et al. Prognostic implications of the magnetic resonance imaging appearance in papillary renal cell carcinoma. *Eur Radiol.* 2013; 23:579–587. [PubMed: 22903703]
72. Yamada T, Endo M, Tsuboi M, et al. Differentiation of pathologic subtypes of papillary renal cell carcinoma on CT. *AJR Am J Roentgenol.* 2008; 191:1559–1563. [PubMed: 18941101]
73. Vargas HA, Chaim J, Lefkowitz RA, et al. Renal cortical tumors: use of multiphasic contrast-enhanced MR imaging to differentiate benign and malignant histologic subtypes. *Radiology.* 2012; 264:779–788. [PubMed: 22829683]

74. Chandarana H, Rosenkrantz AB, Mussi TC, et al. Histogram analysis of whole-lesion enhancement in differentiating clear cell from papillary subtype of renal cell cancer. *Radiology*. 2012; 265:790–798. [PubMed: 23175544]
75. Vargas HA, Delaney HG, Delappe EM, et al. Multiphasic contrast-enhanced MRI: single-slice versus volumetric quantification of tumor enhancement for the assessment of renal clear-cell carcinoma fuhrman grade. *J Magn Reson Imaging*. 2013; 37:1160–1167. [PubMed: 23152173]
76. Gilet AG, Kang SK, Kim D, et al. Advanced renal mass imaging: diffusion and perfusion MRI. *Curr Urol Rep*. 2012; 13:93–98. [PubMed: 22081252]
77. Notohamiprodjo M, Sourbron S, Staehler M, et al. Measuring perfusion and permeability in renal cell carcinoma with dynamic contrast-enhanced MRI: a pilot study. *J Magn Reson Imaging*. 2010; 31:490–501. [PubMed: 20099364]
78. Sourbron SP, Buckley DL. On the scope and interpretation of the Tofts models for DCE-MRI. *Magn Reson Med*. 2011; 66:735–745. [PubMed: 21384424]
79. Chandarana H, Amarosa A, Huang WC, et al. High temporal resolution 3D gadolinium-enhanced dynamic MR imaging of renal tumors with pharmacokinetic modeling: Preliminary observations. *J Magn Reson Imaging*. 2013
80. Kang SK, Huang WC, Lee VS, et al. MR renographic measurement of renal function in patients undergoing partial nephrectomy. *AJR Am J Roentgenol*. 2013; 200:1204–1209. [PubMed: 23701054]
81. Lanzman RS, Robson PM, Sun MR, et al. Arterial spin-labeling MR imaging of renal masses: correlation with histopathologic findings. *Radiology*. 2012; 265:799–808. [PubMed: 23047841]
82. 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; 22:484–492. [PubMed: 21877173]
83. Sandrasegaran K, Sundaram CP, Ramaswamy R, et al. Usefulness of diffusion-weighted imaging in the evaluation of renal masses. *AJR Am J Roentgenol*. 2010; 194:438–445. [PubMed: 20093607]
84. Le Bihan D, Breton E, Lallemand D, et al. Contribution of intravoxel incoherent motion (IVIM) imaging to neuroradiology. *J Neuroradiol*. 1987; 14:295–312. [PubMed: 3450796]
85. Le Bihan D, Breton E, Lallemand D, et al. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. *Radiology*. 1986; 161:401–407. [PubMed: 3763909]
86. Chandarana H, Kang SK, Wong S, et al. Diffusion-weighted intravoxel incoherent motion imaging of renal tumors with histopathologic correlation. *Invest Radiol*. 2012; 47:688–696. [PubMed: 22996315]
87. 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; 72:598–602. [PubMed: 18649929]
88. 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; 68:737–740. [PubMed: 17070344]
89. Kim JK, Kim SH, Jang YJ, et al. Renal angiomyolipoma with minimal fat: differentiation from other neoplasms at double-echo chemical shift FLASH MR imaging. *Radiology*. 2006; 239:174–180. [PubMed: 16507752]
90. Krishnan B, Truong LD. Renal epithelial neoplasms: the diagnostic implications of electron microscopic study in 55 cases. *Hum Pathol*. 2002; 33:68–79. [PubMed: 11823975]
91. 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; 265:468–477. [PubMed: 23012463]
92. Choi HJ, Kim JK, Ahn H, et al. Value of T2-weighted MR imaging in differentiating low-fat renal angiomyolipomas from other renal tumors. *Acta Radiol*. 2011; 52:349–353. [PubMed: 21498374]
93. 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*. 2012; 263:160–168. [PubMed: 22344404]

94. Berland LL, Silverman SG, Gore RM, et al. Managing incidental findings on abdominal CT: white paper of the ACR incidental findings committee. *J Am Coll Radiol*. 2010; 7:754–773. [PubMed: 20889105]
95. Sahni VA, Ly A, Silverman SG. Usefulness of percutaneous biopsy in diagnosing benign renal masses that mimic malignancy. *Abdom Imaging*. 2011; 36:91–101. [PubMed: 20049430]
96. Sahni VA, Silverman SG. Biopsy of renal masses: when and why. *Cancer Imaging*. 2009; 9:44–55. [PubMed: 19602467]
97. Quinn MJ, Hartman DS, Friedman AC, et al. Renal oncocytoma: new observations. *Radiology*. 1984; 153:49–53. [PubMed: 6473802]
98. Cochand-Priollet B, Molinie V, Bougaran J, et al. Renal chromophobe cell carcinoma and oncocytoma. A comparative morphologic, histochemical, and immunohistochemical study of 124 cases. *Arch Pathol Lab Med*. 1997; 121:1081–1086. [PubMed: 9341588]
99. Davidson AJ, Hayes WS, Hartman DS, et al. Renal oncocytoma and carcinoma: failure of differentiation with CT. *Radiology*. 1993; 186:693–696. [PubMed: 8430176]
100. Gudbjartsson T, Hardarson S, Petursdottir V, et al. Renal oncocytoma: a clinicopathological analysis of 45 consecutive cases. *BJU Int*. 2005; 96:1275–1279. [PubMed: 16287444]
101. 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; 452:285–293. [PubMed: 18196270]
102. Kim JI, Cho JY, Moon KC, et al. Segmental enhancement inversion at biphasic multidetector CT: characteristic finding of small renal oncocytoma. *Radiology*. 2009; 252:441–448. [PubMed: 19508984]
103. McGahan JP, Lamba R, Fisher J, et al. Is segmental enhancement inversion on enhanced biphasic MDCT a reliable sign for the noninvasive diagnosis of renal oncocytomas? *AJR Am J Roentgenol*. 2011; 197:W674–W679. [PubMed: 21940539]
104. Millet I, Doyon FC, Hoa D, et al. Characterization of small solid renal lesions: can benign and malignant tumors be differentiated with CT? *AJR Am J Roentgenol*. 2011; 197:887–896. [PubMed: 21940576]
105. O'Malley ME, Tran P, Hanbidge A, et al. Small renal oncocytomas: is segmental enhancement inversion a characteristic finding at biphasic MDCT? *AJR Am J Roentgenol*. 2012; 199:1312–1315. [PubMed: 23169723]
106. Rosenkrantz AB, Hindman N, Fitzgerald EF, et al. MRI features of renal oncocytoma and chromophobe renal cell carcinoma. *AJR Am J Roentgenol*. 2010; 195:W421–W427. [PubMed: 21098174]
107. Silverman SG, Gan YU, Morteale KJ, et al. Renal masses in the adult patient: the role of percutaneous biopsy. *Radiology*. 2006; 240:6–22. [PubMed: 16709793]
108. Ginzburg S, Uzzo R, Al-Saleem T, et al. Coexisting hybrid malignancy in a solitary sporadic solid benign renal mass: implications for managing patients following renal biopsy. *J Urol*. 2013
109. Jewett MA, Mattar K, Basiuk J, et al. Active surveillance of small renal masses: progression patterns of early stage kidney cancer. *Eur Urol*. 2011; 60:39–44. [PubMed: 21477920]
110. 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; 98:1331–1334. [PubMed: 16985252]
111. Nguyen MM, Gill IS, Ellison LM. The evolving presentation of renal carcinoma in the United States: trends from the surveillance, epidemiology, and end results program. *J Urol*. 2006; 176:2397–400. pt 1. [PubMed: 17085111]
112. Abou Youssif T, Kassouf W, Steinberg J, et al. Active surveillance for selected patients with renal masses: updated results with long-term follow-up. *Cancer*. 2007; 110:1010–1014. [PubMed: 17628489]
113. Abouassaly R, Lane BR, Novick AC. Active surveillance of renal masses in elderly patients. *J Urol*. 2008; 180:505–508. discussion 8–9. [PubMed: 18550113]
114. Boorjian SA, Uzzo RG. The evolving management of small renal masses. *Curr Oncol Rep*. 2009; 11:211–217. [PubMed: 19336013]

115. 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; 175:425–431. [PubMed: 16406965]
116. Crispen PL, Viterbo R, Fox EB, et al. Delayed intervention of sporadic renal masses undergoing active surveillance. *Cancer*. 2008; 112:1051–1057. [PubMed: 18286513]
117. Volpe A, Panzarella T, Rendon RA, et al. The natural history of incidentally detected small renal masses. *Cancer*. 2004; 100:738–745. [PubMed: 14770429]
118. Crispen PL, Wong YN, Greenberg RE, et al. Predicting growth of solid renal masses under active surveillance. *Urol Oncol*. 2008; 26:555–559. [PubMed: 18774473]
119. Hartman DS, Davis CJ Jr, Johns T, et al. Cystic renal cell carcinoma. *Urology*. 1986; 28:145–153. [PubMed: 3739121]
120. Jhaveri K, Gupta P, Elmi A, et al. Cystic renal cell carcinomas: do they grow, metastasize, or recur? *AJR Am J Roentgenol*. 2013; 201:W292–W296. [PubMed: 23883243]
121. Smith AD, Remer EM, Cox KL, et al. Bosniak category IIF and III cystic renal lesions: outcomes and associations. *Radiology*. 2012; 262:152–160. [PubMed: 22106359]
122. Suzigan S, Lopez-Beltran A, Montironi R, et al. Multilocular cystic renal cell carcinoma : a report of 45 cases of a kidney tumor of low malignant potential. *Am J Clin Pathol*. 2006; 125:217–222. [PubMed: 16393684]
123. Hindman NM, Bosniak MA, Rosenkrantz AB, et al. Multilocular cystic renal cell carcinoma: comparison of imaging and pathologic findings. *AJR Am J Roentgenol*. 2012; 198:W20–W26. [PubMed: 22194510]
124. Karellas ME, O'Brien MF, Jang TL, et al. Partial nephrectomy for selected renal cortical tumours of ≥ 7 cm. *BJU Int*. 2010; 106:1484–1487. [PubMed: 20518765]
125. Sun MR, Wagner AA, San Francisco IF, et al. Need for intraoperative ultrasound and surgical recommendation for partial nephrectomy: correlation with tumor imaging features and urologist practice patterns. *Ultrasound Q*. 2012; 28:21–27. [PubMed: 22357225]
126. Bertini R, Roscigno M, Freschi M, et al. The extent of tumour fat invasion affects survival in patients with renal cell carcinoma and venous tumour thrombosis. *BJU Int*. 2011; 108:820–824. [PubMed: 21166759]
127. da Costa WH, Moniz RR, da Cunha IW, et al. Impact of renal vein invasion and fat invasion in pT3a renal cell carcinoma. *BJU Int*. 2012; 109:544–548. [PubMed: 21711437]
128. Bertini R, Roscigno M, Freschi M, et al. Renal sinus fat invasion in pT3a clear cell renal cell carcinoma affects outcomes of patients without nodal involvement or distant metastases. *J Urol*. 2009; 181:2027–2032. [PubMed: 19286201]
129. Feifer A, Savage C, Rayala H, et al. Prognostic impact of muscular venous branch invasion in localized renal cell carcinoma cases. *J Urol*. 2011; 185:37–42. [PubMed: 21074196]
130. Flanigan RC, Mickisch G, Sylvester R, et al. Cytoreductive nephrectomy in patients with metastatic renal cancer: a combined analysis. *J Urol*. 2004; 171:1071–1076. [PubMed: 14767273]
131. Flanigan RC, Salmon SE, Blumenstein BA, et al. Nephrectomy followed by interferon alfa-2b compared with interferon alfa-2b alone for metastatic renal-cell cancer. *N Engl J Med*. 2001; 345:1655–1659. [PubMed: 11759643]
132. Mickisch GH, Garin A, van Poppel H, et al. Radical nephrectomy plus interferon-alfa-based immunotherapy compared with interferon alfa alone in metastatic renal-cell carcinoma: a randomised trial. *Lancet*. 2001; 358:966–970. [PubMed: 11583750]
133. Polcari AJ, Gorbonos A, Milner JE, et al. The role of cytoreductive nephrectomy in the era of molecular targeted therapy. *Int J Urol*. 2009; 16:227–233. [PubMed: 19207114]
134. Choueiri TK, Xie W, Kollmannsberger C, et al. The impact of cytoreductive nephrectomy on survival of patients with metastatic renal cell carcinoma receiving vascular endothelial growth factor targeted therapy. *J Urol*. 2011; 185:60–66. [PubMed: 21074201]
135. Kassouf W, Sanchez-Ortiz R, Tamboli P, et al. Cytoreductive nephrectomy for metastatic renal cell carcinoma with nonclear cell histology. *J Urol*. 2007; 178:1896–900. [PubMed: 17868729]
136. Upton MP, Parker RA, Youmans A, et al. Histologic predictors of renal cell carcinoma response to interleukin-2-based therapy. *J Immunother*. 2005; 28:488–495. [PubMed: 16113605]

137. Shuch B, Said J, La Rochelle JC, et al. Cytoreductive nephrectomy for kidney cancer with sarcomatoid histology is up-front resection indicated and, if not, is it avoidable? *J Urol*. 2009; 182:2164–2171. [PubMed: 19758641]
138. Molina AM, Tickoo SK, Ishill N, et al. Sarcomatoid-variant renal cell carcinoma: treatment outcome and survival in advanced disease. *Am J Clin Oncol*. 2011; 34:454–459. [PubMed: 21127411]
139. Dutcher JP, Nanus D. Long-term survival of patients with sarcomatoid renal cell cancer treated with chemotherapy. *Med Oncol*. 2011; 28:1530–1533. [PubMed: 20717755]
140. Haas NB, Lin X, Manola J, et al. A phase II trial of doxorubicin and gemcitabine in renal cell carcinoma with sarcomatoid features: ECOG 8802. *Med Oncol*. 2012; 29:761–767. [PubMed: 21298497]
141. Nanus DM, Garino A, Milowsky MI, et al. Active chemotherapy for sarcomatoid and rapidly progressing renal cell carcinoma. *Cancer*. 2004; 101:1545–1551. [PubMed: 15378501]
142. Mian BM, Bhadkamkar N, Slaton JW, et al. Prognostic factors and survival of patients with sarcomatoid renal cell carcinoma. *J Urol*. 2002; 167:65–70. [PubMed: 11743277]
143. Rosenkrantz AB, Chandarana H, Melamed J. MRI findings of sarcomatoid renal cell carcinoma in nine cases. *Clin Imaging*. 2011; 35:459–464. [PubMed: 22040791]
144. Takeuchi M, Urano M, Hara M, et al. Characteristic MRI findings of sarcomatoid renal cell carcinoma dedifferentiated from clear cell renal carcinoma: radiological-pathological correlation. *Clin Imaging*. 2013
145. Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. *N Engl J Med*. 2007; 356:2271–2281. [PubMed: 17538086]
146. Baccala A Jr, Hedgepeth R, Kaouk J, et al. Pathological evidence of necrosis in recurrent renal mass following treatment with sunitinib. *Int J Urol*. 2007; 14:1095–1097. [PubMed: 18036049]
147. Cowey CL, Fielding JR, Rathmell WK. The loss of radiographic enhancement in primary renal cell carcinoma tumors following multitargeted receptor tyrosine kinase therapy is an additional indicator of response. *Urology*. 2010; 75:1108–1113. [PubMed: 19931124]
148. Hittinger M, Staehler M, Schramm N, et al. Course of size and density of metastatic renal cell carcinoma lesions in the early follow-up of molecular targeted therapy. *Urol Oncol*. 2012; 30:695–703. [PubMed: 21865061]
149. Nathan PD, Vinayan A, Stott D, et al. CT response assessment combining reduction in both size and arterial phase density correlates with time to progression in metastatic renal cancer patients treated with targeted therapies. *Cancer Biol Ther*. 2010; 9:15–19. [PubMed: 20009542]
150. Schmidt N, Hess V, Zumbunn T, et al. Choi response criteria for prediction of survival in patients with metastatic renal cell carcinoma treated with anti-angiogenic therapies. *Eur Radiol*. 2013; 23:632–639. [PubMed: 22918564]
151. van der Veldt AA, Meijerink MR, van den Eertwegh AJ, et al. Choi response criteria for early prediction of clinical outcome in patients with metastatic renal cell cancer treated with sunitinib. *Br J Cancer*. 2010; 102:803–809. [PubMed: 20145618]
152. Smith AD, Lieber ML, Shah SN. Assessing tumor response and detecting recurrence in metastatic renal cell carcinoma on targeted therapy: importance of size and attenuation on contrast-enhanced CT. *AJR Am J Roentgenol*. 2010; 194:157–165. [PubMed: 20028918]
153. Smith AD, Shah SN, Rini BI, et al. Morphology, Attenuation, Size, and Structure (MASS) criteria: assessing response and predicting clinical outcome in metastatic renal cell carcinoma on antiangiogenic targeted therapy. *AJR Am J Roentgenol*. 2010; 194:1470–1478. [PubMed: 20489085]
154. Kang HC, Tan KS, Keefe SM, et al. MRI assessment of early tumor response in metastatic renal cell carcinoma patients treated with sorafenib. *AJR Am J Roentgenol*. 2013; 200:120–126. [PubMed: 23255750]
155. Krajewski KM, Guo M, Van den Abbeele AD, et al. Comparison of four early posttherapy imaging changes (EPTIC; RECIST 1.0, tumor shrinkage, computed tomography tumor density, Choi criteria) in assessing outcome to vascular endothelial growth factor-targeted therapy in patients with advanced renal cell carcinoma. *Eur Urol*. 2011; 59:856–862. [PubMed: 21306819]

156. Choyke PL, Dwyer AJ, Knopp MV. Functional tumor imaging with dynamic contrast-enhanced magnetic resonance imaging. *J Magn Reson Imaging*. 2003; 17:509–520. [PubMed: 12720260]
157. Katabathina VS, Lassau N, Pedrosa I, et al. Evaluation of treatment response in patients with metastatic renal cell carcinoma: role of state-of-the-art cross-sectional imaging. *Curr Urol Rep*. 2012; 13:70–81. [PubMed: 22143974]
158. Flaherty KT, Rosen MA, Heitjan DF, et al. Pilot study of DCE-MRI to predict progression-free survival with sorafenib therapy in renal cell carcinoma. *Cancer Biol Ther*. 2008; 7:496–501. [PubMed: 18219225]
159. Hahn OM, Yang C, Medved M, et al. Dynamic contrast-enhanced magnetic resonance imaging pharmacodynamic biomarker study of sorafenib in metastatic renal carcinoma. *J Clin Oncol*. 2008; 26:4572–4578. [PubMed: 18824708]
160. de Bazelaire C, Alsop DC, George D, et al. Magnetic resonance imaging-measured blood flow change after antiangiogenic therapy with PTK787/ZK 222584 correlates with clinical outcome in metastatic renal cell carcinoma. *Clin Cancer Res*. 2008; 14:5548–5554. [PubMed: 18765547]
161. Schor-Bardach R, Alsop DC, Pedrosa I, et al. Does arterial spin-labeling MR imaging-measured tumor perfusion correlate with renal cell cancer response to antiangiogenic therapy in a mouse model? *Radiology*. 2009; 251:731–742. [PubMed: 19474376]

FIGURE 1. Bilateral AMLs. Axial in-phase (A), opposed-phase (B), water-only (C), and fat-only (D) reconstructed MR images from 3D 2-point Dixon sequence in a 40-year-old man, demonstrating a dominant lipid-rich AML (dotted arrow) in the posterior right kidney as well as multiple smaller AMLs bilaterally (solid arrows).

FIGURE 2. Clear cell RCC. Axial 3D T1-weighted, fat-suppressed gradient-echo precontrast (A), corticomedullary-phase postcontrast (B), and axial in-phase (C) and opposed-phase (D) T1-weighted gradient-echo MR images of a 59-year-old man with a clear cell RCC, demonstrating characteristic avid hypervascularity in the corticomedullary phase (B) and loss of signal on opposed-phase images (asterisk), indicating the presence of intravoxel fat.

FIGURE 3.

Clear cell RCC with central necrosis. Coronal (A) and axial (B) single-shot fast spin-echo T2-weighted MR images and ADC map (C) of a 53-year-old man with a clear cell RCC, which contains central necrosis (asterisk) and peripheral areas of low ADC (arrow); focal high-grade components were identified on histopathologic evaluation.

FIGURE 4.

Tumor extension into the right renal vein and inferior vena cava. Axial 3D T1-weighted, fat-suppressed gradient-echo precontrast (A); corticomedullary-phase postcontrast (B); coronal single-shot fast spin-echo T2-weighted (C); and coronal 3D T1-weighted, fat-suppressed gradient-echo excretory-phase postcontrast (D) MR images of a 57-year-old man with a clear cell RCC with renal vein and inferior vena cava tumor thrombus (arrows). Tumor thrombus enhanced compared with precontrast images (not shown).

FIGURE 5. Papillary RCC. Coronal single-shot fast spin-echo T2-weighted (A); axial T1-weighted, fat-suppressed gradient-echo corticomedullary-phase (B) and nephrographic-phase (C) postcontrast MR images; and ADC map (D) of a 45-year-old man with pRCC. This lesion demonstrates T2 hypointensity (dotted arrow), low-level enhancement (dashed white arrow), and decreased ADC (solid arrow), which are typical of this diagnosis.

FIGURE 6.

Type 2 pRCC with invasive and metastatic features. Axial 3D T1-weighted, fat-suppressed gradient-echo precontrast (A) and corticomedullary-phase postcontrast (B); coronal single-shot fast spin-echo T2-weighted (C); and subtracted coronal T1-weighted, fat-suppressed gradient-echo excretory-phase (D) MR images in a 44-year-old man. This type 2 pRCC demonstrates T1 hyperintense hemorrhagic products (dashed white arrow) and shows focal invasion of the renal collecting system (solid white arrow). There is also an adjacent metastatic retroperitoneal nodal mass (asterisk).

FIGURE 7.

Type 2 pRCC. Coronal single-shot fast spin-echo T2-weighted (A) and axial 3D T1-weighted, fat-suppressed gradient-echo corticomedullary-phase postcontrast (B) MR images of a 50-year-old man with type 2 pRCC with an infiltrative appearance (dashed arrows) and invasion of the renal vein, which contains hypoenhancing (compared with unenhanced images, not shown) tumor thrombus (solid arrow).

FIGURE 8.

Chromophobe RCC with central scar. Coronal (A) and axial (B) single-shot fast spin-echo T2-weighted and axial 3D T1-weighted, fat-suppressed gradient-echo corticomedullary-phase (C) and nephrographic-phase (D) postcontrast MR images of a 67-year-old woman with RCC, chromophobe subtype. Similar to the oncocytoma, with which it shares a common cell of origin, this lesion may exhibit a central stellate T2 hyperintense (asterisk), nonenhancing (solid arrow) scar.

FIGURE 9.

Minimal-fat AML. Axial single-shot fast spin-echo T2-weighted (A); axial 3D T1-weighted, fat-suppressed gradient-echo corticomedullary-phase (B) and nephrographic-phase (C) postcontrast; and in-phase (D) and opposed-phase (E) T1-weighted, gradient-echo MR images of a 53-year-old woman with an AML with minimal fat, which demonstrates no signal loss on the dual-echo imaging (D and E), homogeneous low signal intensity on T2-weighted imaging (solid arrow), and homogenous avid arterial enhancement (dashed arrow) with delayed washout (dotted arrow).

FIGURE 10.

Renal oncocyoma. Axial fat-suppressed turbo spin-echo T2-weighted (A); axial 3D T1-weighted, fat-suppressed gradient-echo corticomedullary-phase (B); and coronal single-shot fast spin-echo T2-weighted (C) MR images of a 51-year-old woman with a renal oncocyoma. There is a central T2 hyperintense, nonenhancing central stellate scar (solid arrow), which demonstrates peripheral enhancement during the corticomedullary phase. The scar is a suggestive but nonspecific finding.

FIGURE 11.

Stable renal mass in a patient undergoing active surveillance. Baseline coronal single-shot fast spin-echo T2-weighted (A) and axial subtracted 3D T1-weighted, fat-suppressed gradient-echo corticomedullary-phase (B) MR images, as well as corresponding sequences obtained on follow-up MRI 3 years later (C and D, respectively), of a 62-year-old man with a T2 hypointense (solid arrow) mass, which exhibits low-level enhancement (dashed arrow) on postcontrast images (compared with precontrast images, not shown) and remained entirely stable in size and imaging features on the follow-up examination.

FIGURE 12.

Baseline coronal single-shot fast spin-echo T2-weighted (A) and axial subtracted 3D T1-weighted, fat-suppressed gradient-echo corticomedullary-phase (B) MR images, as well as corresponding images obtained on follow-up MRI more than 3 years later (C and D, respectively), in an 80-year-old woman with a heterogeneous T2 avidly enhancing mass (solid arrows), which demonstrated interval increase in size between the 2 examinations. The MRI features are most characteristic of the clear cell subtype of RCC.

FIGURE 13.

Axial single-shot fast spin-echo T2-weighted (A) and axial subtracted 3D T1-weighted, fat-suppressed gradient-echo nephrographic-phase (B) MR images of a multilocular cystic RCC in a 54-year-old man. Thick enhancing septations (solid arrow) resulted in interpretation of this mass as a Bosniak 3 cystic lesion.