

Localized MRS of Human Pancreas

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Introduction: Type 2 diabetes occurs when insulin secretion is inadequate for the prevailing insulin sensitivity. Obesity is well known to negatively influence insulin sensitivity, but its direct effect on insulin secretion is still debated, mostly due to lack of an adequate in vivo experimental set-up. The lipotoxicity hypothesis provides a unifying link between chronic positive energy balance and metabolic syndrome abnormalities: excess energy that cannot be stored in the adipose tissue is redirected in the form of triglycerides to ectopic sites (1). Accumulation of fat in the human liver, skeletal muscle, and the heart, along with associated decline in the function of these organs, has been confirmed by previous clinical studies (2), yet data on fat accumulation in the human pancreas is limited to autopsy reports (3), and there is very limited information regarding the relationship between insulin secretion and pancreatic fat accumulation (4). We performed studies in humans to determine whether proton-localized magnetic resonance spectroscopy (MRS) can be used to noninvasively assess pancreatic steatosis. We performed a series of studies in healthy human volunteers to document the reproducibility of the pancreatic triglyceride measurement in vivo and examined the cross-sectional relationship between pancreatic triglyceride content, body mass index (BMI), and glycemic status.

Materials and Methods: Human experiments were approved by the Institutional Review Board at University of Texas Southwestern Medical Center and subjects provided informed consent for the study. Study volunteers (N=33) underwent clinical evaluation, anthropometric measurements, an Oral Glucose Tolerance Test, and MRS for pancreatic triglyceride measurement. To assess reproducibility of MR measurement in the clinical setting we measured the pancreatic triglyceride content in duplicate within 2 weeks.

MRS measurement of pancreatic triglyceride content: MR scanning was performed in fed state. We used 1.5 Tesla clinical whole body MR system (Gyroscan Intera, Philips Medical Systems, North America). High-resolution images through the abdomen were collected to locate the pancreas while patients were holding the breath at exhalation. We tested the volume of 2cc ($10 \times 10 \times 20 \text{ mm}^3$) carefully placed within the pancreas using three perpendicular views and avoiding peri-visceral fat (Figure 1A). The spectroscopic data were collected as patients breathed freely with triggering at exhalation. Spectra were collected using a cardiac synergy coil. PRESS sequence (PointRESolvedSpectroscopy) was used for spatial localization and signal acquisition. The average length of the pancreatic MRI/MRS experiment was 30 minutes.

Reproducibility of the total pancreatic triglyceride measurement by MRS: The intraclass correlation coefficient between the two measurements was 0.9 (Figure 1B).

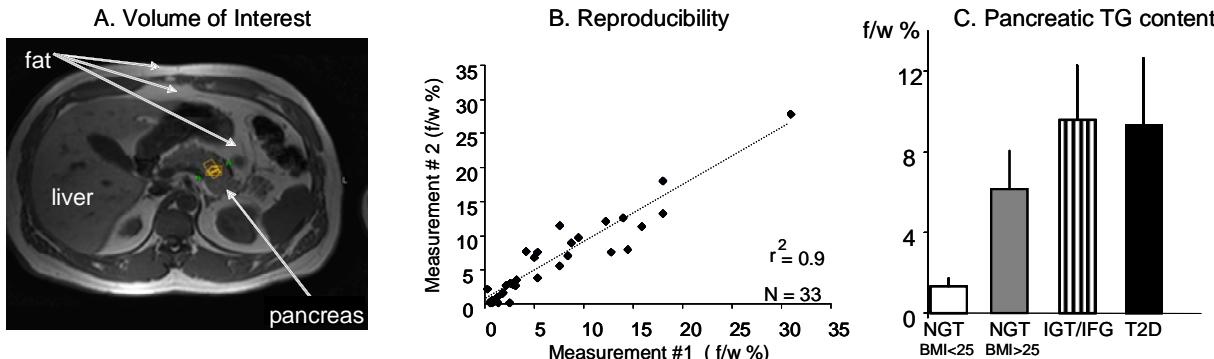


Figure 1: A. The experimental setup for the measurement of a pancreatic TG content using localized Magnetic Resonance Spectroscopy in human. B. Reproducibility of the MRS measurement of pancreatic fat levels. C. Cross-sectional study.

Cross-sectional study of pancreatic triglyceride content in humans: Volunteers were grouped based on their BMI and glycemic status: (1) normal BMI with normal glucose tolerance (control); (2) abnormal BMI with normal glucose tolerance; (3) pre-diabetes (IGT and/or IFG); (4) diabetes. The pancreatic triglyceride content (Figure 1C) was lowest in the control group, the lean normoglycemic volunteers. Pancreatic triglyceride content was significantly higher in the second group when compared with the control group (1.3% versus 6.16%, $p=0.02$). Pancreatic triglyceride levels were even higher in the groups with abnormal glucose levels (IFG/IGT) and diabetes (9.57%, $p=0.006$ versus control group). Pancreatic triglyceride content was not different between volunteers with pre-diabetes and those with diabetes.

Conclusions: MRS based measurement of pancreatic triglyceride content in vivo in humans is a highly reproducible method. We demonstrated using this novel technique, that pancreatic triglyceride content increases with obesity and is further elevated in volunteers with abnormal blood glucose levels. MRS-based measurement of pancreatic triglyceride content is not only a valuable research tool for clinical studies evaluating the biology of obesity and its complications, but a potential clinical tool to identify individuals at high risk of developing diabetes, in whom early intervention could prevent progression to disease.

References: 1) RH Unger, 2008; (2) LS Szczepaniak, 2007; (3) Saisho, 2007; (4) Tushuizen, 2007.