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Efficacy of 3D VIBE Dixon fat quantification for differentiating clear-cell from non-clear-cell renal cell carcinoma

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AIM: To assess the efficacy of three-dimensional (3D) volumetric interpolated breath-hold examination (VIBE) magnetic resonance imaging (MRI) with Dixon quantification for differentiating clear-cell from non-clear-cell types of renal cell carcinoma (RCC).

MATERIALS AND METHODS: The 3D VIBE Dixon renal MRI examinations of 44 patients with 45 histologically confirmed RCCs was analysed. The fat fractions and signal intensity indexes (SI_{index}) of the solid portions of clear-cell and non-clear-cell RCCs were measured and compared using Student's *t*-test and receiver operating characteristic (ROC) curves. The agreement of measurements among observers was evaluated by the intraclass correlation coefficient (ICC), and Bland–Altman plots.

RESULTS: The mean values of fat fraction (13.16±7.16%) and SI_{index} (22.64±15.7%) in clear-cell RCCs were significantly higher than that in non-clear-cell RCCs (7.7±2% and 7.9±4.8%; $p<0.001$, respectively). With the area under the ROC curve (AUC) of the fat fraction at 0.811, 75% (95% CI: 55.1–89.43%) sensitivity and 76.5% (95% CI: 50.1–93.2%) specificity for diagnosing clear-cell RCC were obtained at a cut-off fat fraction value of 8.9%. With a cut-off value of 8.89%, the diagnostic sensitivity and specificity were 85.7% (95% CI: 67.3–96%) and 70.6% (95% CI: 44–89.7%), respectively. The AUC of the SI_{index} was 0.870 (0.766–0.973). ICC and Bland–Altman plots show excellent agreement of the tumour fat fraction and SI_{index} measurement between the two observers.

CONCLUSION: Intracellular lipid content analysis using the 3D Dixon technique can help to differentiate clear-cell from non-clear-cell RCCs.

Introduction

Clear-cell renal cell carcinoma (RCC) is the most common histological subtype accounting for 65–80% of all RCCs. Non-clear-cell RCC includes papillary (10–15%), chromophobe (4–5%), collecting duct (1–2%), and other rare or

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unclassified (4–5%) subtypes.[1,2] Each subtype of RCC is associated with a different prognosis. Compared with common types of non-clear-cell RCC, such as papillary RCC and chromophobe RCC, clear-cell RCC have an unfavourable prognosis, with a 5-year survival rate of 44–69%, and it accounts for 94% of metastatic RCC.[3] Differentiating clear-cell from non-clear-cell subtypes is crucial for prognosis assessment and treatment management. Clear-cell RCC typically presents as a heterogeneous hyper-vascular mass with a variable amount of intracellular lipid. Magnetic resonance imaging (MRI) signal intensities (SIs) and contrast enhancement patterns, apparent diffusion coefficient values on diffusion-weighted imaging (DWI), and the presence of macro- or microscopic fat on chemical shift imaging (CSI) have been used to differentiate clear-cell from non-clear-cell RCC.[4–8] Previous investigators have reported conflicting results of detecting or quantifying intracellular lipid on CSI for differentiating subtypes of RCC. Clear-cell RCC was reported to exhibit a decrease in SI on out-of-phase compared with in-phase CSI because of its intracellular lipid content.[6] Other studies showed that non-clear-cell RCC also demonstrated SI drop on out-of-phase CSI.[9,10] These observations were based on quality analysis or calculation of the SI index (SI_{index}); however, qualitative analysis of focal or diffuse SI drop on out-of-phase CSI showed no significant association with histology.[9,11,12] The objective of this study was to assess the value of three-dimensional (3D) volumetric interpolated breath-hold examination (VIBE) MRI sequences with Dixon quantification of intracytoplasmic lipid for differentiating clear-cell from non-clear-cell RCCs.

Materials and methods

The study was conducted in accordance with ethical guidelines for human research, the Health Insurance Portability and Accountability Act and was approved by the institutional research ethics committee. Written informed consent was obtained from all patients. From November 2014 through September 2017, consecutive patients with suspected RCC on ultrasound or computed tomography (CT) who underwent renal MRI before treatment at The First Affiliated Hospital of Sun Yat-sen University were enrolled in the study. Patients with other renal pathology or no histology confirmation were excluded. All renal MRI examinations were performed on a 3 T MRI system (Magnetom Trio, Siemens Medical Solutions, Erlangen, Germany) with an eight-channel phased-array coil. Axial and coronal 3D T1-weighted VIBE Dixon images (5.5 ms repetition time [TR], 2.5 ms echo time 1 [TE1], 3.7 ms TE2, 10° flip angle, 504 Hz/pixel bandwidth, 1 echo train length, 32–40 cm field-of-view [FOV], 320×240 matrix, 2 mm section thickness) and two-dimensional (2D) T2-weighted (W) periodically rotated overlapping parallel lines with enhanced reconstruction (BLADE) images (3,875 ms TR, 78 ms TE, 140° flip angle, 240 Hz/pixel bandwidth, 9 echo train length, 32–40 cm FOV, 320×240 matrix, 5 mm section thickness) of the kidneys were obtained. Axial and coronal 3D T1-weighted VIBE sequences (4.37 ms TR, 1.45 ms TE, 13° matrix, 210 Hz/pixel bandwidth, 1 echo train length, 32–40 cm FOV, 384×204 matrix, 5 mm section thickness) were then acquired at 5 seconds, 50 seconds, 2 minutes, and 4 minutes after intravenously injecting 0.1 mmol/kg body weight of Gd-DTPA (Magnevist, Bayer-Schering Pharma, Berlin, Germany) at 3 ml/s followed by 15 ml of normal saline flush using a power injector (EmpowerMR, ACIST Medical Systems, Eden Prairie, Minnesota, USA).

In the present study, only the Dixon images and the fat content maps were evaluated. Other images, such as T2W imaging and contrast-enhanced images, were referred to when necessary, but were not specifically analysed for the purpose of this study.

Lesion size, defined as the largest dimension on axial T2W images, was measured by one radiologist with 5 years of MRI experience. None of the tumours contained macroscopic fat. The 3D T1W VIBE Dixon sequence produced in-phase, out-of-phase, fat-only (SI_{fat}), and water-only (SI_{water}) images. Fat content maps were generated by an image-processing program, ImageJ (Version 1.51s, National Institutes of Health, Bethesda, Maryland, USA) according to the following algorithm:

$$\text{Fat fraction} = SI_{fat}/(SI_{water}+SI_{fat}).$$

The quality of the images were analysed, and it was determined whether the images were acceptable for further analysis or not. Those with lesion size <1 cm, with poor image quality or were composed mainly of cystic or necrosis areas were excluded from the study. Two experienced abdominal radiologists (reader 1 with 10 years of experience; reader 2 with 5 years of experience) independently defined the regions of interest (ROIs) without knowledge of the pathology results.

The measurement results were averaged between the two readers for further analyses. The axial or coronal 3D T1-weighted VIBE Dixon images, fat content maps and 3D T1-weighted contrast enhanced images were displayed simultaneously and ROIs were drawn to encompass most of the solid tumour without cystic degeneration, necrosis, or haemorrhage by another radiologist with 10 years of abdominal MRI experience without knowledge of the pathology results (Fig 1). The axial plane was first observed and assessed. If image quality or the depiction of the lesion were not satisfactory, the coronal plane was then observed and assessed. The five ROIs were drawn in five axial planes or five coronal planes. The interval between planes was approximately 20%. That is to say, the five planes were located approximately at the 10%, 30%, 50%, 70%, and 90% thickness of the tumour. A freehand ROI was defined on the in-phase or out-of-phase images, T2WI and post-contrast images were referred to for verification of the solid portion of the tumours and lesion boundaries. The ROI was then defined and added in “ROI Manager”, where ROIs can be stored. The ROIs than applied to the corresponding Dixon images and fat content maps. Care was taken to exclude cystic or necrotic areas from the ROIs, which was unenhanced after intravenous injection of contrast media. For each lesion, five ROIs from five axial or coronal slices of the

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