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Abbreviations:

FDG = 2-[fluorine 18]fluoro-2-deoxy-D-glucose

SUV = standardized uptake value

SUV_{bsa} = SUV calculated by using body surface area

SUV_{bw} = SUV calculated by using body weight

SUV_{ibw} = SUV calculated by using ideal body weight

SUV_{lbm} = SUV calculated by using lean body mass

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Reevaluation of the Standardized Uptake Value for FDG: Variations with Body Weight and Methods for Correction¹

PURPOSE: To reevaluate the relationships between standardized uptake values (SUVs) and body weight by using positron emission tomography (PET) with 2-[fluorine 18]fluoro-2-deoxy-D-glucose (FDG).

MATERIALS AND METHODS: FDG PET scanning was performed in 138 female patients with known or suspected primary breast cancers. SUVs in blood and tumor ($n = 79$) were calculated by using body weight (SUV_{bw}), ideal body weight (SUV_{ibw}), lean body mass (SUV_{lbm}), and body surface area (SUV_{bsa}) on images obtained 50–60 minutes after the injection of FDG.

RESULTS: There was a strong positive correlation between the blood SUV_{bw} and body weight ($r = 0.705$, $P < .001$). The blood SUV_{ibw} reduced the weight dependence but showed a negative correlation with body weight ($r = -0.296$, $P < .001$). Both the blood SUV_{lbm} and SUV_{bsa} eliminated the weight dependence and showed no correlation with body weight ($r = -0.010$, $P = .904$ and $r = 0.106$, $P = .215$, respectively). Although there was a wide variance in the tumor SUV_{bw}, it showed a weak but significant positive correlation with body weight ($r = 0.207$, $P = .033$). Plots of the tumor SUV_{lbm} and SUV_{bsa} versus body weight showed relatively flat slopes.

CONCLUSION: SUV_{lbm} and SUV_{bsa} are weight-independent indices for FDG uptake, and SUV_{lbm} appears to be more appropriate for quantifying FDG uptake to avoid overestimation of glucose utilization in obese patients.

The radiopharmaceutical 2-[fluorine 18]fluoro-2-deoxy-D-glucose (FDG) has been shown to accumulate in malignant tumors because of their increased glucose metabolism (1). In the past several years, positron emission tomography (PET) with FDG has been widely used for differentiating malignant tumors from benign tumors and for assessing treatment efficacy in patients with various cancers (2). The standardized uptake value (SUV), which is defined as the ratio of activity in tissue per milliliter to the activity in the injected dose per patient body weight, has been proposed as a simple useful semiquantitative index for FDG accumulation in tissue (3). The SUV has also been referred to as the differential uptake ratio (4) or the distribution absorption ratio (5). Blood SUV is important, as the uptake of FDG in tumors and normal organs requires the delivery of the FDG via blood.

Although many investigators have been using SUV as a practical semiquantitative index for FDG uptake in tissue, it has been reported recently that SUV shows a strong positive correlation with patient body weight and rises 70%–98% from low-weight to high-weight patients (6,7). Zasadny and Wahl (6) reported that the SUV calculated by substituting lean body mass for total body weight (SUV_{lbm}) shows weight-independence for FDG accumulation in blood. Kim et al (7) also reported that the SUV obtained by substituting body surface area for total body weight (SUV_{bsa}) is less dependent on patient body weight than is the SUV.

It has been reported that heavy patients have relatively higher percentages of fat in their

bodies than have light patients (8). FDG uptake in fat in the fasting state is very low. This observation (ie, fat contributes to body weight but accumulates very little FDG in the fasting state) has been considered to be the explanation for why the SUVs in nonfatty tissues in heavy patients are increased relative to those in light patients (6). Therefore, Zasadny and Wahl (6) have proposed the use of the SUV_{lbm} as a weight-independent index for FDG accumulation in blood (and thus tumor). Although several methods have been reported for estimating lean body mass, a simple formula based on total body weight and height is now one of the most commonly used methods (9). However, in the report by Zasadny and Wahl (6), the lean body mass was calculated from a simple formula in which patient height alone was used (lean body mass = $45.5 + 0.91[\text{height} - 152]$ [10]). Some now believe this formula can be used to better predict ideal body weight than lean body mass (9).

Although SUV shows a strong positive correlation with patient body weight and although the corrections for lean body mass and body surface area proposed by Zasadny and Wahl (6) and Kim et al (7) are more independent of weight, these corrections were evaluated in only a relatively small number of patients and were not confirmed in a larger number of patients. In the current study, we calculated SUVs in blood and tumor by using the actual body weight of the patient; the lean body mass, as proposed by Zasadny and Wahl (6) (which is equivalent to ideal body weight); the lean body mass, based on the recent formula; and the body surface area. Thus, we reevaluated the relationships between these indices and body weight in a larger number of patients. Such standardization is viewed as important, given the continued growth in FDG PET imaging.

MATERIALS AND METHODS

Patient Population

Between July 1989 and February 1998, 157 eligible and consenting patients (two men, 155 women) with newly diagnosed or suspected breast cancer were examined at FDG PET. PET was performed as part of the prospective studies that were used to assess the utility of PET in differentiating or staging tumors and/or in assessing treatment response. Twenty-eight of these patients were included in the previous study of the SUV_{lbm} (6). All patients provided written informed consent for the

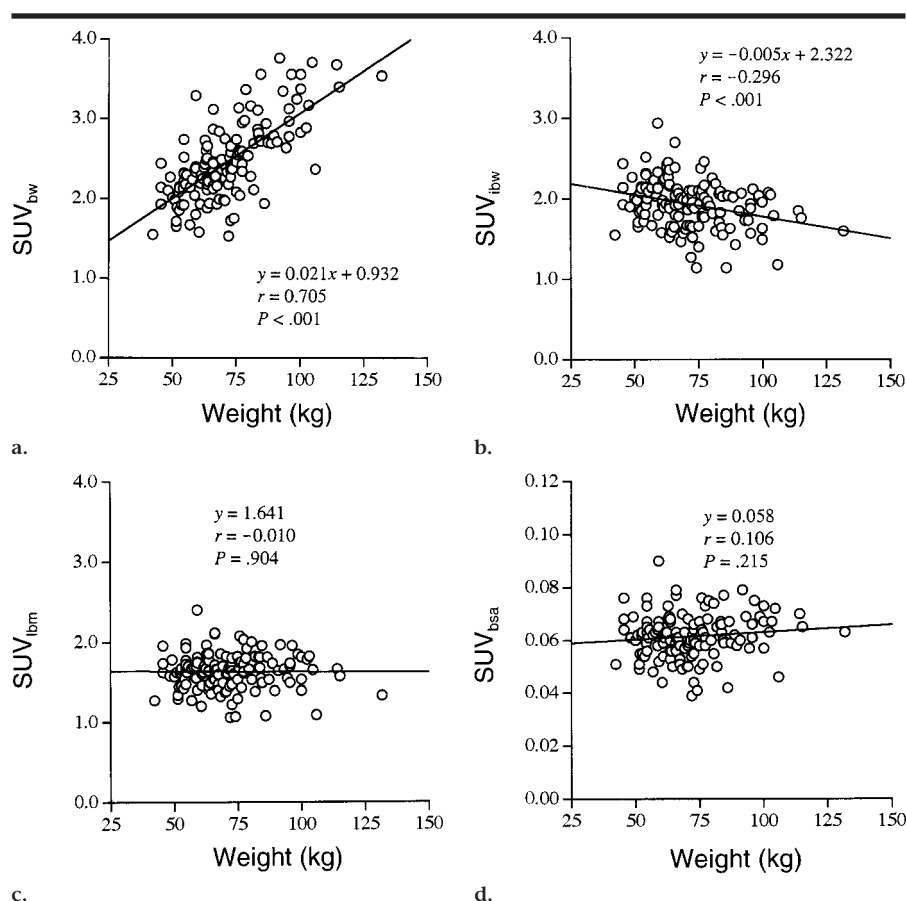


Figure 1. Graphs depict the relationships between patient body weight and blood SUVs: (a) SUV_{bw} , (b) SUV_{lbw} , (c) SUV_{lbm} , or (d) SUV_{bsa} . Note the strong positive correlation between SUV_{bw} and body weight and the lack of weight dependence for SUV_{lbm} and SUV_{bsa} .

imaging study, which was approved by the institutional review board and which was conducted under the guidelines for a physician-sponsored investigation of a new drug application for FDG. In the current study, 138 female patients who had no known glucose intolerance and in whom the PET studies and the administration of FDG were successfully completed were included in the subsequent analysis. Patient ages ranged from 26 to 79 years (mean age, 51 years \pm 13 [SD]), and body weights ranged from 42 to 132 kg (mean, 71 kg \pm 16). Patients fasted at least 4 hours before the administration of FDG, and mean plasma glucose values at the time of the PET study were 87 mg/dL \pm 16 (4.8 mmol/L \pm 0.89).

PET Scanning

FDG PET scanning was performed with either an Ecat 931/08 scanner (15 scanning planes, 10-cm longitudinal field of view; Siemens Medical Systems, Iselin, NJ) or an Ecat 921/Exact scanner (47

scanning planes, 15-cm longitudinal field of view; Siemens Medical Systems). The reconstructed x-y resolution, with a Hanning filter cut-off value of 0.3, was approximately 1.2 cm, full-width at half-maximum, for both scanners. Before the injections of tracer material were administered, at least one transmission image of at least 10-minute duration was obtained by using germanium 68 ring or rod sources to correct the attenuation on the emission images. Sequential dynamic images at the level of the suspected tumors were obtained immediately after the intravenous administration of approximately 370 MBq of FDG, which was produced as described previously (10). Dynamic images were acquired from 0 to 60 minutes in 17–25 frames.

Data Analysis

Images were reconstructed with a 128×128 matrix by using a filtered back-projection algorithm with a Hanning filter cut-off value of 0.3. To determine the

blood activity in each patient, a small square region of interest was placed inside the ascending aorta (4-pixel region of interest) or left atrium (16-pixel region of interest) on the last frame (obtained at 50–60 minutes) of the dynamic image (11). The maximal counts per pixel within the aorta were averaged over two (Ecat 931/08) or three (Ecat 921/Exact) contiguous planes, and only one plane was used in the left atrium.

For semiquantitative analysis of FDG uptake in blood and tumor, SUVs were calculated with patient body weight (SUV_{bw}), ideal body weight (SUV_{ibw}), lean body mass, and body surface area, as follows: (a) SUV_{bw} was decay-corrected tissue concentration (in kilobecquerels per milliliter) divided by the injected dose per body weight (in kilobecquerels per gram) (3). (b) SUV_{ibw} was decay-corrected tissue concentration (in kilobecquerels per milliliter) divided by the injected dose per ideal body weight (in kilobecquerels per gram). (This index was previously reported by Zasadny and Wahl [6] as the SUV calculated with lean body mass.) (c) SUV_{lhm} was decay-corrected tissue concentration (in kilobecquerels per milliliter) divided by injected dose per lean body mass (in kilobecquerels per gram). (d) SUV_{bsa} was decay-corrected tissue concentration (in kilobecquerels per milliliter) divided by the injected dose per body surface area (in kilobecquerels per meters squared) (7).

The ideal body weight (previously reported as lean body mass by Zasadny and Wahl [6]), lean body mass, and body surface area in women were calculated with the following formulas: (a) Ideal body weight (in kilograms) = $45.5 + 0.91(\text{height} - 152)$. Or, the ideal body weight was the weight, if the ideal body weight was greater than the weight (6,12). (b) Lean body mass (in kilograms) = $1.07(\text{weight}) - 148(\text{weight}/\text{height})^2$ (9). (c) Body surface area (in meters squared) = $(\text{weight} [\text{in kilograms}]^{0.425} \times (\text{height} [\text{in centimeters}]^{0.725} \times 0.007184$ (13).

We calculated SUVs for primary tumors in 79 patients and evaluated the relationships between the tumor SUVs and patient body weight. We did not calculate tumor SUVs in the other 59 patients because they had undergone excisional biopsy for their tumors before PET, because their PET images showed no obvious FDG uptake, or because their tumors were diagnosed as benign. We reviewed images in all planes that covered the tumor. A maximal FDG uptake in a small square (4×4 -pixel) region of interest was defined within a large region of interest

that covered the whole tumor by using a computerized, semiautomated algorithm. The maximal, single pixel within the 16-pixel region of interest in the tumor was used to minimize partial volume effects.

The relationships between the SUVs (in the blood and tumor, as defined previously) and patient body weight were assessed by means of the Pearson coefficient r and were plotted with a linear regression equation by using computerized statistical software (STATVIEW, version 4.5; Abacus Concepts, Berkeley, Calif). The significance of the correlations was assessed with the Fisher z test. P values for differences in the blood SUVs were assessed by using the two-tailed tests. According to the hypothesized correlation that was derived from the results of the positive or negative correlations for blood SUV_{bw} or SUV_{ibw} with body weight, the one-tailed tests were used to define P values for the tumor SUV_{bw} or SUV_{ibw} versus body weight. P values less than .05 were considered to indicate a significant difference.

RESULTS

The relationships for various formulations of SUVs in blood and patient body weight are shown in Figure 1. There was a significant positive correlation between the blood SUV_{bw} and patient body weight ($r = 0.705, P < .001$) (Fig 1a). The plot for SUV_{ibw} showed an approximate 4.2-fold decrease in the magnitude of the slope; however, the SUV_{ibw} showed a significant negative correlation with body weight ($r = -0.296, P < .001$) (Fig 1b). In contrast, the SUV_{lhm} and SUV_{bsa} remarkably reduced the dependence on body weight (both the slopes were flat); there was no significant correlation between the SUV_{lhm} or SUV_{bsa} and patient body weight (Fig 1c, 1d). The mean values for blood SUV_{bw} , SUV_{ibw} , SUV_{lhm} , and SUV_{bsa} were 2.46 ± 0.49 , 1.93 ± 0.30 , 1.63 ± 0.22 , and 0.062 ± 0.008 , respectively, and the coefficients of variation (percentage of the SD of the mean value) were 20%, 16%, 13%, and 13%, respectively.

The relationships between the various SUVs (SUV_{bw} , SUV_{ibw} , SUV_{lhm} , and SUV_{bsa}) in tumors and patient body weight are shown in Figure 2. Although there was a wide variance in the tumor SUV_{bw} in the patients, the tumor SUV_{bw} showed a weak but significant positive correlation ($r = 0.207, P = .033$) with body weight. The SUV_{ibw} , SUV_{lhm} , and SUV_{bsa} showed nonsignificant and very weak

negative correlations with body weight ($r = -0.152, P = .091$; $r = -0.077, P = .498$; and $r = -0.027, P = .811$; respectively); the slopes of the regression lines were relatively flat compared with the slope of the line for SUV_{bw} .

The relationships between patient body weight and ideal body weight or lean body mass are shown in Figure 3. The ideal body weight ranged from 42.3 to 73.6 kg (mean weight, $55.5 \text{ kg} \pm 6.5$), and the lean body mass ranged from 34.6 to 63.1 kg (mean mass, $46.9 \text{ kg} \pm 5.0$). Each of the ideal body weights was larger than the lean body mass, although the ideal body weight was similar to the lean body mass in some heavy patients.

DISCUSSION

In this study, the blood SUV_{bw} showed a significant positive correlation with patient body weight ($r = 0.705, P < .001$), and this result was similar to those previously reported by Zasadny and Wahl (6) for SUV_{bw} in blood and by Kim et al (7) for SUV_{bw} in normal liver. The SUV_{ibw} significantly reduced the weight dependence, which was consistent with the previous results of Zasadny and Wahl (6), but it now showed a significant negative correlation with patient body weight ($r = -0.296, P < .001$) in our larger patient group. Both the SUV_{lhm} and SUV_{bsa} essentially eliminated the dependence of SUV_{bw} on body weight; there was no significant correlation between the SUV_{lhm} or SUV_{bsa} and patient body weight. Moreover, the coefficients of variation were smaller for the SUV_{lhm} or SUV_{bsa} than for the SUV_{bw} or SUV_{ibw} .

In a previous study, Zasadny and Wahl (6) reported that lean body mass was calculated from patient height alone, but this formula is now considered by some to be more predictive of ideal body weight (9,12). Since actual body weights could be smaller than the calculated ideal body weight in light (thin) patients, Zasadny and Wahl (6) applied body weight to correct SUV in such light patients (ie, ideal body weight = weight, if calculated ideal body weight > weight). Thus, the ideal body weight did not represent "real" lean body mass, and each of the calculated ideal body weight values was larger than the lean body mass (Fig 3). In light patients, the SUV_{ibw} showed relatively larger values compared with those for the SUV_{lhm} . As a result, the plot for SUV_{ibw} showed a significant negative correlation with patient body weight, whereas the plot for SUV_{lhm} showed a very flat slope

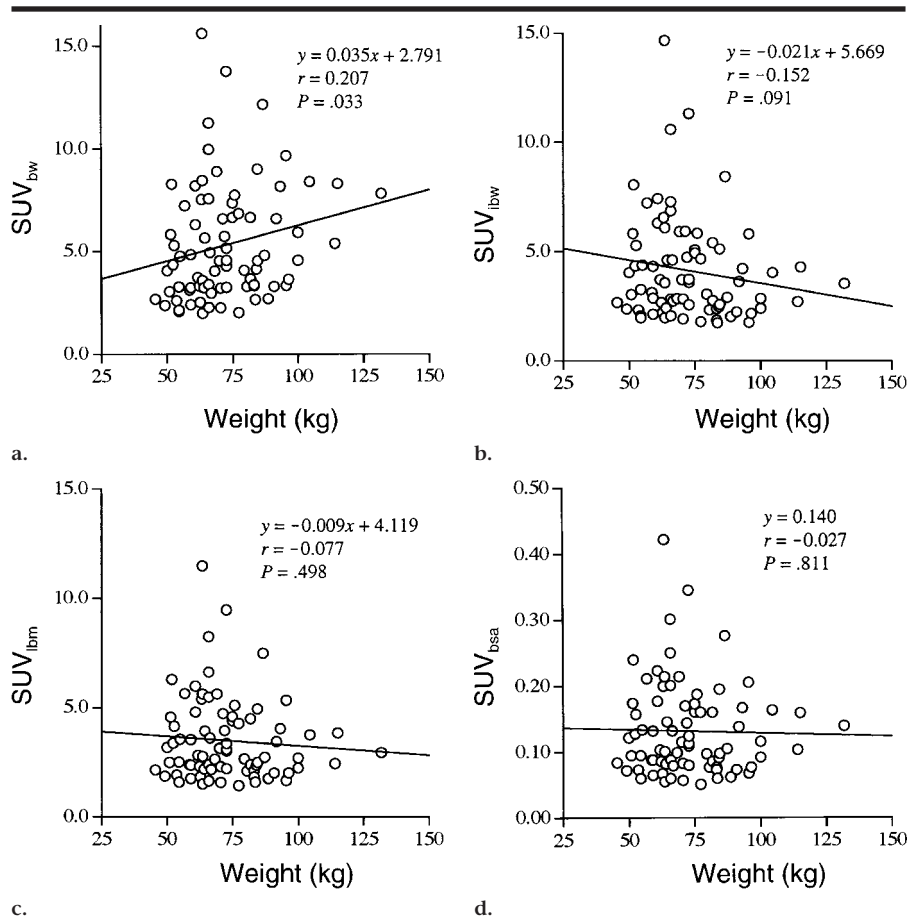


Figure 2. Graphs depict the relationships between body weight and tumor SUVs: (a) SUV_{bw} , (b) SUV_{ibw} , (c) SUV_{lbm} , or (d) SUV_{bsa} . Note the weak but significant positive correlation between SUV_{bw} and body weight and the relatively flat slopes for the plots for SUV_{lbm} and SUV_{bsa} .

and showed no significant correlation with body weight (Fig 1b, 1c).

Lean body mass is defined as the mass that comprises body cell mass, extracellular water, and nonfatty intercellular connective tissue (9). Since lean body mass includes essential fat that is present even during starvation, lean body mass is slightly different from fat-free mass. Consideration of lean body mass seems to be relevant in obese patients because there is an increase in lean body mass and fat. It has been considered that the distribution volume of a variety of chemotherapeutic agents correlates very well with lean body mass (9).

The SUV_{bsa} remarkably reduced dependence on body weight, which was similar to the previous findings by Kim et al (7), and there was no significant correlation between the SUV_{bsa} and patient body weight (Fig 1d). Both body surface area and lean body mass were calculated on the basis of patient body weight and height; there was a strong positive correlation between both indices ($r = 0.898$ in

this study). Although the SUV_{bsa} and the SUV_{lbm} are weight-independent indices, we recommend using the SUV_{lbm} rather than the SUV_{bsa} since body surface area is obviously an index with units that are different from those for lean body mass, ideal body weight, or body weight. That is, body surface area has units for area (meters squared), whereas lean body mass has units for mass (kilograms), which are similar to those for body weight. The SUV_{lbm} is similar in magnitude to the conventional SUV (SUV_{bw} in this study), whereas the SUV_{bsa} is not as simply comparable.

There are some limitations in this study. Since the percentage of fat relative to body weight can vary with patient age, lean body mass could also vary with age (8,9). However, the formula for lean body mass that was used in this study did not account for age. When we plotted the SUV_{lbm} versus patient age, there was a weak (but significant) positive correlation between the SUV_{lbm} and patient age ($r = 0.297$, $P < .001$) (Fig 4). Thus, it might be

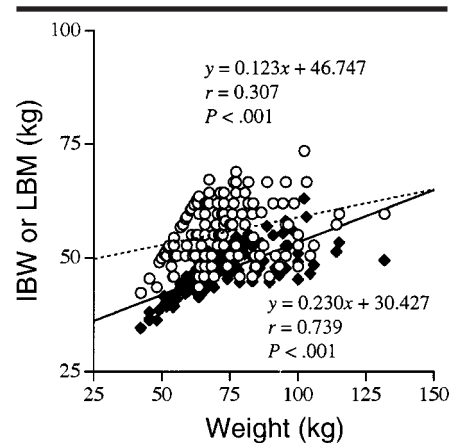


Figure 3. Graph depicts the relationships between ideal body weight (IBW , \circ) or lean body mass (LBM , \blacklozenge) and weight. Note the difference between ideal body weight and lean body mass in each patient (ideal body weight > lean body mass).

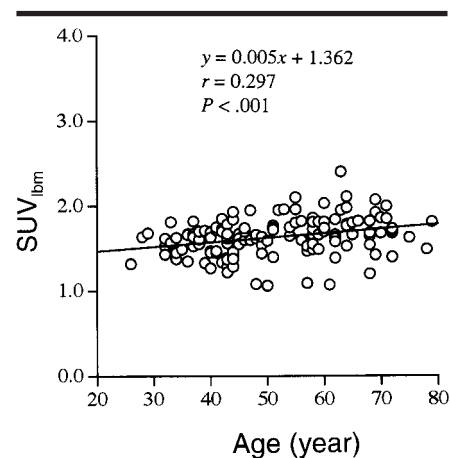


Figure 4. Graph depicts the relationship between blood SUV_{lbm} and patient age. Note the weak but significant positive correlation.

expected that tumor SUV_{lbm} could also rise slightly with age. In the current study, we evaluated only female patients, and patient ages ranged from 26 to 79 years. Similar studies in male patients (the formula for lean body mass in men is as follows: lean body mass in kilograms = $1.10[\text{weight}] - 120[\text{weight}/\text{height}]^2$ [9]) and studies in younger or older patients would be of interest.

Moreover, although FDG accumulates much less in fat than in lean tissues in the fasting state, it has been reported that the accumulation of FDG in fat could be increased (or relatively preserved) with high levels of serum glucose and/or insulin (14,15). It is, therefore, uncertain if the distribution volume of FDG would correlate well with lean body mass after

feeding and/or in the presence of insulin. It is also uncertain if the SUV_{lbm} would be independent of patient body weight in such conditions.

The correlation between the tumor SUV_{bw} and patient body weight had less robust significance ($P = .033$) (Fig 2a), which was only somewhat similar to the results for the blood SUV_{bw} . This more modest relationship could have been due to the wide biologic variance in tumors. Indeed, the tumor characteristics (histologic type, tumor size, stage, etc) were different in each patient, and there were expected biologic differences in tumor glucose utilization; that is, more aggressive tumors could have used more glucose and could have had a greater FDG uptake. If we could have selected the tumors that have similar biologic characteristics, we would have expected the relationship between tumor SUV_{bw} and patient body weight to be more clearly demonstrated. We also would have expected that, in a given patient, if the blood SUV were overestimated, the tumor SUV also would have been overestimated. This, of course, could be of great practical importance if the SUV were being used to predict quantitatively whether a given tumor is malignant or benign.

It has been reported that quantitative assessment of FDG uptake is useful in the differentiation of malignant tumors from benign tumors (such as lung cancer) and in the assessment of treatment response in cancer patients (3,5,16–19). SUVs have shown higher specificity than visual analysis in the differentiation of malignant tumors from benign tumors (18,19). Minn et al (11) reported that the SUV_{lbm} or influx constant Ki was more reproducible from study to study than were the complex metabolic parameters derived from kinetic modeling. Further, an excellent correlation was seen between SUV_{lbm} and the influx constant. Since SUVs can be determined from a static image and although Ki or kinetic modeling param-

eters require several dynamic frames and longer times for acquisition, we can propose that, in clinical practice, SUVs would be simple and reproducible indices for glucose metabolism in tumors; the correction to SUV_{lbm} appears reasonable.

In summary, the SUV_{bw} showed a positive correlation with body weight, and the SUV_{ibw} reduced the weight dependence but showed a weak negative correlation with body weight; in contrast, both the SUV_{lbm} and the SUV_{bsa} essentially eliminated the weight dependence, and plots of these SUVs versus body weight showed relatively flat slopes. SUV_{lbm} or SUV_{bsa} would be more appropriate than SUV_{bw} or SUV_{ibw} for quantifying FDG uptake in nonfatty tissues. We propose that SUV_{lbm} may be the more practical index for FDG uptake in tumors and for routine clinical application.

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