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3D Formulation of SUV Measurements to Improve Partial Volume Effects in PET/CT Image Quantitation.

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ABSTRACT:

Purpose: Partial volume effect is one of the most degrading factors in PET imaging quantitation. The aim of the study was to create three dimensional (3D) representation of the recovery coefficients (RCs) taking into consideration lesion size as well as lesion contrast to improve standardized uptake value (SUV) calculations. **Materials and Methods:** Several phantom studies with fillable spheres have been conducted at significantly wide range of lesion contrast ratios including 3:1, 5:1, 8:1, 10:1, 12:1, 14:1 and 15:1. The phantom studies were then classified into two groups; one for generating a three dimensional function taking into consideration the sphere size as well lesion to background contrast ratio whereas the other group of phantom data were used to validate the 3D formulation obtained from the first group. A PET segmentation threshold algorithm was generated based on lesion contrast and lesion size. In addition, another four 3D of the RC of the SUV mean and SUV max were formulated taking into account lesion volume (or diameter) and lesion contrast. Validation of the new algorithms has considered both phantom and clinical studies. **Results:** Volume threshold optimization revealed significant differences of the threshold value required for the various sphere dimensions at any given contrast ratio. A 3D form has been created that is able to individually segment a PET lesion provided lesion contrast and CT volume. Four functional forms were generated for RCs of the

SUV mean and SUV max taking into account lesion volume or diameter while being able to employ lesion contrast in the same formalism. Phantom validation and clinical data suggested the comparable results of the different algorithms with an error of less than or equal to 10%. **Conclusion:** It has been successful to generate 3D mathematical formulation of the SUV recovery coefficients taking into consideration the most influential factors including lesion size and lesion contrast. Validation studies in phantom and clinical data were suggestive of the good performance of the new algorithms generated to correct for partial volume effect. However, further studies are underway to ensure the performance of the proposed algorithms in PET lesion well below the sensitive region of the partial volume effect.

Keywords: Partial volume correction, positron emission tomography-computed tomography, Recovery coefficient, standardized uptake value.

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INTRODUCTION:

Positron emission tomography (PET) combined with x-ray computed tomography has several features in the world of diagnostic oncology. It has a number of merits in terms of patient diagnosis, staging, restaging, stratification and disease prognosis. What really makes PET a unique imaging modality is its quantitative capability of tracer deposition at any time point of radiopharmaceutical uptake and clearance. The most common traditional quantitative method is the standardized uptake value (SUV). This quantitative index has several formulations and associated uncertainties. SUV is mathematically calculated using the ROI/VOI tracer concentration divided by the injected dose normalized to patient weight. A number of mathematical variants has been devised in order to obtain a more reliable and consistent representation of the tracer uptake. Those variants have considered variation due to body weight, body habitus, mass index or lean body mass and also whether the measured concentration is due to maximum, mean, peak, or others [(1)]. There are a quite significant number of variables that affect the accuracy and reproducibility of the SUV measurements.

One of the most crucial is the partial volume effect lesions of small sizes typically less than twice or thrice the full width at half maximum(FWHM) is variably underestimated based on lesion volume taken for measurements. However, this phenomenon is described by the mutual contamination of the lesion to the surrounding structures and vice versa or namely what is called spill out and spill in respectively. Another important factor is the level of the background and how this could potentially impact the quantitative accuracy and hence the metabolic activity of the lesion [(2)].

The simplest form taken to correct for PVE in SUV measurements was to create a sort of calibration curve of lesion SUV versus sphere size and fitting the curve into two dimensional (2D) mathematical formulas provided the same contrast is used. This method generally lacks the variation that could be introduced due to lesion to background ratio or what is called lesion contrast. In this report we sought to generate a 3D formulation of the SUV recovery coefficients taken into consideration both the lesion size as well lesion contrast [(3)].

The potential of PET/CT is to quantify the concentration of radiopharmaceuticals within the human body, but these measurements are severely hampered by the partial volume effect (PVE).

PVE is basically an effect caused by limited spatial resolution and sampling and results in unreliable quantitative values, especially in small objects, as well as qualitatively impaired images. The consequences of overlooking PVE can be especially severe when using PET to measure the response to tumor therapy. This research is one of the most persistent attempts to overcome the negative drawback of PVE through finding the values of the RC considering the different lesion to background ratios [(1, 4).]

MATERIALSAND METHODS:

Phantom Studies

The work has been commenced in Kasr-Al Ainy Centre for Radiation Oncology and Nuclear Medicine, Cairo University Hospital.

A number of phantom studies were acquired at clinically relevant and different sphere to background ratios. The PET images were acquired using the Ingenuity TF 64 (Philips Healthcare, Cleveland, OH, USA) which is a PET/CT scanner combining a modular, LYSO-based PET component with a 64-channel CT component.

The phantom used consisted of two parts; a hollow cylinder having diameter 18.6 cm and length 21.6 Cm and multiple spheres.

The sphere assembly contained five spheres of varying internal diameter ranging from 12.43 mm to 31.27 mm (i.e., 12.43, 15.43,24.82, and 31.27 mm) and volume ranging from 1 ml to 16 ml (i.e., 1, 2, 4,8 and 16 mL).

As a first step to determine the appropriate activity to be used in filling the hollow spheres to resemble patient's lesions, a number of random clinical studies were selected from our daily routine. The activity concentrations as well as background were measured in units of nCi/ml. A total of 63 random lesions were selected and resulted in a mean contrast ratio of 15.3±10.9 nCi and 8.6±5.7 nCi/ml as SUV max and SUV mean respectively. The average activity concentration measured was used to fill the spheres was 340 nCi/ml ± 80 nCi/ml.

The phantom was filled with water containing ^{18}F-Fluorodeoxyglucose (FDG) to make the sphere versus background activity concentration (μCi/ml) ratio as 2:1, 3:1, 5:1, 8:1, 10:1, 12:1, 14:1 and 15:1. In each image acquisition, the spheres were centered in the field of view and only one bed position was acquired for 3 min which is the same as the routine acquisition in our clinic.

Image Reconstruction

The scanner's built-in reconstruction protocols were used, in which data are typically reconstructed into static, gated ordynamic images. While there are different reconstructions including variable field of view of FOV are supported, the whole body acquisition protocol was used in the present study to simulate clinical data acquisition.

A 576 mm FOV was used in all scans providing a volume dimension of 288x288×90 voxels or slice thickness of 2 mm. Images were reconstructed using a TOF, list-mode, blob-based, ordered subsets maximum likelihood expectation maximization algorithm (TOF-OSEM). Corrections performed in the reconstruction model account for detector efficiency using a component - based method. Scatter using a combination of single scatter and Monte Carlo simulation, and random using smoothed delay-line coincidence data [5, 6, 7 and 8].

The reconstruction software compensates for changes in TOF resolution as a function of measured detector count rate by setting the TOF kernel width based on the average singles rate in each frame (e.g. each bed position within a whole body Study or each time-frame within a Dynamic study, the TOF resolution is determined based on the average singles rate within that frame [9].

Image analysis

Volume segmentation threshold

It has been evident that the use of a fixed threshold to segment a PET lesion bears variable degrees of inaccuracies. Therefore, attempts were made herein to optimize the segmentation threshold level based on the several phantom studies acquired at significantly wide range of lesion to background ratios (i.e from 3:1 up to 15:1). The following steps were followed to obtain a three dimensional optimization (3D) of the threshold level given the lesion contrast level as well as the measurement of the SUV max.

For every reconstructed PET image of the 7 contrast ratios, every sphere of the five was segmented at several threshold values starting from 30% up to 80% in a step of 10% resulting in 6 volumes of the respective threshold. An exponential fit was then generated of the resulting sphere volume and different thresholds applied. The best threshold value was then obtained from the exponential fit and knowledge of the true sphere volume.

This process resulted in a new set of threshold values that adapted to segment PET lesions with different sizes and different contrast ratios.

These measurements permitted to formulate a three dimensional representation in two independent variables namely lesion volume and contrast ratio providing an appropriate estimate of the PET lesion volume. Validation of the 3D function with respect to other contrast ratios revealed normalized mean square error (NMSE) of 4.35

3D Formulation of RCs

The RC can be calculated using Eq.1

$$RC = \frac{\text{Measured activity Conc.} - \text{Measured Background activity Conc.}}{\text{Actual activity Conc.} - \text{Actual Background activity Conc.}}$$ (1).

The reconstructed PET images of the five contrast ratios 2:1, 3:1, 8:1, 12:1, and 15:1 were used to generate another 3D formulation for corrections of SUV mean and SUV max.

This has been created using a 3D array such that one dimension represented the lesion SUV max (or SUV mean obtained from the optimized threshold value) while the other dimension represented the lesion contrast ratio and the third dimension represented the dependent variable which is the SUV max r SUV mean recovery coefficient. In order to account for the lesion contrast as well as the lesion size (e.g. volume or diameter) we had to formulate a three dimensional form that include the results of phantom studies of the lesion contrast and lesion size simultaneously. The new functional form produced was in x,y,z coordinates such that the x and y refer to lesion size (volume or diameter) and lesion contrast respectively while the z coordinate refers to the recovery coefficient of the SUV max or SUV mean.

Validation studies: In order to ensure the 3D formulation of the recovery coefficients is valid, the reconstructed images of the contrast ratios 5:1, 10:1, and 14:1 were used as a measure of the accuracy of the results. The normalized mean square error was calculated using the formula: $NMSE = \sqrt{\frac{\sum_1^n (x_m - x_e\ )}{n}}$ (2) Where x_m and x_e are the measured and calculated RCs of the SUV (mean or max) and n is the number of data points (n=18). In order to investigate the performance of the different 3D functions used to restore the true value of the SUV measurements, a pilot study of 8 lymphoma patients with 9 lesions were randomly selected. The SUV mean and SUV max of the 9 lesions were corrected using the four 3D formulae generated as described above.

RESULTS:

The volume threshold optimization process is demonstrated in figure 1 where there is a decreasing response in volume measurements as the threshold value is increased. The resulted 3D function for calculation of threshold knowing the lesion/background ratio and lesion size revealed the following formula: $z = 87.7 - 14.3 \times ln(x) - 5.9 \times ln(y)$ (Eq.3) Where x is the lesion/background ratio and y is the lesion volume with NMSE = 4.35.

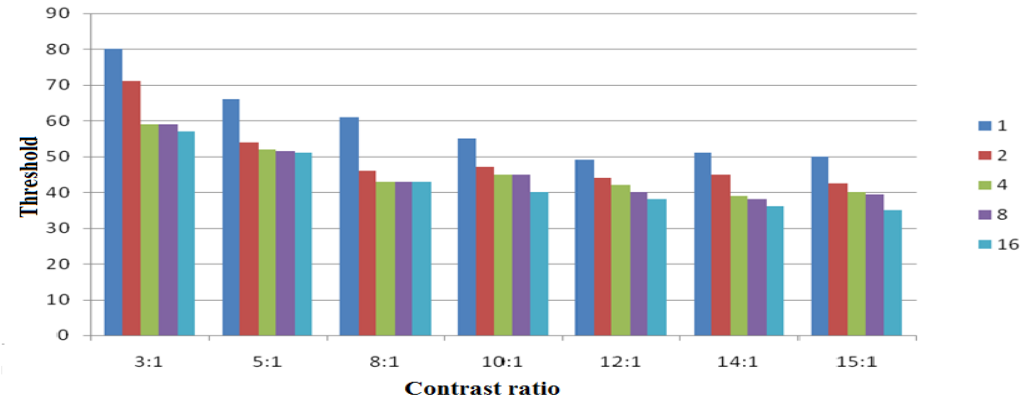

Figure 1. Threshold value is varied for each sphere as the contrast ratio is changed

Recovery coefficients using SUV max versus sphere diameters is shown in ***(figure 2)***. The pattern was similar in the 8 phantom studies performed. ***Figure 3*** represents the relation between recovery coefficients based on SUV mean versus sphere diameters. ***Figures 4 and 5*** describe the relationship between the sphere volumes versus recovery coefficients for the 8 phantom studies using SUV max and SUV mean respectively. As described above, the contrast ratios of 3:1, 5:1, 8:1, 12:1 and 15 were used in generating the 3D form of the RC (Table 1) whereas the other three contrast ratio 2:1, 10:1, and 14:1 were used in the validation studies. The expected logarithmic function was obvious in all of the RC data sets. The median volumes of the PET lesions investigated was 7.5 ml in a range of 2 ml to 83 ml. Comparison of measurements among the different corrections methods revealed a non-significant difference in the SUV max and SUV mean measurements.

Table 1 The various 3D functions generated for RC $_{max}$ and RC $_{mean}$ provided lesion contrast and lesion size (volume or diameters).

		x: sphere size y: contrast ratio	ERROR		
			Min	Mean	Max
Diameter	**SUV** max	**Z=-1.1+0.56ln(x)+0.122ln(y)**	0.2	5.6	16.9
	SUV mean	**Z=-0.86+0.45ln(x)+0.067ln(y)**	10	11.5	29
Volume	**SUV** max	$\mathbf{z = 1 - e^{(-0.173(x+0.486)y^{0.587})}}$	0.08	7	19
	SUV mean	**Z=0.137+0.169ln(x)+0.09ln(y)**	0.5	11.9	31

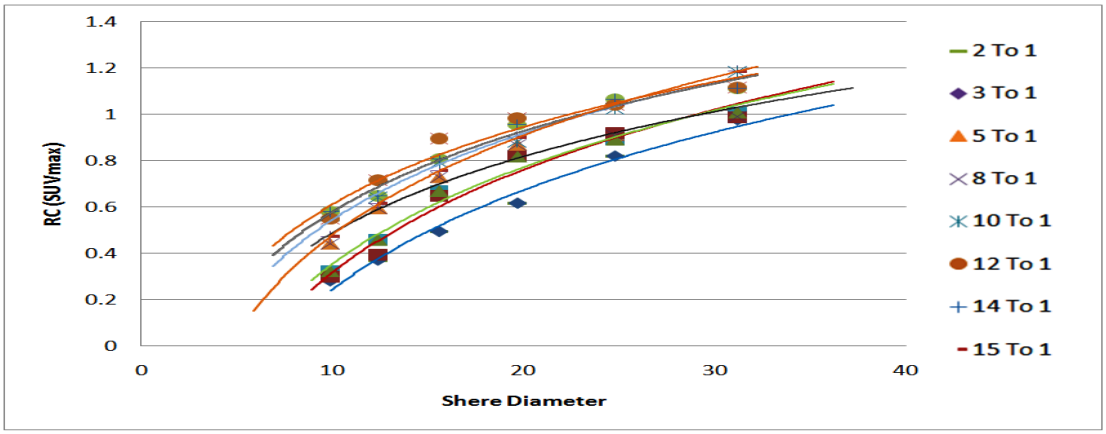

Figure 2.Relation between sphere diameters and RC of SUV max.

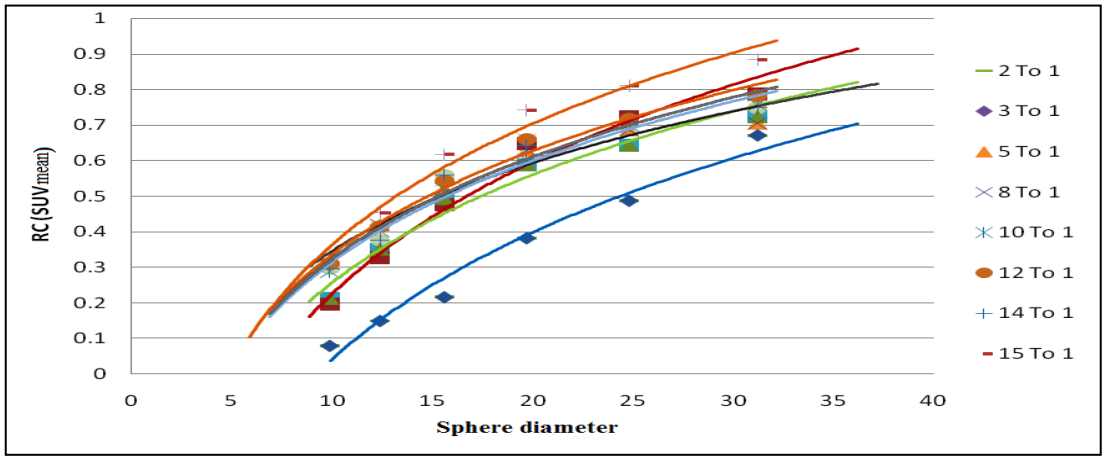

Figure 3 Relation between sphere diameters and RC of SUV mean

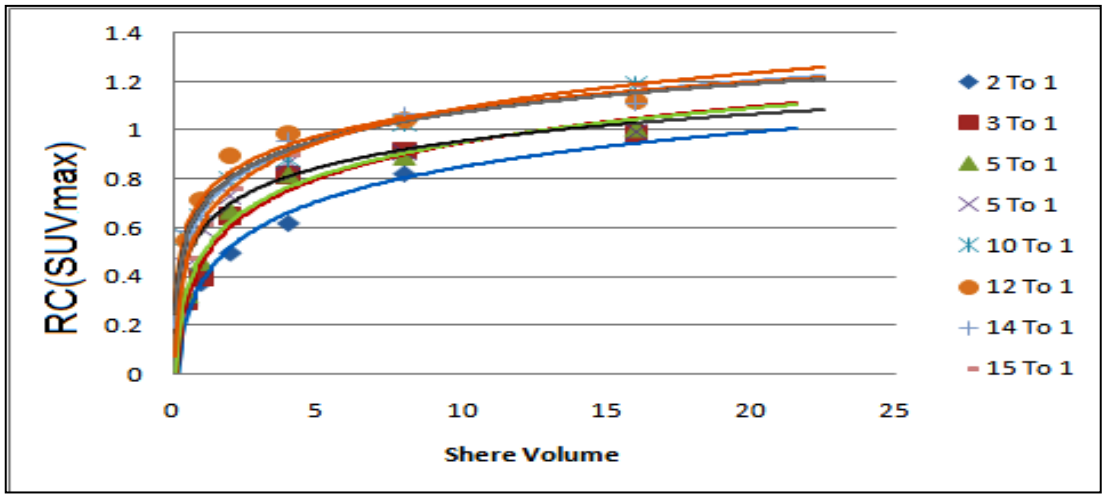

Figure 4 Relation between sphere volumes and RC of SUVmax

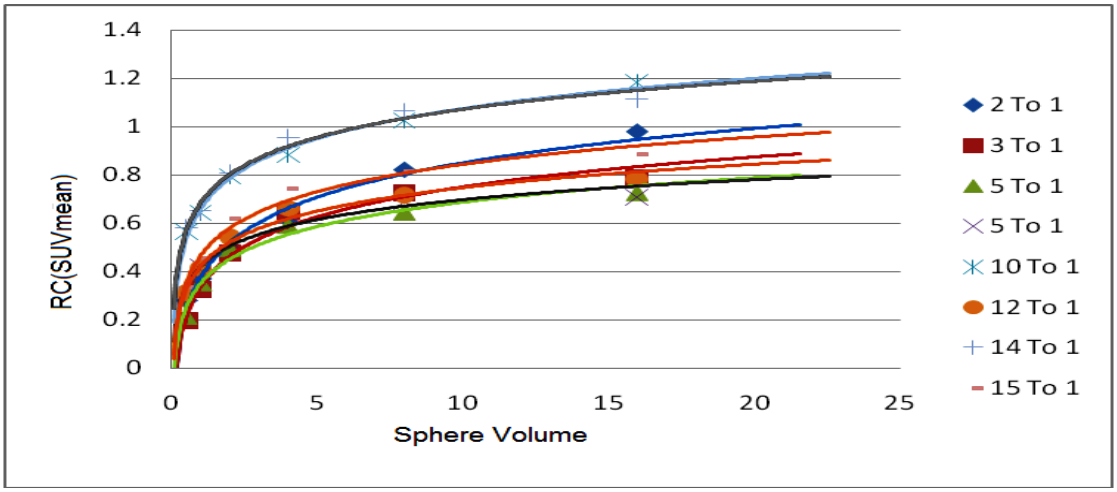

Figure 5 Relation between sphere volumes and RC considering SUV mean

DISCUSSIONS:

Partial volume effect remains one of the most influential parameters that significantly impact image quality and degrade quantitative accuracy.

A relatively large number of reports were released to address this issue with wide range of flexibility, precision and accuracy. One of the major features of partial volume effect is SUV underestimation especially when the lesion size is twice to thrice times less than the full width at half maximum of the system spatial resolution [10, 11].

The attempt made here was to optimize the threshold value that accurately segments a given PET lesion when the volume is measured with CT. A number of measurements were taken to ensure an adequate coverage of the impact of PVE on lesion size at relatively wide range of lesion to background ratio (i.e. contrast ratio) ***(Figure 1)***.

Then validation studies were conducted on different contrast ratios to verify that the generated formula (Eq.3) of the volume segmentation threshold is valid. The error associated with using an adapted threshold value was well below 10% (i.e. NMSE=4.35) when the algorithm was used in comparison to CT lesion volume. However, the error in 19 clinical lesions was about 10%. Four 3D functions were generated to restore the SUV mean and SUV max measurements provided two independent parameters including lesion dimension (volume or diameter) and the measured SUV (mean or max).

The independent variables were treated in the recovery coefficient simultaneously such that the user has to provide both in

Order to get the corrected SUV. Therefore, those combinations resulted in 4 data sets of variable accuracies and precisions.

The best results obtained were those coming from SUV max and sphere diameter, where the error of the RC was around 5.6%. Interestingly, the second best results were also related to SUV max but with volume inclusion. The lowest performance was due to the use of the SUV mean with large dispersion when lesion volume is used and being slightly less with lesion diameter.

Clinical data provided important outcomes when different methods were used to recover the SUV measurements. The median volume of the PET lesions investigated was 7.5 ml in a range of 2 ml to 83 ml.

The range of volumes used was not entirely in the sensitive region of PVE and hence a little impact is expected of the corrected SUV.

Therefore, the four SUV max methods provided comparable results and there was no significant difference in the mean values measured ($p>0.05$). This could indirectly infer the relative equal performance of the RCs in restoring the true value of SUV max.

Similarly, the three methods of SUV mean were not significant at the 0.05 level. Therefore, further studies are warranted to investigate the proposed 3D functions devised in this study on different clinical conditions and in large group of patients.

CONCLUSION:

It has been successful to generate 3D mathematical formulation of the SUV recovery coefficients taking into consideration the most influential factors including lesion size and lesion contrast. The lesions size considered was either volume or diameter whereas lesion contrast was taken either with respect to SUV mean value or SUV max. Validation studies in phantom and clinical data were suggestive of the good performance of the new algorithms generated to correct for partial volume effect. However, further studies are underway to ensure the performance of the proposed algorithms in PET lesion well below the sensitive region of the partial volume effect.

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