Functional Magnetic Resonance Gadolinium Enhanced Imaging of the Kidney: Detection of a physiological change in renal GFR in response to an amino acid challenge test.

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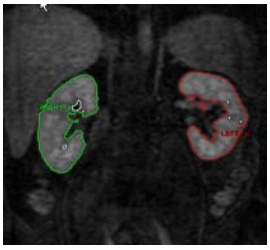
Introduction: Management of patients with impaired renal function is significantly limited by the lack of non-invasive clinically available tests. Techniques for determining glomerular filtration rate (GFR) using MRI combined with dynamic imaging of the kidney following administration of a gadolinium-chelate (Gd) have been developing, and are referred to here as MR Nephrourography (MRN). This approach relies on Gd having renal filtration as the primary method of elimination from the intravascular space, without active excretion or reuptake, and application of a multi-compartment kinetics model to estimate the GFR. In order to further validate MRN, it is useful to demonstrate the ability to detect predictable changes in renal filtration within individuals. It has been well established in both animals and humans that a normal kidney will hemodynamically respond to an ingested protein meal or an amino acid infusion by up-regulating the GFR. In this study, we challenge a series of normal subjects with a standardized amino acid infusion and determine that gadolinium enhanced MRN can reproducibly detect predictable changes and that the measured changes are statistical significance.



Purpose: To demonstrate sensitivity of MRN to detect physiological change in renal GFR.

Methods:

Subjects Ten healthy volunteers (6 male and 4 female, age 25-45) without history of renal disorders participated in the study after obtaining IRB-approved informed consent. Subjects abstained from food and caffeine overnight prior to the study, but consumed water ad libitum.

Imaging Renal perfusion imaging was performed during the first-pass of 0.1mmol/kg Gd-DTPA (Magnevist) using a 3D spoiled gradient echo technique with fat saturation and centric-radial k-space acquisition using a 430mm^2 FOV, 96 matrix (60% scan percentage, recon to 256), TR/TE/flip = 3.7/1.7ms/30, 30 slices at 2.8mm slice thickness, TFE factor = 120, 0.9s per dynamic, and SENSE factor = 3. A paired student's t-test was used to compare pre- and post-AA challenge, with significance being <0.05.

Amino Acid (AA) Infusion A 20% balanced salt amino acid solution (Baxter, Deerfield, Il) was infused over 60 min. The gadolinium enhanced MRN images were obtained at the end of this infusion. Control "pre-AA" MRN images were obtained on another day, either 24-48 hours before (in half) or after (in half), with images acquired 60 min after intravenous infusion of normal saline but without amino acids.

Image Analysis Kidneys were individually segmented with regions of interest (Fig 1) propagated to each slice and for each acquisition (Fig 1) to derive volumes of interest and perfusion-time curves from which kinetic modeling was performed.

Kinetic Modeling Uptake in the kidney was modeled with 3 compartments: blood; extracellular space (ECS); and glomerular filtration. The ECS equilibrates quickly with the blood while the glomerular filtration compartment irreversibly traps Gd over the duration of the analyzed images. The final model and derived equation is described by equation 1, showing the relation between the vascular space (k1) and the clearance of contrast from the vascular space (k2).

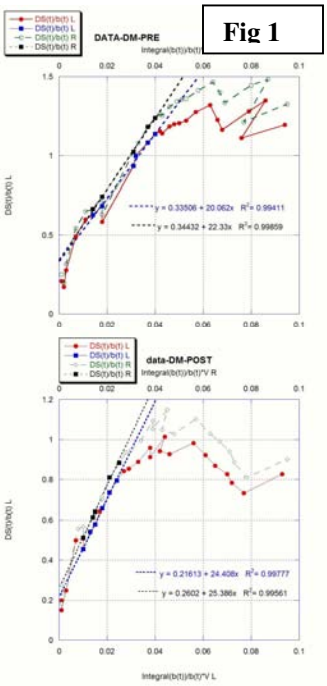


Fig 1

Fig 2

Results: Best fit analysis demonstrated optimal sampling from between 15 and 90 seconds after contrast arrival. Figure 2 shows plotted results from one subject pre-AA (upper graph) and post-AA (lower graph). The GFR is proportional to the fitted slope and shows statistically significant increase post-AA challenge (Table 1).

Table 1. Average estimated GFR of all subjects (N=10)

	Left Kidney		Right Kidney	
	Pre-AA	Post-AA	Pre-AA	Post-AA
Avg +/- SD	62.9 +/- 14.2	83.1 +/- 17.5	63.8 +/- 15.7	88.6 +/- 26.0
P-value	0.00044		0.00022	

$$\frac{K(t)}{c(t)} = k_1 + \frac{k_2 \cdot \int_0^t c(u)du}{c(t)}$$

Equation 1

Conclusions: This study demonstrates that physiological changes in renal function induced by an amino acid challenge may be detected by MRN and that the changes correlate in magnitude with prior reports using traditional laboratory-based methods such as inulin clearance. This provides important support for the expected ability of MRN to detect changes related to disordered renal function, and also demonstrates the potential for using a physiological or pharmacological test for renal responsiveness in combination with MRN.