

Visual identification of brown adipose tissue in adult humans using Dixon MRI

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TARGET AUDIENCE: Radiologists, endocrinologists and those with an interest in bariatric imaging.

INTRODUCTION: There is on-going interest in human brown adipose tissue (BAT) following its identification in human adults using ¹⁸F-FDG PET-CT and its potential role as a pharmacological target in the treatment of obesity. A reliable means of imaging BAT is essential to monitor response to such pharmacological stimulation. PET-CT relies on the uptake of the radioactive isotope ¹⁸F-FDG and therefore only identifies metabolically active BAT. The lower fat content of BAT compared to white adipose tissue (WAT) has been exploited using Dixon based MRI imaging methods to visualize BAT in rodents [1], in a human infant [2] and in adult humans [3]. However, a reliable means of identifying BAT prospectively in adult humans on MR has proved elusive. Based on a single case in which we also obtained immuno-histochemical confirmation of BAT, we postulated it may be possible to identify BAT in human adults by visual inspection of Dixon imaging [4].

AIM: To determine the accuracy of visually identifying BAT in adult humans on Dixon based MRI imaging, by comparison with ¹⁸F-FDG PET-CT.

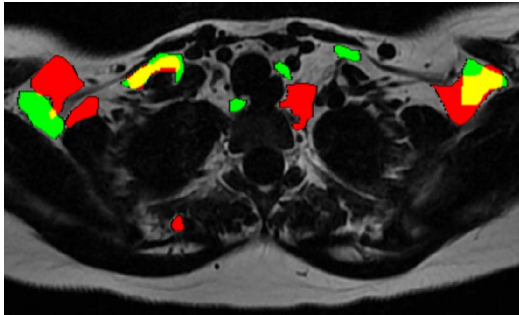


Figure 1: Colocalization of BAT_{PET} (red) and BAT_{MRI} (green), and areas of intersection (yellow).

visual identification of areas of low signal intensity with respect to WAT ('BAT_{MRI}'). BAT volume was calculated using Mirada XD (for PET) and ImageJ (for prospectively identified BAT on MR) and compared using a Bland-Altman plot. Colocalization analysis was performed using the ImageJ plugin JACoP ('Just Another Colocalization Plugin') using the technique described by Bolt *et al* [5] to assess the degree of coincidence between BAT_{PET} and BAT_{MRI} regions of interest (figure 1).

RESULTS: BAT_{MRI} underestimated BAT volume when compared with metabolically active BAT on PET, and the bias increased with larger BAT volumes ($r^2=0.21$, figure 2). No correlation between the accuracy of the technique and BMI was observed ($r^2=0.04$, figure 2). Mander's correlation coefficient describing the degree of overlap between BAT_{MRI} and BAT_{PET} (were 0=no correlation, 1=perfect correlation) was highest in volunteers with high BAT volumes ($r^2=0.36$, $P = 0.01$, figure 4).

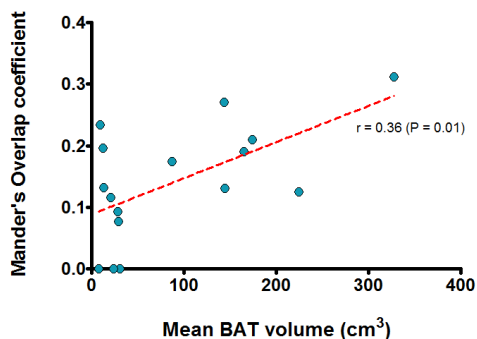


Figure 4: Scatterplot showing a positive correlation between mean BAT volume and Mander's correlation coefficient.

DISCUSSION: In volunteers with metabolically active BAT on PET-CT, visual identification of BAT tended to underestimate BAT volume (figure 2) when compared with PET, particularly in those with high BAT levels (figure 2) and females (figure 3). PET-CT is also known to underestimate BAT, as it only identifies metabolically active tissue. As the technique relies on identifying subtle difference in signal intensity between BAT and WAT one would expect MRI to be less accurate than PET-CT in individuals with low BMI, due to partial volume artefact, but no correlation was observed between BMI and the differences between each test (figure 3). Bland-Altman plots give no indication of whether BAT_{PET} and BAT_{MRI} occur in the same areas therefore the degree of correlation between BAT_{PET} and BAT_{MRI} depots was assessed using Mander's correlation coefficient; the degree of colocalization increased with increasing volumes of BAT (figure 4). The low correlation coefficients may also be due to difficulties with image registration and in part due to the relatively small difference in signal between 'brown' and 'white' fat.

CONCLUSION: Our implementation of Dixon MRI underestimates BAT volume when compared with PET-CT.

REFERENCES: [1] Hu *et al*, JMIR 2010; 31(5): 1195-1202 [2] Hu *et al*, JMIR 2012; 35(4): 938-942 [3] Holstila *et al*, Metabolism 2013; 62(8): 1189-1198 [4] Reddy *et al*, JCEM; in press [5] Bolte *et al*, J Microsc 2006; 224(3): 213-232.

METHOD: 16 volunteers were recruited on the basis of having BAT on ¹⁸F-FDG PET-CT performed for clinical reasons. Each underwent a 3-echo TSE IDEAL sequence on a GE 3T HDxt scanner (GE Medical Systems, Milwaukee, USA) using the cardiac coil. 2.5 - 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) = 440/10-7-11.1/512X512/3/30-40. This generated water-only and fat-only images, of which the latter were used for subsequent analysis.

Metabolically active BAT was identified on PET-CT on the basis of ¹⁸F-FDG uptake within fat with a standardized uptake value (SUV) >2.5 g/ml. BAT depots were delineated by semi-automatically defining isocontours set at an SUV of 2.5 g/ml around the depots ('BAT_{PET}'). PET-CT images were registered with the fat-only MR images using commercially available image fusion software (Mirada XD 4.3, Mirada Medical, Oxford, UK) to facilitate direct comparison. A single blinded observer identified areas of potential BAT on MRI by

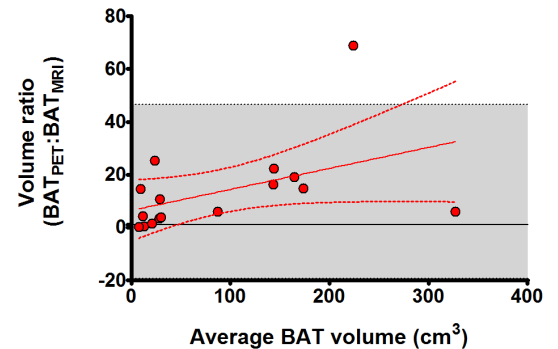


Figure 2: Bland-Altman plot with 95% confidence intervals showing ratio of BAT volume on PET (BAT_{PET}) and MRI (BAT_{MRI}).

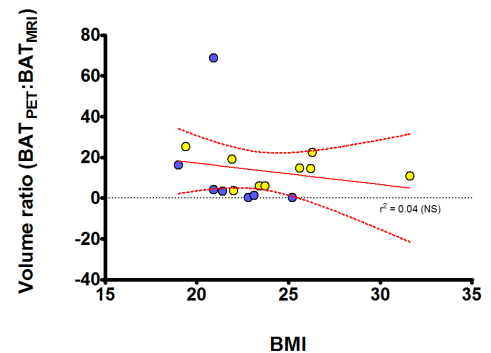


Figure 3: Difference between the ratio of BAT volume on PET (BAT_{PET}) and MRI (BAT_{MRI}). Females are plotted as yellow and males as blue.