Direct Determination of Lean Body Mass by CT in F-18 FDG PET/CT Studies: Comparison with Estimates Using Predictive Equations

Chang Guhn Kim · Woo Hyoun Kim ·
Myoung Hyoun Kim · Dae-Weung Kim

Received: 25 February 2013 / Revised: 23 April 2013 / Accepted: 24 April 2013 / Published online: 7 May 2013
© Korean Society of Nuclear Medicine 2013

Abstract

Purpose The purpose of this study was to estimate lean body mass (LBM) using CT (LBM CTs) and compare the results with LBM estimates of four different predictive equations (LBM PEs) to assess whether LBM CTs and LBM PEs can be used interchangeably for SUV normalization.

Methods Whole-body F-18 FDG PET/CT studies were conducted on 392 patients. LBM CT1 is modified adipose tissue-free body mass, and LBM CT2 is adipose tissue-free body mass. Four different PEs were used for comparison (LBM PE1–4). Agreement between the two measurement methods was assessed by Bland-Altman analysis. We calculated the difference between two methods (bias), the percentage of difference, and the limits of agreement, expressed as a percentage. **Results** For LBM CTs vs. LBM PEs, except LBM PE3, the ranges of biases and limits of agreement were −3.77 to 3.81 kg and 26.60–35.05 %, respectively, indicating the wide limits of agreement and differing magnitudes of bias. For LBM CTs vs. LBM PE3, LBM PE3 had wider limits of agreement and greater positive bias (44.28–46.19 % and 10.49 to 14.04 kg, respectively), showing unacceptably large discrepancies between LBM CTs and LBM PE3.

Conclusion This study demonstrated that there are substantial discrepancies between individual LBM CTs and LBM PEs, and this should be taken into account when LBM CTs and LBM PEs are used interchangeably between patients.

Keywords Lean body mass · Adipose tissue · Body composition · Computed tomography · Positron emission tomography

Introduction

The use of the standardized uptake value (SUV) normalized by lean body mass (LBM) has been recommended for PET Response Criteria in Solid Tumors [1]. However, the determination of LBM usually relies on various predictive equations (PEs) [2–5]. Although it is not precisely defined or universally agreed upon, there are two principal methods of estimating LBM: as fat-free body mass (FFM) or adipose tissue-free body mass (ATFM) [6–9]. Traditionally, LBM was defined as FFM, which was originally based on the unique measurable component of fat. After the introduction of CT and MRI technology into the field of body composition research, another definition of LBM, ATFM, was often used interchangeably with FFM. The terms *fat* and *adipose tissue* (AT) refer to different components of the body composition [9–11]. Fat is a chemical unit that consists almost entirely of triglycerides and is primarily present in AT. Most PEs estimate this fat content, but not AT. AT is an anatomical entity that can be classified as subcutaneous AT (SAT), visceral AT (VAT), interstitial AT (IAT), or yellow bone marrow (YBM) [10, 11]. AT typically contains 80 % fat; the remaining 20 % is water, protein, and minerals [9, 10]. Computed tomographic (CT) methods for quantifying AT volume or mass have been validated in animals [12], human cadavers [13, 14], and living humans [15, 16]. CT is now considered the most accurate method available for directly measuring AT volume *in vivo* [17, 18]. Many investigators using CT or MRI to measure total body fat and total AT have found that these two parameters are highly correlated or similar, although not identical [11, 19]. However, there are no published reports comparing whole-body CT (using modern PET/CT systems) with various PEs as methods for

C. G. Kim (✉) · W. H. Kim · M. H. Kim · D.-W. Kim
Department of Nuclear Medicine, Wonkwang University School
of Medicine, 344-2 Shinyong-Dong,
Iksan 570-711, Korea
e-mail: leokim@wonkwang.ac.kr

C. G. Kim · D.-W. Kim
Institute of Wonkwang Medical Science, 344-2 Shinyong-Dong,
Iksan 570-711, Korea

determining LBM in a large number of patients. We investigated agreement between LBM calculated with CT and LBM estimated with PEs to assess whether CT-based LBM and PE-based LBM can be used interchangeably for SUV normalization.

The purpose of this study was to determine LBM by CT in whole-body F-18 FDG PET/CT studies and to compare the results with LBMs estimated with four different PEs.

Materials and Methods

Whole-body F-18 FDG PET/CT studies (Biograph 16, Siemens, Knoxville, TN, USA) were conducted in 392 patients for routine purposes. Patients with heavy body habitus who exceeded the field of view (FOV) were excluded. Patient characteristics are summarized in Table 1. This study was approved by an institutional review board. Patients were positioned feet first and supine, with their arms beside their body, while being scanned from head to foot. The maximum scan length from head to foot was 183 cm.

The CT acquisition parameters were as follows: tube voltage, 120 kVp; tube current, 60 mA with automated current modulation; tube rotation speed, 0.5 s; table feed, 36 mm·s⁻¹; beam collimation, 1.5×16 mm; image matrix size, 512×512; FOV, 70 cm; slice thickness 5 mm for reconstructed images, with 3-mm spacing.

Intravenous and oral contrast agents were not administered.

A blank CT scan of the scanner table, including the head rest set and the abdominal binder, was conducted three times to determine the number of voxels erroneously assigned to AT depending on the patient's height (500–700 cm³). This volume was subtracted from the total AT volume of each patient. The patient's body weight (BW) was corrected for the weight of the hospital gown (about 610 g).

Measurements and Data Analysis

AT was defined as voxels identified and measured by CT as having CT numbers between −140 and −30 Hounsfield

units, as previously reported [20]. A built-in software package provided by the manufacturer was used to calculate total AT volume. An AT density of 0.95 kg·l⁻¹ and an AT fat content (fraction) of 80 % were applied to convert AT volume to AT mass or fat mass [9, 10, 21].

LBM was defined by two different methods. First, the AT that was measurable by CT was assessed. The fat mass in that AT was then calculated using fat fraction of AT (80 %) (i.e., modified ATFM):

$$\text{LBM CT1 (kg)} = \text{BW} - \text{fat in AT} = \text{BW} - \text{AT volume} \times 0.95 (\text{kg} \cdot \text{l}^{-1}) \times 0.8 \text{ (Fig. 1a)}$$

The second method for determining LBM is as follows:

$$\text{LBM CT2 (kg)} = \text{BW} - \text{AT mass} = \text{BW} - \text{AT volume} \times 0.95 (\text{kg} \cdot \text{l}^{-1}) \text{ (Fig. 1b)} \text{ (i.e., ATFM)}$$

For comparison, we used four different PEs to estimate LBM PE1-4. These PE1-4s were originally developed to

Fig. 1 Graphical illustrations show two LBM CT models and the relationship between AT and body fat components. The shaded areas indicate LBM CT1 (a) and LBM CT2 (b). AT adipose tissue, CT computed tomography, IAT interstitial AT, LBM lean body mass, Le essential lipid, Ln nonessential lipid, RAT retroperitoneal AT, SAT subcutaneous AT, VAT visceral AT, YBM yellow bone marrow, Modified from [28]

Table 1 Patient characteristics ($n=392$)

Characteristics	Mean $\pm$ SD (range)
Men:women	198: 194
Age (years)	59.2 $\pm$ 13.4 (22~88)
Weight (kg)	59.0 $\pm$ 10.4 (36.1~93.0)
Height (cm)	160.3 $\pm$ 8.48 (139~180)
BMI (kg/m ²)	22.92 $\pm$ 3.28 (15.1~36.3)
LBM CT1 (kg)	44.88 $\pm$ 8.44 (27.0~74.1)
LBM CT2 (kg)	41.33 $\pm$ 8.46 (24.4~70.1)

BMI body mass index, LBM lean body mass, CT computed tomography

estimate body fat mass; thus, these formulae were rearranged to estimate LBM PE1–4 as follows [2–5]:

LBM PE1 (for males) = $1.1 \times BW - 128 \times (BW \div \text{height})^2$, and
LBM PE1 (for females) = $1.07 \times BW - 148 \times (BW \div \text{height})^2$ [2];

LBM PE2 = $BW - \{BW \times [1.2 \times (BW \div \text{height})^2 + (0.23 \times \text{age}) - (10.8 \times \text{sex}) - 5.4] \div 100\}$ [3];

LBM PE3 (for males) = $48.0 + 1.06 \times (\text{height} - 152)$, and
LBM PE3 (for females) = $45.5 + 0.91 \times (\text{height} - 152)$ [4]; and
LBM PE4 = $BW - \{BW \times [76 - 1097.8 \times (\text{height}^2 \div BW) - (20.6 \times \text{sex}) + (0.053 \times \text{age}) + 95.0 \times (\text{height}^2 \div BW) - (0.044 \times \text{age}) + 154 \times \text{sex} \times (\text{height}^2 \div BW) + (0.034 \times \text{sex} \times \text{age})] \div 100\}$ [5], where sex = 1 for males and 0 for females; BW is in kilograms; and height is in meters in LBM PE2 and LBM PE4 and in centimeters in LBM PE1 and LBM PE3.

Agreement between LBM CTs and LBM PEs was assessed using the Bland-Altman analysis [22]. Differences between LBM PE1 and LBM CT1 were calculated for each patient (LBM PE1 – LBM CT1, $\bar{d} \pm \text{SD}$). Bias was defined as the mean difference ($\bar{d}$). Percentages of differences were calculated to compare the magnitudes of differences, which were calculated as $100 \times$ the difference between LBM CT1 and LBM PE1 divided by the mean of the two methods for each patient. The 95 % limits of agreement (limits of agreement, for short) between the two methods were defined by Bland-Altman analysis as $\bar{d} - 2\text{SD}$ to $\bar{d} + 2\text{SD}$. To compare relative magnitudes of the limits of agreement, the percentage of limits of agreement was calculated as follows: $100 \times 4 \text{ SD of the differences} \div \text{the average of the global mean of LBM CT1 and LBM PE1}$ [23].

Analyses of LBM CT1 vs. LBM PE2–4 and LBM CT2 vs. LBM PE1–4 were conducted in a similar way.

Statistical Analysis

Statistical analysis was performed using PASW Statistics 18 (SPSS Inc., Chicago, IL, USA). The normal distribution of the differences was tested using the Kolmogorov-Smirnov test. The differences were normally distributed in six paired data sets, but the differences between LBM CTs and LBM PE3 (2 paired data sets) were slightly skewed. However, this was not considered to have had a serious effect on the overall interpretation of the results. $P < 0.05$ was considered statistically significant.

Results

For LBM CTs vs. LBM PEs, except LBM PE3, the ranges of biases ($\bar{d}$), SDs of percentage of difference, and percentage limits of agreement were -3.77 to 3.81 kg, 6.63 – 8.96 %, and

26.60 – 35.05 %, respectively, thereby indicating the wide limits of agreement and differing magnitudes of bias (Fig. 2, Table 2). A representative Bland-Altman plot showing discrepancies between LBM CT2 and LBM PE2 in individual patients is shown in Fig. 3. For LBM CTs vs. LBM PE3, the corresponding figures were 10.49 to 14.04 kg, 10.63 – 10.97 %, and 44.28 – 46.19 %, respectively; compared with other LBM PEs, these were greater values for limits of agreement and had a large positive bias (Fig. 2, Table 2). Thus, there were unacceptably large discrepancies between LBM CTs and LBM PE3.

Discussion

The aim of the current study was to investigate whether LBM CTs and LBM PEs can be used interchangeably for SUV normalization.

To assess agreement between the two measurement methods, the Bland-Altman analysis was performed, which is commonly used to measure agreement between clinical measurement methods [22]. The 95 % limits of agreement define the range within which 95 % of all differences between measurements by the two methods

Fig. 2 Irrespective of the magnitudes of biases (bars), wide limits of agreement (error bars, actual LBM values in kg, mean difference ± 2 SD) were observed between LBM CT1 and LBM PE1–4 (a) and between LBM CT2 and LBM PE1–4 (b)

Table 2 Comparison of Lean Body Mass Estimated by CT and Predictive Equations ($n=392$)

	LBM PE1	LBM PE2	LBM PE3	LBM PE4
LBM PEs (kg)	45.14±7.36	41.11±7.99	55.37±9.70	43.36±7.80
LBM CT1 (44.88±8.44, kg)				
Difference ^a ($\bar{d} \pm$ SD, kg)	0.26±2.99	-3.77±3.06	10.49±5.79	-1.52±3.19
Percentage difference ^b (%)	0.99±6.63	-8.90±7.18	21.02±10.97	-3.29±7.14
Percentage limits of agreement ^c (%)	26.60	28.47	46.19	28.91
LBM CT2 (41.33±8.46, kg)				
Difference ($\bar{d} \pm$ SD, kg)	3.81±3.60	-0.22±3.61	14.04±5.35	2.03±3.32
Percentage difference (%)	9.52±8.96	-0.36±8.94	29.42±10.63	5.25±8.06
Percentage limits of agreement (%)	33.30	35.05	44.28	31.38

Values are mean $\pm$ SD. CT computed tomography, LBM lean body mass, PE predictive equation

^aLBM PEs-LBM CTs

^bDifference (d)/mean of two methods

^c4 SD/average of global mean of two methods

will lie: $\bar{d} - 2$ SD through $\bar{d} + 2$ SD (more precisely, $\bar{d} \pm 1.96$ SD) (Fig. 3). If differences within the limits of agreement would not be clinically significant, the two measurement methods could be used interchangeably.

For example, if actual male patients A and B are similar in weight and height: 57.68 kg and 163 cm, and 57.48 kg and 163 cm, respectively, then the LBM PE1s for patients A and B are 47.42 kg and 47.31 kg, respectively. However, the LBM CT2s for patients A and B are 52.50 kg and 39.84 kg, respectively. The difference in LBM CT2 between the two patients is 12.66 kg. The difference between LBM CT2 and LBM PE1 for the whole group is 3.81 ± 3.60 kg ($\bar{d} \pm$ SD) (Table 2). Thus, the difference in LBM CT2 between the two patients approaches 4 SD of the difference (33.30 % limit of agreement, i.e., 2 SD in opposite directions from the mean difference) (Table 2). This limit of agreement (33.30 %) should be acceptable in order for these two values to be used interchangeably. When the SUVs are normalized by LBM CT2 and LBM PEs, they should not be compared with each other if these limits of agreement are not acceptable [22].

Fig. 3 A Bland-Altman plot depicts discrepancies between LBM CT2 and LBM PE2 in individual patients. The percentage limit of agreement is the interval between $\bar{d} - 1.96$ SD and $\bar{d} + 1.96$ SD, divided by the average of the global mean of the two methods. Regression analysis revealed no statistically significant relationship between measured differences (y-axis) and measured averages (x-axis) ($p=0.332$)

Interestingly, body fat mass estimated by PE1 was slightly smaller than fat mass measured by the LBM CT1 model in our patient population (13.86 vs. 14.12 kg, Table 2). In the LBM CT1 model, the fat mass in AT that is measurable by CT is smaller than the total fat mass because not all of the AT can be measured by CT. Furthermore, a small amount of fat is also present in non-AT, such as the liver (hepatocytes), muscle (myocytes), and blood (as lipoproteins) (Fig. 1a). If the assumed AT fat fraction of 80 % is true in our study population, this finding might suggest that PE1 underestimated body fat and, consequently, overestimated LBM.

PE1 is probably the most commonly used equation for SUV normalization. It was first described in 1976 by James [2]. In some published reports, the value 128 in LBM PE1 was printed as 120 [24, 25] and adopted in the PET community [26, 27]. If 120 is used instead of 128 in LBM PE1, the mean difference would increase further.

PE2 was described in 1991, and it was based on an underwater weighing method (i.e., hydrodensitometry) [3]. The LBM CT2 model was suited to PE2 for our patient sample with regard to near absence of bias (-0.36 % mean difference), but wide discrepancy similar to other PEs is still present. On average (the mean difference or bias), LBM CT2 and LBM PE2 are almost identical. This may suggest that AT mass calculated by CT (i.e., the LBM CT2 model) and body fat mass measured by the traditional criterion method using hydrodensitometry, on which PE2 is based, may also be very similar, as previously reported by many investigators (1.24 % difference between AT and fat mass in the current study) [11, 19]. In this regard, the current study could be regarded as a validation study for PEs. This may be supported by the observations that the percentage differences between LBM CTs and LBM PEs (except LBM PE3) were less than 10 % as a whole group.

There were unacceptably large discrepancies between LBM CTs and LBM PE3 (Fig. 2, Table 2). This suggests that normalization of the SUV with an ideal body weight (estimated by PE3) should be performed with caution. PE3 was described in 1974 and was based on a concept of ideal body weight based only on height [4].

PE4 was proposed for Asian subjects in 2000, and it was based on a four-component model of body fat measurement. The same paper proposed another PE for African Americans and whites. We did not use this PE in the current study, but it yields results similar to those of PE4 (data not shown).

PEs are very useful methods for estimating LBMs when direct measurement of individual LBM is not feasible in the clinical setting. In contrast, routine whole body CT can be used for attenuation correction and localization of FDG uptake in FDG PET/CT study, and consequently, direct determination of individual LBM can be obtained in clinical practice. Either LBM CTs or LBM PEs, respectively, can be used for SUV normalization in FDG PET/CT studies. In other words, they can be used to compare, for example, LBM PE2 for patient A with LBM PE2 for patient B; however, it may be inappropriate to compare LBM CT2 for patient A with LBM PE2 for patient B. Apart from which measurement method is more accurate and precise than others, we intended to assess whether LBM CTs and LBM PEs can be used interchangeably for SUV normalization.

We compared CT-based SUV with PE-based SUV in 453 patients and reported that substantial discrepancies were observed between these two methods [28]. Herein, we emphasized the rationale for CT-based direct determination of LBM for SUV normalization in FDG PET/CT studies, as we have previously described [29].

The clinical implications of our results are as follows:

First, the current study demonstrated that, irrespective of magnitudes of bias, there are wide limits of agreement between individual LBM CTs and LBM PEs, although percentage differences are less than 10 % (except LBM PE3) as a whole group. Thus, direct measurement of LBM by CT instead of using PEs may be one of the most useful methods when accurate measurements of individual LBMs are required, for example, for clinical trials in drug development where even small changes in LBMs with subsequent SUVs may affect the interpretation of the results obtained.

Second, LBM CT2 and LBM PE2, on average, are almost identical (−0.36 % mean difference), implying that AT mass determined by the LBM CT2 model and body fat mass *directly* measured by the criterion method with hydrodensitometry (not by PE2) would also be very similar (this deduction was made based on the very small percentage difference between LBM CT2 and LBM PE2). Hence, if PEs are used for LBM estimation, PE2 is preferred to other PEs, at least for our patient population (however, these values again may be inappropriate for interchangeable use with LBM CT2, but can be used alone as discussed above).

The results of the current study correspond well with a previous study that reported a wide range of discrepancies (32–56 % limits of agreement, calculated based on published data) in LBMs using various PEs,

including all of the PEs we analyzed when compared with measurements using dual-energy X-ray absorptiometry as a reference method [30].

Recently, CT-based direct measurement of LBM in 18 patients has been reported in the nuclear medicine literature [31]. In this study, 26 whole-body CT image data sets (head to toe) obtained from 18 patients were used to predict whole-body LBM of patients who underwent limited whole-body scans (for example, the skull base to mid-thigh). In addition, a CT number range for AT of −190 HU to −30 HU was applied to both contrast-enhanced (14/18 patients) and non-enhanced CT images to calculate AT mass. To our knowledge, however, the CT number range for AT on contrast-enhanced CT images has not been reported, and the CT number range used in this study was different from that used in our studies [28, 29, 31].

The principal limitation of whole-body CT for quantification of LBM is that it is not applicable to patients with large body habitus who exceed the FOV because of truncation artifacts. An increase in radiation dose, although small relative to the total dose, is required. However, the additional dose required was minimized in the current study by using a low-dose CT technique (60 mA) for attenuation correction.

Further studies of other patient samples are necessary to verify these observations.

Conclusion

This study demonstrated that there are substantial discrepancies between individual LBM CTs and LBM PEs, and this finding should be taken into consideration when comparing these values between patients.

Acknowledgments This study was supported by Wonkwang University in 2011.

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

References

1. Wahl RL, Jacene H, Kasamon Y, Lodge MA. From RECIST to PERCIST: evolving considerations for PET response criteria in solid tumors. *J Nucl Med: Off Publ So Nucl Med*. 2009;50 Suppl 1:122S–50S.
2. James WPT. Research on obesity. London: Her Majesty's Stationery Office; 1976. p. 8–12.
3. Deurenberg P, Weststrate JA, Seidell JC. Body mass index as a measure of body fatness: age- and sex-specific prediction formulas. *Br J Nutr*. 1991;65(2):105–14.
4. Devine B. Gentamicin therapy. *Drug Intell Clin Pharm*. 1974;8:650–5.

5. Gallagher D, Heymsfield SB, Heo M, Jebb SA, Murgatroyd PR, Sakamoto Y. Healthy percentage body fat ranges: an approach for developing guidelines based on body mass index. *Am J Clin Nutr*. 2000;72(3):694–701.
6. Bellisari A, Roche AF. Anthropometry and ultrasound. In: Heymsfield SB, Lohman TG, Wang Z, Going SB, editors. *Human body composition*. Champaign: Human Kinetics; 2005. p. 109–27.
7. Chowdhury B, Sjoström L, Alpsten M, Kostanty J, Kvist H, Lofgren R. A multicompartiment body composition technique based on computerized tomography. *Int J Obes Relat Metab Disord: J Int Assoc study of Obes*. 1994;18(4):219–34.
8. Shen W, St-Onge MP, Wang Z, Heymsfield SB. Study of body composition: an overview. In: Heymsfield SB, Lohman TG, Wang Z, Going SB, editors. *Human body composition*. Champaign: Human Kinetics; 2005. p. 3–14.
9. Wang ZM, Pierson Jr RN, Heymsfield SB. The five-level model: a new approach to organizing body-composition research. *Am J Clin Nutr*. 1992;56(1):19–28.
10. Basic anatomical and physiological data for use in radiological protection: reference values. A report of age- and gender-related differences in the anatomical and physiological characteristics of reference individuals. ICRP Publication 89. *Annals of the ICRP*. 2002;32(3–4):18–9, 72–6, 205–6.
11. Shen W, Wang Z, Punyanita M, Lei J, Sinav A, Kral JG, et al. Adipose tissue quantification by imaging methods: a proposed classification. *Obes Res*. 2003;11(1):5–16.
12. Ross R, Leger L, Guardo R, De Guise J, Pike BG. Adipose tissue volume measured by magnetic resonance imaging and computerized tomography in rats. *J Appl Physiol (Bethesda, MD: 1985)*. 1991;70(5):2164–72.
13. Mitsiopoulos N, Baumgartner RN, Heymsfield SB, Lyons W, Gallagher D, Ross R. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. *J Appl Physiol (Bethesda, MD: 1985)*. 1998;85(1):115–22.
14. Rossner S, Bo WJ, Hiltbrandt E, Hinson W, Karstaedt N, Santiago P, et al. Adipose tissue determinations in cadavers—a comparison between cross-sectional planimetry and computed tomography. *Int J Obes*. 1990;14(10):893–902.
15. Seidell JC, Bakker CJ, van der Kooy K. Imaging techniques for measuring adipose-tissue distribution—a comparison between computed tomography and 1.5-T magnetic resonance. *Am J Clin Nutr*. 1990;51(6):953–7.
16. Sjoström L, Kvist H, Cederblad A, Tylen U. Determination of total adipose tissue and body fat in women by computed tomography, ⁴⁰K, and tritium. *Am J Physiol*. 1986;250(6 Pt 1):E736–45.
17. Mattsson S, Thomas BJ. Development of methods for body composition studies. *Phys Med Biol*. 2006;51(13):R203–28.
18. Ross R. Advances in the application of imaging methods in applied and clinical physiology. *Acta Diabetol*. 2003;40 Suppl 1: S45–50.
19. Kullberg J, Brandberg J, Angelhed JE, Frimmel H, Bergelin E, Strid L, et al. Whole-body adipose tissue analysis: comparison of MRI, CT and dual energy X-ray absorptiometry. *Br J Radiol*. 2009;82(974):123–30.
20. Kim WH, Kim CG, Kim D-W. Optimal CT number range for adipose tissue when determining lean body mass in whole-body F-18 FDG PET/CT studies. *Nucl Med Mol Imaging*. 2012;46(4):294–9.
21. Martin AD, Daniel MZ, Drinkwater DT, Clarys JP. Adipose tissue density, estimated adipose lipid fraction and whole body adiposity in male cadavers. *Int J Obes Relat Metab Disord: J Int Assoc study of Obes*. 1994;18(2):79–83.
22. Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res*. 1999;8(2):135–60.
23. Hanneman SK. Design, analysis, and interpretation of method-comparison studies. *AACN Adv Crit Care*. 2008;19(2):223–34.
24. Cheymol G. Effects of obesity on pharmacokinetics implications for drug therapy. *Clin Pharmacokinet*. 2000;39(3):215–31.
25. Morgan DJ, Bray KM. Lean body mass as a predictor of drug dosage. Implications for drug therapy. *Clin Pharmacokinet*. 1994;26(4):292–307.
26. Kelly M. SUV: Advancing Comparability and Accuracy. 2009. http://www.medical.siemens.com/siemens/en_US/gg_nm_FBAs/files/whtpap/wp_09_trued_suv_supporting_better_accuracy_and_comparability.pdf. Accessed December 29 2011.
27. Sugawara Y, Zasadny KR, Neuhoff AW, Wahl RL. Reevaluation of the standardized uptake value for FDG: variations with body weight and methods for correction. *Radiology*. 1999;213(2):521–5.
28. Kim WH, Kim CG, Kim D-W. Comparison of SUVs normalized by lean body mass determined by CT with those normalized by lean body mass estimated by predictive equations in normal tissues. *Nucl Med Mol Imaging*. 2012;46(3):182–8.
29. Kim CG, Kim WH, Kim D-W, editors. Direct determination of individual lean body mass by using CT image data in 18F-FDG PET/CT studies: Comparison with lean body mass estimated by using various predictive equations. SNM Annual Meeting; 2011 June 7, 2011; San Antonio, Texas.
30. Erselcan T, Turgut B, Dogan D, Ozdemir S. Lean body mass-based standardized uptake value, derived from a predictive equation, might be misleading in PET studies. *Eur J Nucl Med Mol Imaging*. 2002;29(12):1630–8.
31. Chan T. Computerized method for automatic evaluation of lean body mass from PET/CT: comparison with predictive equations. *J Nucl Med: Off Publ Soc Nucl Med*. 2012;53(1):130–7.