ASL, BOLD, and Phase Contrast MRI Measurements in the Kidneys of Normotensive and Hypotensive Swine.

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INTRODUCTION

Invasive probes which measure total renal blood flow, regional oxygenation and perfusion have been used to study renal physiology in animals and extrapolated to humans ([1, 2, 3]). Functional MR imaging techniques are an active area of research, as they provide non-invasive methods for studying renal physiology in animals and humans. Furthermore, these methods could be used in humans to study the kidney *in vivo*, during different disease states and following treatments aimed to improve kidney function. Our group has developed a non-contrast-enhanced suite of functional MR techniques including phase contrast (PC) techniques to measure blood flow in the renal artery, arterial spin labeling (ASL) MR imaging to measure regional perfusion and blood oxygen level dependent (BOLD) MR imaging to measure regional oxygen bioavailability. The purpose of this study is to measure the renal blood flow in the main renal artery, cortical and medullary perfusion and cortical and medullary oxygenation in normotensive and hypotensive swine using our techniques.

MATERIALS AND METHODS

This study was approved by the Institutional Animal Care and Use Committee. The investigation was performed on ten female swine (mass = 34-38kg). Anesthesia was induced using a mixture of xylazine hydrochloride (2.2 mg kg^{-1}) and telazol (7 mg kg^{-1}) and continued with propofol (10 mg kg^{-1} hr^{-1}) and fentanyl (0.0035 mg kg^{-1} hr^{-1}). High-dose isoflurane (3%) was administered for two hours in order to lower the mean arterial blood pressure (MAP) to below 80 mmHg. PC, ASL perfusion and BOLD MR images were acquired at the initiation of the experiment when all swine were normotensive (MAP > 80 mmHg) and then again after 2 hours of isoflurane, when the swine were hypotensive (MAP < 80 mmHg).

All images were acquired using a 1.5 T MR scanner (GE Healthcare, Milwaukee, WI, USA) and an eight-element phased array torso coil. PC images aligned perpendicular to the renal arteries were acquired rectilinearly with the following parameters: TR/TE/flip/BW = 6.7ms/3.2ms/30°/±31.25kHz, slice thickness = 5 mm, through-plane flow encoding, phase encoding values = 128, FOV = 24x12 cm^2, and 14 phases. ASL-FAIR (Flow-sensitive Alternating Inversion Recovery) 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° / ±41.67 kHz, FOV = 34cm, 128 x 128 matrix, NEX = 1.0, delay time = 1.2s, and 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. BOLD MR 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.

PC images were analyzed with CV Flow (Medis, The Netherlands) to calculate the renal blood flow in the right and left renal arteries. ASL perfusion exams were analyzed with custom scripts written in MATLAB (MATLAB version 8.0, The MathWorks Inc., Cambridge, MA, USA) to determine the cortical and medullary perfusion measurements. Average R2* values for the cortex and medulla were obtained from the BOLD images using previously described methods ([4]).

Data from each image analysis were divided into two groups based on the MAP at the time of acquisition. Data associated with a MAP greater than 80 mm Hg (beginning of the experiment) made up the normotensive group, and those associated with a MAP less than 80 mm Hg (after 2 hours of isoflurane) made up the hypotensive group. PC, ASL and BOLD MR data were compared between the two groups using a two-tailed paired t-test with significance defined as $P < 0.05$.

RESULTS AND DISCUSSION

Table 1 displays the results for both normotensive and hypotensive groups. The hypotensive group had significantly lower renal artery blood flow, lower cortical perfusion and higher cortical R2* (corresponding to *decreased* oxygen bioavailability) compared to the normotensive group. These results indicate ischemic conditions in the cortex when the MAP is below 80 mm Hg.

Table 1: Results for normotensive and hypotensive swine. Values are mean ± SD.

	Normotensive State	Hypotensive State	*P*
MAP (mm Hg)	**94 ± 11.8**	**55 ± 10.6**	**<0.001****
Phase contrast renal artery blood flow (ml min^{-1})	**256 ± 98.7**	**89 ± 31.5**	**<0.001****
ASL Cortical Perfusion (ml min^{-1} (100 g)$^{-1}$)	**195 ± 43.4**	**77 ± 54.2**	**<0.001****
ASL Medullary Perfusion (ml min^{-1} (100 g)$^{-1}$)	**46 ± 29.8**	**30 ± 31.5**	**0.027****
Cortical R2* (sec^{-1})	**10 ± 1.3**	**14 ± 6.2**	**0.029****
Medullary R2* (sec^{-1})	14 ± 3.4	13 ± 4.6	0.70

**Significant differences between groups are highlighted in bold.

The medullary perfusion was significantly lower in the hypotensive group compared to the normotensive group; however, the medullary R2* was not different between groups. Thus, while the perfusion to the medulla decreased, the oxygenation state of the medulla appears to be maintained. This is consistent with previous studies using invasive probes, which demonstrated the medulla's ability to maintain its oxygenation status despite decreases in total renal blood flow and regional tissue perfusion [1].

Finally, note that the fractional change in total renal blood flow between the normotensive and hypotensive states is similar by PC (65% decrease) and ASL (56% decrease), indicating some consistency between two fundamentally different approaches to the measurement of tissue perfusion.

CONCLUSIONS

This study demonstrates the feasibility of using non-contrast-enhanced functional MR imaging techniques to non-invasively monitor renal artery blood flow, regional tissue perfusion and oxygen bioavailability in the cortex and the medulla of swine kidneys during normotensive and hypotensive states. As previously demonstrated with invasive techniques in animals, medullary oxygenation is maintained despite a decrease in renal artery blood flow and regional tissue perfusion. Future applications of these techniques in humans may be used to non-invasively study renal blood flow and oxygenation simultaneously under normal physiologic and pathologic conditions and may be helpful in monitoring the kidney's response to treatments aimed at improving renal function.

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