Functional Magnetic Resonance Imaging of the Kidneys—With and Without Gadolinium-Based Contrast

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Assessment of renal function with magnetic resonance imaging (MRI) has been actively explored in the past decade. In this review, we introduce the principle of MRI and review recent progress of MRI methods (contrast enhanced and noncontrast) in assessing renal function. Contrast-enhanced MRI using ultra-low dose of gadolinium-based agent has been validated for measuring single-kidney glomerular filtration rate and renal plasma flow accurately. For routine functional test, contrast-enhanced MRI may not replace the simple serum-creatinine method. However, for patients with renal diseases, it is often worthy to perform MRI to accurately monitor renal function, particularly for the diseased kidney. As contrast-enhanced MRI is already an established clinical tool for characterizing renal structural abnormalities, including renal mass and ureteral obstruction, it is possible to adapt the clinical MRI protocol to measure single-kidney glomerular filtration rate and renal plasma flow, as demonstrated by recent studies. What makes MRI unique is the promise of its noncontrast methods. These methods include arterial spin labeling for tissue perfusion, blood oxygen-level dependent for blood and tissue oxygenation, and diffusion-weighted imaging for water diffusion. For each method, we reviewed recent findings and summarized challenges.

Key Words: Magnetic resonance imaging, Glomerular filtration rat, Tissue oxygenation, Tissue perfusion, Diffusion coefficient

The term "functional MRI" was coined to denote brain magnetic resonance imaging (MRI) for investigating brain activation[1] but in this article is used for MRI that studies tissue function, as opposed to structural MRI. Functional MRI of the kidneys started early, eg, Prasad and colleagues in 1996,[2] but its early development was slow. In the past 10 to 15 years, functional MRI of the kidneys has progressed rapidly, partially because of the awareness that progressive renal dysfunction is a significant health problem and accurate characterization by noninvasive imaging tool would be valuable. The MRI methods include gadolinium contrast-enhanced technique and vast choices of noncontrast techniques. With the methods, multiple functional parameters of the kidneys can be estimated, including glomerular filtration rate (GFR), renal plasma flow (RPF), water diffusion, and tissue oxygenation. These parameters would enable characterization of CKDs with much more confidence than simply serum-based GFR or urine test. In the following, we start with a brief introduction of MRI basics; then for each MRI method, we briefly introduce the principle, review new studies in the past 2 to 3 years, and lastly suggest future work. This review will not cover structural MRI for the kidneys, such as "renal masses" and ureteral obstruction, but we do realize the value and the feasibility of incorporating the functional methods into current structural MRI protocols for these diseases. Readers should also read other reviews written in recent years.[3-5]

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PRINCIPLE OF MRI

MRIs are formed of radiofrequency (RF) signals originated from atoms with odd number of protons; for clinical imaging, the most widely explored atom is hydrogen. Each hydrogen atom has a magnetic moment, a property that makes the atom behave like a tiny magnetic needle. Specifically, when placed in magnetic field of an MRI scanner, magnetic moments of hydrogen atoms, or magnetization, are aligned to the direction of the magnetic field. We define this original direction as z-axis. To emit signals, the atoms need to be first excited by RF pulses, which are produced by RF coils (part of MR hardware). When calibrated to the right frequency, RF pulse is able to tilt the magnetic moments of hydrogen atoms away from their original direction, so that the magnetization has a nonzero component in the x-y plane. The atoms are "excited" now or in a high-energy state. With the RF pulse switched off, the excited moments would recover to their original direction, a process called "relaxation" that usually takes few seconds. The relaxation process can be decomposed into (1) recovery of the z-component of magnetization (quantified by spin-lattice relaxation time T_1, Fig 1A) and (2) and decay of the x-y component (quantified by spin-spin relaxation time T_2, Fig 1B). It is the relaxation process that differentiates hydrogen in different tissue types, eg, fat vs muscle. In other words, different types of tissues have different values of T_1 and of T_2. For structural imaging, contrast between different tissues of interest can be created in the acquired images, by properly selecting acquisition parameters to make the acquired signals T_1 or T_2 weighted. For quantitative analysis, images with different T_1 or T_2 weighting are collected and then are processed to generate a map of T_1 or T_2. One major application of T_1 mapping is dynamic contrast-enhanced MRI, where concentration of contrast in tissue is estimated by the T_1-shortening effect of the contrast. More details of contrast-enhanced MRI are given in section "contrast-enhanced MRI." What makes MRI versatile, and unique among all imaging

modalities, is its capability of sensitizing to multiple physiological processes in tissue. In the following, we will give more details of both contrast-enhanced and noncontrast MRI techniques and review their applications in renal function assessment.

CONTRAST-ENHANCED MRI

Contrast-enhanced MRI is widely used in clinical practice, not for assessing renal function but for detecting and characterizing structural abnormalities, such as renal masses and "ureteral diseases." In the following, we introduce the principle of contrast-enhanced MRI, its typical protocol, and then review its progress based on recent studies.

The idea of injecting exogenous contrast to enhance imaging is widely adopted for many imaging modalities, and for the kidneys, the most established technique is planar scintigraphy using technetium-99m diethylenetriamine-pentaacetic acid (DTPA) or mercaptoacetyltriglycine (MAG3). Compared with renal scintigraphy, contrast-enhanced MRI has multiple advantages. First, MRI can achieve high spatial resolution (~1 mm^3) and covers the entire 3-dimensional (3D) volume of the kidneys. Second, MRI uses nonradioactive contrast agent, and one-fifth to one-fourth of clinical dosage is adequate for functional assessment of the kidneys. Here is the typical protocol most studies used. Via an antecubital vein, contrast agent is injected using an automatic power injector with flow rate of 2 to 4 mL/s. Typical dose of 0.025 to 0.05 mmol/kg is much lower than clinically recommended dose of 0.1 mmol/kg because kidneys have high blood perfusion. Also, one can choose to use body weight-calibrated dosage (eg, 0.025 mmol/kg) or fixed volume (eg, 4 mL). One reason that many clinical studies preferred body weight-calibrated dosage is that with such dosage, arterial contrast concentration would be relatively consistent between subjects of different size. Nowadays such consideration is not necessary for contrast-enhanced MRI as arterial input function (AIF) can be directly sampled from the dynamic images and then we remove its impact from tissue contrast enhancements in postprocessing.[6] The injected contrast circulates in the heart and the lungs and then enters the kidneys through renal arteries. This is the first pass of the contrast in the circulation system, followed by later passes when the contrast returns to the heart by veins. To record the process, multiple MR images are acquired, from the instant of contrast injection to several minutes afterward. All the images cover the same field of view, over the kidneys, and the abdominal aorta (for AIF). Representative images are displayed in Figure 2. To resolve the first-pass peak in AIF and in kidney contrast enhancement curves, the imaging should be fast enough (2-4 s per image) and continue for the initial period (~30 seconds) after contrast injection. As contrast concentration in the later passes does not change as quickly as in the first pass, the imaging can be performed with a slower speed, eg, 1 image per 1 min. To avoid respiratory motion, the subject is usually asked to hold breath whenever the imaging is on. The most used sequences for renal contrast-enhanced MRI include spoiled gradient-recalled echo (or termed as fast low angle shot)[7,8] and ultrafast gradient echo (prepared with an initial 180° pulse).[9,10] More recent research on fast acquisition sequences are introduced in next section. In postprocessing of the dynamic images, multiple physiological parameters can be obtained. The first step of the postprocessing is to extract contrast enhancement curves from kidney tissue and from an aortic region (for AIF), using image segmentation methods. AIF is the temporal profile of contrast concentration in the flowing blood through aorta or artery. Renal enhancement curve records the uptake and excretion of contrast agent by the kidneys, and the shape of the curve is determined by RPF, GFR, and tubular transit time. For example, a high value of GFR would lead to a high contrast concentration in the kidney during the tubular phase (from ~30 seconds to few minutes after contrast injection). To quantify these parameters from the curve, one can use proper tracer kinetic model.[7,8,11]

CLINICAL SUMMARY

- Contrast-enhanced magnetic resonance imaging (MRI) is an accurate tool for assessing renal function and can be incorporated into clinical MRI protocol of renal mass and ureteral obstruction.
- Noncontrast MRI methods hold much promise in noninvasive assessment of multiple aspects of renal function; more work is needed for quantifying physiological parameters from the MRI data.

Free-breathing acquisition has been achieved for contrast-enhanced MRI of the kidneys in the past 2 to 3 years. As we introduced earlier, in most protocols, patients are asked to hold breath during imaging to avoid respiratory motion. One innovative approach is to use radial sampling in MR image acquisition. The method has been shown to outperform conventional Cartesian sampling in reducing the impact of respiratory motion.[12] Acquiring spoiled gradient echo signals with a stack-of-stars sampling trajectory and reconstructing images using 3D through-time radial generalized autocalibrating partial parallel acquisition method, Wright and colleagues[13] achieved free-breathing 3D acquisition with spatial resolution of 2.2 to 2.3 mm^3 and temporal resolution of 2.1 to 2.9 seconds per frame. Riffel and associates[14] used a similar stack-of-stars radial sampling in data acquisition and demonstrated the high flexibility of retrospectively choosing desired balance between temporal and spatial resolutions. However, a study comparing the radial and the Cartesian samplings for a group of healthy subjects[15] found that GFR estimated from the radial sampling was significantly lower than conventional Cartesian sampling acquisition (70 ± 30 vs 103 ± 11 mL/min/1.73 m^2). In their shown example, we note that there seems to be a systematic bias between the signals acquired by the 2 sampling methods. Further work is needed to accurately quantify contrast concentration from radial-sampling MR signals. Other techniques were also applied in recent