Rationale and Validation of a 3-Compartment Kinetic Model for Determining Glomerular Filtration on Gadolinium Enhanced MR Imaging of the Kidney

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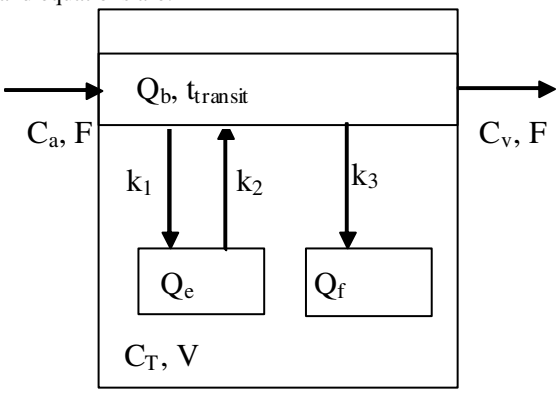
Introduction: Management of patients with impaired renal function is significantly limited by the lack of a non-invasive clinically available test to follow renal function, diagnose causes of renal dysfunction, or monitor treatment response, and there are no readily available tests to detect early or indolent changes of chronic renal disease. 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. Like inulin, Gd is a filtered agent and is therefore potentially useful as an agent for determining GFR. There remains a need for technique rationalization, development, and validation.

Purpose: To develop a 3-compartment kinetic model to describe Gd distribution in the renal artery and kidney, apply the model requirements to an optimized MR imaging technique, and to implement the theoretical model to extract measured renal blood flow and GFR.

Materials and methods:

Kinetic Modeling - Uptake in the kidney was modeled with 3 compartments: blood, extracellular space, and glomerular filtration. The extracellular, Q_e, compartment equilibrates quickly with the blood while the glomerular filtration compartment, Q_f, irreversibly traps Gd over the duration of the experiment. Gd that does not enter either of these compartments remains in the blood and leaves the kidney after a transit time delay, $t_{transit}$. The model and equations are:



$$\frac{dQ_b}{dt} = (F - k_1 - k_3)\{C_a(t) - C_a(t - t_{transit})\}$$

$$\frac{dQ_e}{dt} = k_1 C_a - k_2 * Q_e \quad (t>t_{transit})$$

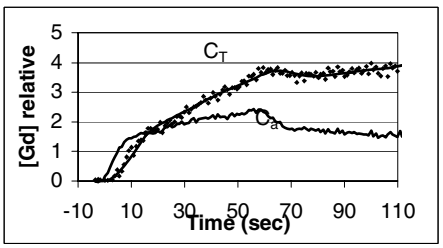
$$\frac{dQ_f}{dt} = k_3 C_a$$

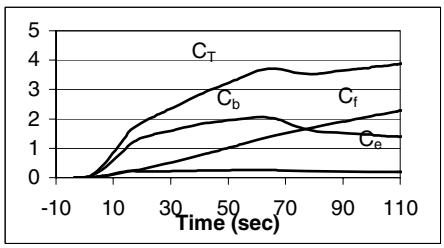
$$C_T V = Q_b + Q_e + Q_f$$

where C's represent concentrations and Q's represent total Gd; k_1 and k_3 (ml/s) represent flow times extraction into the extracellular and filtration compartments; k_2 (1/s) is the rate that Gd leaves the extracellular compartment; F (ml/s) is the total blood flow into the kidney; and the glomerular filtration rate, GFR, (ml/min) is identified as k_3*60. The equations were numerically solved and the five parameters determined using Powell's method to minimize the squared difference between the measured and calculated kidney curves. Corrections for hematocrit and Gd signal changes in plasma versus urine are not included here for the purpose of simplifying this presentation. A linear relation between Gd signal and concentration was assumed.

Renal MRI – Imaging was performed on healthy volunteers after informed IRB approved consent. To achieve optimal curve fitting, highly accelerated 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. The Gd was infused at a constant rate over either 60 or 90 seconds. The kidneys and descending aorta were segmented to derive arterial blood and total kidney time activity curves.

Results: A typical model fit is shown below; the dots are the measured kidney data with the model calculation overlaid. The arterial curve (divided by 2 for display purposes) is also shown for reference. The right graph shows the calculated [Gd] in each of the compartments and the total kidney. There are three distinct phases in the first 90 seconds of uptake in the kidney. Before $t_{transit}$, (approximately 15 s) Gd accumulates in the blood and extracellular compartments producing a rapid rise in the total tissue curve. After $t_{transit}$, the extracellular compartment is at equilibrium, and after the end of infusion (60 s), Gd clears from the blood and extracellular compartments. During the entire experiment, Gd accumulates in the filtration system. Quantitative results are shown in the table. The flow results are not statistically different from that determined by phase contrast imaging. Subjects 4 and 5 are the same person before and after amino acid challenge. The expected increase in both flow and GFR is readily seen.





	Left		Right	
	F	GFR	F	GFR
1	9.46	93	8.14	99
2	9.03	83	7.65	73
3	6.82	66	5.68	66
4	6.25	51	6.79	59
5	8.15	96	9.32	125

Conclusions: This modeling of Gd uptake in the kidney is possible because of the rapid acquisition rate made possible by the imaging protocol presented here. Infusing Gd for the entire experiment, rather than as a rapid bolus, has two advantages: the arterial concentration changes only slowly so it can be measured more accurately, and there is a relatively constant accumulation of Gd in the filtration system. Both of these lead to increased accuracy and stability of the flow and GFR determinations in a very short imaging time. This technique would be straight forward to apply in the clinic.