Comparing Brown Adipose Tissue in Infants and Teenagers by Chemical-Shift Water-Fat MRI

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Target Audience – This work is relevant to investigators surveying applications of water-fat MRI and researchers engaged in obesity-related studies.

Purpose – PET/CT studies in adults have shown an inverse association between age and body adiposity vs. the presence of **brown adipose tissue (BAT)**. Overweight subjects with high body-mass-indices (BMI) typically do not exhibit BAT uptake of 18-FDG in comparison to leaner subjects. Younger subjects also exhibit greater prevalence of tissue uptake. Whereas the detection of BAT by PET/CT is dependent on tissue function and 18-FDG uptake, the intrinsic morphological differences between BAT and **white adipose tissue (WAT)** give rise to **fat-signal fraction (FF)** and T_2^* variations that can be jointly detected by chemical-shift water-fat MRI. FF can reflect the relative amount of triglycerides present in BAT [1] while T_2^* can reflect the level of blood oxygenation and tissue perfusion [2]. Based on previous findings that BAT FF and T_2^* values are significantly lower in lean vs. obese mice [3], the purpose of this work was to determine whether such trends can be similarly observed in lean and overweight teenagers. A second goal was to compare BAT from water-fat MRI in infants and teenagers.

Methods – Cohort: 9 infants (2M, 7F, mean age: 1.5 months, age range: 0 to 4.2 months) and 18 teenagers (17M, 1F, mean age: 12.5 years, age range: 9.7 to 15.2 years) participated. The teenagers were further divided into two sub-groups (lean, average BMI: 18.3±2.1 kg/m^2 vs. overweight, average BMI: 26.6±4.7 kg/m^2) based on a BMI stratification at the 85th percentile.

– Imaging: MRIs were performed on a Philips 3T system (Achieva R3.2). A research mDIXON water-fat sequence was utilized. Setup for the 3D spoiled-gradient-echo sequence was: supine, coronal or axial acquisition, TR=13-16msec, first TE=1.2–1.4msec, ΔTE=1.2msec, 6 echoes, non-flyback readouts, 1 mm isotropic voxels, flip angle=3°, bandwidth=1.3 kHz/pixel, and SENSE×2. Scan time was 2-3 minutes in infants and 5-7 minutes in teenagers while keeping a 1 mm resolution. Typical R/L FOV in the infants was 15-20 cm and 40+ cm in the teenagers to fully encompass the shoulders. An 8-ch head coil was used in the infants and a 16-ch torso array was used in the teenagers. mDIXON employed a seven-peak spectral model of fat. No additional strategies were used to stimulate BAT, such as cooling or drugs. Infants were not sedated; they were bottle-fed prior to MRI and swaddled. Teenagers were awake.

– Analysis: Image analysis was performed with SliceOmatic software to compute FF and T_2^* values from the bilateral adipose tissue depots within the supraclavicular fossa. Measurements are reflective of the relative amount of BAT within the fat pad. If the fat pad consists mostly of triglyceride-rich WAT adipocytes, higher FF values would be expected. Conversely, if it is abundant with BAT, lower FF values would be anticipated. Similar arguments can be made on the basis of T_2^* and BAT activity. In SliceOmatic, Regions-of-Interests (ROIs) were drawn on water/fat/out-of-phase series using the "Region Growing" tool followed by an "Erode" procedure to minimize partial volume edge voxels. Blood vessels and muscles were thus excluded. The ROIs were then transferred to the FF and T_2^* maps for quantification.

Results – Fig. 1 scatter plots show lower BAT FFs in infants than teenagers; T_2^* values were similar and not statistically different. FFs and T_2^* values were statistically lower in the lean teenagers than their overweight counterparts. Fig. 2 provides representative images. Two infants are shown, one with a weight percentile of 10% (Fig. 2A-B), and the other with a weight percentile of 61% (Fig. 2C-D). The latter has significantly greater subcutaneous WAT. Matching outlines highlight the supraclavicular BAT depots. These outlines are for illustration only and are not the ROIs drawn with SliceOmatic. Results from two teenagers are also shown, one lean (Fig. 2E-F) and one overweight (Fig. 2G-H). BAT depots in the lean teenager are characterized by noticeably lower FF and T_2^* values. Note in the overweight subject that BAT appears nearly indistinguishable from WAT on both FF and T_2^* maps.

Discussion – The lower proportion of fat in brown adipocytes, coupled with a higher degree of blood perfusion during metabolic activity, likely contributes to the overall reduction of FF and T_2^* values of the tissue in comparison to triglyceride-rich WAT. The present observations that BAT FF and T_2^* values are lower in lean than overweight teenagers reinforce PET/CT reports that BAT is inversely related to body adiposity. We also speculate that BAT was metabolically active in all of the infants and in the sub-group of lean teenagers. In contrast, we suspect that BAT was non-functional in the sub-group of overweight teenagers. These speculations support the notion that prolonged BAT inactivity leads to an accumulation of triglycerides and an enlargement of intracellular fat vacuoles, thereby causing the tissue to mimic a WAT phenotype. It is also plausible that the density of BAT within the supraclavicular fossa of overweight subjects is low. Small clusters of a few brown adipocytes can become over-ridden by WAT adipocytes, leading to partial-volume effects and low detectability.

Fig.1: Comparison of **(A)** fat-signal fraction and **(B)** T_2^* values between infants (n=9) and teenagers (n=18). **(C, D)** Further stratifying the teenagers into two sub-groups based on the 85th BMI percentile, similar plots are shown.
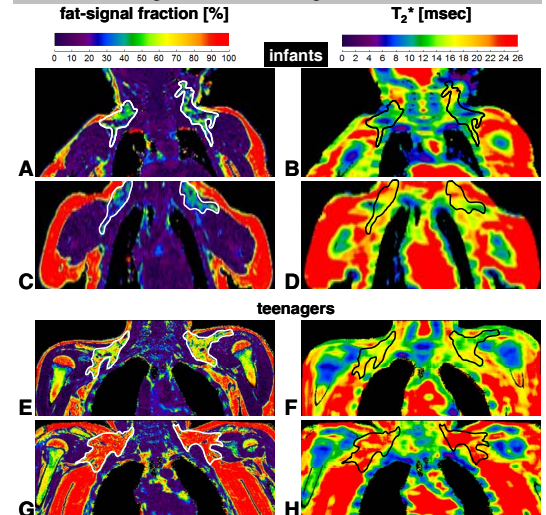
Fig.2: Representative fat-signal fraction **(A, C, E, G)** and T_2^* **(B, D, F, H)** maps from two infants **(A-D)** and two teenagers **(E-H)**. One infant has a low weight percentile of 10% **(A, B)**, while the other has a higher weight percentile of 61% **(C, D)**. Bilateral BAT depots are similarly outlined in white and black traces. These traces are for illustration only and do not represent the ROIs drawn using SliceOmatic. Lean **(E, F)** and overweight teenager **(G, H)** highlight difference in fat-signal fraction and T_2^* within the supraclavicular BAT depot. It is markedly evident that BAT in the lean subject is characterized by lower values.

Conclusion – PET/CT remains at present the preferred modality for investigating metabolically active BAT. There is a paucity of BAT data in pediatric populations. This work has offered evidence that MRI is capable of safely characterizing BAT in vivo, particularly in infants. The intrinsic differences between BAT and WAT, and more importantly the observation that there exists inter-subject BAT variations which give rise to FF- and T_2^*-based signal contrasts, promote the use of MRI to comparatively study BAT cross-sectionally and longitudinally.

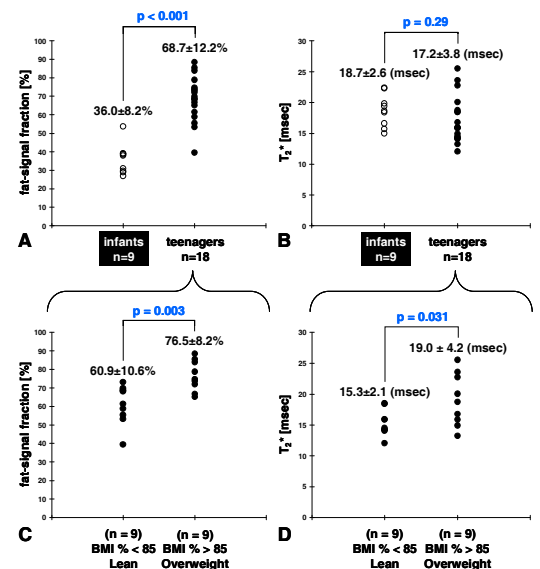**[1]** Hu HH, et al. *JMRI* 2012; 35:938-942. **[2]** Khanna A & Branca RT. *MRM* 2012; 68:1285-1290. **[3]** Hu HH, et al. *MRI* 2012; 30:323-329.