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Title of Defense: Manganese Enhanced Functional Magnetic Resonance Imaging of Endogenous Pancreas and Isolated Human Islets

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ABSTRACT

It is well established that diabetes is of critical importance in the world as the number of people affected increases globally. Although a great deal is known about the pancreas and its function, there are still unanswered basic questions about normal pancreatic physiology/function. Presently, pancreatic endocrine function is assessed using biochemical tests of insulin release or serum glucose. Knowing the functional efficiency of the pancreas would certainly be beneficial in the development of novel therapies aimed at maintaining or increasing endocrine function particularly during progressive pathologies. Here we present an application of functional MRI to the rodent pancreas using manganese (Mn) enhanced imaging (MEMRI) in response to glucose stimulation. To image rodent pancreas is extremely difficult for many reasons including organ size, tissue density, location, and motion. To overcome these constraints, a novel application of Magnetization Prepared RAPid Gradient Echo (MP-RAGE) was applied to achieve significant T1 weighted contrast in response to glucose stimulation. A pre- and post glucose activation in rodent pancreas indicated a signal increment or

decrement depending on the dynamic of the stimulant. A simultaneous injection of stimulant with Mn has shown an overall increase of 20% to 26%, signal enhancement. Uptake of Mn was confirmed via atomic absorption and insulin release via ELISA.

In addition, the research also focused to aid islet transplantation by developing a method to make pre-transplant functional assessments of isolated human islets as they were subjected to both physiological and mechanical stress during isolation. As proposed, the islets labeled with a contrast agent (manganese) would alter their molecular magnetic properties such as longitudinal (T1) and transverse (T2) relaxation time, and there as a result there would be a change in their signal intensity. This change in signal intensity has been exploited to distinguish between adjacent soft tissues, to delineate pathologic tissues, and, in principle, to characterize tissue viability. μ MRI-of isolated islets revealed a significant change in T1 and diffusion coefficient between the controls versus stimulated islet where no changes was observed in transverse relaxation.