# Renal Functional and pH Imaging in Mice by Dual-Bolus Dynamic Contrast-enhanced MRI

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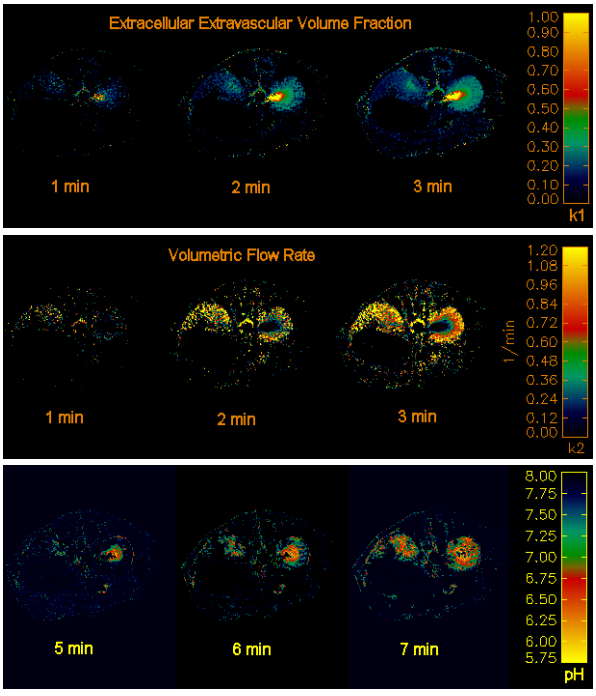
**Introduction.** Knowledge of the glomerular filtration rate (GFR) is vital for the diagnosis and treatment of several renal diseases. Perturbations of pH, another important renal physiological parameter, are also indicative of abnormal renal function. Dynamic contrast-enhanced MRI (DCE-MRI) techniques for measurement of either renal function or pH have been reported in the literature [1,2,3]. We report here a technique for measuring both renal function and pH on a pixel-by-pixel basis in the same animal by DCE-MRI following sequential boluses of two contrast agents, Gd-DOTP (pH-insensitive) and Gd-DOTA-4AmP (pH-sensitive).

**Methods**. MRI was performed on a Bruker Biospec 4.7 T system with 20 G/cm self-shielded gradients, using a 25 mm Helmholtz coil. Mice were anesthetized by inhaled isoflurane (1.5%, rest $O_2$ at 1 L/min), and circulating warm water jackets were used to keep animals warm in the magnet. Mouse body temperature was monitored during all MRI experiments using a rectal fluoroptic temperature probe (Luxtron Corporation, Santa Clara, CA, USA). Mice were cannulated at the tail vein prior to positioning in the magnet, and contrast agent (0.015-0.025 mmole/Kg) and saline chase (0.12 mL) were administered via this catheter at the appropriate time during each experiment. All images were acquired using a fat-suppressed radial spin-echo sequence. Pre-contrast $T_1$ maps were calculated from images acquired prior to administration of contrast agent with the following parameters: TR = 3.0, 0.5 and 0.1 s, TE = 9 ms, no. of radial lines = 256. During the dynamic portion of the imaging experiment, radial lines were collected repetitively with the above parameters and TR = 0.1 s for 30 minutes, with Gd-DOTP & saline chase being injected over 30 seconds 8.5 minutes after start of imaging. The dynamic portion of the experiment was then repeated using Gd-DOTA-4AmP. Images were reconstructed offline via filtered back-projection using a sliding window moving 64 lines per image, yielding an effective temporal resolution of 6.4 s. A "vascular input function" was obtained for each injection from pixels which enhanced at least 3-fold and reached maximum enhancement within 60 seconds after start of injection. The pharmacokinetics of signal enhancement following the Gd-DOTP bolus were fitted to a two-compartment model which incorporated the contribution of intravascular contrast agent. The model yielded two fitted parameters: $k_1$, related to the extracellular extravascular volume fraction (dimensionless), and $k_2$, the flow rate per unit tissue volume ($min^{-1}$). It was assumed that $k_1$ and $k_2$ calculated in a given pixel for Gd-DOTP would also describe the behavior of Gd-DOTA-4AmP in that pixel. This permitted the computation of an in vivo relaxivity of Gd-DOTA-4AmP in each pixel at each time which could be converted to pH using a published titration relationship [3].

**Results.** Calculated maps of $k_1$, $k_2$ and pH from a control mouse are shown at right. The calculated extracellular extravascular volume fraction, $k_1$, visible to the gadolinium at any time ranges from 10-20% in the cortex to 100% in the renal pelvis. The calculated volumetric flow rate, $k_2$, is related to the per-pixel GFR in the cortex at early times post-injection. The cortex is seen to have very high $k_2$ values at 3 min post-injection, while values are low elsewhere. The physiological interpretations of $k_1$ and $k_2$ depend on time post-injection of the contrast agent. Similarly, the calculated pH would also be expected to depend on time post-injection, as this determines the location (blood *vs.* filtrate) of the contrast agent within the nephrons. Between 5-7 min post-injection, as the contrast agent travels from the medullary limbs of the nephrons to the cortex, an apparent decrease in calculated pH in cortical pixels is seen (right), corresponding to filtrate pH.




**Conclusions.** A dual-contrast-agent method has been developed to image both renal function and pH in mice. Assumptions of the two-compartment pharmacokinetic model and slow water-exchange rates between renal compartments will affect the calculated renal physiological and functional parameters, and these have been analyzed.

**References:**

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