Diffusion Weighted µMRI of Isolated Human Pancreatic Islets

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Introduction:

Unfortunately diabetes is quickly becoming a world-wide problem and pancreatic islet transplantation is emerging as an alternative therapeutic treatment. Insulin is released from the ß-cells and although they are the primary cell type within an islet an accurate assessment of their functional mass has yet to be determined. This is important in order to understand how they are affected by disease and pathology such as diabetes and pancreatic cancer. We have previously demonstrated how Mn^{+2} enhanced magnetic resonance micro-imaging (µMRI) of pancreatic islets can be used to image glucose activation (1). Diffusion weighted MRI has been extensively used to study the intra and extracellular physical and chemical environment of water molecules in the brain and has been applied to other tissues (2). Here we present data demonstrating how diffusion weighted µMRI (DW- µMRI) can be used to characterize the physical integrity (viable vs. non-viable) and function (control vs. glucose stimulated) of isolated human islets. DW- µMR images were acquired and apparent diffusion coefficients were mapped. Our data indicate a significant decrease in diffusion in viable versus non-viable and stimulated versus non-stimulated islets.

Methods:

Isolated human islets were incubated in 5mM glucose Krebs-Ringer Buffer (KRB) solution for 30 minutes. One set was then stimulated for 30 minutes in high (16.7 mM) glucose KRB while the control was kept at low (5mM) glucose. Islets were rinsed in 5mM glucose KRB and transferred into a microcapillary sample tube (ID 570 µm). Diffusion coefficients of viable versus non-viable islets and stimulated versus non-stimulated islets were compared to each other and to the surrounding media. Diffusion coefficients were calculated based on the method of Stejskal and Tanner (2). Viability was tested via trypan blue staining before and after imaging. All experiments were conducted using a 750 µm radius home built Archimedes surface coil (1), mounted on a Bruker Micro 5 Imaging Probe (triple axes gradients of maximum strength 2000 gauss/cm).in a 56-mm vertical bore 11.7 T magnet using a Bruker DRX Avance Spectrometer (Bruker, Billerica, MA). Each experiment was performed using diffusion weighted spin echo with 14 b-values ranging from 190 to 3200 mm^2/s. ROIs were selected and SNR intensities computed. Apparent diffusion coefficients were calculated using Matlab (The Mathworks Inc, Natick, MA). Image acquisition parameters were FOV = 0.4 x 0.4 cm, TR = 700 ms, TE = 27 ms, slice thickness = 0.3mm, matrix size = 128 x 128, Δ= 18ms, δ= 4ms.

Result and Discussion:

The diffusion coefficient of the extracellular islet media was used as a reference of D = 2.14± 0.80 μm^2 /ms. Preliminary diffusion data of the islet indicate a fast and slow component which was fitted to the biexponential model (3). Figure 1 is a DW contrast image of control and stimulated islets while figure 2 is a plot of the signal intensity and b-factors both demonstrating a decrease in diffusion with stimulation. Stimulated islets have a fast and slow component of diffusion coefficient of 0.70± 0.35 μm^2 /ms and 0.0850± 0.03 μm^2 /ms compared to control islets of 1.90± 0.53 μm^2 /ms and slow is 0.22± 0.14 μm^2 /ms. Similar measurements were made to compare the diffusion between viable and non-viable islets to assess the physical integrity of the islet as shown in Figure 3. Figure 4 is an apparent diffusion coefficient (ADC) map which correlates a decrease in diffusion with activation.

Conclusion:

Preliminary data indicate that DW- µMR images can be used to assess pancreatic islet integrity as well as functionality of the pancreatic ß-cells and possible ß-cell mass.

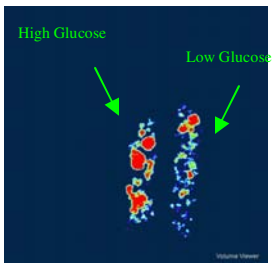

Fig.1 DWI- µMR images of stimulated and control human islet b= 1587 mm/sec, Mtx = 256 x 256, Nex = 20

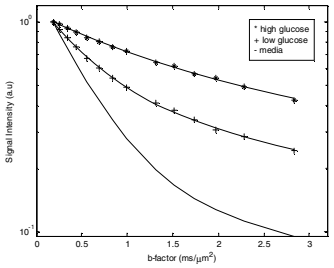

Fig. 2 Diffusion decay curve from media, stimulated and non-stimulated islet

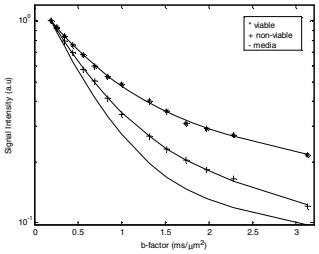

Fig. 3 Diffusion decay curve from media, viable and non-viable islet

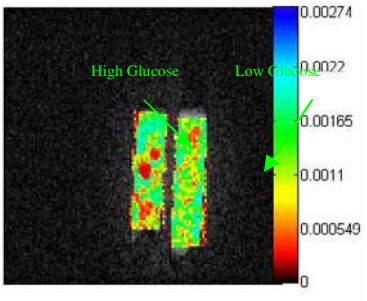

Fig. 4 ADC map of stimulated and non-stimulated islet

Reference:

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