

Metabolic imaging differentiates ischemia reperfusion injury severity in a translational mouse model

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Introduction: Renal IRI commonly complicates conditions like renal transplantation, surgery, and sepsis, resulting in significant morbidity and mortality. Despite significant morbidity, biopsy is standard of care, emphasizing the need for noninvasive diagnostic strategies to inform prognosis. Here, we used co-polarized pyruvate and urea to investigate the effect of IRI severity on kidney metabolism and probe uptake in a mouse model. Our results demonstrate the potential of both probes to provide prognostic insights into renal IRI.

Methods: Wild-type C57BL/6 mice underwent left-side renal warm-ischemia for 28 (moderate) or 45 (severe) minutes. $1\text{-}^{13}\text{C}$ pyruvate and ^{13}C urea were polarized in a Hypersense DNP Polarizer, and 80 mM pyruvic acid with 64 mM urea were injected (6.7 mL/kg) via central line over 10 seconds. Coronal echo-planar spectroscopic images were acquired in a 7.0T MRI system from 5 seconds post-injection, every 3.5 seconds, with a 12×12 matrix, 60 ms TR, 2×2 mm resolution, 10° flip angle, and 6.5-7 mm slice thickness.

Results: Figure 1 shows AUC analysis, with IRI metabolite signal intensity and IRI-to-Contralateral metabolite ratio plots. In severe IRI, left-kidney pyruvate signal rose markedly from day 0 to day 1 ($p = 0.0038$) and then fell by day 7 ($p = 0.0141$). Analysis of IRI:Contralateral pyruvate ratios revealed that pyruvate ratios increase at Day 1 and Day 7 relative to Day 0 ($p = 0.00004$ and $p = 0.00048$) in severe IRI. Figure 2 shows summed lactate maps 2.5 hours post-IRI.

Conclusions: Our results demonstrate that HP pyruvate and urea are promising noninvasive biomarkers for renal ischemia/reperfusion injury. The distinct signal differences observed across timepoints suggest that these markers can accurately differentiate injury severity and serve as an early prognostic biomarker. These findings support further exploration of HP MRI for real-time metabolic evaluation of renal injury.

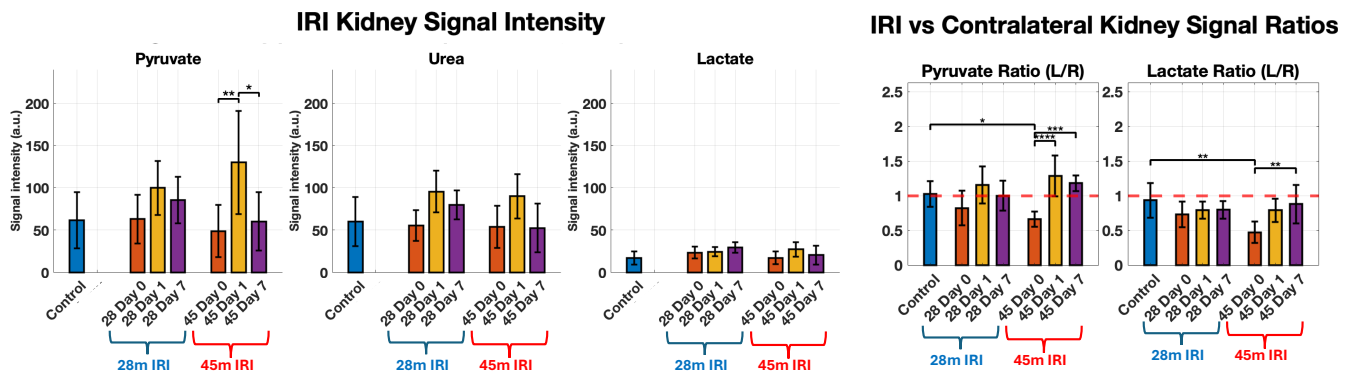


Figure 1: Top) Signal intensity for ischemic kidneys across groups. Bottom) Ratios of ischemic to contralateral kidney.

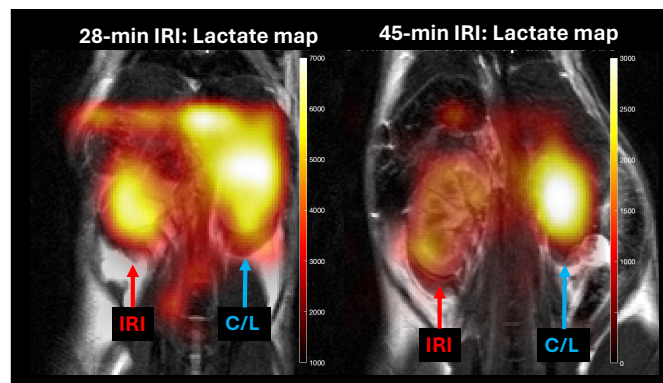


Figure 2: Representative summed lactate maps for 2.5 hours post moderate (left) and severe (right) IRI