Determinants of human brown adipose tissue prevalence and volume on $^{18}$F-FDG PET/CT scans
A retrospective analysis of 3,295 cases

TA Jones, NL Reddy, SC Wayte, O Adesanya, TM Barber, CE Hutchinson

INTRODUCTION
PET/CT studies have shown brown adipose tissue (BAT) to be far more prevalent in adult humans than previously thought. It is facultative to maintain thermal homeostasis by means of non-shivering thermogenesis. Consequently it is highly variable in both incidence and volume between and within individuals.

This retrospective analysis sought to identify determinants of BAT occurrence and volume on a large series of PET/CT scans.

METHODS
Retrospective analysis of 3,295 $^{18}$F-FDG PET/CT scans (2,685 patients) was performed. BAT deposits were segmented semi-automatically using an isocontour set at an SUV of 2.5 g/ml and volumes calculated using Mirada XD 3.4 (Mirada Medical Ltd, Oxford, UK).

Multivariate binomial logistic regression was used to identify determinants of BAT prevalence. Volume data were not normally distributed data (due to the high proportion of scans with no BAT activity) therefore non-parametric multivariate linear regression (Tobit) analysis was performed to identify determinants of BAT volume. Conventional multivariate linear regression analysis was also performed on normalised volume data (i.e. after exclusion of scans with no BAT uptake).

RESULTS

BAT prevalence
BAT prevalence was 5.3% - significantly higher in women (8.7%) than men (2.5%; OR 3.9, 95% CI 2.6-5.1; p<0.01). BAT prevalence increased the more PET/CT scans an individual underwent, increasing by 5.8% for each additional scan, plateauing at 33.3% after 6 scans.

BAT tended to occur in individuals who were younger (48.4 ± 19.6 years vs 64.2 ± 14.2 years, p<0.01) and with a lower BMI (24.3 ± 4.5 kg/m² vs 26.6 ± 5.4 kg/m²; p<0.01) than those in whom it was absent.

There was a strong inverse correlation between BAT prevalence and mean monthly temperature ($r_s$=-0.74, figure 1) and time of day ($r_s$=-0.89, p<0.01, figure 2). BAT was most prevalent in February and least prevalent in August.

Regression analysis of normalised volume data returned a model in which only age (p<0.01) and minimum temperature on the preceding day (p=0.01) were significant predictors of BAT volume.

DISCUSSION
Point prevalence of 5.3% is comparable to values reported in similar retrospective PET studies [1]. The dynamic nature of BAT means its detection on PET is opportunistic, consequently retrospective studies underestimate its true prevalence. Dedicated prospective studies suggest a prevalence of between 33% and 100% [2,3], which accords with our estimates of cumulative prevalence.

Predictors of BAT volume were similar to those for prevalence, likely due to data being skewed by the large proportion of BAT negative scans (3,210/3,295).

Some individuals with no BAT activity on PET/CT may genuinely lack BAT, and no amount of stimulation would be sufficient activate it. Therefore regression analysis of all PET scans may be inappropriate. Analysis of BAT positive scans identified only age and temperature as significant predictors of BAT volume.

CONCLUSION
Different factors may be predictive of BAT prevalence and volume on PET/CT. Large BAT volumes may require sustained exposure to stimuli to induce hyperplasia, whereas prevalence is likely a more dynamic phenomenon reflecting activation state.

REFERENCES

Statistical advice by Ric Crossman is gratefully acknowledged.