Identification of Brown Adipose Tissue in Mice Using IDEAL Fat-Water MRI

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Introduction – Studies in rodents have suggested brown adipose tissue (BAT) as a possible regulator of energy balance and obesity, but the underlying biological mechanisms remain unknown [1]. This link has raised renewed interest of BAT in human obesity research [2, 3]. Whereas white adipose tissue (WAT) is primarily a lipid storage reservoir, BAT is involved in thermogenesis, is characterized by smaller lipid droplets, and has a higher energy turnover. Studies of human BAT are nearly non-existent due to the lack of reliable detection techniques and the presence of BAT in very small quantities *in vivo*. Furthermore, BAT is often in a mixture with WAT *in vivo*. Recently, a spin-echo based three-point Dixon approach has been used to identify interscapular BAT in rats [4]. In this work, we use the chemical-shift IDEAL gradient-echo method [5], which facilitates rapid data acquisition and robust decomposition of fat (F) and water (W) signals, as well as the computation of an accurate fat-signal fraction $F/(F+W)$ on a per-voxel basis. We investigate the use of the IDEAL fat-signal fraction to differentiate BAT and WAT, and hypothesize that the fat-signal fraction will be lower in BAT than in WAT. Results from excised tissue and whole-mice are presented.

Methods – MRI experiments were performed on a GE 3 Tesla scanner with a wrist coil. Fat-water decomposition modeled lipid with a primary peak at -440 Hz (aliphatic spins) relative to water as well as three other smaller fat peaks (e.g. multi-peak IDEAL) [6]. Samples of excised BAT and WAT from mice were first collected (Fig. 1a). A spoiled-gradient-echo IDEAL pulse sequence was used with: 0.6 mm isotropic voxel, BW = ±125 kHz, flip angle = 5° to minimize T1-bias in the fat-signal fraction [7], TR = 10 ms, and TE = {2.1, 2.8, 3.5} ms. The same imaging parameters were then used to study four whole-mice (two 4-weeks-old juveniles, two 12-weeks-old adults). Imaging time for the mice was approximately 10 minutes.

Results – Fig. 1 illustrates results from the excised tissue samples. The two vials of BAT have markedly lower signal intensity in the reconstructed fat image (Fig. 1b, arrows) in comparison to the WAT samples. Figs. 1c and 1d show clear differentiation of BAT and WAT based on the quantitative fat-signal fraction map, with BAT's lower values indicative of their decreased lipid content. The average fat-signal fractions for the four samples were: 0.92 (WAT), 0.51 (BAT), 0.93 (WAT), and 0.62 (BAT). Note that the BAT samples have greater variability in their fat-signal fractions, nearly three to four-fold than that of the WAT samples. Nonetheless, the two are both visually (Figs. 1a, b) and quantitatively (Figs. 1c, d) distinguishable.

Fig. 2 illustrates results from whole mice. A coronal slice highlights the interscapular BAT (Fig 2a: red contours) in each animal. Fig. 2b shows axial reformats of the interscapular BAT along the dorsal aspects of the animals. The same color map is used from Fig. 1c. The heterogeneous appearance of BAT is apparent. The BAT in mouse #2 is surrounded by an evident layer of WAT. Note in Fig. 2b that the mean BAT fat-signal fractions from adult mouse #1 (0.64) and #2 (0.52) (top row) are approximately 10-15% *greater* than that of juvenile mouse #3 (0.42) and #4 (0.39) (bottom row). This is indicative of the juvenile's higher metabolic activity and energy expenditure in thermogenesis and is expected due to the juvenile's larger surface/volume ratio. Thus, juvenile BAT contains less fat content. The interscapular BAT volumes for mice #1-4 were about 402, 396, 381, and 103 mm^3, respectively. Fig. 2c is a superposition of regional fat-signal fractions and anatomy from mouse #1, identifying perirenal (top) and intercostal/thoracic (bottom) BAT sites.

Fig. 1
(a) Excised WAT and BAT.

(b) Reconstructed fat image. Arrows highlight the two BAT samples.

(c, d) Fat-signal fractions.

Discussion – This work has demonstrated that IDEAL-MRI provides a rapid and sensitive mechanism for identifying BAT *in vivo*. BAT from excised tissues and *in vivo* were found to have a fat-signal fraction range of 39-62%, which can be easily distinguished from more lipid-rich WAT. This non-invasive approach will be attractive in studies to better understand BAT's biological role, as it potentially allows serial tracking of BAT depots in animals without requiring sacrifice. Additional work is ongoing to further validate this work against cryosection in mice, and the potential for studying BAT in humans remains to be investigated. In circumstances where fat has infiltrated into organs and skeletal muscles such as in hepatic steatosis, the regional fat-signal fractions may be similar to the range occupied by BAT. However, false-positive identification of BAT can be minimized by corresponding with knowledge of several common BAT sites (neck, perirenal, periaortic, intercostal) in animals and humans [2].

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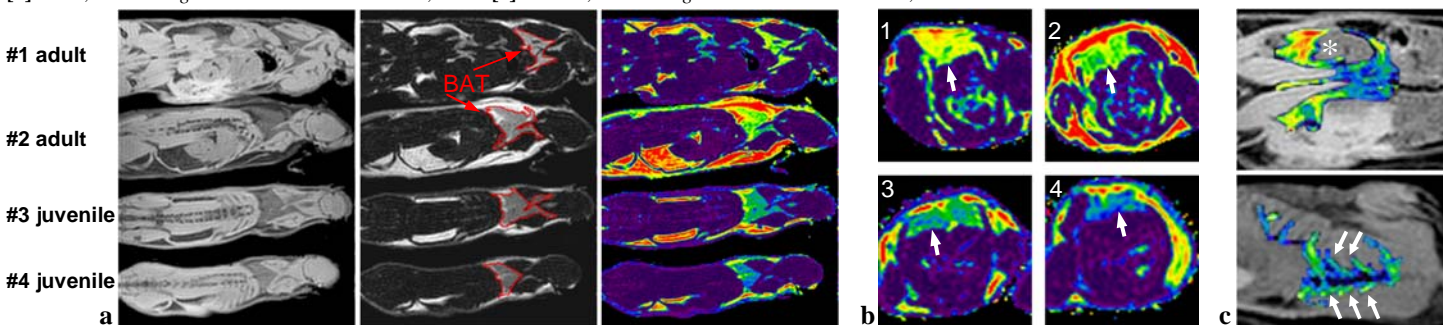
Fig. 2 – (a) Water, fat, and fat-signal fraction images. (b) Axial fat-signal fraction. Red contours in fat image in (a) and arrows in (b) highlight the interscapular BAT depot. The size of this depot varied from 103 mm^3 in mouse #1 to 402 mm^3 in mouse #4. (c) Perirenal BAT (* = kidney) and intercostal (arrows) BAT between ribs.