An Apparatus for In Vivo Simultaneous Oxygen Probe Measurements during Renal BOLD MRI in a Porcine Model

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TARGET AUDIENCE: Investigators studying kidney disease with BOLD MRI

PURPOSE: Renal parenchymal hypoxia plays a central role in the progression of chronic kidney disease (CKD)[1], which afflicts over 10% of the world's population. Renal BOLD MRI shows some promise in depicting renal hypoxia, but multi-parametric models are necessary to translate BOLD signal to pO_2. Invasive measurements of kidney pO_2 are essential to develop and calibrate these models. Pig kidneys are suitable for invasive experiments due to their similar size and histologic architecture compared to human kidneys. Previous measurements of renal oxygen levels in pigs have used Clark electrodes that have metallic parts[2], precluding simultaneous BOLD MRI. More recently, rat kidney oxygenation has been investigated with simultaneous BOLD MRI and fiber-optic oxygen probe measurements at a ~5 minute temporal resolution[3,4]. To our knowledge, ours is the first report of simultaneous invasive oxygenation measurements and renal BOLD MRI in pig kidneys in vivo. We share our technical methods that have achieved excellent agreement in tissue oxygenation, under varying physiologic conditions, between BOLD MRI and the invasive reference probe.

METHODS: With IACUC approval, real-time in vivo oxygen (pO_2) data was acquired in vivo with a fiberoptic oxygen sensor (OxyLite Pro, Oxford Optronix) inserted into a female pig kidney with ultrasound guidance (**Fig 1**) through a 7cm 8Fr. paracentesis catheter (Cook Medical). Small custom plastic clamps (made in-house) were sutured to the skin to secure the fiber-optic probes and limit their movement.

Sagittal renal BOLD images were obtained at 3T: TR = 80ms, TEs = 5, 10, 15, 20, 25, 30ms, flip angle = 25°, matrix = 256x256, voxel size = 0.78x0.78x8mm, FOV = 200x200x8mm, averages = 1, scan time = 20 seconds, with suspended respiration of the intubated pig during imaging. After baseline BOLD imaging, 20 mg iv furosemide was administered. BOLD imaging was performed at 1 min intervals for 7 min.

RESULTS: We successfully implanted oxygen probes in the renal medulla of a female pig using ultrasound guidance, enabled by the large size of the pig kidney (12 cm length) and visibly distinctive cortex and medullas (**Fig 2**).

The real-time OxyLite pO_2 results (**Fig 3**) have much higher temporal resolution (1 sec) than BOLD images. Rapid and slow pO_2 changes that have not been previously observed with MR imaging. For instance, pO_2 decreases (up to 6mmHg) were observed when urine was removed from the bladder (**Fig 3B**), suggesting that bladder filling significantly affects kidney oxygenation. In addition, the saw-tooth appearance that occurred with suspended respiration (indicated with red bars in **Figs 3,4**) is not an artifact, but reflects an immediate and reproducible decrease in renal medullary pO_2 (~2 mmHg) every time the respiration was suspended for 20 sec for the BOLD acquisitions.

The real-time OxyLite pO_2 results show prompt changes in pO_2 within 1 sec (**Fig 4**), from ~31 mmHg up to ~36 mmHg, following furosemide administration that persisted for ~10 minutes and had a maximum roughly 5 minutes after administration. BOLD T2* values followed a pattern very similar to the in vivo oxygen probe measurements, increasing from ~32 ms up to a maximum of ~37 ms (**Fig 4**).

Invasive OxyLite pO_2 is plotted versus BOLD T2* measurements (**Fig 5**) and shows an excellent agreement between T2* and pO_2 measurements.

DISCUSSION: We have developed a successful method for in vivo validation of BOLD MR measurements of porcine renal oxygenation with simultaneous oxygen probe measurements and MRI. We have shown that changes in renal oxygenation measured by invasive probes mirrored the changes in renal BOLD T2* maps. We have also demonstrated large variations in minute-to-minute medullary pO_2 related to factors such as bladder filling and suspended respiration, which may have important implications for human BOLD experiments.

CONCLUSION: We have successfully demonstrated simultaneous high temporal resolution measurement of renal oxygenation with invasive probes and renal BOLD MRI in pigs in vivo. This experimental model provides a valuable platform for investigation of the renal BOLD signal and calibration of models used to estimate renal oxygen levels from MRI BOLD signal. Because of the anatomic similarity between pig and human kidneys these invasive animal experiments may provide valuable data to aid the non-invasive quantification of renal oxygen in humans.

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REFERENCES: 1. Heyman SN, et al. Am J Nephrol 2008;28(6):998. 2. Warner L, et al. Invest Radiol 2011;46(1):41-47. 3. Pohlmann A, et al. Acta Physiol (Oxf) 2013;207(4):673. 4. Pohlmann A, et al. Invest Radiol 2014; 49(8):547.

Figure 1: A paracentesis catheter is inserted into a pig kidney under ultrasound visualization for placement of a fiber-optic O_2 probe. Customized plastic clamps secured the probes to limit their movement after placement.

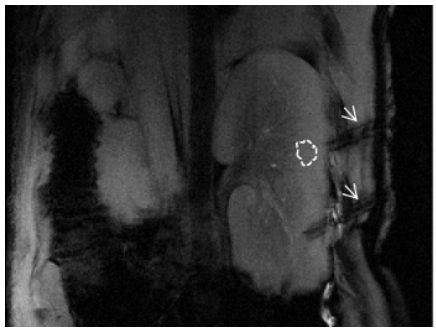

Figure 2: A 2D BOLD image clearly demonstrates the location of the oxygen probes (arrows). The tip of the probe is exactly 5mm beyond the end of the paracentesis catheter. An ROI (outlined) shows where the T2* average was compared to invasive pO_2 measurements.

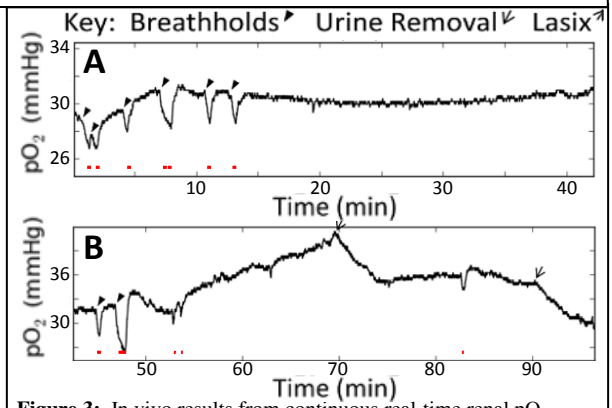

Figure 3: In vivo results from continuous real-time renal pO_2 measurements. (A) Dark triangles indicate the beginning of breath-hold experiments that caused immediate pO_2 decreases that were not observed during normal breathing cycles. (B) Urine removal decreased the pO_2 by ~4 mmHg.

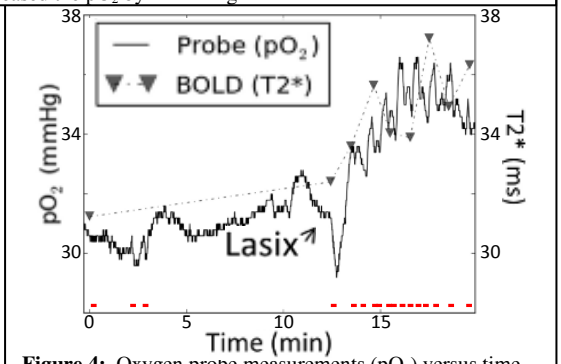

Figure 4: Oxygen probe measurements (pO_2) versus time, and MRI BOLD T2* measurements versus time. Lasix was administered at the point indicated by the upward arrow.

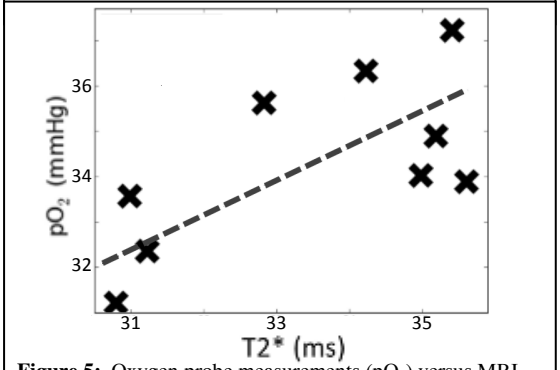

Figure 5: Oxygen probe measurements (pO_2) versus MRI BOLD T2* measurements.