

T_2^* from fat-water MRI is sensitive to local adipose tissue inflammatory changes in a diet-induced obesity mouse model at 15T

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Introduction

Quantitative fat-water MRI (FWMRI) can assess adipose tissue (AT) distribution in obesity, which is linked to numerous health risks such as insulin resistance (IR)¹. In addition to cellular expansion, AT is also known to undergo complex metabolic and endocrine changes in association with chronic inflammation such as macrophage infiltration². Adipocyte iron overload in obesity has also been reported³, which is associated with IR⁴. In this work, we investigated the potential of T_2^* estimates from quantitative FWMRI, which are normally used to improve fat-water separation, to be sensitive to AT inflammatory changes in an established diet-induced obesity mouse model³. Quantitative FWMRI T_2^* may hold the promise of a non-invasive metric capable of tracking AT dysfunction in obesity over time.

Methods

Male C57BL/6J wild type mice at 8 weeks of age were placed on low fat diet (LFD, 10% kcal from fat, N=3) or high fat diet (HFD; 60% kcal from fat, N=3). Dietary iron was controlled in both LFD and HFD. Food was purchased from Research Diets (New Brunswick, NJ, USA). Mice had free access to food and water.

MRI was performed at baseline, 4, and 8 weeks after diet placement. Imaging was performed on a 15.2T Bruker Biospec horizontal bore scanner. A 3D multi GRE image with slab excitation was acquired on each mouse using the following parameters: 128×128×32, FOV = 32×32×48 mm³, number of acquisitions = 2, FA = 5°, echoes = 12, TE/ΔTE = 1.2/0.78 ms, BW = 500 kHz, and TR = 50 ms.

All images were processed using a recently proposed 3D fat-water separation algorithm⁵. Employing a 9 peak model of the lipid signal, the algorithm outputs a water image, a fat image, a single component T_2^* map, and an off-resonance map. The water and fat images can then be combined to produce a fat signal fraction (FSF) map. In this preliminary analysis, we focused on perirenal AT. ROIs around both kidneys were first identified on the magnitude images. Voxels with a value greater than 90% on the FSF maps were identified and their corresponding T_2^* values were recorded.

Results and Discussion

Fig. 1 shows sample magnitude images and FSF maps of LFD and HFD mice at 8 weeks after start of diet. It is clear that the AT body fraction increases dramatically in the HFD mice compared with LFD mice. Arrows mark the general perirenal AT regions used in this analysis. Fig. 2 shows normalized T_2^* histograms of perirenal AT in LFD and HFD mice at 4 and 8 weeks after start of diet. Voxels from all mice in their respective diet group were pooled together at each time point. The results suggest a non-Gaussian distribution for AT T_2^* values. Not shown are the histograms at baseline, which were indistinguishable between the HFD and LFD mice. The T_2^* histograms from LFD mice at 4 and 8 weeks do not show appreciable differences (LFD_{4wk} = 5.6±0.8 ms, LFD_{8wk} = 5.1±0.9 ms). In comparison, the T_2^* histograms from HFD mice at 4 and 8 weeks show a shift to higher T_2^* values relative to LFD mice. There is also an increase in T_2^* values between 4 and 8 weeks (HFD_{4wk} = 6.7±0.9 ms, HFD_{8wk} = 7.6±0.5 ms).

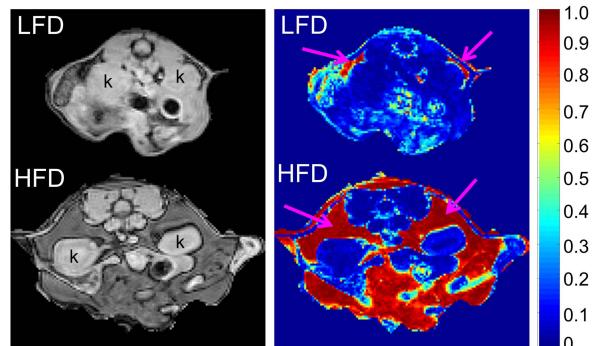


Fig 1. Sample magnitude images and FSF maps of LFD and HFD mice at 8 weeks after diet. Kidneys are labeled in magnitude images with 'k' and perirenal AT is marked with arrows on FSF map.

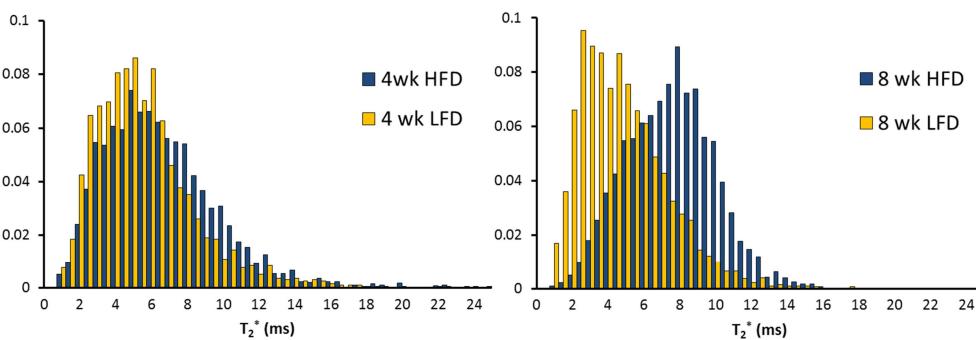


Fig 2. Normalized T_2^* histograms of perirenal AT in LFD and HFD mice at 4 and 8 weeks after diet.

We hypothesize that the changes in T_2^* grossly reflect the complex changes in AT due to obesity which include increased adipocyte size, macrophage infiltration, and variations in intracellular iron content³. While we expected increased adipocyte iron in HFD mice³, T_2^* values actually rose with time. However, the authors in Ref. 3 only reported results after a HFD of 16 weeks and the time course of iron overload is not currently known. This study is ongoing and data will be collected at 12 and 16 weeks after diet as well as repeating this protocol at 7T.

Conclusion

Increased T_2^* values were observed 8 weeks after start of HFD in perirenal AT of obese mice relative to normal-weight mice. Although further work is needed to understand this T_2^* change, quantitative FWMRI T_2^* measurement shows potential for longitudinal non-invasive assessment of AT dysfunction in obesity.

References: 1. Schaffer JE, *Curr Opin Lipidol*, **14**:281 (2003). 2. Weisberg SP, et al, *J Clin Invest*, **112**:1796 (2003). 3. Orr JS, et al, *Diabetes*, In Press (2013). 4. Gabrielsen JS, et al, *JCI*, **122**:3529 (2012). 5. Berglund J, et al, *MRM*, **67**:1684 (2012). **Acknowledgements:** NIH T32 EB001628 and R21DK095456.

Comparison between LFD and HFD T_2^* is confounded by differences in AT size. LFD mice AT depots are markedly smaller and may be more vulnerable to boundary effects and bias towards shorter T_2^* values. Moreover, shorter T_2^* values expected at 15 T may lead to erroneous T_2^* estimates from fat-water separation. Correction for such errors needs to be explored. In this initial examination, only perirenal AT voxels with FSF >90% were analyzed. Lower FSF voxels (<90%) and other AT locations need to be analyzed to confirm the pattern reported here.