Identification of brown adipose tissue using Dixon imaging in a human adult with histological confirmation.

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Introduction: There has been a resurgence of interest in human brown adipose tissue (BAT) in recent years following its identification in human adults using PET-CT [1,2]. In contrast to white adipose tissue (WAT) which is unilobular, has few mitochondria and stores fat, BAT appears multi-lobular, contains numerous mitochondria and metabolizes fat which generates heat. Enhancement of BAT activity holds promise as a therapeutic strategy for the prevention and treatment of human obesity and so there is a need for a safe imaging method to monitor the volume of brown fat. PET-CT has limitations,it only identifies metabolically active BAT, it uses ionising radiation and it is expensive. The lower fat content of BAT compared to WAT has been utilized using Dixon based MR imaging methods to visualize BAT in rodents [3], in a human infant[4] and in adult humans[5,6]. These adult human studies did not histologically confirm the BAT identified using MR. **Aim**: To identify BAT in an adult human using Dixon based MR imaging with histological and immunohistochemical confirmation of the BAT.

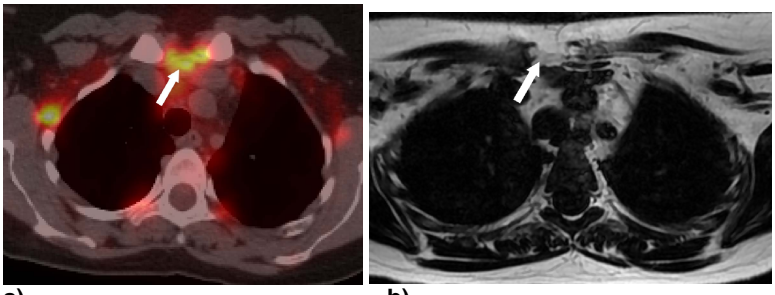
Method: A 25-year old female diagnosed with primary hyperparathyroidism underwent a ^{18}FDG PET-CT scan. This scan revealed multiple areas of high FDG uptake within suprasternal and mediastinal fat (Figure 1a), as well as the neck, supraclavicular fossae and axillae.

A 3-echo IDEAL sequence [7] was performed on a GE 3T HDxt scanner (GE Medical Systems, Milwaukee, USA) using the cardiac coil. 5mm axial images were obtained from the upper cervical to mid-thoracic level. The IDEAL sequence parameters were: TR(ms)/TE(ms)/matrix/NEX/FoV(cm)=440/10.8/320x256/3/30. This generated water-only and fat-only images. The latter were used for subsequent analysis.

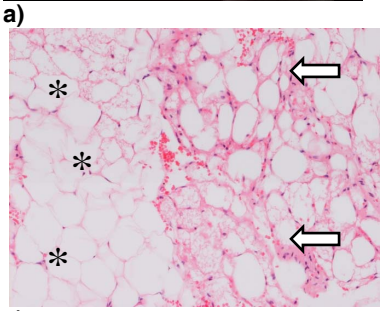
Retrospectively, the fat only MR images were registered with the PET-CT images and BAT ROIs (referred to as BAT_{retro}) were identified on the MR images corresponding to regions of high ^{18}FDG uptake on the PET-CT images. For each BAT_{retro} ROI a corresponding ROI was identified in adjacent WAT, referred to as WAT_{retro}.

Histology and immunohistochemistry were performed on tissue obtained during parathyroidectomy, corresponding with high ^{18}F-FDG uptake on the PET-CT scan and low-signal intensity on the fat-only MR scan (Figure 1).

Prospectively, 4 months later, without reference to the PET-CT scan, BAT and WAT ROIs (referred to as BAT_{prosp}/WAT_{prosp}) were identified on the fat only MR images based on signal intensity and appearance, and then compared with uptake on the PET-CT scan.



a) b)



c)

Figure 1 a) PET-CT showing high tracer uptake in mediastinum (arrow), b) fat only image showing low fat signal intensity in corresponding region (arrow) c) histological specimen from this location with BAT (⇦) and WAT (*) cells

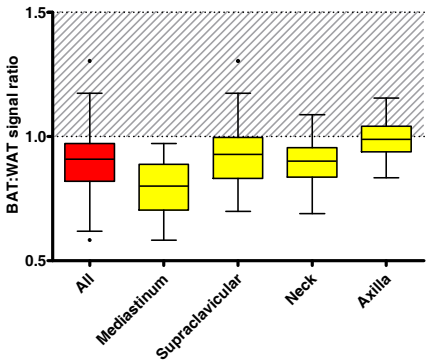


Figure 2: Variation of BAT/WAT signal ratio for a all locations (red) and with anatomical location (yellow).

Results: 111 BAT_{retro} ROIS were identified and 93 (84%) showed corresponding low signal on the MR images (Figure 1). A significant difference ($p<0.0001$) was found between the MR signal within BAT_{retro} and WAT_{retro} ROIs. The BAT_{retro} ROIs had a lower signal than surrounding adipose tissue, and were often delineated by a discrete margin. The overall BAT_{retro}:WAT_{retro} signal ratio was 0.89±0.12, varied according to anatomical location and was lowest in the mediastinum (Figure 2). Histology and immunohistochemistry obtained from the position indicated in figure 1 confirmed BAT. Prospectively, 87% of BAT_{retro} ROIs identified on the MR scans corresponded to increased areas of uptake on the PET-CT scans.

Conclusions: We report the first verification of BAT in a human adult using MR, with histological and immunohistochemical confirmation, with a significant ($p<0.0001$) differentiation between BAT and WAT signal intensity.

References: [1]Nedergaard J et al. Am J Physiol Endocrinol Metab 2007;293: E444-452. [2]Cypess AM et al. N Eng J Med 2009;360:1509-1517. [3]Hu HH et al. JMRI 2010;31: 1195-1202. [4] Hu HH et al. JMRI 2012;35:938-942. [5] Gifford A et al. Proc ISMRM 1269; 2012 [6] Renisch S et al. Proc ISMRM 4100; 2012 [7] Reeder SB et al MRM 2005;54:636–644.