Detection of Brown Adipose Tissue in an Adult Human Using Fat-Water MRI with Validation by Cold-activated PET

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Purpose: The objective of this research is to develop and validate MRI methods for characterizing human brown adipose tissue (BAT), with a focus on differentiating between BAT and white adipose tissue (WAT) under basal and activated conditions. The current imaging method for differentiating BAT and WAT employs a combination of ^{18}F-Fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) and x-ray computed tomography (CT), which requires an undesirable radiation dose. This work is therefore important in developing MRI methods that will replace the current PET-CT methods and enable the study of BAT in many interesting cohorts of human subjects in longitudinal studies without radiation concerns.

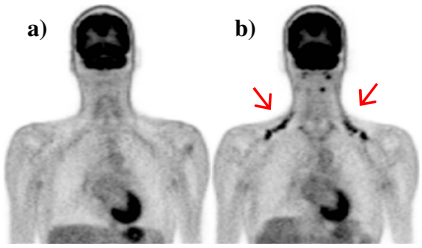

Figure 1. Cold-activation of supraclavicular BAT (red arrows) demonstrated by ^{18}F-FDG PET. Coronal single slice images show minimal 18F-FDG uptake in **a)** thermoneutral (24ºC), and **b)** cold (16ºC) scans performed on the same subject.

Methods: A healthy adult subject was scanned with both Philips Achieva 3T (Philips Healthcare, Best, Netherlands), and GE Discovery PET-CT scanners after obtaining written informed consent. Both MRI and PET-CT scans were performed twice, each scan on a separate day, once under thermoneutral conditions of 24ºC (76ºF), and again under cold conditions of 16ºC (62ºF)[1,2]. In both scenarios the subject spent 2 hours in a temperature-controlled room, with the injection of ^{18}F-FDG administered intravenously for PET-CT scans after the first hour. MRI sequences were performed using the X-tend table with the torso XL coil. Fat-Water MRI (FWMRI) was acquired using a multi-stack, multi-slice, multi-gradient echo (mFFE) acquisition with 7 stacks, 20 contiguous slices per stack. TR = 83ms, 8 echoes (4 echoes x 2 interleaves) TE1/effective ΔTE=1.024/0.779 (ms), flip angle=20º, water fat shift = 0.323 pixels, readout sampling bandwidth=1346.1Hz/pixel, axial in-plane FOV=520mm×408mm, acquired voxel size=2mmx2mmx7.5mm, with SENSE factor=3, and acquisition time=25 sec/stack. PET and CT data were acquired with the same in-plane and through-plane FOV of 0.7m×0.7m×1.1m. PET data had a matrix size of 128×128, with 9 stations, 335 slices 3.27mm thick, and an acquisition=18 minute. CT data had a matrix size of 512×512, was acquired using a helical scan with a pitch=1.675, in under one minute.

Results: Real and imaginary MR images were saved for off-line processing. Three-dimensional water/fat separation and R2* estimation based on a multi-scale whole-image optimization algorithm[3] implemented in C++ was performed for each individual slice stack. Fat was modeled using 9 peaks[4]. The first echo of each 4-echo train was discarded to avoid potential contamination of eddy current in the complex water-fat signal model. The separate 3D stacks of axial fat, water, R2* and static field off-resonance (ΔB_0) images from each table station were collated and reformatted to coronal images using MATLAB (Mathworks Inc., Natick, MA). Fat-fraction maps were used to localize the depots of interest in the supraclavicular region. The thermoneutral and cold PET scans of a 41 y.o. male, BMI = 20.6, show symmetric supraclavicular regions of enhanced uptake of ^{18}F-FDG under cold conditions **Figures 1, 2a-d**, that correspond to areas of adipose tissue (**Figure 2 e,f**). These areas of cold-activated adipose tissue have mean fat-fractions of 73.7%±1.2% (right) and 66.5%±1.9% (left) (mean±95% CI).

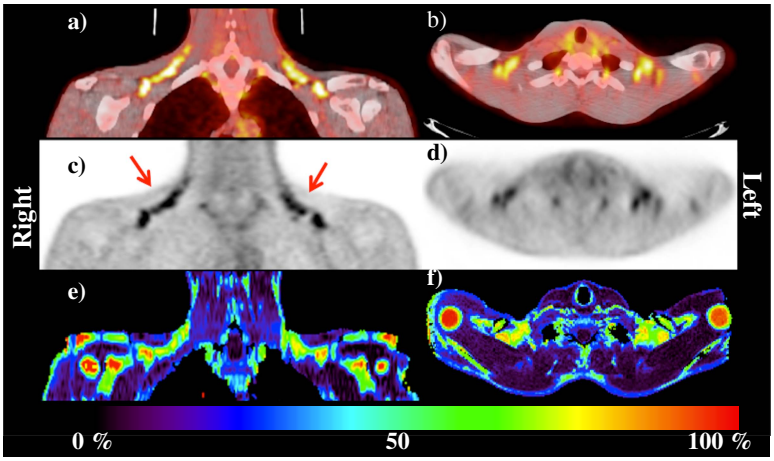

Figure 2. Fused PET-CT **(a,b)**, PET only **(c,d)**, and FWMRI-derived Fat Fraction map (with colorbar) **(e,f)** of coronal and axial slices through the shoulder region. Red arrows in **(c)** point to ^{18}F-FDG uptake into the BAT during the cold PET scan. This region corresponds with the regions of lower fat-fraction in **e)** and **f)**.

Discussion: The fat fractions of the supraclavicular AT depots identified in this study are lower than typical WAT[5,6], but similar to those previously reported for BAT in ex vivo studies in rodents[5]. These AT depots are metabolically silent on ^{18}F-FDG PET under thermoneutral, but hypermetabolic under cold conditions, consistent with the previously described properties of BAT in humans[7]. Taken together, our findings strongly suggest that these low fat fraction AT depots are indeed BAT. To the best of our knowledge, this is the first direct validation of MRI-detected BAT in an adult human using cold-activated PET. Using this approach, we can now begin to characterize the MRI properties of BAT under basal and metabolically active conditions, allowing us not only to refine our ability to distinguish BAT from WAT, but also to determine the metabolic status of BAT. Although recent studies suggest an inverse relationship between BAT and obesity[1,8], it remains unclear whether reduced BAT and/or activity promotes or results from obesity. Studying BAT in human populations of all ages with safe MRI methods for measuring properties reflecting morphology, metabolic activity and molecular composition that can distinguish BAT from WAT will provide investigators with a powerful tool with which to study BAT and its influence on body metabolism and composition.

References: [1] van Marken Lichtenbelt WD, et al. N Engl J Med 360(15); 2009. [2] Virtanen KA, et al. N Engl J Med 360(15); 2009. [3] Berglund J, et al. Magn Reson Med Feb 14. doi:10.1002/mrm.24196 [Epub ahead of print]. [4] Hamilton G, et al. NMR Biomed 24(7); 2011. [5] Hu HH, et al. JMRI 31(5); 2010. [6] Hu HH, et al. JMRI 35(4); 2012. [7] Saito M, et al. Diabetes 58(7); 2009. [8] Yoneshiro T, et al. Obesity 19(9); 2011.