Correlation of Gadolinium Enhanced Time Resolved MR Nephro-Urography and Inulin measurements of Glomerular Filtration Rate in Sickle Cell Disease Nephropathy

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Introduction: Kidney diseases represent one of the major causes of morbidity in the industrialized countries and there remains a need for methods to evaluate renal function to monitor and understand disease and disease therapy. Sickle Cell Disease Nephropathy (SCDN) is a relatively common condition in the United States and results from repeated ischemic injury due to plugging of small caliber vessels. Two of the most commonly used tests for evaluation of renal function are measurement of serum creatinine level and endogenous creatininne clearance. These indirect measures of renal glomerular filtration rate (GFR) are insensitive and non-specific, and do not supply information that would differentiate the right kidney from the left. Recently, the potential of gadolinium-enhanced time-resolved MRI of the kidney, MR nephro-urography (MRU), has emerged as having the capacity to measure GFR [1,2], but there remains need for validation. GFR measured by Inulin clearance is a well established technique and may be used as a reference [3].

Purpose: The aim of this study is to validate MRU against Inulin in normal and sickle cell disease patients.

Methods: HIPPA compliant and institutional ethics committee approved informed consent was obtained from all patients. Five subjects were included: 1 normal; 2 with mild sickle disease; 2 with advanced sickle disease.

MRU: All MRI were performed on a 1.5T Philips Intera system, using phased array 4-element surface flexible body wrap surface coil. To achieve optimal curve fitting, highly accelerated renal perfusion imaging was developed allowing high frequency imaging 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 scan volume***, and SENSE factor = 3. The Gd was infused at a constant rate (0.5ml/s) over 90 seconds. The kidneys and descending aorta were segmented offline to derive arterial blood and total kidney time activity curves.

Kinetic Modeling of Renal Uptake of Contrast Agent Using Analyze version 6.0 software package (AnalyzeDirect, Mayo Clinic Rochester MN), both kidneys were individually segmented with regions of interest on each slice covering the kidneys, then propagated to each dynamic acquisition to derive volumes of interest and perfusion-time curves from which kinetic modeling was performed. Significant motion was corrected manually, as needed. Uptake of gadolinium contrast agent in the kidney was modeled with the assumption that three compartments are involved, i.e., blood; extracellular space (ECS); and glomerular filtration. In this model (Rutland-Patlak analysis), the ECS equilibrates quickly with the blood while the glomerular filtration compartment irreversibly traps Gd-DTPA molecules 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):

$$\frac{K(t)}{c(t)} = k_1 + \frac{k_2 \cdot \int_0^t c(u)du}{c(t)} \qquad \textit{Equation 1}$$

Inulin Test: Determination of GFR using a bolus of Inulin followed by constant infusion as previously described [3]. Statistical analysis was performed by determining the correlation coefficient between the Inulin and MRU values.

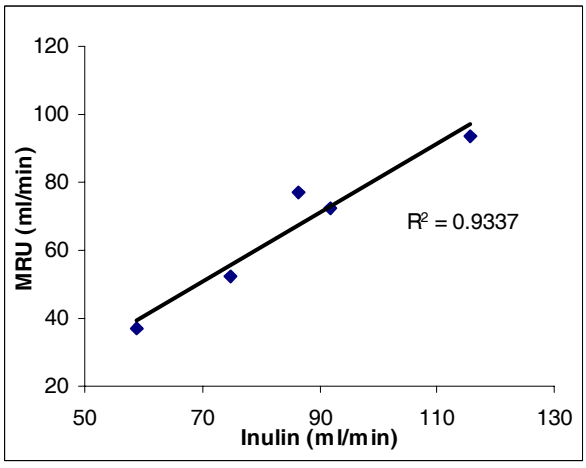

Figure 1. Plot of GFR measured by Inulin and MRU. Least square fit is shown in black and demonstrates a correlation coefficient of 0.9337

Results:
MRU was performed without any complications, and subsequent Patlak analysis resulted in linear fits with an efficacy greater than 0.95 in all cases. This result was achieved despite the use of only semi-automated motion correction. There was a high correlation between the MRU and inulin studies (r2=0.9337) in this subset of patients, as exhibited in Figure 1. Given the range of the inulin data, these results potentially suggest the MRU examination is highly sensitive to a broad spectrum of GFR values.

Conclusions: These findings show good correlation between MRU and Inulin for subjects with a range of renal function, from normal to severe SCDN. These data warrant expansion and further analysis of a larger population for further support of these preliminary results.

References:

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2. Hackstein N. *JMRI* **2005**;22:406-414
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