Non-Invasive Assessment of Renal Tumor Aggressiveness using Hyperpolarized Carbon-13 Magnetic Resonance

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Summary: The ability of hyperpolarized carbon-13 pyruvate to assess tumor aggressiveness is explored by comparing the response of three different renal cell lines to this metabolic probe. Past studies have merely distinguished normal and tumor tissues with this method.

There is a clear research and clinical value for non-invasive molecular imaging biomarkers that inform on specific molecular events associated with oncogenesis and response to therapy. Hyperpolarized (HP) carbon-13 methodology overcomes some of the major shortcomings of magnetic resonance and with a greater than 40,000 fold signal enhancement allows for the imaging of injected molecular probes, in vitro and in vivo. The field's efforts have been focused on using HP 13C pyruvate to image glycolysis in many aggressive and metastatic cancers, where an over production of lactate attributed to the Warburg Effect distinguishes these cancerous tissues from normal. This technique has already been successfully applied to the prostate cancer presence and aggressiveness in animal models (1,2). However, studies to date have merely distinguished normal from cancerous tissue. In this study, we test the hypothesis that HP 13C pyruvate can assess tumor aggressiveness.

In this study, we probe normal renal tubule epithelial cells (HK2 cells), indolent renal cell carcinoma (RCC) (UMRC6 cells), and aggressive/metastatic RCC (UOK262c cells) in cell culture. Steady state metabolite concentrations in each cell line have been measured for proton (Figure 1a) and for carbon-13 after incubation of 4mM [3-13C] pyruvate (data not shown) by high-resolution magic angle spinning (HR-MAS) NMR spectroscopy. Markedly, steady state lactate concentrations increased significantly with aggressiveness of cell lines. Injection of 4mM HP [1-13C] pyruvate allow for a real-time assessment of lactate production in each of the cell lines (Figure 1c) where again lactate production increases with aggressiveness of the cell lines.

Overall, we show that hyperpolarized 13C MR has the potential to noninvasively characterize renal tumor aggressiveness. Specifically, HP [1-13C] lactate may be a useful biomarker for discriminating benign from malignant, and indolent from aggressive renal tumors.