A comphrehensive fat composition measurements in mice In vivo with High Field MR Systems

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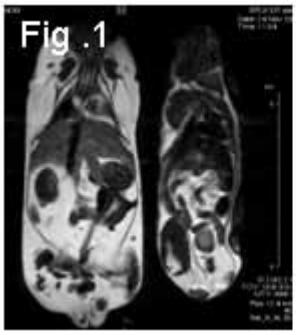
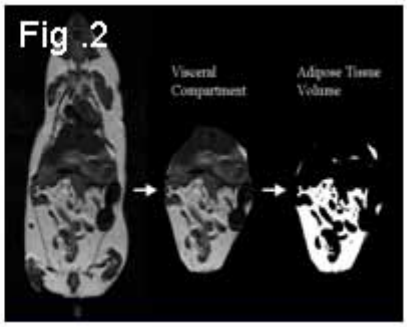
Introduction: Excess bodyweight is among the highest risk factors contributing to the overall burden of disease, in particular to heart disease, diabetes and cancer. Currently, 1.1 billion adults and 10% of children worldwide are classified as overweight or obese. Animal models, especially mice, are widely used in medical research for studying obesity to better understand the disease and its related complications, and response to treatment. While a direct result of obesity is weight gain due to accumulation of adipose tissue throughout the body, fat deposition in liver is important because it is actively involved in fatty acid metabolism. Also, intramyocellular lipid (IMCL) has been frequently linked to insulin resistance (IR) in obese patients. Non invasive measurements that include a comprehensive profile of fat, including total body fat, visceral, liver fat and IMCL should provide a more complete insight into the involvement of fat in obesity. We report a non-invasive study with such a comprehensive fat profile for lean and transgenic obese mice using MRI and MRS techniques.

Methods: Experiments were conducted on a 9.4-T/31-cm Bruker Biospec MR scanner. Whole body composition and compartmental adipose tissue volume were measured using a whole body fast spin echo (FSE) imaging sequence and liver fat and IMCL with localized proton spectroscopy (PRESS). The relevant scan parameters were as follows. FSE: TR/TE=2000/17.3msec, ETL=4, FOV=10cm, 16 slices, slice thickness=1mm (20% gap), NSA=2; SVS (PRESS) TR/TE=2-5sec/7ms, 1uliter voxel, NSA=16 (liver)/256-512(IMCL). Obese mice (ob/ob) (n= 4) and lean wild type C57 mice (n=4) fed with normal chow were anesthetized with 1.5% isofluorane using a nose cone during imaging. The various adipose tissue volumes, such as visceral and subcutaneous, were obtained with image segmentation of MR images. Adipose fraction: total adipose volume / total body volume; Visceral adipose tissue fraction: visceral adipose volume / total adipose volume.

Results: Typical whole body MR images of an obese mouse and a lean mouse in coronal orientation are shown in Figure 1, which reveal clearly the global distribution of adipose tissue in the ob/ob and lean C57 mice. From the 3-dimensional MR images, adipose tissue volumes in various compartments, were determined through image based analysis schematically as shown in figure 2. The results of the study were summarized as follows, the body size, adipose fraction, visceral adipose fraction, and liver fat content of ob/ob, and lean mice (in parentheses) were: 55.8+/-8.5cc (21.0+/-2.6cc), 68.5+/-5.3% (13.5+/-5.9%), 33.3+/-1.7% (55.6+/-8.7%), and 41.7+/-5.7% (1.8%+/-2.2%), respectively. The IMCL peak in the resulting spectrum was found to be 60% higher than the creatine peak for ob/ob mice, while -30% for lean mice. Though the liver fat content and IMCL were low in lean mice, both lipid signals were detectable with MRS.

Conclusions: An MR based assay has been implemented to provide a comprehensive characterization of body fat composition. A valuable set of body composition parameters have been obtained from both lean and ob/ob mice. These readouts, total fat volume, visceral volume, liver fat content, IMCL, etc. are not easily accessible from a living animal with other conventional measurement techniques. A more complete characterization of the body fat changes in progression of obesity and response to various therapeutic agents is now possible in the same animal.





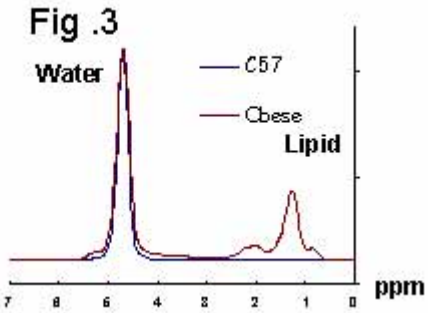


Figure 1: Global distribution of adipose tissue (high signal regions) in the body of an obese (left) and a lean mouse (right). Figure 2: A schematic showing various steps (adipose tissue compartmentalization and fat tissue identification) involved in the determination of visceral fat volume from a MRI image. In the example, the total adipose tissue volumes were found to be 64.9cc and 29.4cc respectively with corresponding visceral fraction of 0.63 and 0.33. Figure 3: Typical localized mouse liver spectra from an obese and lean mouse.