Standardized uptake values of fluorine-18 fluorodeoxyglucose: the value of different normalization procedures

A. Schomburg[1], H. Bender[1], C. Reichel[3], T. Sommer[2], J. Ruhlmann, B. Kozak, H.J. Biersack[1]

[1] Department of Nuclear Medicine, PET Center Bonn, University of Bonn, Germany
[2] Department of Radiology, PET Center Bonn, University of Bonn, Germany
[3] Department of Internal Medicine, PET Center Bonn, University of Bonn, Germany

Received 1 October 1995 and in revised form 29 January 1996

Abstract. While the evident advantages of absolute metabolic rate determinations cannot be equalled by static image analysis of fluorine-18 fluorodeoxyglucose positron emission tomographic (FDG PET) studies, various algorithms for the normalization of static FDG uptake values have been proposed. This study was performed to compare different normalization procedures in terms of dependency on individual patient characteristics. Standardized FDG uptake values (SUVs) were calculated for liver and lung tissue in 126 patients studied with whole-body FDG PET. Uptake values were normalized for total body weight, lean body mass and body surface area. Ranges, means, medians, standard deviations and variation coefficients of these SUV parameters were calculated and their interdependency with total body weight, lean body mass, body surface area, patient height and blood sugar levels was calculated by means of regression analysis. Standardized FDG uptake values normalized for body surface area were clearly superior to SUV parameters normalized for total body weight or lean body mass. Variation and correlation coefficients of body surface area-normalized uptake values were minimal when compared with SUV parameters derived from the other normalization procedures. Normalization for total body weight resulted in uptake values still dependent on body weight and blood sugar levels, while normalization for lean body mass did not eliminate the positive correlation with lean body mass and patient height. It is concluded that normalization of FDG uptake values for body surface area is less dependent on the individual patient characteristics than are FDG uptake values normalized for other parameters, and therefore appears to be preferable for FDG PET studies in oncology.

Key words: Positron emission tomography – Fluorine-18 fluorodeoxyglucose – Standardized uptake value – Semiquantitation

Eur J Nucl Med (1996) 23:571–574

Correspondence to. A. Schomburg, Department of Nuclear Medicine, University of Bonn, Venusberg, D-53105 Bonn, Germany

Introduction

Increased glucose metabolism as studied by positron emission tomography (PET) using fluorine-18 fluorodeoxyglucose (FDG) can be evaluated at different levels of sophistication [1]. Visual analysis of qualitative images and calculation of kinetic constants by means of multicompartment models and arterial blood sampling mark the extremes that have been proposed for the evaluation of studies. Between these extremes, the calculation of standardized uptake values (SUVs) is expected to combine useful semiquantification with the ease of use obligatory for daily clinical routine [2]. Various algorithms for the normalization of FDG uptake have been proposed and appear to be necessary, since the originally introduced SUV(TBW) proved to be highly dependent on body weight, thus overestimating FDG uptake in heavy patients [3]. However, the accuracy of various normalization procedures has not been systemically evaluated in larger patient cohorts.

In an attempt to clarify further the dependency of different SUVs on various patient characteristics and to demonstrate the level of reproducibility that can be attained by the use of semiquantitative measures in daily clinical routine, we prospectively calculated the previously proposed parameters and compared them in a larger than previously reported patient cohort studied for oncological staging. The objective of this study was to determine the optimal procedure for FDG uptake normalization in this setting.

Materials and methods

The study cohort consisted of 126 consecutive patients studied for oncological staging after the histological diagnosis of malignant disease. The majority of tumours in this population included melanoma (n=33), colorectal (n=18), breast (n=18), differentiated thyroid (n=8), ovarian (n=8) and testicular (n=8) tumours, malignant lymphoma of Hodgkin's (n=7) and non-Hodgkin's histology (n=5), bronchogenic carcinoma (n=5) and osteosarcoma (n=3). Patient characteristics are given in Table 1.

Table 1. Patient characteristics and imaging modalities

Reference	Patients (*n*)	Weight (kg)	Age (years)	Fasting (h)	BSL (mg/dl)	Imaging (start min p.i.)
Zasadny and Wahl [3]	28	72±18 (45–107)	54±12 (29–75)	≥4	94±22	50
Kim et al. [4]	44	79.4±19.5 (45–115)	61.5±14.9 (30–89)	NR	NR	60–90
This study	126	72.1±12.5 (42–110)	49.0±17.7 (14–86)	≥12[a]	96.3±17.9 (40–191)	67±31 (40–200)

Indicated are mean values±standard deviations (range)
BSL, Blood sugar level; NR, not reported
[a] Recommended, but not followed in all patients

Whole-body PET was performed according to the methods reported by Dahlbom et al. [4], and emission and transmission scans (10 min per bed, each) were acquired sequentially using multiple bed positions. All of the PET scans performed in this study were acquired on a Siemens ECAT Exact 921/47 (CTI, Knoxville, Tenn., USA). Prior to the patient studies, a 15-min blank transmission scan was acquired every morning. The emission scan was started 67±31 (range, 40–200; median, 55) min after intravenous injection of 6.7±2.1 (range, 2.7–13.3; median 6.6) mCi FDG. Decay correction during the emission scans, attenuation correction, processing and reconstruction by filtered backprojection using a Hann filter (0.4 cycles/pixel cutoff) and manufacturer-provided standard software were performed and the tomograms were displayed in transaxial orientations with a final sclice width of 3.75 mm.

Regional activity concentrations were evaluated by means of standard region of interest (ROI) software provided with CTI scanner systems. Circular ROIs were created on the transaxial tomograms and carefully positioned over areas with homogeneous activity uptake. Two sets of ROIs were selected per patient, with a mean ROI surface of 1326±123 (range, 64–4322) mm^2 and a mean of 1140±96 (range, 60–3335) pixels. The matrix size of the reconstructed images was 128×128, and the pixel size was 1.1 mm^2.

Calculations were based on the ratio of activity found in the tissue to the injected activity and to the patient's total body weight (TBW), body surface area (BSA) or lean body mass (LBM), all of which were calculated using previously published formulae [3, 5]. All tomograms were read by three staff members for analysis of hypermetabolic and eumetabolic findings. ROI areas were localized by a single observer, and standard statistical software packages were used for the determination of correlation coefficients, variation coefficients and significance levels. A P value less than 0.05 was considered statistically significant.

Results

Mean SUVs for the liver were 3.6±1.4 (range, 0.7–7.8; median, 3.6) [SUV(TBW)], 91.6±34.3 (range, 23.5–181.9; median, 92.6) m^{-1} [SUV(BSA)] and 3.3±1.3 (range, 0.5–6.6; median, 3.2) [SUV(LBM)]. The coefficient of variation (CV) was smallest for SUV(BSA), being 37.4%, followed by the CV of SUV(TBW), 38.7%, and the CV of SUV(LBM), 39.4%.

For the lung, mean SUVs were 0.9±0.3 (range, 0.4–2.3; median, 0.9) [SUV(TBW)], 22.9±7.5 (range, 7.9–42.8; median, 23.6) m^{-1} [SUV(BSA)] and 0.8±0.3 (range, 0.4–2.0; median, 0.8) [SUV(LBM)]. The CV was smallest for SUV(BSA), being 32.9%, followed by the CV of SUV(LBM), 35.1%, and the CV of SUV(TBW), 36.0%.

Table 2. Interpendence of SUVs in liver tissue

SUV	*R*	*P*
SUV(TBW)=1.68+0.027×TBW	0.241	0.0001*
SUV(TBW)=3.70–0.0013×LBM	0.007	0.9
SUV(TBW)=2.32+0.71×BSA 0.098	0.1	0.1
SUV(TBW)=4.19–0.0034×HGT	0.021	0.7
SUV(TBW=2.39+0.0127×BSL	0.161	0.01*
SUV(BSA)=89.25+0.032×TBW	0.012	0.8
SUV(BSA)=104.5–0.196×LBM	0.057	0.3
SUV(BSA)=81.97+5.29×BSA 0.029	0.6	0.6
SUV(BSA)=135.6–0.25×HGT 0.065	0.3	0.3
SUV(BSA)=71.67+0.207×BSL	0.109	0.08**
SUV(LBM)=3.31–0.00009×TBW	0.0009	0.9
SUV(LBM)=1.92+0.021×LBM	0.173	0.007*
SUV(LBM)=3.22+0.046×BSA0.007	0.9	0.9
SUV(LBM)=–0.41+0.0022×HGT	0.148	0.02*
SUV(LBM)=2.64+0.0068×BSL	0.096	0.1

TBW, Total body weight (kg); LBM, lean body mass (kg); BSA, body surface area (m^2); HGT, body height (cm); BSL, blood sugar level (mg/dl); *R*, coefficient correlation; *P*, level of significance
* $P<0.05$; ** $0.05<P<0.1$

Correlations of various SUVs with TBW, LBM, BSA, height and blood sugar levels are shown in Table 2 for the liver, and in Table 3 for the lung. In the liver, SUV(TBW) was significantly correlated with patient weight and blood sugar level, SUV(LBM) was significantly correlated with lean body mass and patient height, and SUV(BSA) was independent of all parameters studied (Table 1).

In the lung, SUV(TBW) was also significantly correlated with patient weight and blood sugar level, while SUV(LBM) was also correlated with lean body mass and patient height. With respect to SUV(BSA), there was no statistically significant correlation with any of the parameters evaluated (Table 2).

Table 3. Interdependence of SUVs in lung tissue

	R	*P*
SUV(TBW)=0.338+0.0079×TBW	0.302	0.0001*
SUV(TBW)=0.865+0.0006×LBM	0.025	0.7
SUV(TBW)=0.723+0.001×BSA	0.059	0.3
SUV(TBW)=0.774+0.0008×HGT	0.021	0.7
SUV(TBW)=0.570+0.0035×BSL	0.192	0.002*
SUV(BSA)=20.91+0.027×TBW	0.045	0.5
SUV(BSA)=24.72–0.0285×LBM	0.036	0.6
SUV(BSA)=21.30+0.851×BSA	0.022	0.7
SUV(BSA)=26.99–0.024×HGT	0.028	0.6
SUV(BSA)=17.87–0.052×BSL	0.122	0.05**
SUV(LBM)=0.775+0.0007×TBW	0.03	0.6
SUV(LBM)=0.410+0.006×LBM	0.224	0.0003*
SUV(LBM)=0.939–0.063×BSA	0.042	0.5
SUV(LBM)=–0.407+0.007×HGT	0.217	0.0005*
SUV(LBM)=0.655+0.0018×BSL	0.109	0.08**

TBW, Total body weight (kg); LBM, lean body mass (kg), BSA, body surface area (m^2); HGT, body height (cm); BSL, blood sugar level (mg/dl); *R*, coefficient of correlation; *P*, level of significance * $P<0.05$; ** $0.05 \leq P < 0.1$

Discussion

SUVs are increasingly being used in FDG PET studies, being a semiquantitative compromise between qualitative visual assessment and the measurement of the absolute metabolic rates. The latter cannot be readily adopted in clinical routine and has occasionally been questioned with regard to its feasibility, reproducibility and benefit [1]. However, algorithms based on the separation of malignant from benign tissues on the basis of SUV(TBW) have been shown to be generally useful [2, 6].

The independence of SUV from other patient parameters is crucial for several reasons. Reference ranges in broader study populations can be applied only when a valid normalization has been performed. Especially when monitoring for treatment response, when the therapy given might also change body weight and other patient characteristics, the influence of these variables has to be minimized. In addition, only successful normalization of uptake values might reduce the overlap between benign and malignant lesions.

Zasadny et al. studied a group of 28 women with breast cancer and observed a positive correlation of SUV(TBW) with body weight; in certain organs, the SUV(TBW) was more than twice as high in heavier patients as compared to the lightest patients [3]. This observation was clearly confirmed by our data (Tables 2, 3). We also report a clear dependence of SUV(TBW) on blood sugar levels. The overestimation of FDG uptake in heavy patients using SUV(TBW) is generally explained by the increase in body fat tissue relative to other tissues in patients with higher body weight [3, 5], thus indicating a poor correlation between body mass and whole-body distribution of FDG [5]. Therefore, Zasadny et al. proposed the use of SUV(LBM) to correct for the weight dependency of SUV(TBW). However, our data clearly show that SUV(LBM) is also statistically significantly correlated with lean body mass and patient height. These results are in accordance with data calculated in 44 patients studied by Kim et al.[7].

Kim et al. suggested that the application of SUV (BSA) would be preferable to the use of SUV(TBW), given that it is minimally affected by body size [5]. The use of normalization of FDG uptake for the body surface area in our hands also proved to be clearly superior to normalization for body weight or lean body mass: SUV(BSA) was statistically independent of total body weight, lean body mass, body surface area, patient height and blood sugar levels. Moreover, the CVs for SUV(BSA) were considerably smaller than those for SUV(TBW) or SUV(LBM). This corresponds to the observation by other [5] of a "narrower range" and "smaller standard deviation" for SUV(BSA).

The weak correlation of SUV(BSA) with body weight and body surface area observed by Kim et al. [5, 7] could not be reproduced in our patient cohort. While overall SUV parameters measured in our study are comparable with the magnitude of liver and lung FDG uptake values reported by other investigators [3, 5, 7–10], the trend toward discretely higher mean values and wider variability in the present report might be influenced by the hypothetical inclusion of patients with occult metastatic lesions, as was also discussed by Kim et al. [5]. Although special care was taken to place the ROIs outside of obvious metastatic foci, the presence of undiagnosed pathology in these non-selected patients cannot be excluded. The heterogeneity of the patient data can also be deduced from Table 1, demonstrating the broader ranges of both patient age and time of commencement of imaging in our study. While decay correction during the emission scan was performed using manufacturer-provided standard software, the different times of commencement of acquisition were not corrected for. However, the dependence of SUV values on imaging times appears to be plausible and can also be calculated from our data ($R=0.326$; $P<0.05$; data not shown). In addition, patient age might be a factor too little accounted for in previous analyses; according to our data, SUV(TBW) was clearly dependent on age ($R=0.13$, $P=0.03$), while this correlation was not significant for SUV(LBM) and SUV(BSA) ($P=0.66$ and $P=0.27$, respectively; data not shown), all of which might be influenced by the interdependence of body mass and age.

None of the suggested normalization procedures will replace absolute quantitation of glucose utilization. Naturally, the metabolic rate of glucose should be the gold standard against which different SUV algorithms are compared. However, in the absence of absolute data, the different qualities of different SUVs can only be compared in terms of coefficients of regression and variance. This study has calculated several suggested algorithms for normalization of SUV in a considerable number of

patients and demonstrated the level of reproducibility attainable in a PET facility supplied on an FDG satellite basis and operating in a daily routine setting. We found SUV(BSA) to be clearly superior to the other parameters and recommend its use in future semiquantitative approaches for routine patient studies in oncology.

References

1. DiChiro G, Brooks RA. PET quantitation: blessing and curse [editorial]. *J Nucl Med* 1988; 29: 1603–1605.
2. Strauss LG, Conti PS: The application of PET in clinical oncology. *J Nucl Med* 1991; 32: 623–648.
3. Zasadny KR, Wahl RL. Standardized uptake values of normal tissues at PET with FDG: variations with body weight and a method for correction. *Radiology* 1993; 189: 847–850.
4. Dahlbom M, Hoffman EJ, Hoh CK, Schiepers C, Rosenqvist G, Hawkins RA, Phelps ME. Whole-body PET: part I. Methods and performance characteristics. *J Nucl Med* 1992; 33: 1191–1199.
5. Kim CK, Gupta NC, Chandramouli B, Alavi A. Standardized uptake values of FDG: body surface area correction is preferable to body weight correction. *J Nucl Med* 1994; 35: 164–167.
6. Griffeth LK, Dehdashti F, McGuire AH, Perry DJ, Moerlein SM, Siegal BA. PET evaluation of soft-tissue masses with FDG. *Radiology* 1992; 182: 185–194.
7. Kim CK, Gupta NC. Dependency of standardized uptake values of FDG on body "size": body surface area correction versus lean body mass correction [abstract]. *J Nucl Med* 1995; 36: 201P.
8. Hübner KF, Buonocore E, Singh SK, Gould HR, Cotten DW. Characterization of chest masses by FDG PET. *Clin Nucl Med* 1995; 20: 293–298.
9. Wong FCL, Garcia JR, Kim EE, Wong WH, Podoloff DA. Normal organ uptake of FDG and C-11 methionine during PET scans of oncologic patients [abstract]. *J Nucl Med* 1994; 35: 220P.
10. Leskinen-Kallio S, Minn H, Zasadny KR. Standardized uptake values of FDG [letter]. *J Nucl Med* 1994; 35: 1564.