DEVELOPMENT OF QUANTITATIVE MAGNETIC RESONANCE IMAGING TECHNIQUES FOR CELLULAR TRACKING AND MEASURING ORGAN PERFUSION

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ABSTRACT

Magnetic resonance imaging (MRI) is a safe and promising modality for non-invasive, longitudinal, and quantitative evaluation in higher risk populations including pediatrics and obstetrics. The overall goal of this thesis is to develop quantitative MRI techniques for pediatric and in utero studies of disease. Progress with expansion and activation of immune cells has revived interest in cellular-based treatments against incurable or relapsed pediatric cancers. One of the technological shortcomings of translating cellular-based therapies from animal models to clinical application is the inability to non-invasively image therapeutically delivered cells after infusion. Furthermore, several pregnancy complications are correlated to vascular functional deficiencies impeding nutrient exchange in placental tissue, including intrauterine growth restriction (IUGR), maternal gestational hypertensive disorders as well as adverse birth outcomes. There is a clear need for non-invasive, quantitative assessment of vascular function of the placenta in early pregnancy to identify any developing pathophysiologic conditions before their clinical manifestation. MRI methods of immune cell detection and blood perfusion

measurement can improve sensitivity to novel therapies and early disease without using ionizing radiation. To this end, a chemical shift encoded (CSE) fluorine-19 (^{19}F) MRI acquisition and reconstruction is developed and optimized for quantitative imaging of complex cellular labels used to track immune cells. The CSE approach is applied to a ^{19}F cell tracking agent used to detect natural killer (NK) cells in vivo and validation is performed with fluorescence microscopy. This work demonstrates advancements in ^{19}F MRI techniques to detect and accurately quantify ^{19}F concentrations. Additionally, we evaluate arterial spin labeling (ASL) with flow-sensitive alternating inversion recovery (FAIR) to measure placental intervillous perfusion in a pregnant rhesus macaque model and compare with ferumoxytol dynamic contrast-enhanced (DCE) MRI. Differences in contrast dynamics of the endogenous blood label versus the injected ferumoxytol are used to delineate fast and slow components of blood arrival time. Regions of fast and slow arrival appear to be associated with functional units of the placenta that may be useful for measuring and monitoring placental function. Overall, the dissertation provides the foundation for developing longitudinal and quantitative MR techniques to assess immune cell dynamics and measure placental vascular function in human pregnancies.