Comparison of ASL and DCE-MRI for renal perfusion measurements

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Introduction: The injury or loss of renal microvessels is a determinant of renovascular disease severity and progression to end-stage renal failure[1]. Promotion of renal angiogenesis is seen as a promising therapeutic technique. Directly assessing the status of the renal microvasculature using tissue-level perfusion measurements could benefit the assessment of renovascular disease and monitoring of therapeutic interventions. Such an assessment may be achieved using MR perfusion techniques, including quantitative dynamic contrast-enhanced (DCE) MRI and arterial spin labeling (ASL). To extract absolute renal tissue perfusion, quantitative DCE methods generally employ pharmacokinetic analysis of Gadolinium(Gd)-based contrast uptake, whereas ASL exploits endogenous blood water as a contrast agent. In comparison with ASL, DCE-MRI offers increased signal-to-noise ratio (SNR), superior spatial resolution, and the potential to extract the glomerular filtration rate (GFR) - a measure of kidney function. However, limitations of DCE-MRI include the need to measure the arterial input function (AIF) and the risk for nephrogenic systemic fibrosis (NSF), especially for patients with compromised kidney function. Despite distinct advantages for both methods, direct comparisons are limited. The primary objective of the current study was to compare renal perfusion estimates for ASL and DCE-MRI. For DCE-MRI, a dual-bolus approach was adopted to improve AIF, and is validated for the first time in the kidney in this study.

Methods: Imaging studies were performed on six New Zealand white rabbits (4 - 4.5 kg) on a 1.5 T GE scanner. Rabbits were induced with Akmezine, and maintained under anesthetic using 2 % isoflurane. All procedures were approved by our institutional animal care committee. The ASL data were collected from the lower kidney in an 8-channel knee coil using a fluid alternating inversion recovery (FAIR) sequence implemented using spiral imaging: TE = 4 ms, TR = 3.75 s, FOV = 160 mm, matrix = 64 × 64, slice thickness (SL_{TH}) = 5 mm, slice spacing (SL_{SP}) = 1 mm, number of slices (N_{SL} = 3) and post-label delay time = 1.39 s. Arterial and venous saturation pulse were applied, along with background suppression. In total, 64 ΔM (tag - control) images and a M_0 image were collected. For one rabbit the ASL protocol was repeated with 11 different labeling inversion times to assess inflow characteristics. Blood flow was calculated using a general kinetic model, as previously described[2].

Following the ASL acquisition, the rabbit was moved to a quadrature knee coil for the dual bolus DCE acquisition. To acquire the AIF, a low-dose (0.2 mmol/kg) prebolus injection of Gd-DTPA was administered through an ear vein at a rate of 0.5 ml/s, followed by a 2 ml saline 'chaser'. The AIF acquisition was performed using a TRICKS sequence to maximize the temporal resolution. The imaging slices were positioned such that a central slice was centred on the aorta. Imaging parameters included: TE = 1.02 ms TR = 2.94 ms, FA = 20°, FOV = 180 mm with 70 % phase FOV, matrix = 90 x 90, N_{SL} = 10, SL_{TH} = 3 mm, number of averages (N_{AVG}) = 0.75 and temporal resolution = 0.554s. The AIF was acquired in 5 separate acquisitions of 56 phases one minute apart. After 15-20 minutes following the prebolus, we acquired T_1 maps of the kidney using the variable flip angle approach, using three 3D FSPGR scans with the following parameters: TE = 3.1 ms, TR = 7.2 ms, FA = 2, 10 and 21°, FOV = 160 mm, matrix = 256 × 192, SL_{TH} = 4 mm, N_{SL} = 10, N_{AVG} = 4. Following the T_1 map sequence, the main bolus (0.8 mmol / kg) was injected using the same procedure as the prebolus, and renal DCE-MRI scans were obtained using an FSPGR sequence with the following parameters: TE = 1.86 ms, TR = 4.9 ms, FA = 15°, FOV = 160 mm, matrix = 128 × 96, SL_{TH} = 4 mm, N_{SL} = 10, N_{AVG} = 0.75 and temporal resolution = 2.805 s. For the DCE analysis, the AIF was extracted from an aorta ROI, the 'tail' was fit to a bi-exponential decay, and the signal intensity values were converted to units of Gd concentration ([Gd]) using an assumed blood T_1 value of 1270 ms. Pixel-wise kidney T_1 values were generated using the formula for the SPGR signal intensity and corrected for FA variations[3], and used to convert kidney DCE signal to [Gd]. Next, the DCE-MRI data was fit pixel-wise to the separable compartmental model[4]: $C(t) = F_p T_p C_p + F_t e^{-t/T_T} \otimes C_p(t)$, in which F_p is the plasma flow, T_p is the plasma transit time, F_T is the flow in the tubules and T_T is the tubule transit time. The quantitative DCE-MRI measures of renal perfusion were compared with the ASL estimates of blood flow using a Student's t-test.

Results: The fit of the multiphase ASL data to the general kinetic model, and a representative ASL image of renal blood flow are provided in Figure 1. The separable compartmental model provided an adequate fit to the mean renal cortex contrast concentration curve, but not the medulla (Figure 2). Mean DCE estimates of cortical perfusion (3.57 ± 0.96 ml/g/min) and ASL estimate of perfusion (3.28 ± 0.59 ml/g/min) were in agreement (Table 1), with no statistical differences observed. Table 1 also provides the additional DCE-MRI separable compartment model parameters.

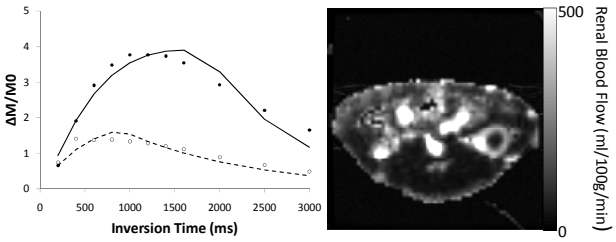

Figure 1. Multiphase ASL fit to the general kinetic model in the kidney (left), and representative renal ASL blood flow map (right)

Discussion: Renal MRI studies could be enhanced with the inclusion of tissue perfusion methods that assess renal microvacular structure and function. To date, one previous study has investigated DCE-MRI and ASL methods in the kidney; however, a comparison of absolute values was not performed[4]. In this study, both techniques generated perfusion estimates that were in close agreement. Pixel-wise DCE-MRI renal cortex blood flow estimates (3.57 ± 0.96 ml/g/min) were similar to a previous report using the separable compartmental model in humans (3.09 ± 0.45 ml/g/min)[5]. Renal cortex ASL perfusion estimates for the current study (3.28 ± 0.59 ml/g/min) were also in agreement with previous ASL studies that reported flows of 2.78 ± 0.55 ml/g/min[6] and 3.23 ±0.59 ml/g/min[7] using similar ASL techniques.

Another novel contribution of this study was the application of the dual bolus approach to quantitative DCE-MRI within the kidney - the first demonstration of the method outside cardiac imaging[8]. This dual bolus technique offered two key advantages: i. the low pre-bolus [Gd] levels avoid the non-linear regime of the ΔR_1 relationship with [Gd] as well as potential MR signal saturation, and ii. it allows for high temporal sampling of the AIF from a major vessel without compromising the spatial resolution of the main DCE scan.

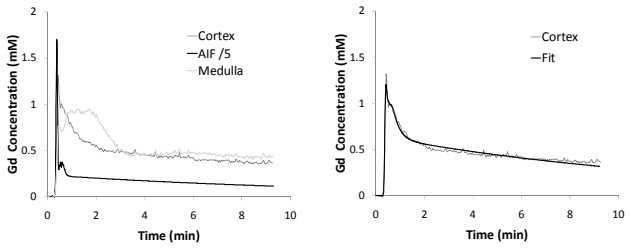

Figure 2. DCE-MRI Gd uptake curve, showing the scaled AIF, and mean signal from the renal cortex and medulla (left), with corresponding fit of the cortical data to the separable compartment model.

In conclusion, we demonstrated agreement between ASL and DCE estimates of absolute perfusion within the renal cortex. These two MR techniques are equally capable of measuring renal perfusion and offer clinicians a choice for different patient groups, e.g., patients with reduced GFR, and at risk for NSF, can be safely imaged using ASL.

	ASL	DCE MRI fit to separable compartment model			
Rabbit	Blood flow	F_p (ml/g/min)	T_p (s)	F_T (ml/g/min)	T_T (s)
A	N/A	2.48	10.5	0.66	38.8
B	3.09	4.10	5.4	1.24	22.5
C	4.24	2.81	7.6	1.07	17.6
D	2.96	2.89	5.9	1.22	15.4
E	2.70	4.80	2.2	1.38	17.8
F	3.41	4.34	3.1	1.22	23.1
Mean	3.28 ± 0.59	3.57 ± 0.96	5.8 ± 3.0	1.1 ± 0.3	22.5 ± 8.5

Table 1. ASL blood flow and DCE-MRI separable compartment model

References: 1. Kang DH *et al.* J Am Soc Nephrol 2002,**133**:806-816; 2. Koziak AM *et al.* Magn Reson Imaging 2008,**264**:543-553; 3. Cheng HL *et al.*, Magn Reson Med 2006, **55**:566-574; 4. Boss A *et al.* Eur Radiol. 2006, **166**:1226-1236; 5. Sourbron SP *et al.* Invest Radiol 2008,**431**:40-48; 6. Roberts DA *et al.* Radiology 1995,**1961**:281-286; 7. Fenchel M *et al.* Radiology 2006;**2383**:1013-1021; 8. Christian TF *et al.* Radiology. 2004,**2323**:677-684.