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Fractional perfusion: A simple semi-parametric measure for clinical translation of hyperpolarized 13C MR?

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Hyperpolarized (HP) 13C magnetic resonance imaging (MRI) is a promising tool for in vivo metabolic interrogation of disease states and treatment efficacy assessment. However, the method is currently limited by the lack of good quantitative measures. This is particularly true in humans where large variations in transport kinetics have been reported [1]. Here we introduce a novel model-free perfusion [2] and area under the curve ratio-metric [3] combined model. We define fractional perfusion as substrate-delivery corrected metabolic conversion, for quantifying the metabolic information in hyperpolarized imaging. Healthy (normoglycemic) and diabetic (hyperglycemic) rats were subjected to unilateral ischemia (IR) with a non-traumatic clamp for 40 min, 8 days before sacrifice. The model proposed fractional perfusion was investigated using HP [1-13C]pyruvate and compared to 1H dynamic contrast enhanced (DCE) perfusion imaging. A similar perfusion assessment was derived from HP [1-13C]pyruvate and DCE ($p=0.65$) in both healthy contralateral (CL) and IR kidneys using the proposed model. Fractional pyruvate to lactate perfusion (FPL) was also comparable between the two methods. Alanine signal significantly increased in the hyperglycemic IR kidney ($p=0.04$) compared to the hyperglycemic CL kidney. However, when accounting for perfusion changes, no alteration in the metabolic conversion is seen. A significantly altered fractional lactate production is seen in the hyperglycemic animals, demonstrating a metabolic shift. Hence, we demonstrate that the use of HP 13C-metabolites could be used to quantify the energetic demand by mapping both the injected biomarker perfusion and metabolic conversion. Therefore, the pyruvate concentration curve can be a surrogate marker for perfusion, in cases where other perfusion assessment is not directly obtainable. Perfusion parameters from DCE MRI or dynamic pyruvate signal therefore enable correction of pyruvate delivery variations. This allows calculation of semi-parametric measures of metabolism per perfusion unit, which could facilitate more quantitative information from HP pyruvate in the future.

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