Effects of a high-fat diet on multiple organ systems in mice: a MRI and MRS study

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Introduction: Nearly ¾ of the US population is currently overweight or obese [1]. Obesity contributes to numerous pathologies, such as cardiovascular diseases, diabetes, cancer [2] and osteoarthritis [3]. Body mass index is very popular to sort people into overweight, obese and extremely obese classes, but is not always accurate. Recent, more adapted methods are based on measurements of body and tissue fat contents by ultrasound, computed tomography or magnetic resonance imaging (MRI). This project shows the efficacy of such a technique (i.e. MRI and MR spectroscopy) to determine whole body fat volume, adipose tissue distribution and affected cardiac functions in mice fed a high-fat diet compared to normal mice.

Material and methods: 20-week old mice fed a high-fat diet (n = 20) or a normal diet (n = 20) were imaged using a 7 Tesla Bruker BioSpin system. Whole body coronal images were obtained with a spin-echo method, the addition of a frequency-selective saturation pulse allowing the acquisition of "water-suppressed" datasets. Cardiac slices were acquired through the short axis of the left ventricle using a cine-MR technique, ten frames per heart cycle. Cardiac 1H spectroscopy data were acquired in a 8 mm^3 voxel positioned across the septum, using a point-resolved spectroscopy method and VAPOR water suppression scheme. Knee images were obtained using a FLASH scheme to acquire 0.5mm-thick sagittal slices across the knee joint. To evaluate the distribution of adipose tissue throughout the whole body and in the knee joint, a semi-automatic thresholding method was implemented to select and count the "fat" pixels from the water-suppressed images. To evaluate cardiac function, the stroke volume, ejection fraction, total heart volume and average wall thickness were assessed from the cardiac MR images. Finally, cardiac contents in taurine, choline, carnitine, total creatine and lipids were obtained from phased, calibrated and integrated cardiac spectra.

Results: High-fat diet mice had slightly hypertrophied hearts, with thicker walls and a reduced ejection fraction. The percent body fat of the fat animals was twice as high as the one from the lean mice (36.7 ± 2.7 % and 14.8 ± 1.1 %, respectively) and correlated with the body weight. Our semi-automated thresholding method allowed us to determine these percent body fats in less than 10 seconds. Both the knee and the heart tissue presented higher lipid contents in the fat animals. The infrapatellar knee fat pad of these mice had a size of 0.68 mm^3 whereas lean animals had an average fat pad of 0.39 mm^3 in size. In conclusion, MRI and MRS allowed us to localize and measure *in vivo* the fat contents of several organ systems, and show the effects of a high-fat diet on cardiac function and joints.

[1] National Health and Nutrition Examination Survey, 2005-2006
[2] J.M. Rutkowski, K.E. Davis and P.E. Scherer, FEBS journal 276: 5738 (2009)
[3] D.M. Okay et al., Prim Care Clin Office Pract 36: 379 (2009)

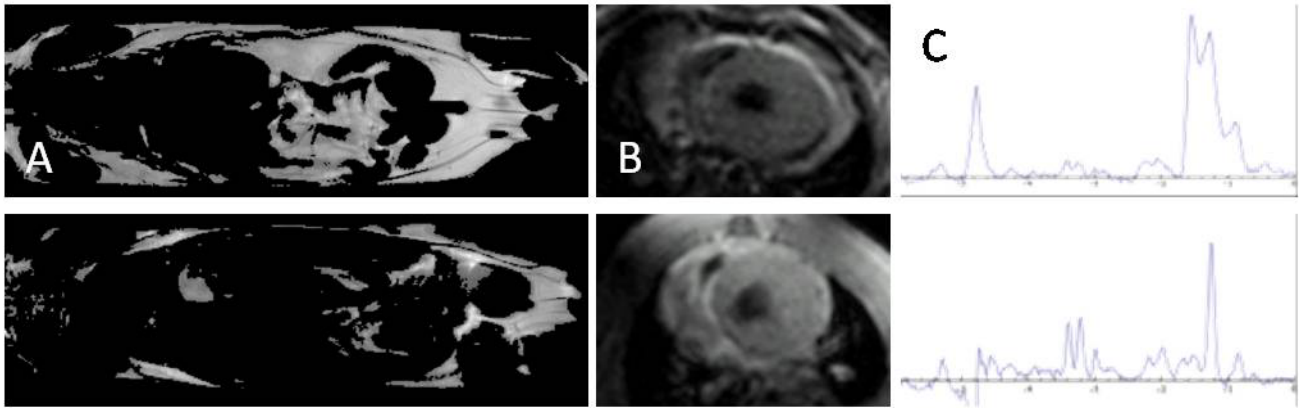

Figure 1: Thresholded coronal "fat" images (A), cardiac image (B) and cardiac 1H spectrum (C) representative of a fat and lean animal (top and bottom row, respectively).