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PICTORIAL ESSAY

Diffusion-weighted MRI of renal cell carcinoma, upper tract urothelial carcinoma, and renal infection: a pictorial review

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Abstract Diffusion-weighted (DW) magnetic resonance imaging (MRI) is a functional imaging technique that derives image contrast from differences in water molecule diffusion within tissues. DW MRI helps detect and characterize renal and urothelial malignancies, may help in differentiating some benign from malignant renal masses, and can also recognize renal and upper urinary tract infections. Patients precluded from receiving intravenous contrast agents may particularly benefit from this technique.

Keywords DWI · Renal cell carcinoma · Magnetic resonance · Urothelial carcinoma · Renal infection

Introduction

Applications of diffusion-weighted (DW) magnetic resonance imaging (MRI) in the body have rapidly expanded in the past several years, coinciding with advances in MRI techniques and hardware technology. DW MRI is a functional imaging technique that derives image contrast from differences in the random motion of water molecules ("Brownian motion") at the cellular level. The ability to depict areas of high cellularity can be helpful in lesion detection and tissue characterization. DW MRI does not rely on intravenous contrast, so patients with renal failure who are at risk for nephrogenic systemic fibrosis or nephrotoxicity may particularly benefit from this technique in the evaluation for renal and upper urinary tract cancer.

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DW MR imaging and analysis

Water molecules exhibit varying levels of restricted motion in biologic tissues, the degree of which inversely correlates with tissue cellularity and cell membrane integrity [1]. Diffusion of water molecules is restricted in highly cellular tissues due to reduced extracellular space and by intact cell membranes that act as barriers to diffusion between the intracellular and extracellular spaces [1]. Highly cellular tissues (i.e., solid neoplasms) will, therefore, demonstrate greater restricted diffusion than tissues with low cellularity (i.e., cysts) and/or defective cell membranes. This forms the basis for DW MRI to derive image contrast. In addition, diffusion characteristics of tissues partly relate to microvascular perfusion. Thus, the kidney is a particularly interesting organ to study due to its high vascularity and inherent fluid transport properties [2].

In general, DW MR in the body uses a fast single-shot echo-planar imaging based sequence. Parallel imaging significantly shortens acquisition time and increases the

signal-to-noise ratio [3]. Breath-hold or respiratory-gated techniques are commonly employed to minimize motion artifact. Alternatively, patients may be instructed on the use of "free-breathing" (shallow breathing throughout image acquisition), a technique that yields diagnostic quality images in many patients. Robust fat suppression also helps eliminate ghosting from respiration and chemical shift artifact [3].

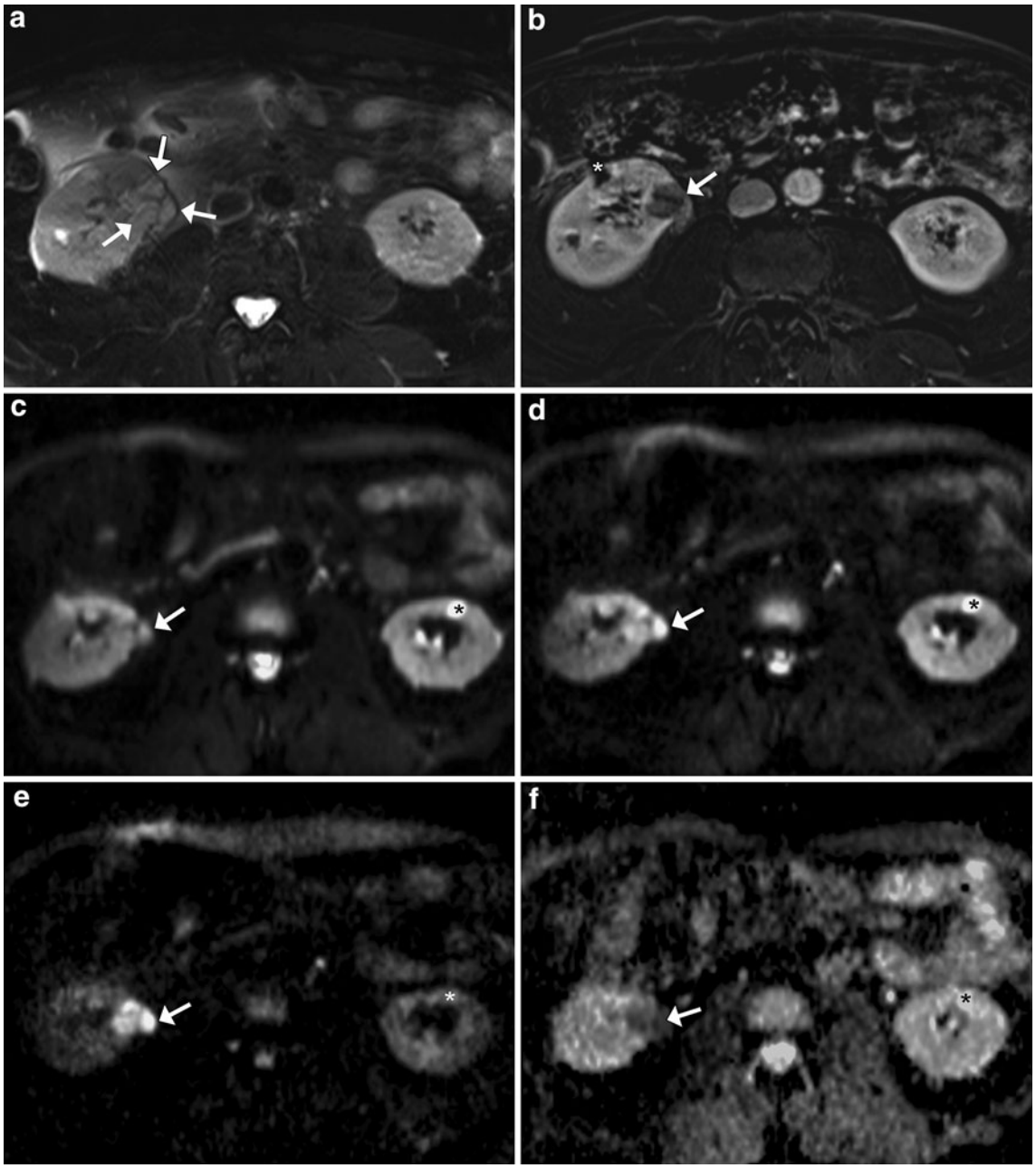


Fig. 1 59-year-old male with RCC (chromophobe type). T2-weighted image with fat-saturation (**a**) demonstrates a small, partially exophytic mass (*arrows*) in the medial lower pole of the right kidney that is nearly iso-intense to adjacent renal parenchyma. Post-contrast T1-weighted subtraction image (**b**) demonstrates low-level enhancement in the mass (*arrow*) compared to a non-enhancing small right renal cyst (*asterisk*). Low b-value (50 s/mm^2) diffusion-weighted image (**c**) shows the mass (*arrow*) to be near iso-intense to adjacent renal parenchyma. Note the hyperintense signal within a simple left renal cyst (*asterisk*). Higher b-value diffusion-weighted images obtained at (**d**) 400 s/mm^2 and (**e**) 800 s/mm^2 demonstrate that the mass (*arrow*) retains hyperintense signal while other tissues, including the small left renal cyst (*asterisk*), and cerebral spinal fluid (CSF) progressively lose signal. Corresponding ADC map (**f**) demonstrates low signal within the mass (*arrow*), confirming restricted diffusion; RCC (chromophobe type) was found at surgery. Note presence of bright signal, or T2 shine-through, in the simple left renal cyst (*asterisk*)

To achieve meaningful interpretation, DW images are acquired with at least two different b-values (i.e., low and high) in order to calculate an apparent diffusion coefficient (ADC) map. By drawing regions of interest on an ADC map, ADC values are derived to allow the quantification of diffusion in specific tissues ("quantitative analysis"). Alternatively, conclusions may be readily drawn by simple visual inspection of the b-value images and the corresponding ADC map ("qualitative analysis"). Images obtained with high b-values (i.e., 800 or 1000 s/mm^2) produce greater signal loss from water molecules [1]. Therefore, tissues that exhibit the greatest degree of restricted diffusion are seen as areas of retained (bright) signal on high b-value images and show low signal intensity on the corresponding ADC map. Renal DW MRI improves lesion conspicuity and may help characterize tissues in a noninvasive manner.

Renal cell carcinoma

DW MR has a promising role in the characterization of renal masses. Highly cellular neoplasms, such as solid renal cell carcinomas (RCCs), typically maintain bright signal intensity compared to normal renal parenchyma on high b-value images. Conversely, renal masses with low cellularity such as benign cysts typically have less restricted water diffusion and lose signal on high b-value images (Fig. 1) [1]. Nonetheless, RCC can have a varied appearance on DW MRI owing to differing degrees of

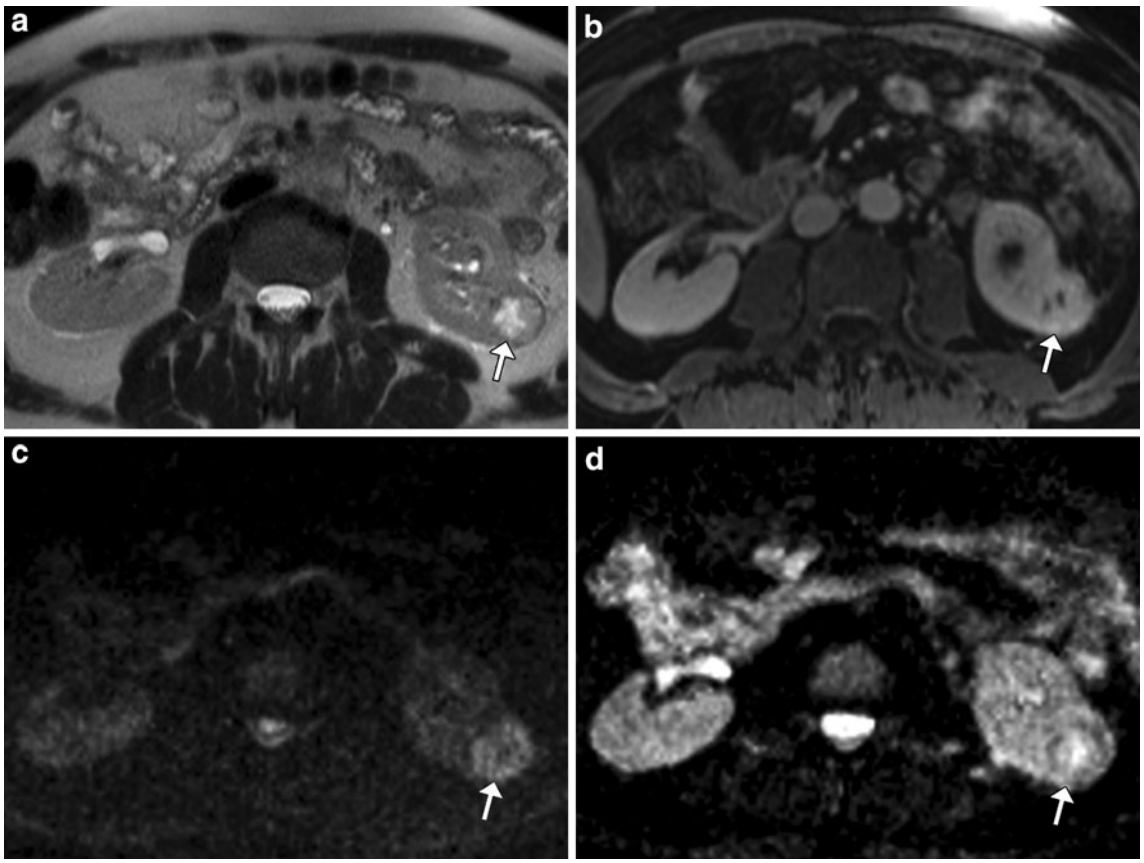


Fig. 2 64-year-old male with clear cell type RCC. Axial half-Fourier acquisition single-shot turbo spin-echo (HASTE) image (**a**) demonstrates a left renal mass (*arrow*) with a peripheral irregular rind of soft tissue and central cystic change or necrosis. Post-contrast T1-weighted spoiled gradient recalled echo (SPGR) image (**b**) demonstrates avid enhancement throughout most of this mass (*arrow*). High b-value (800 s/mm^2) diffusion-weighted image (**c**) shows high signal mostly within the peripheral portion of the mass (*arrow*) and a small central area of low signal corresponding to cystic change or necrosis. ADC map (**d**) confirms restricted diffusion in the periphery of the mass (*arrow*) with T2 shine-through centrally

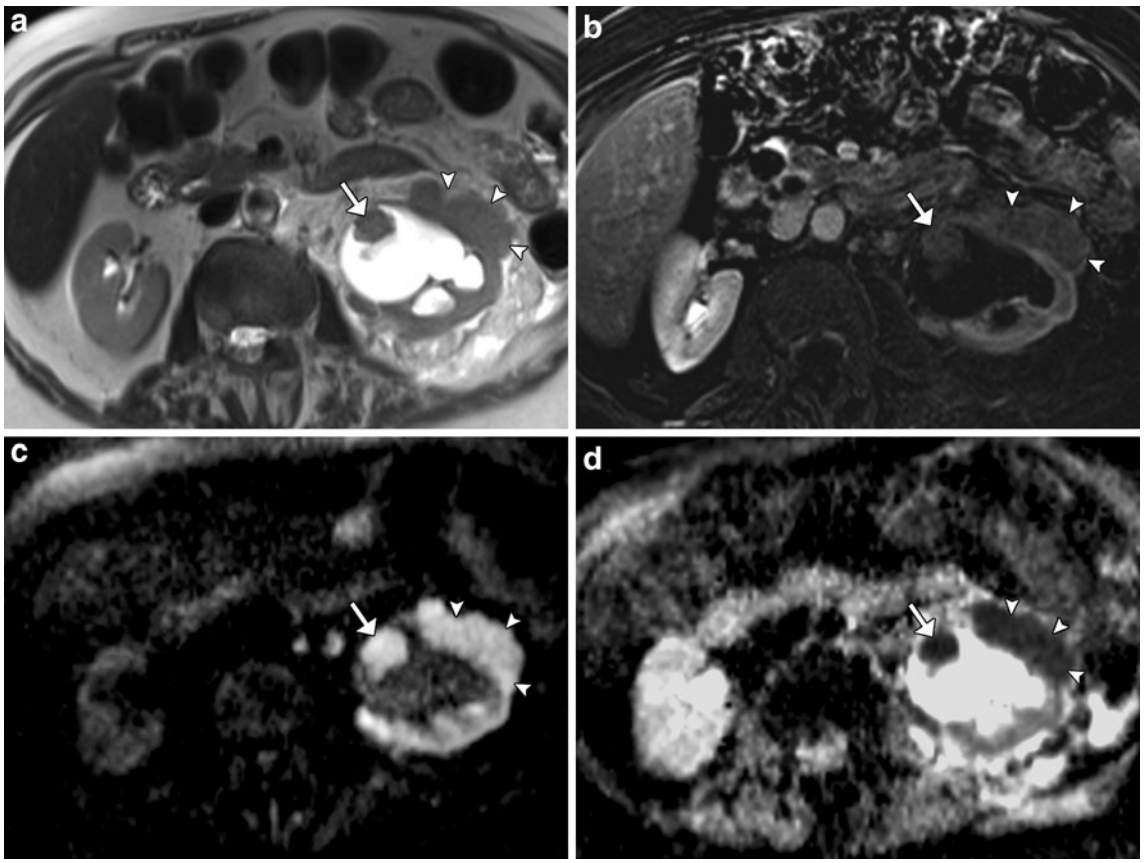


Fig. 3 85-year-old female with surgically proven urothelial carcinoma with perinephric extension. Axial HASTE image (**a**) demonstrates severe left hydronephrosis attributed to an obstructing mass in the renal pelvis (*arrow*). Abnormal soft tissue extends along the anterolateral margin of the kidney (*arrowheads*), representing invasion of the perinephric fat by tumor. Post-contrast T1-weighted subtraction image (**b**) shows mild enhancement throughout the same areas of tumor (*arrow*, *arrowheads*). High b-value (800 s/mm^2) diffusion-weighted image (**c**) shows hyperintense signal in the renal pelvic mass (*arrow*) and perinephric tumor (*arrowheads*), as well as within the obstructed renal parenchyma. Corresponding ADC map (**d**) shows marked hypointensity in the areas of tumor (*arrow*, *arrowheads*), allowing for easier separation from uninvolved renal parenchyma

cellularity and elements of cystic change, necrosis, or hemorrhage. In complex renal masses, solid enhancing tumor components demonstrate lower ADC values than necrotic or cystic regions (Fig. 2) [4]. Areas of restricted diffusion in a mixed solid and cystic renal mass may help differentiate an RCC with cystic or necrotic areas from a benign complicated cyst that might otherwise appear similar on conventional MRI obtained without contrast [4, 5].

With regard to renal masses favored to represent RCC at imaging, some authors suggest that DW MRI may potentially allow differentiation of RCC subtype and histologic grade based upon their respective ADC values. Wang et al. [6] reported statistically significant differences in ADC values among the three major subtypes of RCC at 3.0-T MRI. Papillary RCCs have been demonstrated to have the lowest ADC values, a feature that may relate both to the high cellularity and decreased perfusion or hypovascular nature of this particular RCC subtype [6, 7]. Rosenkrantz et al. [8] reported significantly lower ADC values in high-grade compared to low-grade clear cell RCC. Similarly, Yu et al. [9] found that ADC values decreased with increasing pathological grade of clear cell RCC. With advanced or metastatic RCC, the ability to characterize RCC preoperatively could alter the selection of clinical therapy [8].

Upper urinary tract carcinoma

Urothelial carcinomas also exhibit restricted diffusion due to high cellularity; they stand out as areas of bright

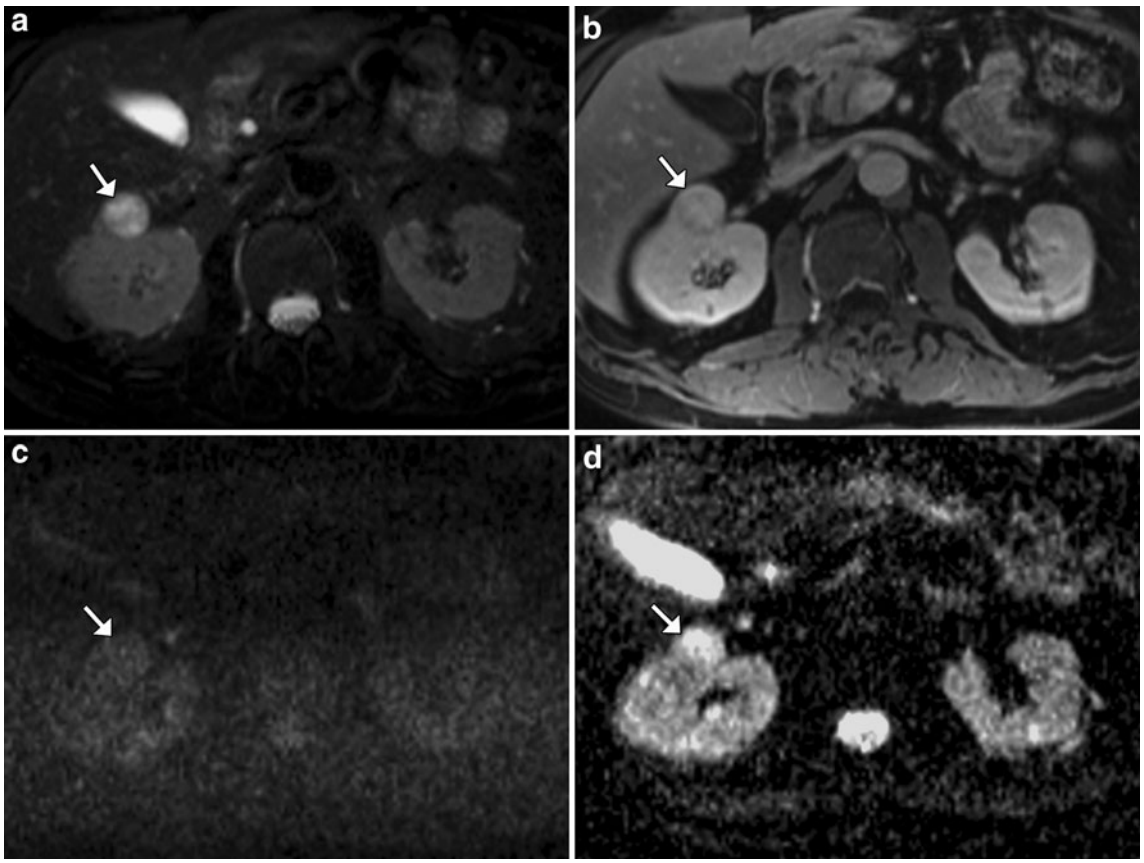
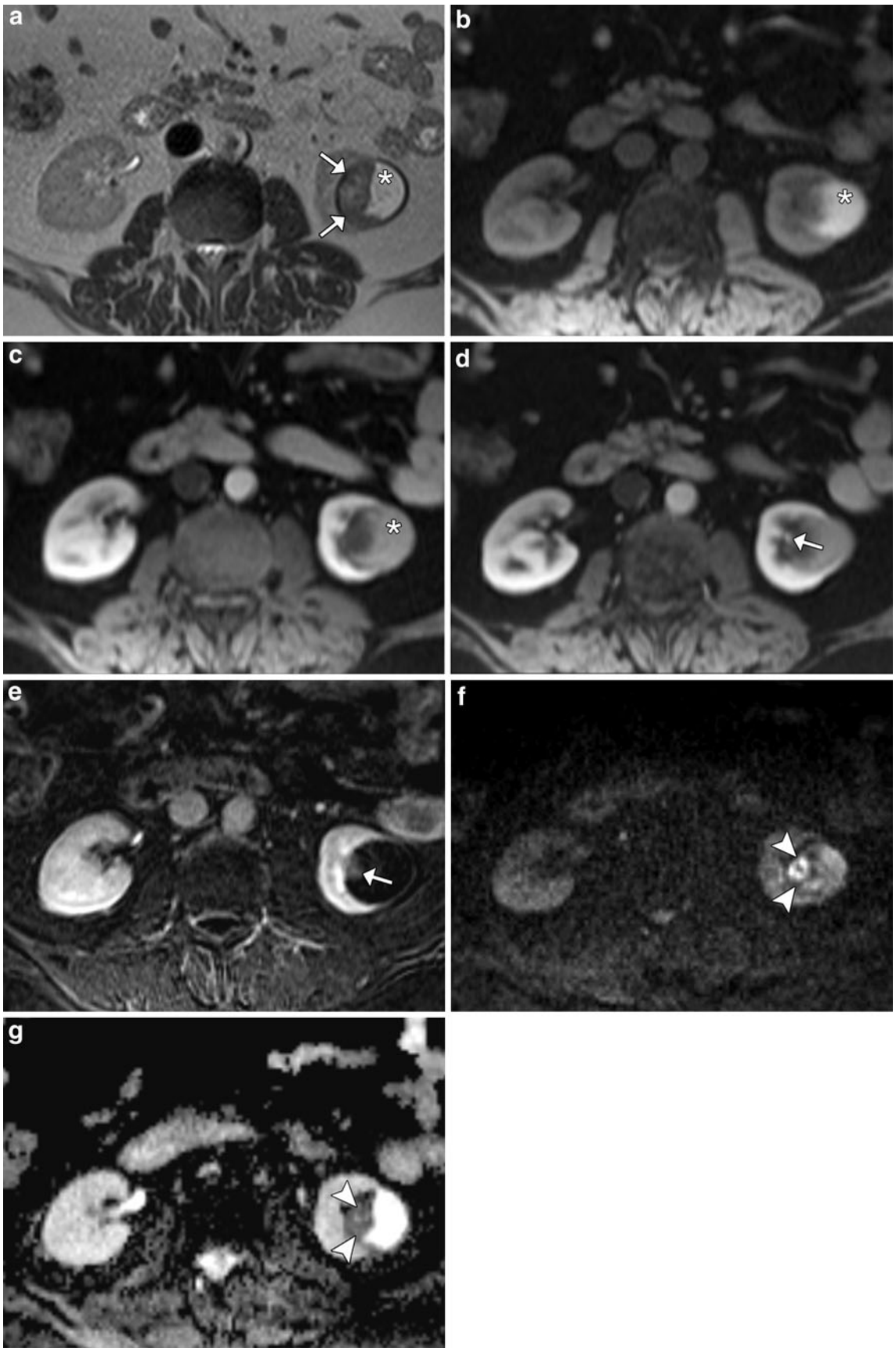


Fig. 4 65-year-old male with surgically proven oncocytoma. T2-weighted image with fat-saturation (**a**) demonstrates a rounded heterogeneous, predominately T2 hyperintense mass (*arrow*) in the right kidney. Postcontrast T1-weighted SPGR image (**b**) demonstrates this to be a solid enhancing mass (*arrow*). High b-value (1000 s/mm^2) diffusion-weighted image (**c**) demonstrates no significant retained bright signal in the mass (*arrow*) relative to normal kidney. Corresponding ADC map (**d**) shows T2 shine-through in the mass (*arrow*), unlike findings of restricted diffusion in the preceding examples of malignancy (Figs. 1, 2, 3)

signal intensity against a background of suppressed signal within the collecting system and adjacent normal renal parenchyma on high b-value images while demonstrating low signal on the corresponding ADC map (Fig. 3). Yoshida et al. [10] found that the accuracy and sensitivity for detecting upper urinary tract carcinoma at MRI can be significantly improved by adding DW imaging to standard anatomic and fluid-sensitive sequences; in fact, the diagnostic abilities of DW MRI alone in comparison to dynamic contrast-enhanced MRI were not markedly different. DW MRI may also be a useful adjunct in preoperative assessments of tumor grade or aggressiveness; Akita et al. [11] reported a significant difference between mean ADC values of high-grade versus low-grade renal pelvic urothelial carcinomas. DW MRI is limited in depicting carcinoma in situ and small lesions less than or equal to 5 mm in size [12]. Additionally, the mere presence of retained bright signal on high b-value images is not entirely specific for malignancy. A benign entity that also exhibits restricted diffusion, such as a focal inflammatory process, could be mistaken for tumor. Thus, DW MRI should be interpreted in conjunction with conventional MRI sequences to allow better morphologic assessment [10].

Differential diagnoses

Investigators have shown ADC values of benign renal lesions to be significantly higher than malignant lesions [4, 5, 7, 13, 14]. Despite this, there has been a general inability to reliably differentiate benign solid renal masses from malignant masses based upon respective ADC values thus far. In one promising exception, however, Taouli et al. [7] reported that renal oncocytomas had significantly higher ADC values than solid RCCs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◀ **Fig. 5** 65-year-old male with a surgically proven hemorrhagic cyst with active bleeding along its wall, mimicking a cystic RCC. Axial HASTE image (**a**) demonstrates a rounded lesion with a T2 hypointense rim, a large cystic-appearing component laterally (*asterisk*), and a more solid appearing portion medially (*arrows*). Pre-contrast T1-weighted SPGR image (**b**) shows that the more cystic-appearing component is intrinsically T1 hyperintense compatible with blood products (*asterisk*). The initial set of post-contrast images shows that this T1 hyperintense component (*asterisk*) and the majority of the more solid-appearing portion do not enhance (**c**), but there is a small peripheral nodular focus of enhancement medially (*arrow*) (**d**). Subtraction image during the nephrographic phase (**e**) confirms a small area of contrast pooling within the medial portion of the lesion (*arrow*). The high b-value (800 s/mm^2) diffusion-weighted image (**f**) shows hyperintense signal in the region of active bleeding (*arrowheads*). ADC map (**g**) demonstrates restricted diffusion medially (*arrowheads*) but not in the more cystic appearing portion laterally. A partial nephrectomy was performed due to concerns over cystic RCC; pathology revealed a hemorrhagic cyst with hemosiderin deposition but without any tumor elements

(Fig. 4). Larger studies are needed to validate these results, and surgical excision is still required for definitive diagnosis. Renal hemorrhagic cysts can sometimes demonstrate very low signal on the ADC map, a finding that may relate to the "T2 blackout" effects of an intrinsically T2 hypointense lesion and/or restricted diffusion in blood products (Fig. 5) [14]. In our experience, fluid–fluid or hematocrit levels can be observed in some hemorrhagic cysts. They characteristically lack solid enhancing components, although small lesion size and motion artifact can limit accurate evaluation.

Renal infection and some associated complications also demonstrate restricted diffusion and should not be mistaken for malignancy. Pyelonephritis results in patchy non-mass-like areas of restricted diffusion in portions of the renal parenchyma, a finding that may relate to inflammatory cell

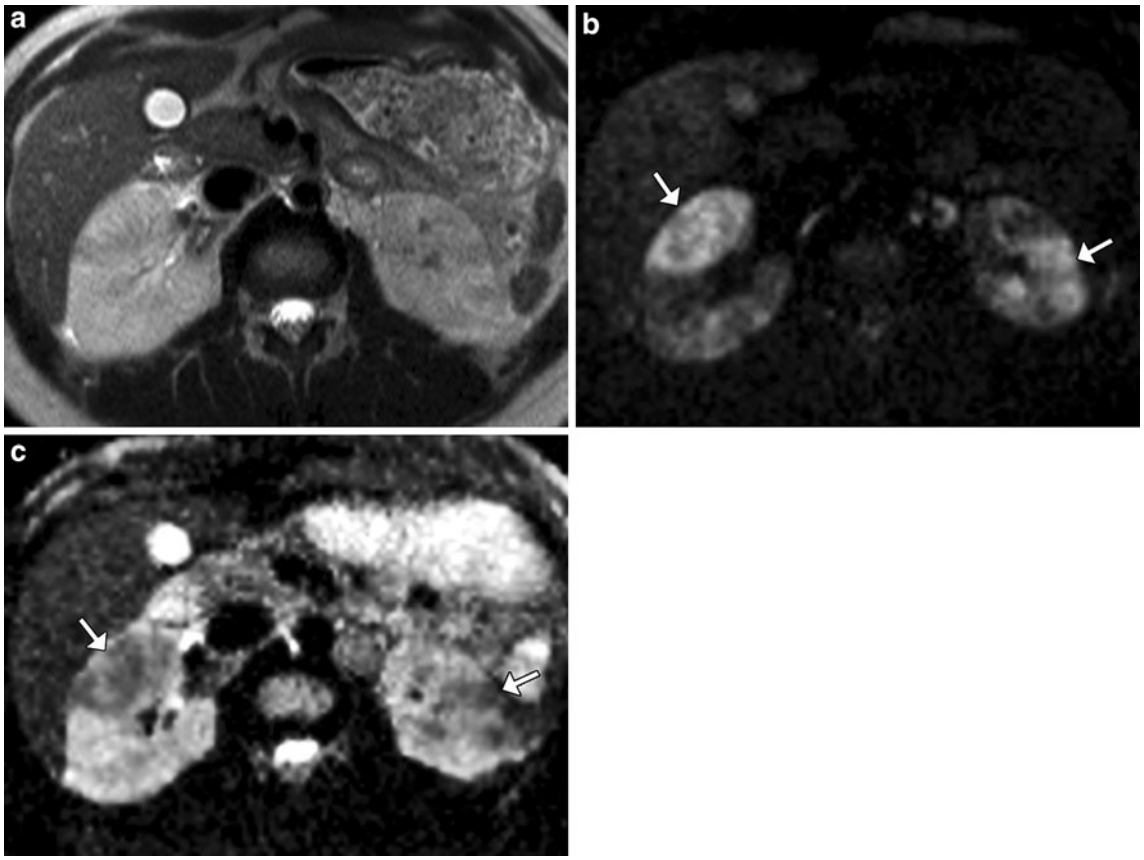

Fig. 6 21-year-old female with persistent fevers after treatment for urinary tract infection, who was found to have bilateral pyelonephritis. Axial HASTE image (**a**) demonstrates subtle non-masslike areas of heterogeneous T2 signal in both kidneys that could easily be overlooked. Gadolinium could not be administered due to impaired renal function. Multifocal areas of restricted diffusion (*arrows*) indicating bilateral pyelonephritis are readily apparent on the high b-value (800 s/mm^2) diffusion-weighted image (**b**) and corresponding ADC map (**c**)

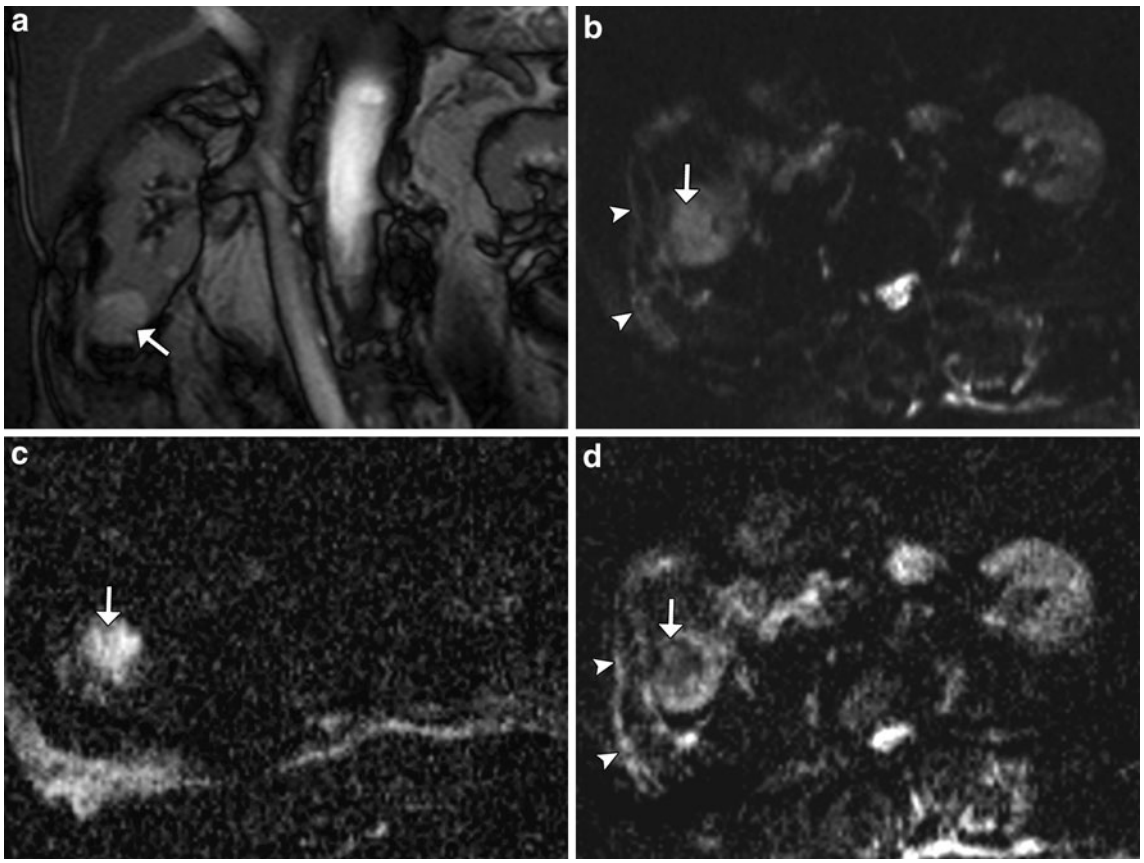

Fig. 7 86-year-old male with a renal abscess after persistent urinary tract infection (*Pseudomonas*) for 2 months. Coronal steady-state free precession image (**a**) demonstrates a rounded mildly T2 hyperintense mass in the lower pole of the right kidney (*arrow*). Low b-value (50 s/mm^2) image (**b**) demonstrates the mass (*arrow*) to be mildly hyperintense with the presence of adjacent perinephric stranding (*arrowheads*). High b-value (800 s/mm^2) diffusion-weighted image (**c**) demonstrates retention of hyperintense signal within the mass (*arrow*) while background tissues and CSF have lost signal. Low signal within the mass (*arrow*) on the ADC map **d** confirms restricted diffusion, a finding that helps to confirm the clinical suspicion for a renal abscess. Perinephric stranding (*arrowheads*) is another clue to the diagnosis

infiltration and possible ischemic effects of infection (Fig. 6) [3, 15]. A renal abscess could simulate a solid renal mass on DW images due to marked restricted diffusion owing to viscous fluid containing bacteria, mucoid proteins, and cellular debris, but an abscess is usually suspected clinically (Fig. 7) [3]. While not easily confused with tumor, the presence of pus within an obstructed collecting system is crucial to recognition; emergent percutaneous decompression is indicated because these patients can become septic and deteriorate rapidly. Differentiation between pyonephrosis and hydronephrosis may not be possible on ultrasound and standard MRI sequences; however, DW MRI easily differentiates the two because pyonephrosis demonstrates marked restricted diffusion (Fig. 8) [15, 16].

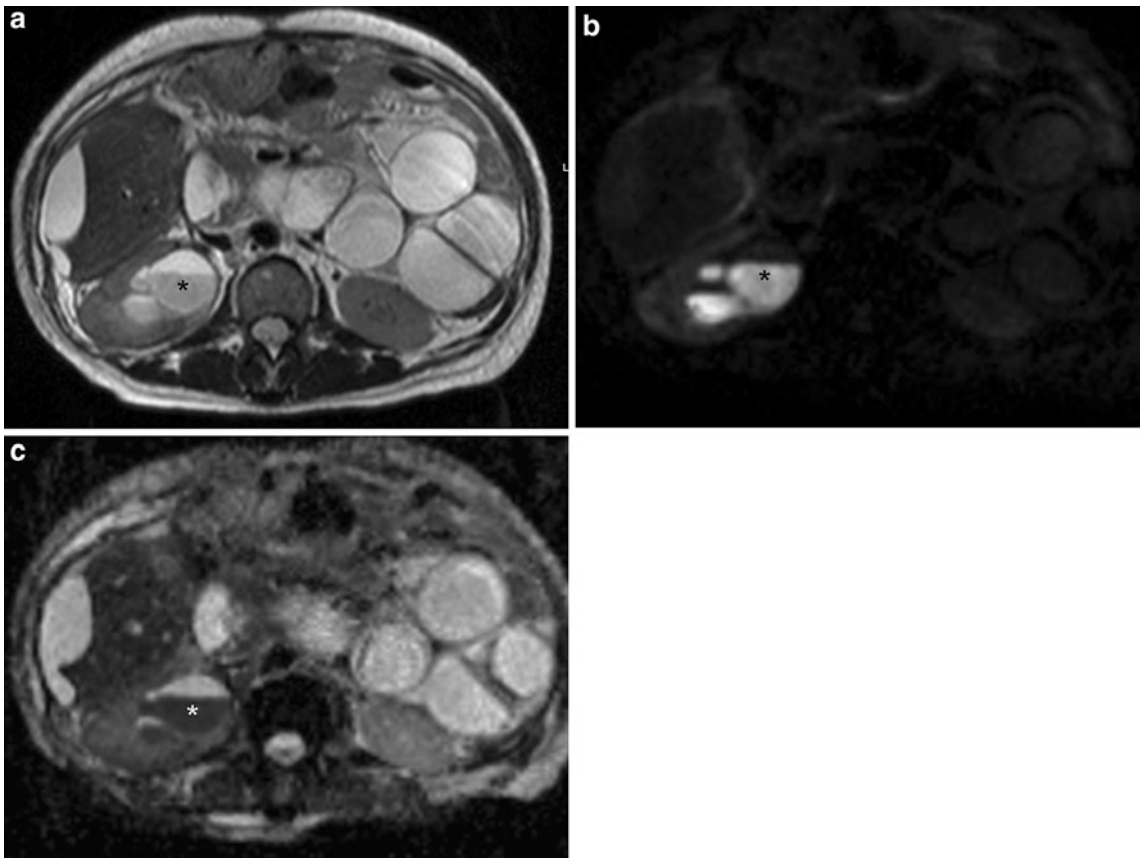

Fig. 8 42-year-old female with sepsis who was found to have right pyonephrosis. Axial HASTE image (**a**) demonstrates moderate dilatation of the right collecting system with the presence of a fluid–fluid level (*asterisk*). High b-value (800 s/mm^2) diffusion-weighted image (**b**) shows marked hyperintense signal involving the more dependent fluid layer (*asterisk*) within the obstructed right collecting system. The corresponding ADC map (**c**) demonstrates marked hypointensity of the dependent fluid level (*asterisk*), confirming the diagnosis of pyonephrosis

Conclusion

This article demonstrates basic principles, imaging features, and current roles of DW MRI in the evaluation of renal and upper urinary tract cancer and infection. DW MRI may be particularly helpful in patients who cannot receive intravenous contrast.

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

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