Sensitivity of Arterial Spin Labeling Perfusion Imaging to Pharmacologically Induced Changes in the Rat Kidneys

Huan Tan[1], Jon Thacker[2], Tammy Franklin[3], and Pottumarthi V Prasad[1,3]

[1]*University of Chicago, Chicago, IL, United States,* [2]*Northwestern University, Evanston, IL, United States,* [3]*NorthShore University HealthSystem, Evanston, IL, United States*

Introduction: Chronic kidney disease (CKD) is a major healthcare problem with annual Medicare costs estimated to be $49 billion (1) with stage 3 accounting for about $32 billion (due to a large number of patients). This is not including care for end stage kidney disease (ESKD), estimated to be another $20 billion (2). With the lack of any measures to predict whom with CKD stage 3 will actually progress towards ESKD, almost all of them are managed similarly. Reduced perfusion and oxygenation are implicated in the initiation and progression of CKD (3). Recently, perfusion estimates in humans with arterial spin labeling (ASL) was shown to demonstrate changes between healthy and subjects with CKD (4). Here, we have evaluated the sensitivity of ASL to pharmacologically induced vasodilation and vasoconstriction in rat kidneys.

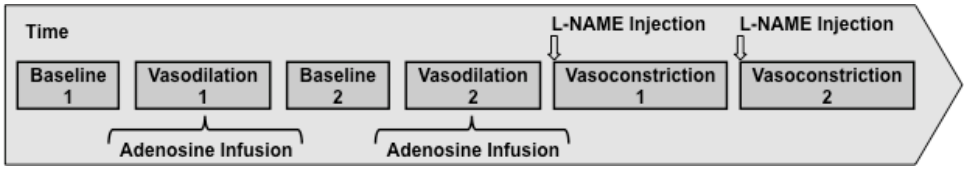


Figure 1. Experiment design.

Methods: All animal handling and experiments were conducted under a protocol approved by the local Institutional Animal Care and Use Committee (IACUC) and in accordance with animal welfare regulations. Experiments were carried out with 7 Sprague Dawley rats (weight 368 - 521g). A catheter was placed in the femoral vein for administration of vasoactive drugs. All procedures were conducted under anesthesia using Inactin (thiobutabarbital sodium, 100 mg/kg i.p., Sigma-Aldrich, St. Louis, MO).

Imaging studies were performed on a Siemens 3T scanner with an eight-channel knee coil. The animal was placed on a cushion at the center of the coil in a right lateral decubitus position. Six perfusion measurements were made in the order scheme shown in Figure 1. Adenosine (for vasodilation) was formulated from 200 mg/kg adenosine hemisulfate salt (Sigma-Aldrich) and dissolved in 10 mL saline. An infusion pump was used to infuse the dissolved adenosine with a rate of 0.05 mL/min. L-NAME (Sigma-Aldrich) was administered into the femoral vein as a 10 mg/kg of rat bolus.

ASL sequence was implemented with a FAIR preparation and a TrueFISP readout (4). Imaging parameters were: FOV/TE/TR = 83mm/2.5ms/6s; flip angle = 21°; slice thickness = 4.5 mm; averages = 30; imaging matrix = 128 x 78 (frequency x phase); post labeling delay = 1.2s; labeling band thickness = 10mm; bandwidth = 651 Hz/Px. The scan time for each ASL sequence was 6 minutes. A proton density weighted image was acquired with the same trueFISP readout with a TR = 10s for perfusion quantification. The delay in between each perfusion scan is about 15 minutes.

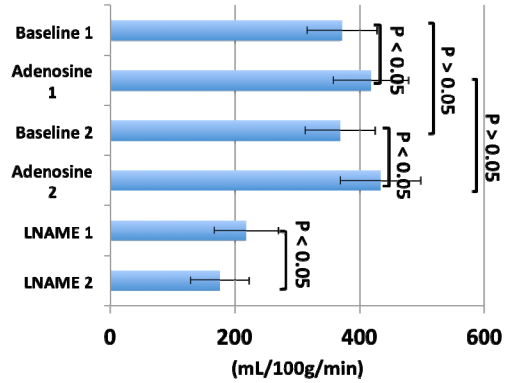
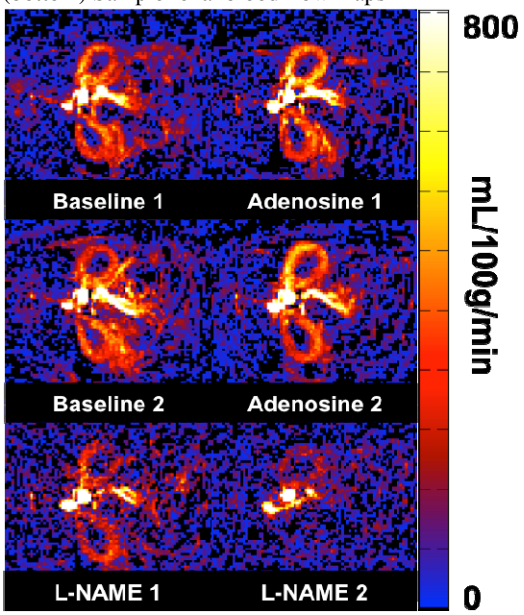


Figure 2. (top) Quantitative renal perfusion rates. (bottom) Sample renal blood flow maps.



Results: One rat died right during the data acquisition after the first L-NAME injection. The mean and the standard deviation of the cortical perfusion rate are shown in Figure 2 top. An illustration of the renal blood flow map for each acquisition is shown in Figure 2 bottom. Signal averaging effectively eliminated motion related artifacts and the final renal blood flow maps were of high quality for analysis. The changes in perfusion rate were significant between baseline and vasodilation ($p < 0.05$) and between baseline and vasoconstriction ($p < 0.01$). The coefficients of variations were 4% and 11.6% for baseline and adenosine measurements, respectively, indicating high reproducibility. The mean perfusion rate difference between the first and second L-NAME injection was 42.45 ± 25.15 ml/100g/min ($p < 0.05$), suggesting that the effect of L-NAME might be cumulative.

Conclusion: In the study, we have shown that ASL is sensitive to pharmacological induced blood volume change in a rodent model. It was demonstrated that changes in supplying blood volume led to changes in the cortical perfusion. The findings suggest that it is feasible to use ASL investigate the various effects on renal blood flow in rodent models (e.g. acute injury, renal artery stenosis, etc.).

References: 1) Honeycutt et. al. JASN, 2013. 2) Khan et. al. JECP, 2008. 3) Fine et. al. KIS, 1998. 4) Tan et. al. MRM 2013.