Lipid content and composition differ in adipose tissues and liver of ob/ob mice

Qiong Ye[1], Alexander Fuchs[1], and Markus Rudin[1,2]
[1]*Institute for Biomedical Engineering, Zürich, Switzerland,* [2]*Institute of Pharmacology and Toxicology, Zürich, Switzerland*

Introduction: When energy intake is higher than expenditure,excessive energy will be stored in both adipose tissue and liver. Adipose tissue, as a major endocrine organ, and the liver are quantitatively the most important tissues involved in fatty acid metabolism (1). Both fat content and composition are closely related to metabolic regulation. Proton magnetic resonance spectroscopy has evolved into a reliable method for measuring both fat content and composition non-invasively. The objective of this study was to assess fat in adipose and liver tissue of ob/ob mice, an established murine model of obesity with mice displaying defective leptin signaling.

Materials and methods: *Animals*: Three male ob/ob mice of 34 weeks of age were used. The mice were anesthetized using isoflurane (1.5%-2.25%) in an oxygen-air mixture (150/400) throughout the experiments with a face mask. The body temperature and respiration were monitored. All animal experiments were performed in strict adherence to the Swiss Law for Animal Protection. *MRS experiment:* All in vivo MRS measurements were performed on a Bruker BioSpec 94/30 (Bruker BioSpin MRI, Ettlingen, Germany) system using a volume resonator for excitation anda surface coil for signal detection. Anatomical reference images were acquired using a TurboRARE sequence. The volume-of-interest(VOI) was carefully placed on these images to avoid contribution from large blood vessels and tissue boundaries. Single-voxel localized ^{1}H MR spectra were acquired using the PRESS sequence with additional outer volume suppression with the following parameters: VOI 2.0*2.0*2.0 mm^3 (neck), 1.5*1.5*1.5mm^3 or 1.0*1.0*1.0 mm^3 (lower belly), 1.5*1.5*1.5 mm^3 (visceral fat), 3.0*3.0*3.0 mm^3 (liver), T_R=6s, T_E=12, 18, 24, 30, 36ms (for correcting the measured signal intensities for T_2 effects), band width=4006.41 Hz, number of sampling points=6009, acquisition time=1499.85 ms, number of averages (NA) =20 or 40 for sufficient SNR. No water suppression was applied.Two VOIs without overlay were acquired for neck, lower bellyand visceral fat. All spectral data have been corrected for T_2 relaxation, while the long T_R values were used rendered T_1 correction unnecessary. *Analysis of MRS data:* All spectroscopy data were processed using LCModel (Version 6.2-1Q, Stephen Provencher, Oakville, ON, Canada). *Calculations:* Peak assignments were based on published data (2). Quantification was done with T_2 correction and no correction for T_1. The fraction of lipid mass, saturated, polyunsaturated and monounsaturated lipids were defined as literatures (3). *Statistical analysis:* All results are presented as mean ± SE. For statistical analysis OriginPro 8.1 (OriginLab, Northampton, MA, USA) has been used.

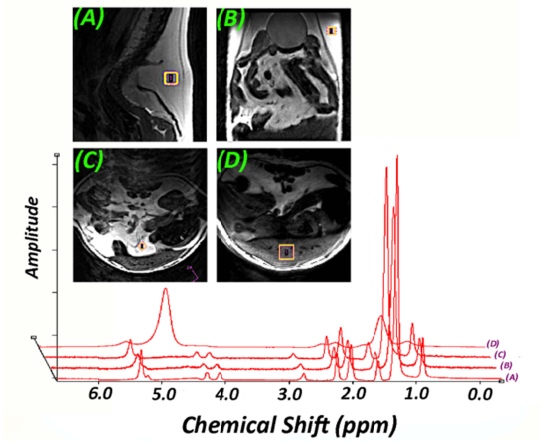

Fig1. Anatomical images from neck (A), lower belly (B), visceral fat (C) and liver (D) in ob/ob mouse. Typical spectrum at TE=12ms from four compartments are shown.

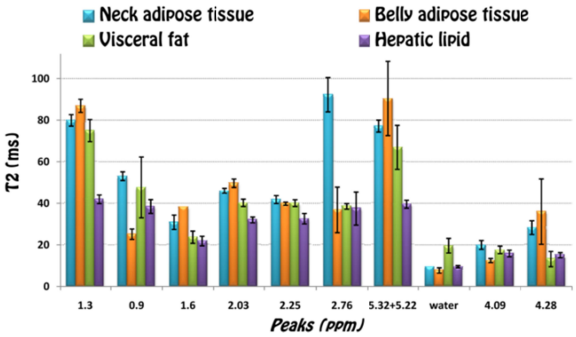

Fig 2. Mean T_2 values and SE of the ten main resonances estimated in adipose tissues and liver.

Results: In Fig.1, Anatomical MR images displaying fat pads at neck (A) and lower belly (B), visceral fat (C), and liver (D) and representative spectra at TE=12ms from these four compartments. Typically ten lipid resonances could be resolved. As shown in Fig. 2, T_2 values of individual peaks differed in various adipose tissues and liver. MRS derived parameters characterizing the fat composition in the four fatty tissues are shown in Figure3. As expected, the lipid mass fraction in the liver is significantly lower than in adipose tissues(~0.2 in liver vs. >0.75 in adipose tissues). The fraction of saturated lipids was significantly higher in belly adipose tissue than the other three compartments. Visceral fat showed a distinctly higher fraction of polyunsaturated lipids, while the fraction of monounsaturated lipids was found to be low in belly adipose tissue when compared to other lipid deposits.

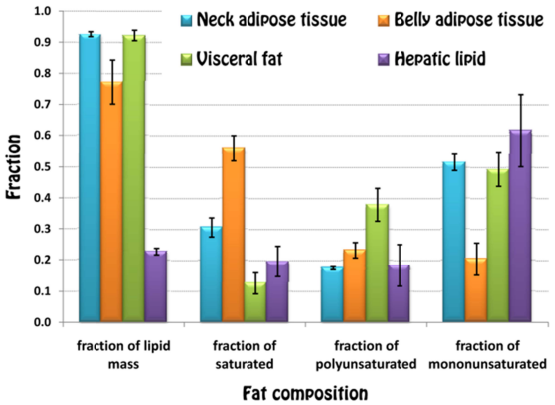

Fig 3. Mean levels and SE of fat content and composition estimated in adipose tissues and liver.

Discussion and conclusion:
The present study demonstrates that in vivo ^{1}H MRS can be an effective method to non-invasively detect accumulation of fat in adipose tissues and liver as well as potentially assess the fat composition. This has attracted great research interest over the last few years, owing to the relevance of lipid metabolism in relation to insulin sensitivity, diabetes, and obesity. The four lipid compartments studied were found to be characterized by specific lipid content/lipid composition profiles reflecting their different metabolic role. Being able to carry out such studies in mice is attractive in view of the many transgenic lines available for mechanistic studies. An attractive application is the monitoring of changes in fat content and composition within the various compartments in response to diet, exercise, and disease.

References:

1. Frayn K. N., P. Arner, H. Yki-Jarvinen. 2006. Fatty acid metabolism in adipose tissue, muscle and liver in health and disease. *Essays Biochem*. **42**: 89-103.
2. Strobel K., J. van den Hoff, J. Pietzsch. 2008. Localized proton magnetic resonance spectroscopy of lipids in adipose tissue at high spatial resolution in mice in vivo. *Journal of Lipid Research*. **49**: 473-80.
3. Mosconi E., M. Fontanella, D. M. Sima, S. Van Huffel, S. Fiorini, A. Sbarbati, P. Marzola. 2011. Investigation of adipose tissues in Zucker rats using in vivo and ex vivo magnetic resonance spectroscopy. *J Lipid Res*. **52**: 330-6.