

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

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**INTRODUCTION:** Recent studies have demonstrated a link between the use of gadolinium-based contrast agents and nephrogenic systemic fibrosis (NSF) [1]. MR perfusion methods, specifically arterial spin labeling (ASL) techniques, for evaluating renal function are important to develop [2]. The goal of this study was to validate the ASL-FAIR perfusion technique in the swine kidney with the use of fluorescent microspheres as a gold standard under baseline conditions, during an acetylcholine and fluid bolus challenge, and during extended isoflurane anesthesia with ice placed on one of the kidneys.

**MATERIALS AND METHODS:** Institutional Animal Care and Use committee approval was obtained prior to this study. To date, five female swine (34-38 kg) were induced with xylazine hydrochloride (2.2 mg/kg) and telazol (7 mg/kg) and maintained for the first 2 hours of the experiment with propofol (10 mg/kg/hr) and fentanyl (0.0035 mg/kg/hr), followed by isoflurane (3%) for the last two hours of the experiment. A 5 French catheter was placed in one carotid artery and a pig tail catheter was inserted into the left ventricle for the injection of fluorescent microspheres (IMT Stason Pharmaceuticals, Irvine, CA, USA). A 6 French aortic catheter was placed through a femoral artery sheath and positioned just above the renal arteries for the administration of acetylcholine (4.5 µg/kg/min) and a 450 cc bolus of 0.9% normal saline. A contralateral femoral sheath was inserted in order to draw reference blood for microsphere measurements of perfusion.

MR acquisitions were performed initially at baseline under the anesthetic propofol, then under continued propofol and during administration of acetylcholine with a bolus of saline (both administered in the suprarenal abdominal aorta), and finally at two time points during isoflurane administration alone. Microspheres were drawn at each time point. In four of the five swine, a bag of ice was placed on the hilum of one kidney at the beginning of isoflurane administration. Swine were euthanized with Beuthanasia-D (0.2 ml/kg) and the kidneys were harvested. Four-six cortical tissue samples (2-3 for each kidney) were excised for microsphere analysis by IMT Stason Pharmaceuticals (Irvine, CA, USA).

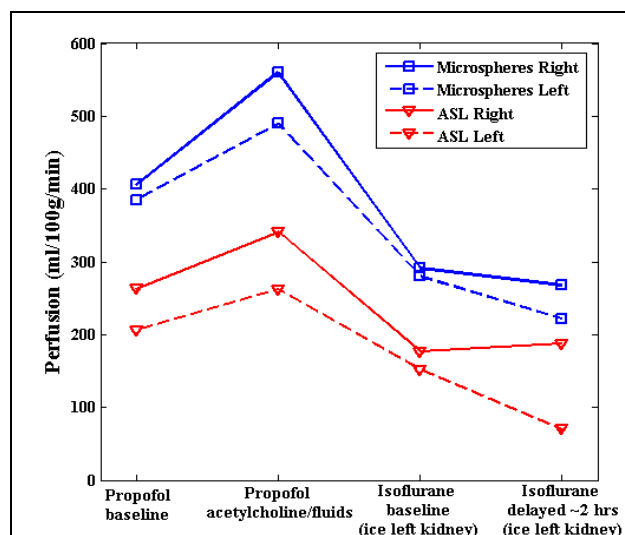
Scans were performed on a 1.5 T MR scanner (Excite HD, GE Healthcare, Milwaukee, WI, USA) with an eight-element phased array cardiac coil (GE Healthcare, Milwaukee, WI, USA). ASL perfusion images were acquired using a FAIR-Fiesta technique [2]; parameters: TR/TE/flip = 4.6/2.3ms/70°, BW = 83.33 kHz, FOV = 34 cm, and 128 x 128 matrix. An 8mm slice was chosen coronal to the kidney. The technique minimizes motion corruption by respiratory triggering the inversion at expiration throughout the scan. Following an inversion time (TI) of 1.2 sec, an image was acquired using a balanced-SSFP readout with centric phase encoding. Non-selective and selective inversion images were alternated until 64 total images (32 pairs) were acquired. Four proton density images were also acquired for normalization purposes by using the Fiesta readout with no prior inversion pulse.

ASL perfusion exams were analyzed using custom scripts written in MATLAB (MATLAB version 8.0, The MathWorks Inc., Cambridge, MA, USA). Following registration, the cortex of the kidney was manually segmented from the image by thresholding techniques. ASL perfusion measurements from all the pixels in the cortex were averaged and compared to the mean of the microsphere perfusion measurements for each kidney, at each time point. Pearson product-moment correlation coefficients were determined for the perfusion data.

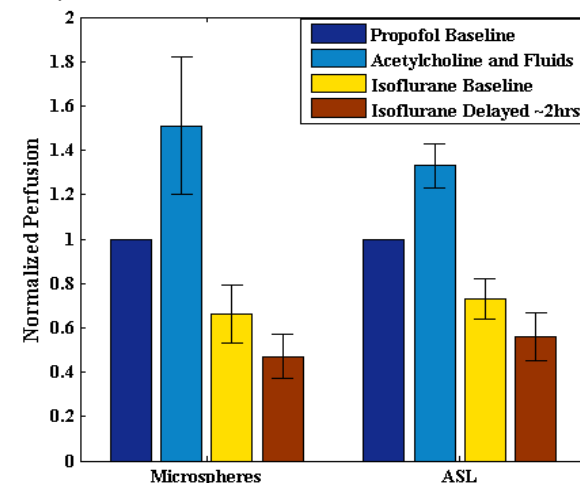
**RESULTS AND DISCUSSION:** Figure 1 demonstrates typical ASL and microsphere perfusion results for the right kidney and left kidney (with ice) of one swine. There is an increase in cortical perfusion demonstrated during the acetylcholine and saline challenge and a decrease in perfusion during isoflurane anesthesia with the left kidney (with ice) as measured by both microspheres and ASL. ASL perfusion measured underestimated perfusion relative to microspheres in all cases. Normalized values for 6 kidneys (no ice) (Fig. 2) demonstrated increased cortical perfusion from baseline in response to the administration of acetylcholine and saline with both ASL and microsphere-based measurements. Cortical perfusion decreased under isoflurane anesthesia compared to baseline (under propofol anesthesia). Including all 10 kidneys (4 with ice + 6 with no ice) ASL and microsphere measurements had a correlation of 0.71.

**CONCLUSIONS:** Preliminary results show that ASL cortical perfusion measurements agree qualitatively with microsphere-based measurements, demonstrating comparable changes during pharmacologic and physiologic alteration in renal blood flow.

**REFERENCES:** [1] Marckmann *et al.* J Am Soc Nephrol. 2006; 17(9): 2359-62. [2] Martirosian *et al.* Magn Reson Med. 2004; 51(2): 353-61.



**Figure 1.** Average cortical microsphere and ASL perfusion measurements at four time points for the right kidney and left kidney (with ice) of one swine.



**Figure 2.** Average cortical microsphere and ASL perfusion measurements normalized to the baseline measurement in 6 kidneys (with no ice) at four time points. Error bars represent the standard error of the mean.