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New magnetic resonance imaging methods in nephrology

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Established as a method to study anatomic changes, such as renal tumors or atherosclerotic vascular disease, magnetic resonance imaging (MRI) to interrogate renal function has only recently begun to come of age. In this review, we briefly introduce some of the most important MRI techniques for renal functional imaging, and then review current findings on their use for diagnosis and monitoring of major kidney diseases. Specific applications include renovascular disease, diabetic nephropathy, renal transplants, renal masses, acute kidney injury, and pediatric anomalies. With this review, we hope to encourage more collaboration between nephrologists and radiologists to accelerate the development and application of modern MRI tools in nephrology clinics.

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Long established as a method to study structural changes in disease, such as renal tumors or atherosclerotic vascular disease, magnetic resonance imaging (MRI) to interrogate renal function has only recently begun to come of age. Functional renal MR approaches render added value for MRI over other conventional imaging modalities, with emerging applications in nephrology. As an example, low doses of the conventional contrast agent used in MRI—gadolinium chelates—can be used to measure glomerular filtration rate (GFR) in individual kidneys.[1,2] Techniques borrowed from functional brain mapping known as blood oxygen level–dependent (BOLD) MRI have recently been applied to interrogate renal oxygenation and metabolic rate.[3,4] Renal perfusion can be measured using MRI either by intravenous injection of an exogenous tracer or with endogenous blood labeling methods that do not require contrast injection.

In this article, we briefly review the principles of MR imaging, introduce some of the most important MRI techniques, and then review current findings on their use for diagnosis and monitoring of major kidney diseases. Specific applications include renovascular disease (RVD), diabetic nephropathy (DN), renal transplants, renal masses, acute kidney injury, and pediatric anomalies. Our purpose is to accelerate the application of modern MRI tools in the clinic and to strengthen the collaboration between MRI physicists, radiologists, and nephrologists. We refer the reader to other reviews[5–14] and the cited papers for more technical details.

MRI PRINCIPLES AND TECHNIQUES

Modern clinical MRI scanners are typically equipped with a large superconducting magnet, which provides a stable homogeneous magnetic field (1.5–3.0 T), and multiple coils for different purposes, including signal transmission, reception, and creating magnetic field gradients. For abdominal imaging, surface coils are available to be applied to the abdomen to improve signal reception. Owing to the strong magnetic field, pacemakers are usually contraindicated with MRI scans, but most vascular stents are compatible.

Most MRI signals originate from hydrogen nuclei or protons, which behave like tiny magnets in the MRI system's magnetic field and their behavior in response to changing magnetic fields forms the basis of MRI. MRI image contrast is achieved by manipulating the magnetic properties of hydrogen protons and thereby distinguishing among various tissue characteristics, including intrinsic MR properties such as the relaxation times T_1 and T_2. Compared with tissues, water (e.g. cysts, cerebrospinal fluid) typically has longer T_1 and T_2 times (Figure 1).

Using MRI, we can also visually distinguish tissues based on other inherent tissue properties such as diffusivity of water within those tissues, capillary perfusion, blood flow or velocity, and even oxygenation. In addition, with the administration of exogenous contrast agents, other tissue characteristics can be explored. Exogenous agents such as gadolinium (Gd)-based chelates are useful for MR angiography and in MR renography (MRR), because they shorten T_1 relaxation time, and for many years they were regarded as one of the safest agents used in medicine. About a decade ago, the associations between high doses (typically double and triple the standard doses) of Gd contrast in patients with renal failure and nephrogenic systemic fibrosis (NSF) were first reported.[15] Recommendations have been made on the use of Gd contrast in patients with renal impairment.[16,17] In the past few years, with adherence to guidelines, no report of new NSF cases has been published.[18]

Below, we review some of the MRI techniques most widely explored for applicability to functional renal imaging. Their characteristics are summarized in Table 1.

MRR and dynamic contrast-enhanced MRI

MRR is a term used to describe one application of dynamic contrast-enhanced (DCE) MRI, specifically the use of Gd-based contrast agents for the noninvasive measurement of GFR. Most Gd chelates have favorable renal properties: they are freely filtered at the glomeruli without tubular secretion or resorption. This means that with the continuous acquisition of high-resolution images through the kidney every few seconds, renal function can be visualized as the passage of contrast material from the aorta through the kidney and out of the collecting system. Calculation of the extraction fraction of the Gd contrast allows determination of GFR. Several technical limitations have slowed the widespread adoption of this method, although recent developments are promising. We review some of the challenges below.

Unlike computed tomography or nuclear medicine, where tracer concentration is approximately linear to signal intensity, in DCE MRI, the relationship is more complex and it depends on the specific pulse sequence used. Methods converting MR signal intensity to concentrations of tracer have been reviewed elsewhere.[19,20] Because of the sensitivity of MRI to Gd contrast agents, 3–4 ml of Gd contrast agent suffices for accurate renal functional measurements. In MRR, signal intensities can be recorded from the whole kidney to determine GFR. For more refined measurements, signal intensities can be recorded from the renal cortex, medulla, and collecting system. With more detailed data, the transit of the bolus of contrast from the artery to the renal cortex can be used to estimate renal perfusion; the transit from cortex to medulla reflects glomerular filtration; and finally from the medulla into the collecting system reflects tubular function.

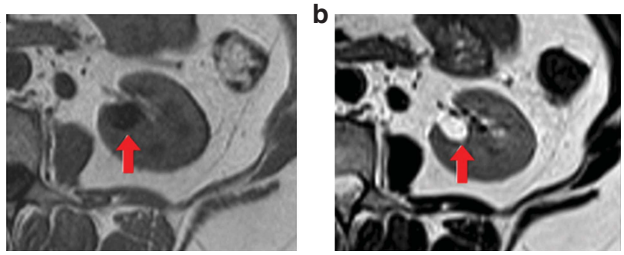

Figure 1 | Conventional anatomic magnetic resonance imaging (MRI) of kidney. The cyst, (**a**) with long T_1, is dark on a T_1-weighted image, and (**b**) with long T_2, bright on a T_2-weighted image.

To extract these functional measurements from signal intensities in the kidney, the method typically assumes a tight bolus of contrast entering the renal artery. Gd contrast is administered intravenously, and therefore accurate measurement of renal function depends on knowing the shape of the bolus of contrast as it arrives in the abdominal aorta, following dispersion during transit through the pulmonary circulation, heart, and thoracic aorta. Direct measurement of the bolus as it arrives at the level of the renal arteries can be taken from images of the abdominal aorta and is termed arterial input function (AIF). Using a mathematical operation called deconvolution, we can eliminate the variable effects of bolus dispersion, as quantified by AIF, on the measurements of tracer in the kidney. Compartmental modeling is typically used to extract renal physiological parameters such as GFR from enhancement curves. The details of the models and their comparison can be found in literature.[2,21–25]

Several studies have shown good agreement between MRR measurements of GFR and reference methods. Hackstein *et al.*[26] found a correlation coefficient of 0.83 between MRR-GFR and GFR measured by iopromide plasma clearance. Using low Gd dose (4 ml) and multiple-compartment modeling technique, Lee *et al.*[2,21,24] measured MRR-GFR with correlation coefficient of 0.82–0.84 with ^{99m}Tc-DTPA (^{99m}Tc-diethylenetriamine pentaacetic acid) plasma clearance.

One major issue with MRR is imprecise measurement of AIF. Cutajar *et al.*[27] found that AIF errors could severely lower the precision of the estimated GFR and renal blood flow. Zhang *et al.*[28] proposed a technique of using patient's cardiac output (measured using phase-contrast MRI) and increased the correlation coefficient between two independent MRR-GFR measurements from 0.83 to 0.92. The cardiac-output approach[28] is promising in correcting for AIF errors, but measurement of the patient's cardiac output with phase-contrast MRI can be cumbersome.[29] The other