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RESEARCH ARTICLE

Determinants of Physiologic ^{18}F-FDG Uptake in Brown Adipose Tissue in Sequential PET/CT Examinations

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Abstract

Purpose: The aim of this study was to assess independent predictors of 2-deoxy-2-[^{18}F]fluoro-D-glucose (^{18}F-FDG) uptake in brown adipose tissue (BAT) in patients undergoing repeated positron emission tomography (PET)/computed tomography (CT) scans.

Procedures: Eight hundred forty-eight (mean age 50.9±16 years) patients in whom PET/CT scan was repeated (mean interval 5±1.5 months) constituted the study group. ^{18}F-FDG uptake in characteristic areas of BAT, with CT density of adipose tissue, greater than background soft-tissue activity was considered as evidence of BAT uptake. Both distribution and maximum standardized uptake values (SUVmax) were registered. Clinical and anamnestic data were collected for each patient.

Results: ^{18}F-FDG uptake in BAT was present in 8.6% patients at first scan. Independent predictors of presence of uptake were age (younger), gender (female), body mass index (lower), and maximum outdoor temperature (lower). Age was the only independent predictor of BAT ^{18}F-FDG uptake distribution, while SUVmax was related to both age and outdoor temperature. Independent determinants of persistence of BAT ^{18}F-FDG uptake at second PET/CT were outdoor temperature at time of second scan and extension of metabolically active BAT at first scan.

Conclusions: Age, body mass index, and outdoor temperature are significant determinants of BAT evidence at ^{18}F-FDG PET/CT. Moreover, extension of BAT and outdoor temperature are the strongest determinants of persistence of BAT evidence on ^{18}F-FDG PET/CT in repeated scan.

Key words: Brown adipose tissue, ^{18}F-FDG, PET/CT

Introduction

Increased 2-deoxy-2-[^{18}F]fluoro-D-glucose (^{18}F-FDG) uptake in brown adipose tissue (BAT) may be seen on positron emission tomography (PET) imaging [1–5], and the development of PET/computed tomography (CT) has allowed better localization and recognition of ^{18}F-FDG in metabolically active BAT. The presence and intensity of ^{18}F-FDG uptake in BAT have been related to several factors: temperature, gender, various agents (beta-blockers, ephedrine, nicotine, and others), and interventions [4–18].

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Recently, two large studies [5, 18] reported clear relationships between ^{18}F-FDG uptake in BAT and female gender, temperature, and body mass index (BMI). The influence of both BMI and temperature on tracer uptake has been further confirmed by an interventional study in healthy men exposed to mild cold [16]. Moreover, it has been clearly demonstrated that such areas of ^{18}F-FDG uptake in healthy adult subjects indeed had histological features of BAT and expresses mRNA and proteins that distinguish it from white adipose tissue [17].

In this study, patients undergoing two ^{18}F-FDG PET/CT scans with an interval of at least 4 months were retrospectively analyzed in order to investigate the variation of ^{18}F-FDG BAT uptake in the same subjects.

Materials and Methods

Patients

Among all patients who underwent ^{18}F-FDG PET/CT scan from January to December 2008, only those undergoing a second scan at least 4 months and no later than 8 months from the first scan were selected; moreover, only patients without any change in therapy or other medical or surgical intervention between the two studies were selected. A total of 848 patients (mean age, 50.9±16 years; median age 53.5 years; age range 17–85 years; 415 females) constituted the study group. The mean interval between the two ^{18}F-FDG PET/CT scans was 5±1.5 months. The majority of patients underwent ^{18}F-FDG PET/CT for oncological purposes.

Image Acquisition

All patients fasted for 8 h before imaging. PET/CT was obtained on a commercial PET/CT scanner (Discovery LS; GE Milwaukee, WI, USA) which combines an Advance NXi PET scanner and a Light Speed Plus four-row multidetector computed tomography (MDCT) system. In all studies, PET/CT imaging was acquired 60 min after intravenous administration of 370–444 MBq of ^{18}F-fluorodeoxyglucose (^{18}F-FDG). MDCT (pitch 1.5; 120 mAs; 120 kVp) was performed without intravenous and/or oral contrast medium as part of the PET/CT scan. PET scanning was subsequently performed with 4 min per bed position and six to eight bed positions per patient, depending on patient height. Raw CT data were reconstructed into transverse images with a 4.25-mm section thickness. Sagittal and coronal CT images were generated by reconstruction of the transverse data. Raw PET data were reconstructed with and without attenuation correction into transverse, sagittal, and coronal images. Attenuation correction was based on the CT attenuation coefficients, which were determined by iterative reconstruction. Blood glucose level was determined in all patients before ^{18}F-FDG administration and a cut-off value of less than 140 mg/dL was considered appropriate to perform examination. Temperature in both injection and waiting room was maintained at a constant 24°C by an air conditioning/heating and thermostats system.

Image and Data Analysis

All images were reviewed at a workstation by using PET/CT fusion software (Volumetrix for PET, GE). Each set of PET/CT studies was interpreted by two experienced (LP and EN) operators by consensus. ^{18}F-FDG uptake in BAT was considered to be present when the uptake in characteristic areas of brown fat localization, having the CT density of adipose tissue (−250–50 Hounsfield units), was greater than background soft-tissue activity. Otherwise, ^{18}F-FDG BAT was considered as absent. In addition, when ^{18}F-FDG BAT uptake was present, the site of uptake was determined as: neck (paravertebral), supraclavicular, thorax (paravertebral), pectoral, and dorsal (shoulder areas). Then, maximum standardized uptake values (SUVmax) were determined by using vendor-provided software (Volumetrix for PET-CT; GE Healthcare) on PET scans. Region of interest diameter was set at 1 cm. SUVmax was body weight-corrected. For each patient showing ^{18}F-FDG BAT uptake, the maximum SUVmax was recorded.

Data on age, gender, height, weight, medications used, diagnosis, coffee intake (≥2 expressos/day), physical activity (in the 24 h before the scan), and smoking history were collected for each patient by using a questionnaire. A patient was considered to be a smoker when smoking at least five cigarettes per day. Daily outdoor temperatures (minimum and maximum) for Naples, Italy were obtained from the weather service of the University of Naples (Osservatorio Metereologico, Università degli Studi di Napoli Federico II).

Statistical Analysis

Data are expressed as mean±one standard deviation or as proportion, as appropriate. A commercial statistical software was used (MedCalc®). Differences between continuous data were assessed using unpaired or paired Student's t test. Categorical data were evaluated by chi-square analysis, Fisher exact test, Mann–Whitney or Wilcoxon test, as appropriate. Relationships between variables were assessed by Pearson or Spearman analysis, as appropriate. Logistic analysis was used to evaluate significant determinants. A p value<0.05 was considered significant.

Results

Prevalence and Determinants of ^{18}F-FDG BAT Uptake

Of the total 848 patients studied, 73 (8.6%) were judged to be positive for BAT at first PET/CT scan. ^{18}F-FDG uptake in BAT was significantly ($p<0.05$) more common in women (53/411, 12.7%) than in men (20/433, 4.6%). The highest prevalence of ^{18}F-FDG BAT uptake occurred in December (16.7%). Figure 1 shows the prevalence of BAT in relation to seasons, as well as the mean outdoor temperature for each month. Inverse significant relationships between prevalence of patients with ^{18}F-FDG BAT uptake and either average

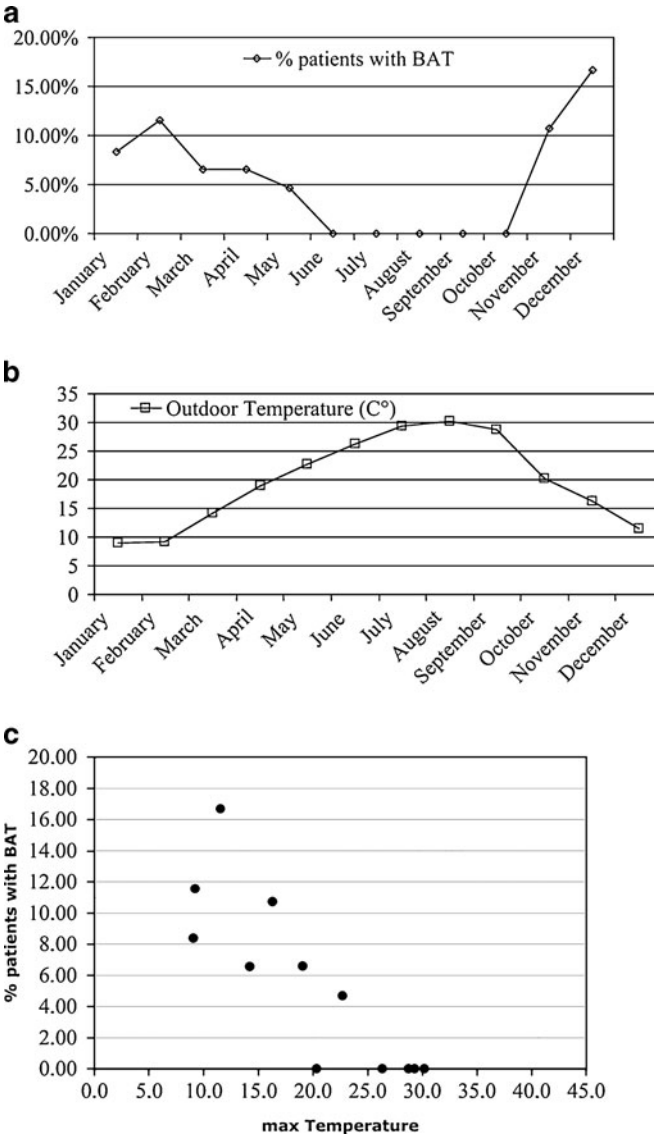

Fig. 1. Monthly incidence of ^{18}F-FDG uptake in brown adipose tissue (**a**) and of outdoor temperature (**b**). Relationship between maximal outdoor temperature (month's average) and incidence of ^{18}F-FDG uptake in brown adipose tissue, $r=-0.85$, $p<0.01$ (**c**). *BAT* brown adipose tissue.

maximum and minimum outdoor temperature ($r=-0.85$ and $r=-0.83$, respectively, $p<0.01$) were observed.

Patients with ^{18}F-FDG uptake in BAT had lower BMI, were younger, and more frequently women than patients without BAT (Table 1). Moreover, outdoor temperature (both minimum and maximum) was significantly lower in the period of PET/CT scan for patients with ^{18}F-FDG BAT uptake (Table 1). Table 2 reports the data of logistic analysis. Only those variables significant at univariate analysis were tested in multivariate analysis. Age (younger), gender (female), BMI (lower), and maximum outdoor temperature (colder) of the day of PET/CT scan were significantly associated with the presence of ^{18}F-FDG uptake in BAT at logistic multivariate analysis (Table 2).

Anatomical Distribution and Activity of ^{18}F-FDG BAT Uptake

Twenty-seven of the 73 patients (37%) with ^{18}F-FDG uptake in BAT had tracer activity in all five anatomical regions considered: neck–paravertebral, supraclavicular, thorax-paravertebral, pectoral, and dorsal; ten patients (14%) had ^{18}F-FDG BAT uptake in four anatomical regions (five in neck–paravertebral, supraclavicular, thorax-paravertebral, and pectoral; four in neck–paravertebral, supraclavicular, thorax-paravertebral, and dorsal; one in supraclavicular, thorax-paravertebral, pectoral, and dorsal); 11 patients (15%) showed tracer uptake in three anatomical regions (seven in neck–paravertebral, supraclavicular, thorax-paravertebral; two in supraclavicular, thorax-paravertebral, pectoral; two in neck–paravertebral, thorax-paravertebral, pectoral); 14 patients (19%) had ^{18}F-FDG BAT uptake in two anatomical regions (eight in supraclavicular, and thorax-paravertebral; four in neck–paravertebral, and thorax-paravertebral; two in neck–paravertebral, and supraclavicular); the remaining 11 patients (15%) had tracer uptake in only one anatomical region (eight in thorax-paravertebral; two in supraclavicular; and one in neck–paravertebral). A different distribution of ^{18}F-FDG BAT uptake in men and women ($p<0.05$) was observed (Fig. 2). Actually, men showed more areas of BAT evidence at ^{18}F-FDG PET/CT than women (4.4±1.6 vs. 3.3±1.6, respectively, $p<0.05$). On the other hand, men were younger than women (27±10 vs. 39±15 years, respectively, $p<0.005$), and extension of ^{18}F-FDG BAT uptake was significantly related to age in both men ($r=-0.47$, $p<0.05$) and women ($r=-0.41$, $p<0.01$). In the whole group of 73 patients, significant relationships between the extension of ^{18}F-FDG uptake in BAT and both age ($r=-0.46$, $p<0.0001$) and BMI ($r=-0.27$, $p<0.05$) were found; however, only age retained a significant correlation at multivariate analysis.

^{18}F-FDG BAT uptake quantified by SUVmax in the 73 patients was 7.9±5.4, and statistically significant difference

Table 1. Characteristics in patients with (BAT) and without (noBAT) ^{18}F-FDG brown adipose tissue uptake

Variable	noBAT (*N*=775)	BAT (*N*=73)	*p* value
Age (years)	54±15	35±15	<0.0001
Gender (female %)	47%	73%	<0.0001
BMI	27±6	23±6	<0.0001
Coffee intake (%)	81%	71%	<0.05
Smoking history (%)	22%	15%	N.S.
Min temperature (C°) average of 3 days	9±5	7±4	<0.05
Max temperature (C°) average of 3 days	15±6	14±6	N.S.
Min temperature (C°) day of PET/CT scan	9±5	7±5	<0.01
Max temperature (C°) day of PET/CT scan	15±5	13±5	<0.005
Physical activity (%)	69%	78%	N.S.
Beta-blocker use (%)	3%	0	N.S.
Benzodiazepine use (%)	4%	5%	N.S.

N.S. not significant, *BMI* body mass index, *BAT* brown adipose tissue

Table 2. Predictors of ^{18}F-FDG brown adipose tissue uptake

Variable	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*p* value	Odds ratio	95% CI	*p* value
Age	0.96	0.91–0.94	<0.0001	0.92	0.90–0.94	<0.0001
Gender (female)	3.09	1.81–5.29	<0.0001	3.86	2.09–7.13	<0.0001
BMI	0.86	0.81–0.91	<0.0001	0.91	0.86–0.96	<0.005
Coffee intake	1.59	1.15–2.24	<0.01	N.S.		
Smoking history	0.62	0.32–1.20	0.1	N.S.		
Min temperature average of 3 days	0.94	0.89–1.00	0.06	N.S.		
Max temperature average of 3 days	0.96	0.92–1.00	0.06	N.S.		
Min temperature day of PET/CT scan	0.93	0.88–0.99	<0.05	N.S.		
Max temperature day of PET/CT scan	0.94	0.94–0.98	<0.01	0.86	0.75–0.99	<0.05
Physical activity	1.59	0.90–2.82	0.1	N.S.		
Beta-blocker use	NA	–	–	N.S.		
Benzodiazepine use	1.37	0.47–3.99	0.6	N.S.		

NA not available, *N.S.* not significant, *BMI* body mass index, *CI* confidence interval

was observed between men and women (9.9±7.1 vs. 7.1±4.5, respectively, $p<0.05$). Significant relationships between SUVmax and age, gender, BMI, and outdoor temperatures were observed (Table 3). At multivariate analysis of these variables, only age and minimum outdoor temperature (average of 3 days) remained significant. Finally, SUVmax and extension of ^{18}F-FDG uptake in BAT were significantly related ($r=0.70$, $p<0.0001$).

^{18}F-FDG BAT Uptake in Repeated PET/CT Scans

At repeated ^{18}F-FDG PET/CT scan (mean interval 5.5± 1.6 months), 16 (21%) of the 73 patients with ^{18}F-FDG BAT uptake at first scan had again evidence of tracer uptake in BAT, while none of the remaining 775 patients did show it. Thus, the 73 patients were subdivided into two groups: BAT-1 showing ^{18}F-FDG BAT uptake only at first scan and BAT-2 showing ^{18}F-FDG BAT uptake at both scans. Age, extension of ^{18}F-FDG BAT uptake at first scan and outdoor temperatures (either minimum or maximum) significantly differed between BAT-1 and BAT-2 groups (Table 4). In the whole group of 73 patients, univariate logistic analysis showed that age, outdoor temperature (both minimum and maximum), and the anatomical extension (i.e., the number of regions) of ^{18}F-FDG BAT were predictors of persistent^{18}F-FDG BAT evidence (Table 5). However, at multivariate logistic analysis, only maximum outdoor temperature (average of 3 days) at the time of second PET/CT scan and extension of ^{18}F-FDG BAT uptake (number of regions) at first PET/CT scan remained significant (Table 5). In BAT-2 group, no significant differences between first and second PET/CT scans were found in SUVmax, extension of ^{18}F-FDG BAT uptake and BMI.

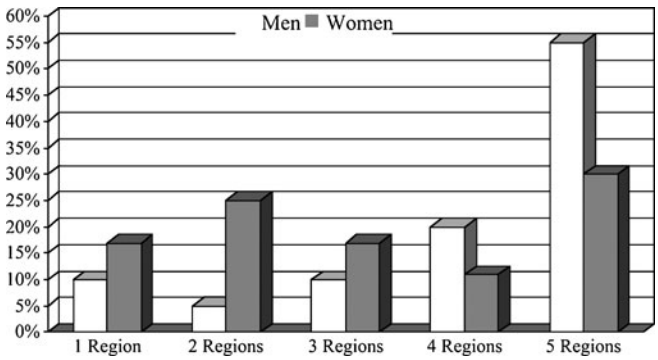

Fig. 2. Prevalence and extension of 18F-FDG uptake in brown adipose tissue in men and women.

Discussion

In the present study, BAT evidence on ^{18}F-FDG PET/CT scan was observed in 8.6% of patients, 12.7% of women, and 4.6% of men. The percentage of patients showing ^{18}F-FDG BAT uptake varied according to season and was significantly associated with mean outdoor temperature of each month. Among several variables analyzed, significant independent predictors of presence of evidence of metabolically active BAT were age (younger), BMI (lower), maximum outdoor temperature of the day of the scan, and female gender. Moreover, 21% of patients showing evidence of BAT at ^{18}F-FDG PET/CT had again evidence of BAT at scan repeated at a mean interval of 5 months.

Table 3. Relationships between intensity (SUVmax) of ^{18}F-FDG brown adipose tissue uptake and characteristics of patients

Variable	*r*	*p* value
Age	−0.39	<0.001
Gender (female)	−0.27	<0.05
BMI	0.16	N.S.
Coffee intake	−0.10	N.S.
Smoking history	−0.17	N.S.
Min temperature (average of 3 days)	0.24	<0.05
Max temperature (average of 3 days)	0.25	<0.05
Min temperature (day of PET/CT scan)	0.24	<0.05
Max temperature (day of PET/CT scan)	0.25	<0.05
Physical activity	−0.10	N.S.
Beta-blocker use	NA	–
Benzodiazepine use	−0.15	N.S.

NA not available, *N.S.* not significant, *BMI* body mass index

Table 4. Characteristics in patients showing ^{18}F-FDG BAT uptake only at first scan (BAT-1) and in those showing ^{18}F-FDG BAT uptake at both scans (BAT-2)

Variable	BAT-1 (*N*=57)	BAT-2 (*N*=16)	*p* value
Age (years)	37±15	28±14	<0.05
Gender (female %)	72%	75%	N.S.
BMI	24±4	24±7	N.S.
Coffee intake (%)	77%	50%	N.S.
Smoking history (%)	17%	6%	N.S.
Min temperature (C°) average of 3 days (second PET/CT)	16±7	11±4	<0.05
Max temperature (C°) average of 3 days (second PET/CT)	23±6	17±8	<0.01
Min temperature (C°) (day of second PET/CT scan)	15±5	11±8	<0.05
Max temperature (C°) (day of second PET/CT scan)	22±6	17±7	<0.01
Physical activity (%)	79%	81%	N.S.
Beta-blocker use (%)	0	0	–
Benzodiazepine use (%)	5%	1%	N.S.
Difference in min temperature (C°) (average of 3 days)	8±8	5±7	N.S.
Difference in max temperature (C°) (average of 3 days)	9±10	3±8	<0.05
Difference in min temperature (C°; day of PET/CT scan)	8±9	5±7	N.S.
Difference in max temperature (C°; day PET/CT scan)	9±9	5±8	N.S.
SUVmax of ^{18}F-FDG BAT uptake (first PET/CT scan)	7.3±5.4	9.8±5.0	N.S.
Extension of ^{18}F-FDG BAT uptake (nr. regions; first PET/CT scan)	3.1±1.5	4.4±1.1	<0.01

N.S. not significant, *BMI* body mass index, *BAT* brown adipose tissue

The incidence of BAT evidence at PET/CT differs in the literature, ranging from 3% up to 80% [6, 18–20]. The percentage of subjects showing ^{18}F-FDG uptake in BAT observed in the largest published studies [6, 18] is slightly less (i.e., 3% and 5%, respectively) than the value observed in the present study (8.6%). This difference could probably be due to differences in the population studied, namely age of the subjects, with those included in our study being younger.

An inverse correlation between the evidence of ^{18}F-FDG BAT uptake and age has been found in the present as well as in previous studies [3, 18, 21]. In the present study, age was found to be the only independent predictor of the extension of BAT, i.e., the number of anatomical regions with BAT at PET/CT, with younger patients showing larger extension. This finding is in agreement with that of Cypess et al. [18] who found the greatest amount of BAT in younger subjects. Moreover, younger patients show higher SUVmax, thus, metabolic activity, in our study. A higher prevalence of BAT evidence in women, as already reported [6, 18], with a women/men ratio of 2.7/1, was observed in the present study. The inverse relationship between ^{18}F-FDG BAT uptake and BMI we observed suggests an interaction between obesity and BAT metabolism, with functionally active BAT in people showing lower BMI, thus confirming previous studies [4, 18, 21, 22]. ^{18}F-FDG uptake in BAT has been reported to be clearly related to temperature [6, 8, 18, 21, 22], and our results show the same relationship. Moreover, the finding of an influence of outdoor temperature the same day of PET/CT scan on BAT evidence in the

Table 5. Predictors of ^{18}F-FDG brown adipose tissue persistent uptake: univariate analysis

Variable	Univariate analysis			Multivariate analysis		
	Odds Ratio	95% CI	*p* value	Odds ratio	95% CI	*p* value
Age (years)	0.95	0.91–0.99	<0.05	N.S.		
Gender (female %)	1.14	0.32–4.07	0.8	N.S.		
BMI	1.01	0.89–1.14	0.9	N.S.		
Coffee intake (%)	0.32	0.10–1.01	0.06	N.S.		
Smoking history (%)	0.29	0.04–2.30	0.2	N.S.		
Min temperature (C°) average of 3 days (second PET/CT)	0.91	0.83–0.99	<0.005	N.S.		
Max temperature (C°) average of 3 days (second PET/CT)	0.89	0.82–0.97	<0.005	0.90	0.82–0.98	<0.05
Min temperature (C°; day of second PET/CT scan)	0.90	0.83–0.99	<0.05	N.S.		
Max temperature (C°; day of second PET/CT scan)	0.90	0.83–0.98	<0.01	N.S.		
Physical activity (%)	1.25	0.31–5.07	0.7	N.S.		
Beta-blocker use (%)	–	–	–	N.S.		
Benzodiazepine use (%)	1.22	0.12–12.6	0.9	N.S.		
Difference in min temperature (C°; average of 3 days)	0.95	0.89–1.01	0.09	N.S.		
Difference in max temperature (C°; average of 3 days)	0.95	0.90–1.00	<0.05	N.S.		
Difference in min temperature (C°; day of PET/CT scan)	0.95	0.88–1.01	0.08	N.S.		
Difference in max temperature (C°; day PET/CT scan)	0.95	0.89–1.01	0.08	N.S.		
SUVmax of ^{18}F-FDG BAT uptake (first PET/CT scan)	1.08	0.98–1.19	0.1	N.S.		
Extension of ^{18}F-FDG BAT uptake (nr. regions; first PET/CT scan)	2.14	1.25–3.69	<0.001	2.03	1.17–3.51	<0.01

N.S. not significant, *BMI* body mass index, *CI* confidence interval

present study, but not of the average outdoor temperature of the 3 days before the scan, do confirm previous observation of FDG uptake in BAT as an acute response to cold [6]. It should be said that we did not find any relationship between ^{18}F-FDG BAT uptake and medications such as beta-blockers or benzodiazepine, as previously reported [10, 18]. However, the number of subjects using these medications in our study is quite low (i.e., <3% and 4%, respectively) and it is thus conceivable that this hampered statistically significant results. On the other hand, cigarette smoking (>5 per day) was not a predictor of BAT ^{18}F-FDG uptake, and this result is in contrast with that reported in an animal study [9].

In patients with ^{18}F-FDG BAT uptake, the most common locations of BAT were shoulders (94%), supraclavicular (80%), and neck (72%). Actually, many patients had BAT evidence at ^{18}F-FDG PET/CT in more than one area, namely 85% of those included in the present study. Moreover, a significant association of BAT distribution and gender was observed, with larger proportion of men showing >3 regions of ^{18}F-FDG BAT uptake than women (75% vs. 42%). This finding is in apparent contrast with the study of Cypess [18] who reported greater mass of BAT in women. However, in our study, women showing BAT were significantly older than men, and age is the strongest single predictor of extension of metabolically active BAT with multivariate analysis. Thus, it is conceivable that our observation of larger extension of BAT in men is mainly, if not exclusively, due to difference in age.

In order to analyze the metabolic activity of BAT, we calculated for each patient the SUVmax in BAT. Although this is a rough estimate, it can be used as an indicator of metabolic activity. From our data, it could be argued that metabolic activity (namely, glucose consumption) in BAT is determined by age (younger) and outdoor temperature (colder). Actually, with multivariate analysis, age and outdoor temperature were the only variables retaining significance. Again, the difference in SUVmax between men and women observed in our study should be attributed to difference in age.

Repeated PET/CT scan in the same patients showed persistence of ^{18}F-FDG BAT uptake in 21% of patients showing ^{18}F-FDG BAT uptake in the first study. To the best of our knowledge, only one study investigated ^{18}F-FDG BAT in serial PET/CT scan [20], and the authors did not find any relationship of tracer uptake and either outdoor temperature or age, while a clear relationship with therapy was observed. However, several differences between the two studies could be responsible for the different results reported. Rousseau et al. [20] investigated only women with a quite narrow age range, while in the present study both men and women with a larger age range have been analyzed. Moreover, in our study, only patients without any change in therapy between the two PET/CT scans were included, while this is not true for Rousseau's investigation due to change in chemotherapy [20]. Patients showing persistence of ^{18}F-FDG BAT uptake were younger and had a larger extension of BAT than those not showing persistence of ^{18}F-FDG BAT uptake. On the other hand, no differences in other well-known predictors of BAT, as BMI and gender, have been observed in the population studied, while significant difference in outdoor temperature at time of second ^{18}F-FDG PET/CT scan was found. Moreover, multivariate analysis showed that only maximum outdoor temperature and extension of BAT evidence were significant predictors of persistence of ^{18}F-FDG BAT uptake in repeated study. While there is a great amount of data on the influence of temperature on BAT evidence on ^{18}F-FDG PET/CT, somewhat more intriguing is the finding of a relationship between extension of ^{18}F-FDG BAT uptake in the first PET/CT scan and the evidence of tracer uptake at second scan. It could be argued that change in outdoor temperature would have greater influence on metabolic activity of the tissue in subjects with larger amount of BAT, and thus, on evidence of ^{18}F-FDG uptake.

In the past several years, mainly when only PET scanners were available, evidence of uptake of ^{18}F-FDG in areas such as neck, supraclavicular, or shoulders was attributed to different factors (i.e., muscle) and sometimes created confusion in the interpretation of the images. The introduction of PET/CT in routine clinical use has lead to clear attribution of uptake in these regions to the presence of BAT. It has been long recognized that BAT is a highly specialized thermogenic tissue playing an important role in regulating body temperature in newborns [23]. The amount of BAT decreases with aging and with increasing BMI [18, 21, 22, 24]. The increasing use of ^{18}F-FDG PET/CT has added new information on BAT in adults. Uptake of ^{18}F-FDG is obviously due to increased metabolic activity and is mediated by glucose transporters. Thus, evidence of BAT at ^{18}F-FDG PET/CT is an estimate of the presence of BAT, since only metabolically active tissue is evidentiated.

The findings of our study show that metabolically active BAT is present in adult humans, with a women predominance, and that age, BMI, and outdoor temperature are significant determinants of its evidence at PET/CT. Moreover, extension of BAT and outdoor temperature are both strong predictors of persistence of BAT evidence at repeated ^{18}F-FDG PET/CT scan. This last finding is of potential clinical use, since methods to decrease ^{18}F-FDG BAT uptake have been proposed [25–27] and thus, can be used in selected patients.

Conflict of Interest Disclosure The authors declare that they have no conflict of interest.

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