The appropriate whole body metric for calculating standardised uptake value and the influence of sex

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**Aim** To compare weight, lean body mass and body surface area for calculation of standardised uptake value (SUV) in fluorine-18-fluorodeoxyglucose PET/computed tomography, taking sex into account.

**Patients and methods** This was a retrospective study of 161 (97 men) patients. Maximum standardised uptake value (SUV$_{\text{max}}$) and mean standardised uptake value (SUV$_{\text{mean}}$) were obtained from a 3-cm region of interest over the right lobe of the liver and scaled to weight, scaled to lean body mass (SUL) and scaled to body surface area (SUA). Mean hepatic computed tomography density was used to adjust SUV$_{\text{mean}}$ for hepatic fat (SUV$_{\text{FA}}$). Hepatic SUV indices were divided by SUV from left ventricular cavity, thereby, eliminating whole body metric, to obtain a surrogate of blood fluorine-18-fluorodeoxyglucose clearance into liver, and multiplied by blood glucose to give a surrogate of hepatic glucose uptake rate (mSUV).

**Results** SUV$_{\text{max}}$, SUV$_{\text{mean}}$ and all scaled to weight indices correlated strongly with weight. SUV$_{\text{mean}}$, SUV$_{\text{FA}}$, SUV$_{\text{mean}}$ and SUV$_{\text{FA}}$, however, correlated weakly or not at all with weight, nor with their corresponding whole body metric in men or women, but correlated strongly when the sexes were combined into one group. This was the result of sex differences in SUL (greater in men) and SUA (greater in women). There was, however, no sex difference in mSUV.

**Conclusion** Weight is unsuitable for calculating SUV. SUL and SUA are also inappropriate as maxima but appropriate as mean and fat-adjusted values. However, SUV is recommended for both sexes because SUA is influenced by both body fat and weight. Sex differences in SUV and SUA give rise to misleading correlations when sexes are combined into one group. 

Keywords: body surface area, fluorine-18-fluorodeoxyglucose, lean body mass, PET, sex, standardised uptake value

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increased in larger persons [13], which would be expected to increase SUV\textsubscript{max}. Sex is also an important consideration because, first, there is evidence to suggest that hepatic glucose metabolism differs between sexes [14, 15], second, men are larger than women, and thirdly, women have more body fat than men [16].

The purpose of the current study was to re-examine the issue of most appropriate whole body metric for calculating SUV using the liver as reference tissue in the context of sex.

**Patients and methods**

**Patients**

This was a retrospective study of 161 (97 men) adult patients, in whom height as well as weight was measured immediately prior to imaging, referred for routine \textsuperscript{18}F-FDG PET/CT almost all for the management of cancer. The population comprised two groups of 101 and 60 patients that have been separately reported in studies elsewhere [6,9,13] and combined into one group for this study. The study received ethical approval from a National Research Ethics Committee of the UK.

**Imaging**

The PET/CT imaging protocol is described elsewhere [6,9,13]. In brief, PET/CT was performed with unenhanced CT-based attenuation correction using a Siemens Biograph, Siemens, Erlangen, Germany. 64-slice PET scanner with immediate nonenhanced CT scanning (120 kVp/50 mA-Care dose\textsuperscript{4D}; slice 5 mm; pitch 0.8; rotational speed 0.5/s). Arms were up, as arms down may result in artificial elevation of the liver \textsuperscript{18}F-FDG signal due to beam-hardening effects. Emission data were acquired at 3 min per bed position. Imaging was performed 60 min after injection of \(\sim 400\) MBq, not scaled for body size, after 6 h of fasting.

**Image analysis**

SUV\textsubscript{max}, SUV\textsubscript{mean} and mean CT density were recorded in a 3 cm diameter ROI over the right lobe of the liver, avoiding any known or suspected regional pathology, as described previously [6,9,13]. Blood pool SUV was obtained from an ROI of 1.5 cm diameter over the left ventricular blood pool (SUV\textsubscript{LV}). Reproducibility of SUV measurement was performed in the group of 60 patients.

**Data analysis**

SUV\textsubscript{mean} was adjusted for hepatic fat using a recently described exponential equation [17] that relates CT density to the proportion of the liver that is fat ($P_F$).

$$P_F = \exp[-0.0238(\text{CTD}+50)].$$

The fat-adjustment procedure was to divide SUV\textsubscript{mean} by $1-P_F$ to give SUV\textsubscript{FA} [18]. SUV\textsubscript{max} is not considered to require correction.

SUV\textsubscript{max} was divided by maximum SUV\textsubscript{LV}, and SUV\textsubscript{mean} and SUV\textsubscript{FA} were divided by mean SUV\textsubscript{LV}. Expressing tissue SUV in relation to blood pool SUV has two desirable effects. Firstly, it eliminates whole body metric and secondly renders SUV a closer surrogate of blood \textsuperscript{18}F-FDG clearance into tissue (i.e. blood clearance of \textsuperscript{18}F-FDG that is phosphorylated) [19]. SUV/SUV\textsubscript{LV} was then multiplied by blood glucose concentration to give mSUV as an estimate of hepatic glucose phosphorylation rate [20].

**Estimation of lean body mass and body fat percentage**

Sex-specific LBM was estimated from the formula of Boer [21] to give $^\text{B}$LBM and from the formulae of Janmahasatian et al. [22] to give $^\text{J}$LBM. Body fat percentage was calculated as: $100 \times (\text{weight} - \text{LBM})/\text{weight}$.

**Estimation of body surface area**

Sex-non-specific BSA was estimated from the formula of Haycock et al. [23] to give $^\text{H}$BSA and from the sex-specific formulae of Tikuisis et al. [24] to give $^\text{T}$BSA.

**Statistical analysis**

Linear regression analysis was used to determine the Pearson correlation coefficients between variables. Student’s unpaired $t$-test was used to determine the significance of the differences of variables between men and women. A $P$ value of less than 0.05 was taken to indicate statistical significance.

**Ethical approval**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

**Results**

**Correlations with body weight**

SUV indices correlated strongly with body weight in both men and women (Table 1). SUV\textsubscript{max} and SUV\textsubscript{Amax} also correlated strongly with body weight. SUV\textsubscript{mean}, SUV\textsubscript{FA}, SUV\textsubscript{mean} and SUV\textsubscript{FA} showed weak or no correlations with body weight in men or women analysed separately but showed some strong correlations when the sexes were combined into one group (Table 1).

**Whole body metric-specific correlations**

In contrast to maximum SUV and SUV\textsubscript{mean} and fat-adjusted SUV and SUA showed no correlations with their whole body metric equivalents in men or women, except for $^\text{T}$SUA\textsubscript{mean} in men (Tables 2 and 3). However, several strong correlations were again noted when the sexes were combined (Fig. 1).
Differences between men and women

CT density, \( P_F \) and blood glucose were all similar between men and women (Table 4). Body fat percentage, however, was higher in women compared with men. LBM and BSA were, as expected, higher in men than women but the ratio of BSA/LBM was higher in women. \( ^{15}SUL \) behaved similarly, although \( ^{15}SUA_{\text{mean}} \) did correlate significantly with \( ^{15}BSA \) in men. \( mSUV \), in contrast, correlated strongly with body weight, which can be explained by the relatively low penetration of \(^{18}F\)-FDG into adipose tissue [1]. These findings are in line with Sugawara et al. [4] and Tahari et al. [5], who favoured LBM, and with Kim et al. [3] and Schomburg et al. [7], who favoured BSA, and are therefore not new. Nevertheless, we believe our study is important as it clarifies the role of sex and shows that ignoring sex results in misleading correlations.

SUV indices were not significantly different between men and women (Table 4). \( ^{15}SUL \) indices, however, were greater in men than women, while in contrast \( ^{15}SUW \) indices were not significantly different between men and women (Table 4).

Discussion

The main finding in this study is that mean and fat-adjusted hepatic SUV showed no significant correlation with LBM in either sex, in spite of the presence of LBM in both co-ordinates, suggesting that LBM is an appropriate whole body metric for the calculation of SUV. \( SUA \) behaved similarly, although \( ^{15}SUA_{\text{mean}} \) did correlate significantly with \(^{15}BSA \) in men. \( SUW \), in contrast, correlated strongly with body weight, which can be explained by the relatively low penetration of \(^{18}F\)-FDG into adipose tissue [1]. These findings are in line with Sugawara et al. [4] and Tahari et al. [5], who favoured LBM, and with Kim et al. [3] and Schomburg et al. [7], who favoured BSA, and are therefore not new. Nevertheless, we believe our study is important as it clarifies the role of sex and shows that ignoring sex results in misleading correlations.

LBM has the potential disadvantage of underestimating SUV because \(^{18}F\)-FDG, at least to a limited extent, accumulates in adipose tissue [1], which SUV ignores. Because women have more adipose tissue than men, this may explain why \( ^{15}SUL \) indices were higher in women. Conversely, BSA has the potential disadvantage of

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**Table 1** Correlation coefficients and their significance levels (\( P \)) of the linear relationships between \( ^{15}SUV \) indices and body weight in men, women and both combined

|            | Men          | Women        | Both         |
|------------|--------------|--------------|--------------|
| \( ^{15}SUA_{\text{max}} \) | 0.62 (<0.0001) | 0.76 (<0.0001) | 0.65 (<0.0001) |
| \( ^{15}SUA_{\text{mean}} \) | 0.48 (<0.001)  | 0.61 (<0.0001) | 0.45 (<0.0001) |
| \( ^{15}SUW_{\text{max}} \) | 0.55 (<0.001)  | 0.67 (<0.0001) | 0.53 (<0.0001) |
| \( ^{15}SUW_{\text{mean}} \) | 0.29 (0.004)  | 0.26 (0.04)   | 0.28 (<0.0001) |
| \( ^{15}SUW_{\text{max}} \) | 0.27 (0.007)  | 0.46 (0.0002) | 0.46 (<0.0001) |
| \( ^{15}SUW_{\text{mean}} \) | 0.06 (NS)    | 0.09 (NS)    | 0.18 (0.02)* |
| \( ^{15}JSUL_{\text{max}} \) | 0.07 (NS)  | 0.21 (NS)  | 0.28 (0.0003)* |
| \( ^{15}JSUL_{\text{mean}} \) | 0.25 (0.01)  | 0.40 (0.001) | 0.27 (0.0005) |
| \( ^{15}JSUL_{\text{max}} \) | 0.13 (NS)  | 0.16 (NS)  | 0.09 (NS) |
| \( ^{15}JSUL_{\text{mean}} \) | 0.14 (NS)  | 0.32 (0.01) | 0.17 (0.03) |
| \( ^{15}JSUL_{\text{max}} \) | 0.21 (0.04)  | 0.08 (NS)  | 0.26 (0.0009)* |
| \( ^{15}JSUL_{\text{mean}} \) | 0.09 (NS)  | 0.03 (NS)  | 0.15 (NS) |

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**Table 2** Correlation coefficients and their significance levels (\( P \)) of the linear relationships between scaled to lean body mass indices and the same lean body mass used to calculate them in men, women and both combined

|            | Men          | Women        | Both         |
|------------|--------------|--------------|--------------|
| \( ^{15}SUL_{\text{max}} \) | 0.28 (0.005)  | 0.42 (0.0006) | 0.49 (<0.0001) |
| \( ^{15}SUL_{\text{mean}} \) | 0.02 (NS)   | 0.1 (NS)    | 0.20 (0.01)* |
| \( ^{15}SUL_{\text{max}} \) | 0.23 (0.02)  | 0.49 (<0.0001) | 0.63 (<0.0001) |
| \( ^{15}SUL_{\text{mean}} \) | 0.09 (NS)  | 0.14 (NS)  | 0.44 (0.001)* |
| \( ^{15}SUL_{\text{max}} \) | 0.10 (NS)  | 0.24 (NS)  | 0.50 (<0.0001)* |

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**Table 3** Correlation coefficients and their significance levels (\( P \)) of the linear relationships between scaled to body surface area indices and the same body surface area used to calculate them in men, women and both combined

|            | Men          | Women        | Both         |
|------------|--------------|--------------|--------------|
| \( ^{15}SUA_{\text{max}} \) | 0.22 (0.03)  | 0.41 (0.0008) | 0.24 (0.002) |
| \( ^{15}SUA_{\text{mean}} \) | 0.09 (NS)   | 0.03 (NS)   | 0.18 (0.02)* |
| \( ^{15}SUA_{\text{max}} \) | 0.03 (NS)  | 0.14 (NS)  | 0.07 (NS) |
| \( ^{15}SUA_{\text{mean}} \) | 0.1 (NS)   | 0.34 (0.006) | 0.13 (NS) |
| \( ^{15}SUA_{\text{max}} \) | 0.21 (0.04)  | 0.07 (NS)  | 0.29 (0.0002)* |
| \( ^{15}SUA_{\text{mean}} \) | 0.09 (NS)  | 0.04 (NS)  | 0.19 (0.02)* |

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**Fig. 1**

There is no significant correlation between lean body mass \( (^{15}LBM) \) estimated from the sex-specific formulae of Janmahasatian et al. [25] and mean SUV \( (^{15}SUW_{\text{mean}}) \) calculated using LBM as whole body metric in women (open circles; \( r = 0.14 \)) or in men (closed circles; \( r = -0.09 \)), but there is a strong correlation when the sexes are combined into a single group (\( r = 0.44; P < 0.0001 \)). "LBM, Janmahasatian lean body mass; \( SUW \), Janmahasatian scaled to lean body mass; SUV, standardised uptake value."

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The finding of significant correlations between SUV indices and whole body metrics when men and women were combined when there was no correlation in either sex analysed separately (Tables 1–3 and Fig. 1) is the result of anthropometric differences and consequent differences in SUV indices between the two sexes. Batallés et al. [26] found higher SUV in men than women, while Demir et al. [25], like us, found SUL, but not SUV, to be higher in men. This sex difference indicates that correlations when the sexes are combined may be misleading. Some of the previous studies either included only women [2,4] or did not distinguish between men and women [3,7].

Division by blood pool SUV renders tissue SUV a closer reflection of $^{18}$F-FDG clearance [19] (referred to as uptake constant in dynamic $^{18}$F-FDG studies), and bypasses whole body metric normalisation, which cancels out. Multiplication of this ratio by blood glucose concentration makes it a closer surrogate of hepatic glucose phosphorylation [20], which in dynamic studies is uptake constant multiplied by blood glucose [27,28]. We found no difference in mSUV between men and women, in keeping with an artefactually lower SUL and artefactually higher SUA in women, as suggested above. However, although division by blood pool SUV bypasses the choice of whole body metric, partial volume effects in relation to blood pool ROI become an issue and may explain why no sex differences in mSUV were seen, because several previous studies have shown differences in glucose metabolism between men and women [14,15], including a higher glucose uptake rate [29].

SUV is sensitive to statistical noise and to hepatic fat content. Thus, in general, SUV$_{max}$ indices, but not SUV$_{mean}$ or SUV$_{FA}$ indices, correlated strongly with all body size metrics, consistent with SUV$_{max}$ being more susceptible to noise, and therefore reaching higher values in large persons in whom there is greater signal attenuation. Adjusting SUV for hepatic fat (to give SUV$_{FA}$) turned out to have no relevance to choice of whole body metric in our study probably because there was no significant difference in liver fat percentage between men and women, and correspondingly no difference in hepatic CT density.

**Conclusion**

We believe in common with others that in general LBM, as a 3-dimensional variable, is the preferred whole body metric for normalising SUV for the purpose of quantifying $^{18}$F-FDG accumulation in pathological tissues, such as tumours, in both men and women. Although LBM tends to underestimate SUV in persons with high body fat percentage, we believe it is preferable to BSA because BSA is artefactually influenced not only by body fat percentage, which is greater in women, but also by body size, which is greater in men.

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**Table 4** Mean (SD) values of computed tomography density (HU), blood glucose (mmol/l), liver fat (%), body fat (%), whole body metrics, SUV indices and mSUV in men and women

|                | Men          | Women        | P       |
|----------------|--------------|--------------|---------|
| Blood glucose  | 5.7 (0.8)    | 5.6 (0.9)    | NS      |
| CT density     | 46 (10)      | 50 (12)      | NS      |
| %Liver fat     | 10.5 (2.9)   | 9.7 (3.0)    | NS      |
| %Body fat (Boer)| 26 (6)      | 32 (10)      | <0.0001 |
| %Body fat      | 25 (7)       | 39 (6)       | <0.0001 |
| Body weight    | 84 (16)      | 71 (18)      | <0.0001 |
| LBM            | 62 (7)       | 47 (6)       | <0.0001 |
| BSU            | 2.63 (0.22)  | 1.79 (0.24)  | <0.0001 |
| BSUFA          | 2.94 (0.18)  | 1.78 (0.21)  | <0.0001 |
| SUWFA          | 3.28 (0.012) | 0.0393 (0.0025) | <0.0001 |
| SUWmax         | 3.02 (0.62)  | 2.84 (0.65)  | NS      |
| SUWmean        | 2.03 (0.41)  | 1.96 (0.29)  | <0.0001 |
| BSULmax        | 1.67 (0.22)  | 1.57 (0.21)  | 0.005   |
| BSULmin        | 0.06 (0.001) | 0.075 (0.011) | NS      |
| BSUmin         | 0.065 (0.007) | 0.06 (0.008) | <0.0001 |
| SuFAmax        | 0.061 (0.008) | 0.066 (0.008) | <0.0001 |
| SuFAmin        | 0.072 (0.011) | 0.075 (0.011) | NS      |
| TSUAmx         | 0.055 (0.007) | 0.060 (0.008) | <0.0001 |
| TSUAmn         | 0.065 (0.008) | 0.066 (0.008) | <0.0001 |
| mSUV FA        | 9.35 (2.17)  | 8.12 (2.71)  | NS      |
| mSUV mean      | 7.96 (1.64)  | 8.22 (2.21)  | NS      |
| mSUV FA        | 8.90 (1.82)  | 9.13 (2.54)  | NS      |

SUW, Boer lean body mass; BSU, Haycock body surface area; LBM, Jaanmahasatian lean body mass; BSUL, Jaanmahasatian scaled to body surface area; BSA, Haycock scaled to body surface area; SUL, Jaanmahasatian scaled to lean body mass; LBM, lean body mass; NS, not significantly different between men and women; SUV, standardised uptake value; SUA, Tikuisis body surface area; SUA, Tikuisis scaled to body surface area; SUL, scaled to weight.

overestimating SUV because, like body weight, it increases, with no change in LBM, when body fat increases, explaining why SUA indices were higher in women. Moreover, as a two-dimensional variable, BSA is relatively higher in small individuals compared with large. It is notable that the sex-specific equations of Tikuisis gave almost identical estimates of BSA as the sex-non-specific formula of Haycock (Table 4). There were no sex differences in SUW. However, because they have more fat, women might have been expected to have higher SUW indices.

The generally stronger correlations between SUV$_{max}$ indices and corresponding whole body metrics compared with their mean and fat-adjusted equivalents are in keeping with the notion that SUV$_{max}$ is influenced by statistical noise and increased in large persons. This tendency, however, is opposed by BSA as a whole body metric because large persons have low BSA relative to their size, explaining why SUA$_{max}$ did not correlate so strongly with BSA compared with the correlations between SUL$_{max}$ and LBM (Tables 2 and 3).
Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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