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Study of an image-derived SUV and a modified SUV using mouse FDG-PET

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Abstract

Introduction—Standard uptake value (SUV) is calculated without consideration of the differences in plasma FDG clearance. Its variability can be affected by changes of the amount of excreted FDG by renal function. Moreover, the estimation of SUV is quite sensitive to errors in the measurements of body weight and injected dose. This study aims to develop an image-based method to obtain an image-derived SUV (iSUV) and a modified SUV (mSUV) to overcome these problems.

Methods—31 tumor-planted SCID mice were scanned in microPET at ~60min post FDG injection, and then scanned in microCT. Using image-based method, the body weight and injected dose were derived from the microPET/CT images to calculate iSUV. The volumes and the total activities of FDG within the bladder and the whole-body were also obtained to calculate mSUV. For the selected targets, the iSUVs and mSUVs were compared against their corresponding SUVs.

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Results—Compared with SUV factor (injected dose/body weight), iSUV factor had an average percentage error of -0.7% . The linear regressions between SUV and iSUV had a slope of 0.99 with correlation coefficient of 0.95. Compared with SUV and iSUV, CV% of mSUV decreased while the tumor-to-background separation of mSUV increased.

Conclusions—Using this image-based method, the iSUV can replace SUV when the actual measurements were missing or unreliable. The mSUV can reduce the inter-subject variability and enhance the tumor-to-background separation in mouse FDG-PET studies.

Keywords

FDG-PET; standard uptake value; image-based method; tumor-to-background separation

Introduction

Positron emission tomography (PET) with 2-deoxy-2-[^{18}F]fluoro-D-glucose (FDG) is a well established oncologic imaging technique which has beneficial effects on clinical routines and preclinical studies [1,2]. In the quantitative analysis for FDG-PET image, standard uptake value (SUV) is frequently used to measure the tracer uptake as a means to differentiate malignancy [3]. However, SUV can be influenced by many factors including the length of uptake period, plasma glucose level, recovery coefficient, partial volume effects [4,5] and the subject preparation [6]. In addition, the body weight may not be the best parameter in SUV calculation due to the lower FDG concentration in body fat. The lean body weight or surface area has been proposed as a substitute [7,8]. Recently the impact of renal function variation has been studied in FDG-PET [9,10], since SUV is regularly defined as the local target concentration normalized by injected dose per unit body weight without regard to the differences in plasma FDG clearance [11]. As a result, changing the amount of excreted FDG by renal function could affect the estimation of SUV, even if the glucose utilization in the rest of the body stays unchanged.

On the other hand, the subject's body weight and injected dose, which are needed in the calculation of SUV, are measured separately from imaging. Generally, the body weight is measured by a scale, and the injected dose is measured by a dosimeter. Because it is difficult to redo these physic measurements sometimes, any missing records would lead to the failure in the calculation of SUV. This is a notable issue in the data reutilization especially for multidisciplinary and inter-institution sharing in education and scientific research, when the data were stored in a shared database such as Mouse Quantitation Program (MQP) [12]. The tumor-to-background ratio (TBR), which is calculated as the ratio of the tracer concentration in tumor over that in normal tissue, is sometimes applied as an index to quantify the tracer uptake without measurements of body weight and injected dose [13,14]. However, to find a suitable normal tissue as background may be difficult for some oncologic imaging [15].

Hence, this study aims to explore a purely image-based method to estimate SUV and, further, to find a way to improve SUV variability that will eventually help the use of SUV for differentiation of malignant from benign lesions. This study is evaluated in a set of mouse FDG-PET studies.

Materials and Methods

1.1 Animals and Image Acquisitions

All animal experiments were conducted in compliance with the Animal Care and Use Program established by the Chancellor's Animal Research Committee of UCLA. Thirty-one SCID mice (20-33g) were implanted with U251 tumor in the left flank at least one week

before the investigation. These mice would undergo the microPET/CT scans after tumor volumes had reached 100 mm³. All the mice were fasted overnight (about 15 hours) before microPET and microCT studies. For each mouse, the body weight was measured using a standard lab weighting scale. The injected dose was measured by a dosimeter and corrected for the residue of dose remained in the syringe. At 60 minutes post intraperitoneal injection of FDG (4.81-5.92 MBq), a 10 minutes static PET scan was performed on a microPET Focus 220 tomography (Siemens Preclinical Solutions, Knoxville, TN), whose imaging field of view (FOV) is 51.2 mm diameter in transverse by 75.6 mm in axial. The spatial resolution at the center of FOV was 1.7 mm full width at half maximum (FWHM). The microPET images were reconstructed using 2D filtered back-projection with a voxel size of 0.4×0.4×0.8 mm³ in a 128×128×95 matrix. The PET image was corrected for scatter radiation, random coincidence, dead time and physical decay. After microPET imaging, a 7-10 minutes microCT scan was acquired on a MicroCAT II tomography (Siemens Preclinical Solutions, Knoxville, TN), which has an imaging field of 51.2 mm in diameter in transverse by 99.2 mm in the axial direction. The microCT image had a voxel size of 0.2×0.2×0.2 mm³ in 256×256×496 matrix. The animals were anesthetized (~2% isoflurane) and placed in an imaging chamber with a heating bed during the scans [16]. The imaging chamber was compatible with the microPET and microCT systems [17,18]. The microCT image was aligned to the microPET image using a predetermined, geometric transformation matrix [19]. The aligned microCT image was used in PET reconstruction for attenuation correction [20].

In the image analysis, AMIDE software [21] was used to manually remove the imaging chamber and nose cone in the microCT image. In every mouse study, ellipsoidal ROIs were drawn for major organs (brain, heart, lung, liver, kidney and muscle) in the microPET image with the guide of the aligned microCT image. To reduce the effects of ROI delineation, the ellipsoidal ROIs for the same major organ were of the same size and were placed in the core part of the organ for all mouse studies. The tumor volume for each mouse was large enough for manually delineating the ellipsoidal ROI on the left flank where the implanted tumor was. The size of the tumor ROI depended on the shape of the lesions in the microPET/CT images. The average and maximum values of tracer concentrations in these ROIs were calculated for further quantitative analysis. The bladder ROIs were also manually delineated with the visual guide from microCT and microPET images by an experienced operator. The volumes of the manually drawn bladder ROIs were used as the standard for validation of the bladder volumes derived from the automatic image-based method described as follows.

1.2 Image-Based Methods for Calculating iSUV and mSUV

An automatic image-based method was explored to obtain the whole-body mask (composed of the bone mask, body mask and lung mask) and bladder mask using the microCT and microPET images. These masks were used to locate the corresponding targets in the microPET and microCT images, and then to get the parameters for calculating iSUV and mSUV. Figure 1 shows the flow chart of this method. The entire process was described as follows.

In the reconstructed microCT image (in Hounsfield units, HU), the threshold method was firstly utilized to segment the mouse body from background using an empirical threshold window of [-250, 4000] HU. That is, the voxels with intensity values higher than -250 HU and lower than 4000 HU were considered as belonging to the rough body mask. Within the rough body mask, the bone tissue was further segmented using another empirical threshold window of [400, 4000] HU. As a result, the voxels with intensity values higher than 400 HU and lower than 4000 HU were set as the rough bone mask. These two rough masks were saved as two binary images in the same matrix dimension as the microCT image.

Secondly, the “morphological opening” operation (Matlab Image Processing Toolbox™) was applied to smooth the boundary of the rough body mask and bone mask. The voxels within the body part that have low density (i.e., lung, trachea and the gas in the alimentary system) were excluded in the rough body mask at the first step. The “morphological fill” operation (Matlab Image Processing Toolbox™) was then applied to fill the holes in the body mask to obtain a whole-body mask that included all the voxles within the body. The lung mask was then derived by subtracting the whole-body mask from the rough whole-body mask in the upper body. The lung mask was then refined by using the “morphological opening” operation to remove the artifacts of the trachea. Using these masks, the microCT image of the whole mouse was separated into three regions, namely soft tissue, lung and bone.

The total voxel numbers of the body, bone and lung regions were counted, and the volumes were calculated by multiplying the voxel number with the voxel volume (0.008mm³). The volumes of these different regions derived from microCT image were used to estimate the subjects’ body weight. The whole-body mask was re-sampled into the image voxel matrix of the aligned microPET to define the whole-body region on the microPET image. The total radioactivity in the whole-body was calculated as the sum of the values of the voxels within the whole body mask in the microPET image times the microPET voxel volume.

In the static microPET image, the bladder had a high radioactivity concentration, which was different from the surrounding tissues, so the max gradient searching method was applied to derive the bladder mask automatically. This method consisted of four steps.

Step 1: Define the bottom region of the microPET image which contained bladder;

Step 2: Calculate the gradient at each voxel within the predefined bottom region as:

$$G(x, y, z) = \sqrt{\left(\frac{\partial C(x, y, z)}{\partial x}\right)^2 + \left(\frac{\partial C(x, y, z)}{\partial y}\right)^2 + \left(\frac{\partial C(x, y, z)}{\partial z}\right)^2} \quad (1)$$

where $C(x, y, z)$ is the value of radioactivity at voxel (x, y, z) .

Step 3: Any voxel with gradient greater than 90% of the maximal gradient within the bottom region would be marked as the bladder boundary. All voxels within the bottom region with image values above the minimal value of bladder boundary voxels were used to form the bladder mask image.

Step 4: Apply the “morphological opening” and “morphological fill” operations to the bladder mask image to remove any residual artifact.

The total bladder volume was calculated by multiplying the voxel number of the bladder mask by the microPET voxel volume (0.4×0.4×0.8 mm³). The total radioactivity in the bladder was calculated as the sum of the radioactivity concentrations for all voxels located within the bladder mask in the microPET image multiplied with the microPET voxel volume.

1.3 Image-derived SUV and Modified SUV

A. Image-derived SUV (iSUV)—iSUV was calculated using a similar formula as SUV, except that the body weight (*BW*) and injected dose (*ID*) were estimated from the microCT and microPET images by the proposed imaged-based method described in 1.2. The equation is shown in (2).

$$iSUV = \frac{C_i}{ID_{\theta}/BW_{\theta}} \quad (2)$$

where ID_{θ} and BW_{θ} are the estimated injected dose and body weight obtained by the imaged-based method. The term in the denominator is referred to as the iSUV factor; C_i is the average or maximum value of tracer concentration within the target ROI.

The iSUV calculated by average tracer concentration within an ROI was noted as $iSUV_{mean}$. Similarly, the iSUV estimated by the maximum ROI value was recorded as $iSUV_{max}$.

The estimated body weight was calculated as the sum of weights of the soft tissue, bone and lung regions as given in (3). The specific densities of soft tissue, bone and lung regions were assumed as 1, 1.14 and 0.28 g/ml, respectively [22,23].

$$BW_{\theta} = V_{nb} \times D_{nb} + V_b \times D_b + V_l \times D_l \quad (3)$$

where BW_{θ} is the estimated body weight; V_{nb} is the soft tissue volume; V_b is the bone volume; V_l is the lung volume; D_{nb} , D_b and D_l are the specific densities of soft tissue, bone and lung, respectively.

The estimated injected dose was calculated as the sum of the radioactivity within the whole body. Since the FOV of microPET is smaller than that of the microCT, some parts of the animal were not imaged by the microPET. The average voxel radioactivity of the part outside the microPET image was assumed to be equal to the average voxel radioactivity of the part inside the microPET image. Thus, the injected dose was calculated by (4).

$$ID_{\theta} = (A_{in} + A_{out}) \times CF = \left(\frac{A_{in}}{V_{wb_in}} \times V_{wb} \right) \times CF \quad (4)$$

where ID_{θ} denotes the estimated inject dose, A_{in} is the total radioactivity of the body within the microPET image, and A_{out} is the radioactivity of the part outside the microPET image (but inside the corresponding microCT image). V_{wb_in} is the body volume within microPET image. V_{wb} is whole-body volume in microCT image, and CF is the calibration factor that converts radioactivity unit from *PET units* to *MBq/ml*.

B. Modified SUV (mSUV)—Because the amount of the extracted tracer by renal function varied among subjects, the variability of SUV can be influenced by the tracer excretion. In order to reduce the variability of SUV, mSUV was calculated based on the target concentration normalized by the total uptake of the whole-body, excluding the amount excreted into the bladder. If the average body density was assumed to be 1 g/cm³, the body volume could be used instead of body weight in the calculation. Thus, mSUV can be calculated by (5). The term in the denominator of (5) will be referred to as the mSUV factor. mSUV calculated by average value of tracer concentration was noted as $mSUV_{mean}$. Similarly, the mSUV estimated by the maximum value was recorded as $mSUV_{max}$.

$$mSUV = \frac{C_i}{(A_{wb} - A_{bl}) / (V_{wb} - V_{bl})} \quad (5)$$

where C_i is the average or maximum value of the tracer concentration within the target ROI (in PET units); A_{wb} and A_{bl} are the total radioactivity in the whole-body and the bladder; V_{wb} and V_{bl} are the volumes of the whole body and the bladder, respectively.

1.4 Statistical Analysis

A. iSUV Validation—The estimated body weight and injected dose were compared with the actual measurements of body weight and injected dose. The percent errors of the estimated body weight and injected dose compared with the actual measurements were calculated. The iSUV factor, which is defined as the ratio between the estimated body weight and injected dose, was compared with the SUV factor calculated by the actual measurements. The percent errors of the $1/(\text{iSUV factor})$ to $1/(\text{SUV factor})$ were also calculated. The linear regression between iSUV factor and SUV factor were performed to evaluate their correspondence. The significant difference between the iSUV factor and SUV factor was evaluated by paired t-test. A p-value <0.05 was considered statistically significant.

Moreover, $\text{iSUV}_{\text{mean}}$ was validated by the SUV calculated by the average value of tracer concentration within the ROI (SUV_{mean}), and iSUV_{max} was validated by the SUV calculated by the maximum value within the ROI (SUV_{max}). The average and standard deviation (SD) of these two sets of SUV and iSUV were compared, and linear regressions were performed both for $\text{iSUV}_{\text{mean}}$ vs. SUV_{mean} and iSUV_{max} vs. SUV_{max} for all target ROIs (major organs and tumor). Paired t-test was also performed to detect the significant difference between the iSUV and the SUV for each target ROI.

B. mSUV Evaluation— $\text{mSUV}_{\text{mean}}$ was compared with $\text{iSUV}_{\text{mean}}$ and SUV_{mean} , while mSUV_{max} was compared with iSUV_{max} and SUV_{max} . The average and standard deviation (SD) of the two sets of mSUV, iSUV and SUV were calculated for all target ROIs. The coefficient of variation (CV%) was used as a measure to evaluate the inter-subject variability. The tumor-to-background separations for these two sets of mSUV, iSUV and SUV were quantified by the Mahalanobis distance that is defined in mathematical classification theory as given by (6).

$$D = \frac{|mean_t - mean_b|}{\sqrt{SD_t^2 + SD_b^2}} \quad (6)$$

where D is the Mahalanobis distance; $mean$ is the population average value of SUV/iSUV/mSUV for tumor or background; SD is the standard deviation of SUV/iSUV/mSUV for tumor or background among the animals.

Experimental Results

1.5 iSUV vs. SUV

In the statistical analysis, average percent errors of the estimated body weight and injected dose to their actual measurements were respectively $-9.5 \pm 7.3\%$ and $-8.5 \pm 11.5\%$, which are shown in Figure 2 by box-and-whisker diagrams. Considering the reciprocal of iSUV factor, its average percent error to the reciprocal of SUV factor was about $-0.7 \pm 14.3\%$. Figure 3 shows the linear regression for 31 pairs of iSUV factor and SUV factor. The corresponding regression equation was $y = 0.83x + 0.037$ with $R^2 = 0.44$. Paired t-test did not show significant difference between SUV factor and iSUV factor.

The $iSUV_{mean}$ and $iSUV_{max}$ for each major organ were validated by their corresponding SUV_{mean} and SUV_{max} . Figure 4 shows the comparisons using box-and-whisker diagrams. The average and standard deviation of SUV_{mean} and $iSUV_{mean}$ for the defined ROIs (major organ and tumor) are listed in Table 1, and those for SUV_{max} and $iSUV_{max}$ are listed in Table 2. Figure 5 (a) shows the linear regression between SUV_{mean} and $iSUV_{mean}$ of all major organs for all mouse studies. The linear regression line was $y=0.99x+0.018$ with $R^2=0.95$. Similarly, Figure 5 (b) shows the plot of SUV_{max} vs. $iSUV_{max}$. The linear regression line was $y=0.99x+0.027$ with $R^2=0.95$. For each major organ, the paired t-test did not detect any significant difference between SUV_{mean} and $iSUV_{mean}$. The same results were found between SUV_{max} and $iSUV_{max}$.

1.6 mSUV vs. SUV

The bladder volume estimated by the automatic image-based method was compared with that obtained from manual definition. Figure 6 shows the linear regression between the two estimates of bladder volume. The linear regression line was expressed as $y=1.10x-4.25$. The regression slope was close to 1 with $R^2=0.97$.

The averages, SDs and CV% for SUV_{mean} , $iSUV_{mean}$ and $mSUV_{mean}$ in each defined major organs ROI are shown in Table 1. Those metrics for SUV_{max} , $iSUV_{max}$ and $mSUV_{max}$ are given in Table 2. From these results, the CV% of $mSUV_{mean}$ decreased by about 1-5% in the brain, heart, lung and liver compared to those of SUV_{mean} , while the CV% of $mSUV_{max}$ decreased by about 1-4% in the comparison with SUV_{max} . For the tumor ROI, the CV% of $mSUV_{mean}$ was 2% lower than that of SUV_{mean} and the CV% of $mSUV_{max}$ was 3% lower than that of SUV_{max} . Compared with $iSUV_{mean}$, the CV% of $mSUV_{mean}$ was decreased by about 1-5% in major organs and tumor, except in the heart the CV% of $mSUV_{mean}$ was increased by about 1%. Similar results were observed in the comparisons between $mSUV_{max}$ and $iSUV_{max}$.

Tumor-to-background separation was increased by using mSUV because of the decrease in the variances of the mSUV values in the tumor and background regions. In this study, lung, liver and muscle were chosen as the background. The Mahalanobis distance (D) was used to quantify the tumor-to-background separation. From the D values given in Table 3, among SUV_{mean} , $iSUV_{mean}$, and $mSUV_{mean}$ the highest D values were obtained from $mSUV_{mean}$ regardless of the background used. Figure 7 (a) shows the tumor-to-background separation distribution of SUV_{mean} , $iSUV_{mean}$ and $mSUV_{mean}$. The result indicated that $mSUV_{mean}$ had the largest separation between the tumor and background, which was about 5% and 20% higher in D values than SUV_{mean} and $iSUV_{mean}$. Similar results were derived by comparing the tumor-to-background separations among SUV_{max} , $iSUV_{max}$ and $mSUV_{max}$ (shown in Table 3). It is clear that $mSUV_{max}$ had the largest separation which is about 8% and 17% higher in D values than SUV_{max} and $iSUV_{max}$. Figure 7 (b) shows the tumor-to-background separation distribution of SUV_{max} , $iSUV_{max}$ and $mSUV_{max}$. In this figure, a threshold of 1 (gray dash line) is given as an example to separate tumor from background. As a result, using SUV_{max} and $iSUV_{max}$ could both yield some false positives, while $mSUV_{max}$ could separate tumor from background without error.

The automatic image-based method was run in Matlab 7.0. It took ~38 seconds to do all the calculations for one animal using a Mac with OS X 10.5.5 (2.4GHz Intel Core 2 Duo, 4GB SDRAM).

Discussion

This study developed a robust and automatic image-based method for calculating $iSUV$ which can be used as a substitute of the regular SUV in mouse FDG PET studies, when the

body weight or injected dose is not available or unreliable. Based on this image-based method, a modification of SUV was applied to reduce the inter-subject variability with regards of the tracer excretion variability among subjects. The microPET/CT images used in the image-based method were obtained in separate scanners. A hardware registration method was applied to minimize the error in the alignment of two modalities images [19]. Moreover, the scans were performed when the implanted tumors had relatively large volumes ($>100 \text{ mm}^3$). This also allowed the reliable PET-to-CT alignment for the tumor lesions.

The results of the mouse studies indicated that the average percent error of estimated body weight was about -9.5% and that of estimated injected dose was about -8.5% . In the worst case, the percentage errors of the estimated body weight and injected dose were -22.5% and -35.1% , respectively. The underestimations of the body weight and the injected dose, however, occurred together, thus resulted in much less error in the ratio (e.g., the iSUV factor). There are several error sources that might affect the accuracy of the estimations using the image-based method. First is the incomplete coverage of the whole body in the microCT and the microPET images, as shown in Figure 8 (a) and (b). In this case, part of the tail and the hind legs were missing because of the limited field of view in microCT. The missing parts are manually sketched out in Figure 8 (c). In addition, the radioactivity outside the field of view of the microPET would introduce out-of-field scatter and influenced the quantitative accuracy of the image values [24]. The accuracy of the injected dose estimate also relied on that of the PET data correction, including the normalization, attenuation correction, scatters correction, random correction, dead-time correction, and the calibration. Urine leakage from the bladder during the microPET scan would also impact the injected dose estimation.

Another source of error is in the assumed values of specific gravity (i.e., density) for various tissues. The densities used in the body weight estimation were assumed uniform in each type of tissue, which were grouped into soft tissue, bone and lung. The lung has only a small impact on the body weight estimation, and its density could be assumed to be zero without great effect on the estimated body weight.

We expect that the major improvement in the accuracy of estimation is to position more consistently the mouse in the imaging chamber, and to fit the entire body in the field of view. This may reduce the influence of the missing regions in the estimation of body weight and injected dose by the image-based method. The studies using the newer microPET scanners (e.g., Inveon Dedicated PET System), which have larger FOVs, are expected to have less variability by covering the entire animal within the FOV. Also, the conversion of the attenuation coefficient from microCT images to that of microPET for attenuation correction could also be improved to give a better estimate of the injected dose. However, the correlated underestimations of body weight and injected dose did not introduce a large estimation error to the iSUV factor, of which the percent error was about -0.7% in average compared with SUV factor. Including all 217 pairs of iSUV and SUV (7 major organs for 31 mice studies) in linear regression, the results in Figure 5 (a) and (b) indicated that iSUV closely match the SUV ($R^2=0.95$), either for $iSUV_{\text{mean}}$ vs. SUV_{mean} or $iSUV_{\text{max}}$ vs. SUV_{max} . These data demonstrated the validity of the iSUV from the automatic image-based method in this study.

In the future, the body surface area could be obtained directly from the microCT image (e.g., by a marching cubes algorithm [25]), and it could be used as the normalization factor instead of body weight. To use of body surface area has been reported in some studies to be preferable in SUV calculation [7], e.g. for obese subjects with increased fraction of body fat.

On the other hand, mSUV was designed to improve SUV reliability for accurate diagnosis of tumor malignancy by removing the variability of tracer excretions among subjects. To a certain extent, mSUV could be considered as the SUV with FDG excretion correction. Bladder voiding performed immediately before a FDG PET scan as part of the animal preparation procedure can achieve the same objective, and can be considered to be equivalent to replacing the image processing procedures for calculating the accumulated bladder radioactivity. However, the renal pelvis beside bladder usually also contained some urine. This could influence the mSUV in the kidney ROI. As a result, CV% of mSUV in kidney was found to be 2% higher than that of SUV both for $mSUV_{mean}$ vs. SUV_{mean} and $mSUV_{max}$ vs. SUV_{max} . It is assumed in this study that the amount of FDG in renal pelvis is much less than that in bladder, and mSUV mainly considered the influence of the FDG excreted into bladder. In the future, the influence from the renal pelvis could be removed in the calculation of mSUV by defining kidney ROIs to exclude the renal pelvis.

In common practical application, a predefined threshold of SUV is usually set for determining malignancy. That is, the lesion would be regarded as malignant when its SUV is higher than the threshold. Therefore, to enlarge the separation between the tumor and background is expected to be helpful for defining a threshold to detect the malignancy and improving the accuracy of diagnosis. mSUV is shown to increase the separation between the tumor target and background in Figure 7. Especially, $mSUV_{max}$ showed its advantage in eliminating the false positive compared with SUV_{max} and $iSUV_{max}$. The Mahalanobis distance was adopted to measure the separation. The results indicated that the tumor to background (liver, lung or muscle) separation all increased using mSUV compared with SUV in light of the higher D values.

The amount of reduction in CV% of tumor mSUV shown in this study is not very large, since all the animals studied were quite uniform in size, in their preparations, and in the study procedure. When the physiological condition of the animals is more variable and the study condition is less uniform, the amount of improvement in mSUV is expected to be increased. Also, other body tissues that have large population variability in FDG extraction could also be excluded, just like the bladder that is addressed in this study. That is, the radioactivity taken up in these tissues and the corresponding volume/weight could be taken out of the injected dose and the body weight, respectively, in the calculation of mSUV. The reliability of the resulted mSUV is expected to be further improved, though further work is needed to demonstrate the amount of improvement in practical situations.

The present study is focused on mouse FDG PET study to improve the reliability of SUV. The underlying concept of mSUV can be extended to whole-body human FDG PET studies. Although the effectiveness of the approach for improving SUV reliability in these human studies needs many future investigations, results from the present study clearly indicated its feasibility and potentials.

Conclusion

This investigation demonstrated that, for mouse FDG PET studies, it is feasible to use microCT and microPET images to calculate iSUV, which could be used as a semi-quantitative index to substitute for SUV when directly measured body weight and/or injected dose are missing or unreliable.

The mSUV is shown to reduce the inter-subject variability of SUV and increase the tumor-to-background separation. Therefore, with further clinical investigations mSUV has the potential to be useful for increasing the accuracy to separate malignancy from benign lesions in FDG PET studies.

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Figure 1.
The flow chart of image-based method for the estimation of iSUV and mSUV.

Figure 2.

Box-and whisker diagrams of estimated error percentage of body weight (BW), injected dose (ID) and 1/iSUVfactor. Box height shows inter-quartile range (IQR). The line in the box is for the median. Whiskers indicate the largest observation (minimum to maximum).

Figure 3.

The linear regression performed for all 31 pairs of SUV factor and iSUV factor. The open circle symbols note the scatter plot of the 31 pairs of iSUV factor and SUV factor. The red solid line is the regression line.

Figure 4.

The comparisons between two sets of SUV and iSUV, SUV_{mean} vs. $iSUV_{mean}$ and SUV_{max} vs. $iSUV_{max}$, for brain (a), heart (b), lung (c), liver (d), kidney (e), muscle (f), and tumor (g) shown by box-and-whisker diagram. In each sub-figure, box height shows inter-quartile range (IQR). The line in the box is for the median. Whiskers indicate the largest observation (minimum to maximum).

Figure 5.

The linear regression plots between SUV and iSUV. (a) Linear regression is performed for 217 (7×31, 7 major organs for 31 mice studies) pairs of iSUV_{mean} and SUV_{mean}. (b) Linear regression is performed for 217 (7×31, 7 major organs for 31 mice studies) pairs of iSUV_{max} and SUV_{max}. The black dot symbols note the scatter plot of pairs of iSUV and SUV. The red solid line is the regression line.

Figure 6.

The validation of bladder volume. The estimated bladder volume obtained by the automatic image-based method is compared to the value obtained by manual method with visual support from microCT image. The open circle symbols denote the scatter plot of the pairs of automatic and manual results. The red solid line is the linear regression line.

Figure 7.

Plot of tumor and background (lung, liver and muscle) SUVs, iSUVs and mSUVs. The values for tumor (square), lung (circle), liver (triangle) and muscle (cross) are grouped for SUV, iSUV and mSUV to compare the tumor-to-background separations (please see the Table 3 for quantitative measurements of the separation). (a) This figure shows that the tumor-to-background separation is increased using $mSUV_{mean}$ compared with using SUV_{mean} and $iSUV_{mean}$. A threshold of 1 (gray dash line) is given as an example to separate tumor from background in this figure. (b) This figure shows that the tumor-to-background separation is increased using $mSUV_{max}$ compared with using SUV_{max} and $iSUV_{max}$. A threshold of 1 (gray dash line) is given as an example to separate tumor from background in this figure.

Figure 8.

The microCT and microPET images and the missing body parts in the images. (a) the microCT image has a field of view of $51.2\text{mm} \times 51.2\text{mm} \times 99.2\text{mm}$. The microCT image voxel size is $0.2\text{mm} \times 0.2\text{mm} \times 0.2\text{mm}$ in a $256 \times 256 \times 496$ matrix. (b) The microPET image has a field of view of $51.2\text{mm} \times 51.2\text{mm} \times 75.6\text{mm}$. The microPET image voxel size is $0.4\text{mm} \times 0.4\text{mm} \times 0.796\text{mm}$ in a $128 \times 128 \times 95$ matrix. (c) The fused microPET-CT image. In this figure, the contour of the whole body, included the missing parts of the mouse body, is sketched out by red solid line.

Table 1

The comparison of SUV_{mean} , $iSUV_{mean}$ and $mSUV_{mean}$ by mean, standard deviation and coefficient of variance

N=31	SUV_{mean}			$iSUV_{mean}$			$mSUV_{mean}$		
	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%
brain	4.14	1.00	24%	4.14	1.09	26%	5.14	1.11	22%
heart	0.71	0.26	37%	0.70	0.24	35%	0.88	0.32	36%
lung	0.41	0.06	15%	0.40	0.06	14%	0.50	0.05	10%
liver	0.51	0.08	16%	0.50	0.08	15%	0.63	0.09	15%
kidney	1.76	0.42	24%	1.77	0.51	29%	2.21	0.58	26%
muscle	0.29	0.08	27%	0.29	0.09	31%	0.36	0.10	27%
tumor	2.05	0.55	27%	2.06	0.63	30%	2.55	0.65	25%

* For each ROI, the lowest CV% among SUV , $iSUV$, and $mSUV$ for each ROI is shaded.

Table 2

The comparison of SUV_{max} , $iSUV_{max}$ and $mSUV_{max}$ by mean, standard deviation and coefficient of variance

N=31	SUV_{max}			$iSUV_{max}$			$mSUV_{max}$		
	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%
brain	5.67	1.31	23%	5.67	1.44	25%	6.90	1.41	20%
heart	1.10	0.42	39%	1.08	0.38	36%	1.32	0.48	36%
lung	0.58	0.09	15%	0.58	0.08	14%	0.71	0.08	11%
liver	0.67	0.13	19%	0.67	0.14	21%	0.82	0.15	18%
kidney	2.35	0.62	27%	2.37	0.73	31%	2.90	0.83	29%
muscle	0.70	0.18	26%	0.70	0.18	25%	0.85	0.21	24%
tumor	2.48	0.64	26%	2.48	0.68	27%	3.02	0.70	23%

* For each ROI, the lowest CV% among SUV , $iSUV$, and $mSUV$ for each ROI is shaded.

Table 3

Comparison of Mahalanobis distance to evaluate SUV, iSUV and mSUV for tumor-to-background separation

	Mahalanobis distance* (D)		
	tumor to lung	tumor to liver	tumor to muscle
SUV_{mean}	2.99	2.80	3.18
iSUV_{mean}	2.61	2.44	2.77
mSUV_{mean}	3.15	2.94	3.34
SUV_{max}	2.95	2.78	2.69
iSUV_{max}	2.77	2.60	2.53
mSUV_{max}	3.27	3.06	2.96

* The higher D value means more separation between tumor and background. The highest D values for each background reference are shaded.