Comparing Kidney Perfusion Using Arterial Spin Labeling and Microsphere Methods in an Interventional Swine Model

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INTRODUCTION: Magnetic Resonance Imaging (MRI) perfusion methods, specifically arterial spin labeling (ASL) techniques, can magnetically label endogenous blood and offers an alternative to contrast enhanced techniques in evaluating renal function. The goal of this study was to validate an ASL-FAIR (Flow Sensitive Alternating Inversion Recovery) cortical perfusion technique in the swine kidney over a range of perfusion measurements using microspheres as a gold standard during pharmacologic and physiologic alterations in renal blood flow.

MATERIALS AND METHODS: For eleven female swine (34-38 kg), MR ASL acquisitions were performed at four interventional time points: 1) under the anesthetic propofol ("baseline"), 2) during administration of acetylcholine and propofol with a 450 cc bolus of saline ("acetylcholine challenge" to increase perfusion), 3) baseline after switching to isoflurane administration ("initial isoflurane") and 4) after two hours of isoflurane ("prolonged isoflurane"). Fluorescent microspheres (IMT Stason Pharmaceuticals) were injected at each intervention as well. In ten of the eleven swine, a bag of ice was placed on the hilum of one kidney at the beginning of isoflurane administration to further reduce perfusion. Swine were euthanized with Beuthanasia-D (0.2 ml/kg) and the kidneys were harvested. Four to six cortical tissue samples (2-3 for each kidney) were excised for microsphere analysis. **ASL Acquisition:** ASL perfusion images were acquired on a 1.5 T MR scanner (Excite HD, GE Healthcare) using a FAIR-bSSFP technique [1] (parameters: TR/TE/flip = 4.6/2.3ms/70°, BW = 83.33 kHz, FOV = 34 cm, matrix = 128 x 128, slice thickness = 8 mm). Imaging was triggered during expiration following a delay time of 1.2 s until 32 control-tag image pairs were acquired (~6 min). Several proton density images were also acquired for normalization purposes. **Segmentation and Processing:** ASL perfusion exams were analyzed with a one compartment ASL model using custom scripts written in MATLAB (version 7.5, The MathWorks Inc.). After automatically aligning each kidney in the image series, the cortex was manually segmented using interactive threshold techniques. The average difference between control and tag was used to calculate a perfusion map based on known scan parameters and assumed values of T1 = 1 sec, and partition coefficient, λ = 80 ml/100g. ASL perfusion measurements from all the cortical pixels were averaged for each kidney and compared to the mean of the microsphere perfusion measurements for each respective kidney at each time point. **Data Analysis:** ASL and microsphere measurements for all eleven swine (22 kidneys) were plotted across interventions. A Pearson correlation coefficient was calculated for ASL and microsphere perfusion using all 22 kidneys across all four intervention time points. Additionally, a paired t-test was used to determine if the perfusion difference between interventions was statistically significant. The t-test was performed for the left and right kidneys separately across all swine.

RESULTS AND DISCUSSION: Example ASL perfusion maps calculated for one swine across the interventions demonstrate an increase in perfusion with acetylcholine and subsequent decrease with transition to isoflurane anesthesia. Perfusion in the iced kidney was lower than the non-iced kidney. (**Fig 1**) Both ASL and microsphere perfusion values demonstrated the expected responses to intervention (**Fig 2**), yielding statistically significant differences in perfusion ($p < 0.05$) for the left and right kidneys from one intervention to the next. ASL perfusion responses showed less variability across swine (**Fig 2**) which may be due to the measurement being averaged over the 6 minute acquisition period, whereas microspheres deposit in a matter of seconds. This consistency of ASL seems desirable for intra-subject longitudinal assessment as well as inter-subject comparison purposes. Comparing ASL and microsphere measurements, the two methods yield a Pearson correlation coefficient of 0.72 (**Fig 3**). However, the relationship between ASL perfusion and microspheres was not linear due to saturation for very high perfusion values. In addition, ASL perfusion values were consistently lower than microspheres (**Fig 2&3**). This underestimation may be a result of imaging at a delay time in which tagged spins had already left the volume due to venous outflow.

Figure 1: ASL perfusion maps across interventions in One

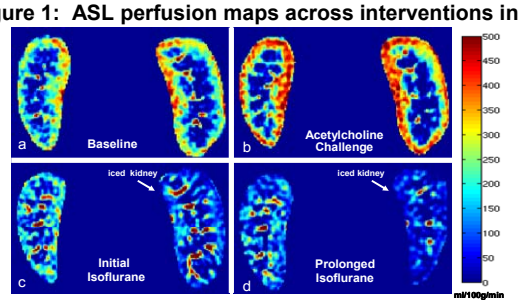


Figure 3: ASL vs Microsphere Correlation

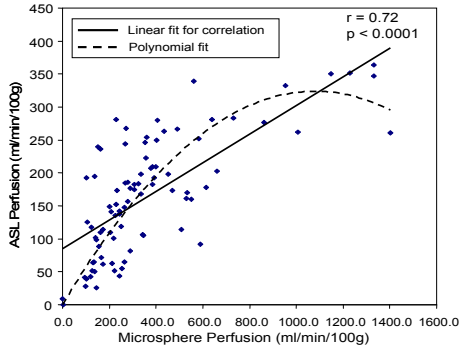
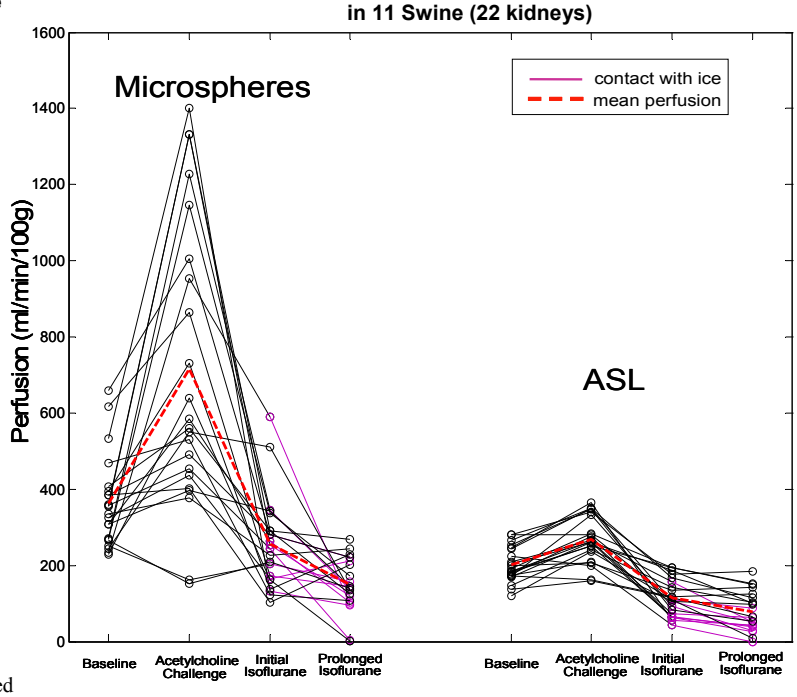


Figure 2: Microsphere and ASL Perfusion vs Intervention in 11 Swine (22 kidneys)



CONCLUSIONS: This non-contrast enhanced ASL technique tracked cortical perfusion changes and correlated with microspheres, providing validation of this technology for relative renal perfusion imaging, especially for evaluating time-averaged perfusion changes that may be observed in chronic disease. Extension of this technique to 3.0 T will further improve perfusion measurement, although additional challenges due to field inhomogeneity will need to be addressed. Human studies are also needed to examine the role of ASL in evaluating renal perfusion in disease and are ongoing in native and transplant kidneys as part of this research effort.

REFERENCES: [1] Martirosian *et al.* Magn Reson Med. 2004; 51(1): 353-61. **ACKNOWLEDGEMENTS:** GE Healthcare, NIH R01 DK 073680, NIH R21 DK070243, and internal department research funds