Title: Evaluating the progress of inflammation in myocardial infarction using hybrid PET/MRI

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Structured Abstract:

Introduction: Cardiovascular disease is the leading cause of death worldwide. Heart failure, specifically, is predominantly caused by dysregulation of inflammation often seen after a heart attack [1]. MRI has shown promise in detecting characteristics that can increase the risk of heart failure, including: infarct size, presence of hemorrhage and presence and size of an area of extreme low blood flow within the infarct called the region of microvascular obstruction (MO) [2]. What is needed is an imaging method that can distinguish between pro-inflammatory (neutrophils and M1 macrophages) and anti-inflammatory (M2 macrophages) cells as dysregulation occurs when the pro-inflammatory phase is prolonged.

It has been shown that FDG-PET can, in principle, distinguish between the pro- and anti-inflammatory cell types [3] however post heart attack there are three problems: a) FDG cannot penetrate the MO after intravenous bolus injection, b) resting healthy myocardium also has uptake of FDG and hence must be suppressed and c) partial volume effects interfere with identification of MO tissue. A constant infusion may be able to penetrate the MO while simplifying kinetic modelling [4,5]. Here we present results addressing these three issues post-myocardial infarction using PET/MRI imaging during a simultaneous constant infusion of FDG and an extracellular MRI contrast agent (a gadolinium chelate e.g. Gd-DTPA) in canines and humans.

Methods: 1) Evaluate the safety of combining FDG and Gd-chelates in one syringe. 2) Compare kinetic modeling results of bolus injection, constant infusion and bolus followed by constant infusion. 3) Assess whether a long constant infusion of Gd-DTPA penetrates the MO. 4) Evaluate the effectiveness of myocardial glucose uptake suppression. 5) Use a clinically relevant constant infusion method in a longitudinal study. 6) Conduct a human study based on the canine work.

Results: Radiochromatography showed no change in the FDG or Gd-DTPA. The baseline study showed no difference between injection methods. It was found that a long constant infusion reduces the apparent MO volume by 90%. The slope of the time-activity curve decreased after suppression in remote tissue but not in infarcted tissue. The longitudinal study showed significant correlation between infarct volume and amount of inflammation.

Discussion: It was found that injecting FDG and Gd-chelates was safe and that a constant infusion or bolus followed by constant infusion could be used to accurately identify glucose metabolism and extracellular volume in canines. It was found that a constant infusion can effectively penetrate the MO and be used to study the myocardium post-MI. This work has provided a method to image inflammation post-MI even in the presence of an MO.