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Utility and limitations of 3-Tesla diffusion-weighted magnetic resonance imaging for differentiation of renal tumors

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ABSTRACT

Objective: To investigate utility and limitations of 3-Tesla diffusion-weighted (DW) magnetic resonance imaging (MRI) for differentiation of benign versus malignant renal lesions and renal cell carcinoma (RCC) subtypes.
Materials and methods: Sixty patients with 71 renal lesions underwent 3 Tesla DW-MRI of the kidney before diagnostic tissue confirmation. The images were retrospectively evaluated blinded to histology. Single-shot echo-planar imaging was used as the DW imaging technique. Apparent diffusion coefficient (ADC) values were measured and compared with histopathological characteristics.
Results: There were 54 malignant and 17 benign lesions, 46 lesions being small renal masses ≤4 cm. Papillary RCC lesions had lower ADC values ($p = 0.029$) than other RCC subtypes (clear cell or chromophobe). Diagnostic accuracy of DW-MRI for differentiation of papillary from non-papillary RCC was 70.3% resulting in a sensitivity and specificity of 64.3% (95% CI, 35.1–87.2) and 77.1 (95% CI, 59.9–89.6%). Accuracy increased to 83.7% in small renal masses (≤4 cm diameter) and sensitivity and specificity were 75.0% and 88.5%, respectively. The ADC values did not differ significantly between benign and malignant renal lesions ($p = 0.45$).
Conclusions: DW-MRI seems to distinguish between papillary and other subtypes of RCCs especially in small renal masses but could not differentiate between benign and malignant renal lesions. Therefore, the use of DW-MRI for preoperative differentiation of renal lesions is limited.

1. Introduction

Renal cell carcinoma (RCC) survival is improving because of both improved therapeutic strategies and early detection through the increased use of imaging studies [1]. New imaging techniques have also led to an increased detection of incidental renal tumours [2], most of which are <4 cm at detection and therefore known as "small renal masses" (SRM). SRMs are often detected in elderly individuals with multiple morbidities who are potential candidates for active surveillance [3]. Up to 20% of SRMs are indeed benign, underscoring the need for diagnostic tools which could aid in the differentiation between benign and malignant lesions [4].

Recently, the introduction of diffusion-weighted magnetic resonance imaging (DW-MRI) in oncologic imaging has improved the discrimination between benign and malignant tumours in the brain, breast, liver, prostate and some female pelvic organs [5–8]. The diagnostic role of DW-MRI in the characterization of renal lesion is yet unclear. Early reports on preoperative DW-MRI have shown results for differentiating between benign and malignant renal tumours and for discriminating between the various subtypes of RCCs [9–16]. Obviously, such findings would have great clinical impact and could be used for presurgical risk stratification, especially in the context of observation/active surveillance

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for SRMs and in patients with impaired renal function. However, the current literature remains inconclusive, with inconsistent classification results and varying quantitative diffusivity values [9–16].

Consequently, our study aimed to investigate the diagnostic utility and limitations of 3-Tesla DW-MRI for differentiation of benign and malignant renal lesions and for characterization of various RCC subtypes, using histopathology as the gold standard.

2. Methods

Sixty patients (mean age 64.0 years range 21–85 years), scheduled for biopsy or surgery of suspicious renal lesions, were eligible for this retrospective, institutional review board-approved, single-center study. Seventy patients with 81 renal lesions were enrolled between February 2007 and September 2012. Ten patients with 10 lesions were excluded because of insufficient image quality due to gross motion artifacts. All patients gave written informed consent to the examination.

Two board-certified uropathologists blinded to the DW-MRI results reviewed the histological specimens. Lesions were classified as benign or malignant. Malignant lesions were subcategorized as clear cell carcinoma, chromophobe carcinoma, papillary carcinoma or unclear. Benign lesions were categorized as oncocytoma, angiomyolipoma, or benign mixed epithelial stroma tumour.

Histological results of the surgical resection ($n = 56$) or image-guided biopsy ($n = 15$) were used as the reference standard for lesion characterization.

2.1. MRI protocol

All examinations were performed using a whole body MRI system at a field strength of 3-Tesla (TIM Trio, Siemens, Erlangen, Germany). A dedicated, phased-array body coil was used as the receiver while the standard body coil was used as the transmitter. The imaging protocol included unenhanced T2-weighted Turbo-Spin-Echo and T1-weighted gradient echo sequences. Diffusion Weighted Imaging (DWI) was performed using a respiratory triggered Echo Planar Imaging (EPI) sequence (TR: 1700 ms; TE_{eff}: 73 ms; 3 *b*-values of 0, 500, and 1000 s/mm^2). Apparent Diffusion Coefficient (ADC) maps were calculated using mono-exponential linear regression, performed by the scanner software on a pixel-by-pixel basis. After DWI, a dynamic contrast enhanced T1-weighted gradient echo sequence completed the protocol.

DW data were analyzed by 2 observers (a board-certified radiologist with an MRI specialization and 7 years of experience in body DW and a urologist with 10 years of experience in renal tumour diagnosis and treatment). All imaging data, including contrast-enhanced images, were reviewed using a dedicated workstation (Siemens Leonardo MMWP, Munich, Germany). Solid parts of the investigated lesions were carefully identified and interrogated using a small (5–10 pixels) circular region of interest (ROI). This ROI was placed on high *b*-value DWI images and automatically transferred to the ADC map in order to obtain mean Apparent Diffusion Coefficient (ADC) values. Lesion size was measured using electronic calipers on the MRI image.

2.2. Statistical analysis

Descriptive statistics, clustered boxplots, and statistical testing were performed using SPSS 19.0 (IBM, Armonk, NY, USA). Normal distribution of data was confirmed by the Kolmogorov Smirnoff test. Group comparisons were performed by two-sided unpaired *t*-tests and Levene's test was used to test the equality of variances. *P* values of <0.05 were considered significant.

Table 1
Clinico-pathological characteristics of renal cell carcinomas.

	n	%
T-stage		
pT1a	23	46.0
pT1b	1	2.0
pT2a	3	6.0
pT2b	0	0
pT3a	22	44.0
pT3b	1	2.0
pT3c	0	0
pT4	0	0
N-stage		
N0 + Nx	49	98.0
N1	1	2.0
M-stage		
M0	47	94.0
M1	3	6.0
RCC subtypes		
Clear cell	29	53.7
Papillary	15	27.8
Chromophobic	6	11.1
Fuhrmann grade		
G1	18	36.0
G2	24	48.0
G3	8	16.0
G4	0	0

3. Results

The 71 lesions, from 60 patients, had a mean size of 4.2 ± 3.0 cm (median 3.5 cm, IQR 3.4 cm, range, 1.0–19.8 cm). Histological specimens were acquired through radical nephrectomy ($n = 25$), partial nephrectomy ($n = 15$). One patient received both radical nephrectomy on one side and partial nephrectomy on the other side. Four patients underwent nephroureterectomy. Fifteen patients were biopsied under imaging guidance. Therefore, 61 surgical procedures were performed in 60 patients. The mean time interval between MRI examination and surgery/imaging-guided biopsy was mean 19.3 ± 29.8 (median 7.5, IQR 28.8) days.

Seventeen of the 71 lesions (27.8%) were histo-pathologically benign and 54 (88.5%) were malignant. The benign lesions included 10 oncocytomas, three angiomyolipomas, and one case of mixed epithelial stromal and mesenchymal tumour. In two cases, image-guided biopsy did not identify malignant tissue but fibrosis. The malignant subtypes included 29 clear cell RCCs, 15 papillary RCCs, 6 chromophobe RCCs, and 4 urothelial cell carcinomas. TNM classifications of the tumours and Fuhrmann grade distribution are shown in Table 1. Twenty-three of 54 (42.6%) lesions had no necrotic components.

ADC values differed significantly between solid (46/71, 64.8%) and non-solid (25/71 partially cystic, 35.2%) lesions (mean 1176 ± 363, median 1124, IQR 559 × 10^{-6} mm^2/s versus mean 1472 ± 699, median 1361, IQR 780 × 10^{-6} mm^2/s; $p = 0.021$) but not between benign and malignant renal lesions ($p = 0.45$, Table 2). Papillary RCCs showed significantly lower ADC values than clear cell and chromophobe RCCs ($p = 0.029$, Fig. 1). A clinical example of clear cell carcinoma is given in Fig. 2.

Receiver operating characteristics (ROC) analysis revealed an area under the ROC curve of 0.703 ($p = 0.018$); at an ADC cut-off value of ≤0.954 × 10^{-6} mm^2/s, sensitivity and specificity for diagnosis of papillary RCC were 64.3% (95% CI, 35.1–87.2) and 77.1 (95% CI, 59.9–89.6%), respectively.

Histopathological grades were not associated with ADC measurements ($p = 0.86$, cf Fig. 3). Furthermore, ADC values did not differ significantly between malignant lesions with or without necrosis (mean, 1163 ± 374, median 1137, IQR 683 × 10^{-6} mm^2/s