Simultaneous Hyperpolarized 13C Pyruvate and Urea Perfusion Parameterizations in Cancer

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Introduction- The correct characterization of cancer is an important problem for the clinical control of individual cancers(1). The purpose of this study was modeling the perfusion of both hyperpolarized pyruvate and urea in healthy and cancerous tissues. In cancerous tissue there is both existing vasculature and neovascularization as different kinds of lesions surpass the normal blood supply, including small circulation disturbance in some of the abnormal vessels. Tumor perfusion data available with pyruvate metabolic data would be valuable in exploring the complicated relationship between perfusion and cancer metabolism at both preclinical and clinical research levels(2,3).

Methods - For total pyruvate perfusion, we propose a parameterization: $P_p \propto \int_0^{\infty} \bar{M}_{zP}(t) + \bar{M}_{zL}(t) + \bar{M}_{zA}(t)\,dt$, while for the urea perfusion we propose: $P_u \propto \int_0^{\infty} \bar{M}_{zU}(t)dt$, where $\bar{M}$ is the metabolites longitudinal magnetization that was calculated by a kinetic model fitting that accounts for arbitrary RF flip angles. We used a 3D hyperpolarized 13C dynamic MRSI acquisition with multiband excitation pulses and a compressed sensing acquisition and reconstruction (REF). The sequence was started immediately following the 12 sec injection of a 350 uL solution containing 80 mM [1-13C]-pyruvate and 80 mM 13C-urea. 4 transgenic prostate tumor model (TRAMP) mice and 4 double transgenic liver tumor model mice were studied.

Results- The variation of pyruvate perfusion and urea perfusion can be observed for the healthy and cancerous tissues. The amount of pyruvate perfusion in Fig1-c in liver is very low. Overall, we observed an elevated ratio of our proposed pyruvate perfusion to urea perfusion parameterizations in both prostate and liver tumors compared to healthy tissues (Fig. 3). We believe this is due to increased uptake (and subsequent metabolic conversion) of pyruvate compared to urea, which is primarily in the vasculature.

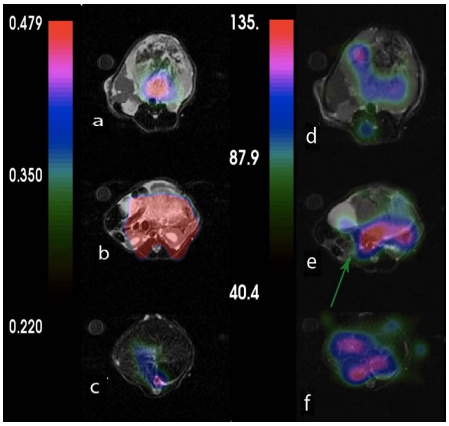

Fig 1. (a-c) Proposed pyruvate total perfusion for prostate cancer, kidney, and liver slices, respectively. (d-f) Proposed urea perfusion for the same slices.

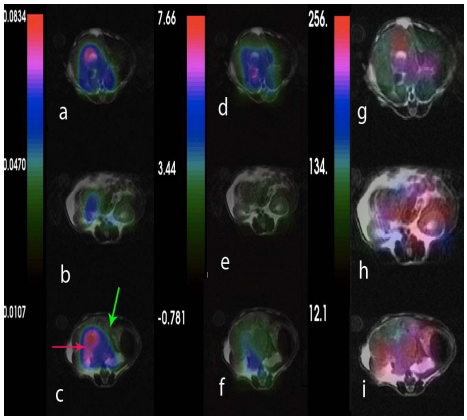

Fig 2.Comparison of (a-c) Kpl (d-f) Pp and (g-i) Pu in a liver tumor (red arrow).

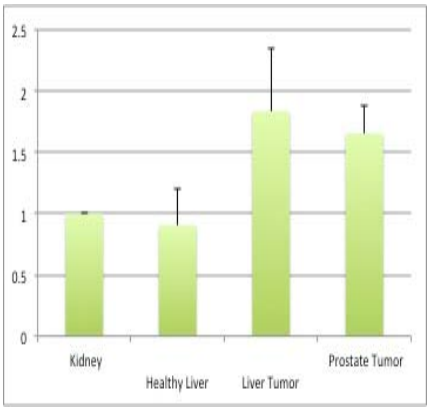

Fig3.The perfusion ratio between pyruvate and urea, Pp:Pu, in liver and prostate tumor were significantly different than healthy kidney and liver tissue ($p < 0.001$). (Metabolite perfusion was normalized to kidney.)

Discussion- The urea perfusion is primarily representing the vasculature delivery in each specific tissue and it stays in the vessels, while the pyruvate perfusion, which is the accumulation of all source and derived metabolites related to the pyruvate including pyruvate, lactate, and alanine, can also be a marker for vascular delivery but also includes tissue uptake. We hypothesize that when the pyruvate perfusion is higher in some tissues relative to urea perfusion it represents higher amount of uptake of the pyruvate that is flowing into the tissue. Measurement of urea perfusion at each organ is proportional to urea concentration in the tissue and can be a marker vascular delivery since urea primarily stays in the vasculature. Liver is a very vascular organ and the opened capillary shape of liver vasculature likely caused high urea perfusion and concentration in liver. The kidneys take up more urea due to their high vasculature and are also responsible for concentrating urine for removal in the urine. The urea perfusion from tumors is more sporadic and random. Urea cannot perfuse well in some parts of tumor particularly in suspected necrotic regions. On the other hand, some parts of tumor have more metabolic activity and, therefore, these parts need more blood and more vessels, and consequently more urea perfusion.

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