Functional Magnetic Resonance Imaging of Liver: Effect of Glucose

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Introduction

Diabetes is a chronic disease in which the pancreas either does not produce enough insulin (type I), or the body fails to utilize it (type II). Insulin resistance, defined as a decrease in sensitivity or responsiveness of its action, is the primary cause in humans to develop type II diabetes. Therefore, quantifying insulin sensitivity or resistance is of a great importance for early diagnosis and prevention of subsequent complication such as cardiovascular disease, hypertension, retinopathy etc. One of the primary functions of insulin is disposal of blood glucose and inhibition of hepatic glucose production (HGP). Incomplete suppression of HGP is a strong indication of insulin resistance. Current gold standard to assess insulin sensitivity/responsiveness is insulin clamp technique [1], but, it is rarely performed in clinical care because it is complicated, invasive and poses a potential danger of hypoglycemia. A non-invasive functional imaging of liver to assess insulin function will not only indicate presence of any insulin resistance. Therefore here, for the first time, we attempt to visualize insulin function in liver by stimulating with glucose. In liver, glucose is metabolized via non-oxidative pathways [2], and an increase in endogenous insulin results in a change in the role of liver from a glucose producer to glycogen storage. We hypothesized that this change in roles may be associated with a change in hepatic oxygenation and can be detected by blood oxygenation level dependent (BOLD) MRI.

Materials and Methods

Six healthy volunteers (age 24.6 ± 10.4) and four Yucatan mini pigs (weight of 51.2 ± 2.9 kg) liver were image pre and post hyperglycemia. All studies were approved by Institutional Animal Care and Use Committee (IACUC) or Institutional Review Board (IRB). Both animals and human were subjected to over night fasting prior to scanning. Hyperglycemia was induced by oral ingestion in human and was infused in swine with the final dose of 0.5g/kg and 1.0g/kg in swine respectively. In addition to baseline, two more serum glucose level were measurements at 30 and 60 minute post ingestion in human and 5 and 30 minute post infusion in swine.

Imaging Protocol

All MRI scans were performed on a whole 3.0 T scanner (Siemens Verio). T2* weighted images of the liver was obtained using multiple gradient recalled echo (mGRE) sequence with 11 echoes from 3.1 through 44.6 ms. Other imaging parameter include: TR = 62 ms, no. of slices = 3, slice thickness 3.0 mm, FOV = 25.7 x 37.5 cm, matrix 192 x 512. R2* (=1/T2*) measurements were performed by drawing a circular region of interest (ROI), placed on the T2* map. Statistical significance was determined by paired one tail Student's t-test. Additionally, R2* color maps were generated offline using Matlab (Mathwork, Natick MA).

Results

Figure 1 illustrates representative R2* maps of the liver in swine and human subject. There is a clear decrease in R2* in the liver in both species during hyperglycemia, although the magnitude of change is less in humans. The absolute magnitude of change observed in swine liver (110.41 ± 14.1 s-1 to 72.22 ± 5.7 s-1) and in humans (55.84 ±3.8 s-1 to 50.6 ±0.5 s-1) before and after glucose reached statistical significance ($p < 0.05$) by one tail Student's t-test. Figure 2 is a summary plot illustrating changes in R2* with corresponding serum glucose level at two time intervals following administration of glucose in both species. The mean R2* values averaged over all the three slices per subject and over all the subjects. Data from one volunteer and swine were removed from the analysis due to motion related technical difficulties.

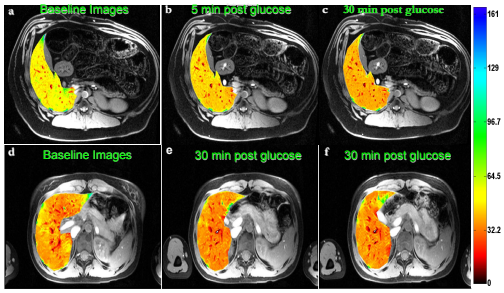

Figure 1. R2* maps of swine and human liver: The top row illustrates liver R2* maps in a representative swine: (a) baseline or pre-glucose, (b) 5 minute post glucose infusion, (c) 30 minute post glucose infusion. The bottom row similarly shows the liver R2* map in a representative human subject: (d) baseline image, (e) 30 minute post glucose ingestion, (f) 60 minute post glucose ingestion. All the maps are scaled from zero to 165 (red to blue) representing oxygen saturation to severe hypoxia

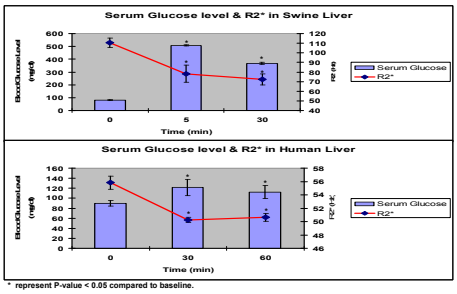

Figure 2. Top plot histogram shows the glucose level at baseline, 5, and 30 minute post glucose infusion in swine where as line plot illustrates the corresponding changes in R2*. Bottom plot histogram similarly shows pre and post serum glucose changes in human at baseline, 30, and 60 minute post glucose ingestion where as line plot shows the corresponding changes in R2*.

Conclusions: Functional magnetic resonance imaging of the liver using BOLD contrast is feasible to study insulin response with suitable stimulus such as glucose. A significant change in hepatic R2* was observed post glucose both in swine liver and human.

Reference:

1. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol 979;237(3):E214-223.
1. Roden, M *Clinical Diabetes Research: Methods and Techniques chap 4, pp 43-76*London, Great Britain, Wiley's, 2007.