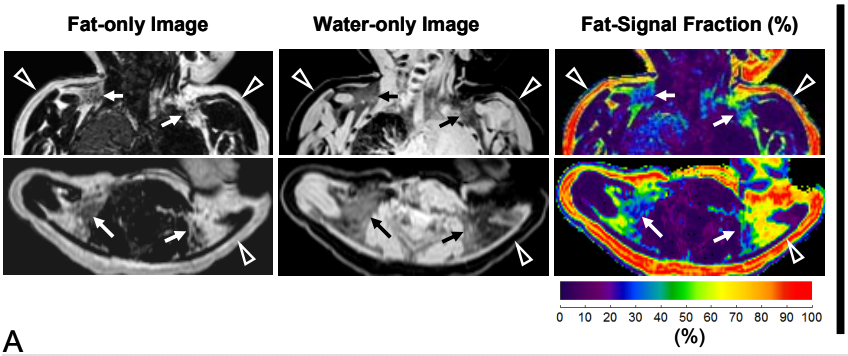
Identification of Brown Adipose Tissue in a Human Infant

Houchun Harry Hu[1,2], Jason P. Tovar[3], Zdena Pavlova[3], Thomas G. Perkins[4], and Vicente Gilsanz[1]

[1]*Radiology, Children's Hospital of Los Angeles, Los Angeles, California, United States,* [2]*Electrical Engineering, University of Southern California, Los Angeles, California, United States,* [3]*Pathology, Children's Hospital of Los Angeles, Los Angeles, California, United States,* [4]*Philips Healthcare, Cleveland, Ohio*

INTRODUCTION – Recent findings of brown adipose tissue (BAT) in adult humans by PET/CT have reinvigorated interest in the tissue's role in metabolism and obesity [1, 2]. In contrast to white adipose tissue (WAT), which functions to store fat, BAT metabolizes fat and generates heat. BAT is vascularized, rich in mitochondria, and innervated by the sympathetic nervous system, not unlike skeletal myocytes. WAT adipocytes contain a single large intracellular lipid droplet, a peripherally located nucleus, limited cytoplasm, and little intracellular and extracellular water. In contrast, BAT adipocytes are smaller, contain multiple lipid vacuoles, and have centrally located nuclei. PET/CT imaging of BAT has limitations. It is restricted to oncology patients and not applicable to the general population, particularly children, due to radiation and ethical restrictions. PET/CT can only detect metabolically active BAT that uptakes the injected radionuclide tracer. Recently, several studies have demonstrated BAT MRI in rodents by exploiting the cellular differences between BAT and WAT to generate signal contrasts based on fat-signal fraction from chemical-shift MRI [3], T1 relaxation [4], and intermolecular zero-quantum coherence spectroscopy [5]. In this work, we report the unequivocal identification of metabolically inactive BAT in a *three month-old human body* (cadaver) by MRI and CT, with confirmation by post-mortem histology. We demonstrate in this case study that the intrinsic differences between BAT and WAT morphology lends to unique complementary signal contrasts, based on fat-signal fraction in MRI, and X-ray tissue attenuation (e.g. Hounsfield Units - HU) in CT [6].

METHODS – This 95 day-old female developed severe respiratory distress a few hours after birth, followed by persistent pulmonary hypertension. A diagnosis of alveolar capillary dysplasia was confirmed. Within 48 hours after the patient was pronounced deceased, MRI, CT, and tissue biopsy procedures were performed. ***MRI:*** MRI was implemented on a 3T platform (Achieva, R2.6.3, Philips Healthcare). The head, neck, chest, and thorax regions were placed inside an eight-channel head coil. A chemical-shift 2-point 3D spoiled GRE sequence was used [7]. Imaging parameters for the coronal scan were: TR/TE1/TE2=3.9/1.4/2.5ms, full Cartesian echoes, flip angle=5°, FOV=35cm (S/I) and 17.5cm (R/L), 350×350 matrix, 2 mm overlapping slices, 2 averages, and BW=1.3 kHz/pixel. For 100 slices, the scan time was 68 sec. T1-weighted (T1w) fat (F), water (W), and fat-signal fraction maps [F/(F+W)] were generated. Additionally, adjunct non-fat-sat T1w (TR/TE: 221/9.2ms, TSE factor: 3) and T2w (TR/TE: 2406/80ms, TSE factor: 15) turbo spin echo scans were also performed. ***CT:*** A CT exam was performed (LightSpeed QX, R10.5, GE Healthcare). Acquisition mode was helical and parameters were: kVp = 120 Volts, 160 axial 2.5 mm slices, and an in-plane resolution of 0.54 mm. ***Histology:*** Supraclavicular BAT depots identified by both MRI and CT were presented to two pathologists, who then performed biopsies and extracted tissue samples for histological analysis.



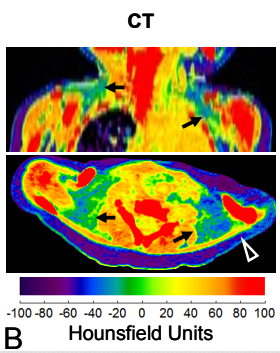


FIG. 1: (A) BAT by chemical shift MRI, illustrating bilateral BAT depots (arrows) near the neck. BAT has appreciable signal in both fat and water images. In contrast, lipid-rich WAT (arrowheads) exhibits dominant signal only in the fat image. T1-weighted fat-signal fractions show intermediate values (blue, green, yellow) for BAT, in contrast to higher values for WAT (orange, red). **(B)** On CT, WAT (dark blue, purple) exhibits more negative X-ray attenuation HU than BAT (light blue, green).

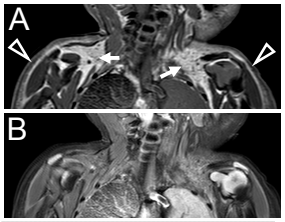


FIG. 2: (A) T1w and **(B)** T2w TSE showing high signal contrast of BAT against other tissues in the former, but not the latter.

RESULTS – Fig. 1A shows coronal and axial images from chemical-shift MRI. Arrowheads point to the layer of lipid-rich subcutaneous WAT, which exhibits high signal intensity. On the water-only image, WAT is expectedly devoid of signal. In contrast, arrows in the fat-only image point to bilateral BAT depots, adjacent to the scapula and clavical. Note that BAT exhibits intermediate gray intensities and is visible on both the fat and water images. It is hypointense to WAT in the fat-only image and hyperintense to WAT in the water-only image. In the T1w fat-signal fraction map, BAT has distinctively lower fat-water ratios **(41.9±6.25%)** than lipid-rich WAT (>90%). Fig. 1B shows CT images with colored HU. Note that the subcutaneous WAT is represented in dark blue and purple, in the range of -60 to -100 HU. In contrast, the bilateral BAT depots are distinctly visible in light blue and green **(-20.76±3.37 HU)**, suggestive of greater water content and tissue density. Fig. 2A and 2B show images from T1w and T2w TSE scans, respectively. The bilateral BAT depots are highly visible in the T1w image and appears hyperintense to WAT. On the T2w image, overall BAT tissue contrast is poor, except for a granular appearance. Fig. 3 shows a microscope slide from histology. WAT can be identified by their large lipid droplets (black arrowheads), in contrast to the BAT with their multiple lipid vacuoles and surrounding capillaries (blue arrows). In this subject, we measured a total of 17 ml of supraclavicular BAT.

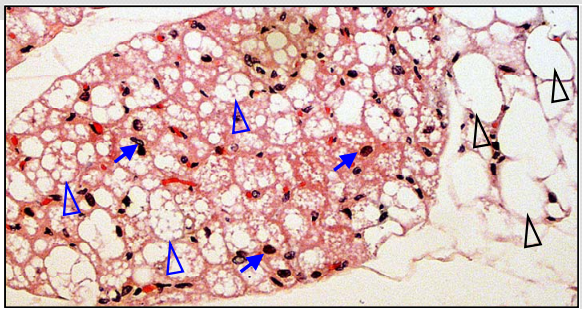


FIG. 3: Histological specimen at 10x magnification taken from the interscapular BAT depots. Black arrowheads point to the large white adipocytes each with a single intracellular vacuole of lipids, approximately 100-120 μm in size. Blue arrowheads point to brown adipocytes, with multiple intracellular lipid droplets, 25-40 μm in size. Furthermore, BAT is perfused by capillaries (blue arrows).

CONCLUSION – In this case study, we have demonstrated that BAT can occupy a signal range that is intermediate to WAT and surrounding muscle in both MRI and CT images. BAT and WAT signal contrast is visually recognizable and manifests from differences in intrinsic tissue properties. This finding supports MRI as a suitable platform and PET/CT alternative to further study BAT, especially in children where BAT is more prevalent.

REFERENCES – [1] Cannon B. Physiol Rev 2004:84:277-359. **[2]** Nedergaard J. Cell Metab 2010:11:268-272. **[3]** Hu H. JMRI 2011:34:468-473. **[4]** Hamilton G. JMRI 2011:34:468-473. **[5]** Branca R. MRM 2011:65:313-319. **[6]** Hu H. JCAT 2011:35:65-71. **[7]** Eggers H. MRM 2011:65:96-107.