Measurements of Renal Perfusion and Oxygenation in Swine: Preliminary Results

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INTRODUCTION

Recent studies have demonstrated a link between the use of gadolinium-based contrast agents and the development of nephrogenic systemic fibrosis (NSF) [1]. Given growing concerns of developing NSF, it has become important to investigate non-contrast methods of evaluating renal function. We have developed an MRI perfusion technique employing arterial spin labeling (ASL) [2] that allows for the measurement of cortical blood flow in the kidneys without the use of contrast. The goal of this study was to correlate ASL perfusion measures of cortical blood flow with blood oxygen level dependent (BOLD) MRI measures of oxygen bioavailability and vital signs during pharmacologic and physiologic alterations in renal blood flow.

MATERIALS AND METHODS

Institutional Animal Care and Use Committee approval was obtained prior to this study. To date, four female swine (34-38 kg) were induced with xylazine hydrochloride (2.2 mg/kg) and telazol (7 mg/kg) and maintained for the first two 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 6 French aortic catheter was placed through a femoral sheath and positioned just above the renal arteries for the administration of acetylcholine (4.5 µg/kg/min) and a 450cc bolus of 0.9% normal saline. A contralateral femoral sheath was used to invasively monitor the blood pressure and heart rate. A catheter was placed in the bladder to monitor urine output.

Scans were performed on a 1.5 T MR scanner (GE Healthcare, Milwaukee, WI, USA) with an eight-element phased array torso coil. BOLD images were acquired with the following parameters: TR/TE/flip/BW = 87ms/7-41.8ms/40°/±62.5kHz, FOV = 32-34cm, and 256 x 128 matrix. Three coronal slices were acquired, each during a separate 12-second breath hold. ASL perfusion images were acquired in the coronal plane using a balanced SSFP 2D imaging sequence (FIESTA) with the following parameters: TR/TE/flip/BW = 4.6ms/2.3ms/70°/±41.67kHz, FOV = 34cm, 128 x 128 matrix, NEX = 1.0, slice thickness = 8mm. Non-selective and selective inversion images were alternated until 64 total images (32 pairs) were acquired. For normalization, four proton-density images were acquired with a FIESTA readout without a prior inversion pulse. MR acquisitions were performed at four time points: first during baseline under the anesthetic propofol, second under the influence of acetylcholine administered in the suprarenal abdominal aorta along with a 450cc bolus of saline, third at the start of isoflurane and finally after two hours of isoflurane. After imaging, swine were euthanized with Beuthanasia-D (0.2 ml/kg).

BOLD images were analyzed as previously described by Sadowski et al [3]. ASL perfusion exams were analyzed with custom scripts written in MATLAB (MATLAB version 8.0, The MathWorks Inc., Cambridge, MA, USA). Average cortical R2* measurements and average cortical perfusion measurements were plotted for the right kidney of one pig. Mean arterial pressure, heart rate, and urine output were plotted for each phase of the experiment for the same pig. Measurements of cortical R2* and perfusion were tabulated from the four pigs studied thus far.

RESULTS AND DISCUSSION

There was increased cortical perfusion and decreased cortical R2* (increased oxygen bioavailability) from baseline to the administration of acetylcholine/fluid (Figure 1). Due to space constraints, only data from the right kidney are shown. Over the 2 hours the swine were anesthetized with isoflurane, cortical perfusion decreased and cortical R2* increased (decrease in oxygen bioavailability). The use of acetylcholine and a saline bolus caused a moderate increase in mean arterial pressure, a moderate decrease in heart rate, and a substantial increase in urine output. The prolonged use of isoflurane anesthesia corresponded to a decrease in mean arterial pressure, heart rate, and urine output (Figure 2). Table 1 shows average BOLD and perfusion values from the kidneys of four swine.

CONCLUSIONS

The fMRI measurements of cortical blood flow and R2* demonstrate expected changes with pharmacologic and physiologic maneuvers to increase renal blood flow (acetylcholine and fluid) and with a pharmacologic maneuver to decrease renal blood flow (isoflurane). Furthermore, increases in renal blood flow corresponded with an increase in blood pressure and urine output, whereas a decrease in renal blood flow corresponded with a decrease in blood pressure and urine output.

REFERENCES

[1] Marckmann et al. J Am Soc Nephrol. 17(9): 2359-62. [2] Martirosian et al. Magn Reson Med. 51(2): 353-61. [3] Sadowski et al. Radiology. 236(3): 911-9.
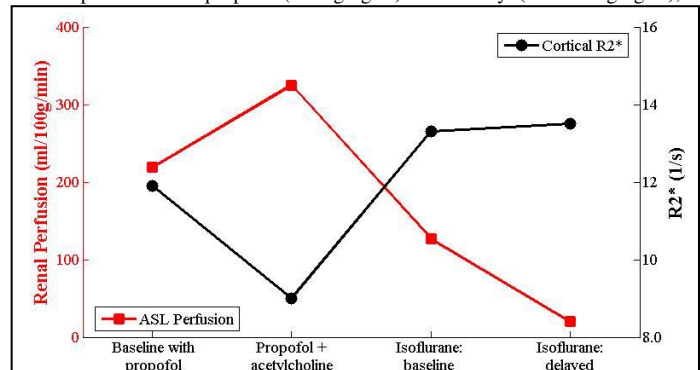
Figure 1. Exemplary results demonstrating renal perfusion and R2* in the cortex of the right kidney in one swine at four time points. Similar results were observed in the left kidney.
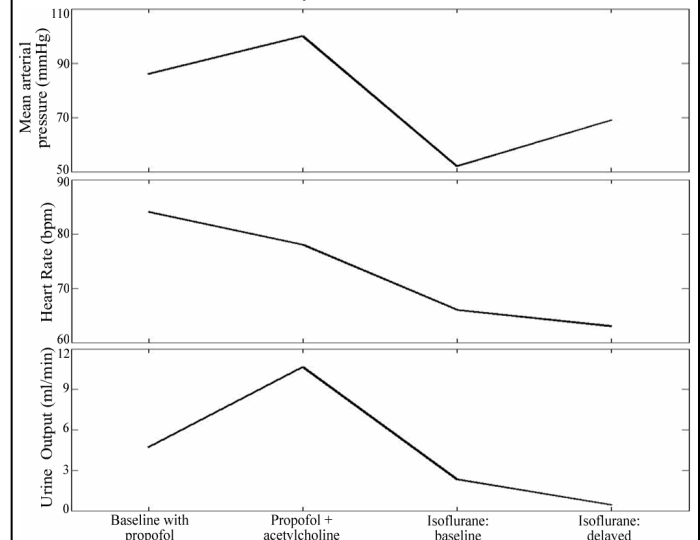

Figure 2. Measurements of mean arterial pressure, heart rate, and urine output in one pig during baseline under the anesthetic propofol, under the influence of acetylcholine and a saline bolus, and finally at two time points under the influence of isoflurane as an anesthetic.

Table 1. ASL Perfusion and BOLD R2* measurements in the cortex of the right kidneys in four swine. Measurements are shown for the four time points corresponding to the figures above. Similar results were observed in the left kidney.

	R2* (1/s)				ASL Perfusion (ml/100g/min)			
	Prop.	Prop + Ach	Iso: base	Iso: Delayed	Prop.	Prop + Ach	Iso: base	Iso: Delayed
Pig 01	13.3	11.4	13.2	13.4	220	291	169	164
Pig 02	10.9	9.4	10.2	10.8	292	331	182	180
Pig 03	11.9	9.0	13.3	13.5	219	325	127	20
Pig 04	13.2	11.8	12.4	16.0	153	191	91	79