Method to Determine the Standard Deviation of SUV Parameters

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Method to determine the standard deviation of SUV parameters

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Abstract

Some of the parameters used for the quantification of Positron Emission Tomography (PET) images are the Standardized Uptake Value (SUV)Max, SUVMean and SUVPeak. In order to assess the significance of an increasing or decreasing of these parameters for diagnostic purposes it is relevant to determine their standard deviation. In this study we present a method to determine the range of statistical variation of the SUV in PET images.

Our method is based on dividing an original dataset into subsets of shorter time-frames. The variation between the SUV parameters of the subsets is used to estimate the standard deviation of the of the original acquisition. This method was tested on images of a NEMA quality phantom with acquisition time of 150 s per bed position and foreground to background activity ratio of F^{18}-2-fluoro-2-deoxy-D-glucose (FDG) of 10:1. This original dataset has been reconstructed with different reconstruction lengths, generating new data subsets. The SUVMax, Mean and Peak were calculated for each image in the subsets. Their standard deviation has been calculated per subset for the different spheres included in the phantom. The variation of each subset has then been used to estimate the expected variation between images at 150 s reconstruction length.

We report the largest standard deviation of the SUV parameters for the smallest sphere, and the smallest variation for the largest sphere. The expected variation at 150 s reconstruction length does not exceed 6% for the smallest sphere and 2% for the largest sphere, but we report an higher coefficient of variation (up to 30%) for shorter reconstruction lengths. We also report significant differences in the variation of SUV parameters for the larger spheres. With the presented method we are able to determine the standard deviation of SUV parameters only due to and the statistical variation. The method enables us to evaluate the effect of parameter selection and lesion size on the standard deviation, and therefore to evaluate its relevance on the total variation of the SUV value between studies.

Introduction

Positron Emission Tomography (PET) has become an indispensable diagnostic tool over the last decades. Computed Tomography (CT) is added to the PET modality for the purpose of attenuation correction and furthermore PET-CT imaging provides a combined view of functional and morphological information.

The radio-ligand FDG has ensured the success of PET-imaging. The glucose component of the molecule provides a higher uptake of FDG in malignant than in healthy cells [1], the fluor-18 component provides the detectability in the PET-CT system.
PET-CT images can be reported visually by the nuclear medicine physician, however an important advantage of PET imaging is that the uptake can be quantified in absolute measures.
Quantification of FDG PET enables the staging of cancer and the comparison of follow-up studies to track the evolution of cancer and response to tumour therapy [2].

The proposed framework for PET Response Criteria in Solid Tumours (PERCIST) suggests to consider a 30% change in Standardized Uptake Value (SUV) as significant variation of tumour activity between images of the same patient [3]. The most used methods of the SUV parameter are the SUVMax and the SUVMean. In the SUVMax only the voxel with the highest uptake is considered, while in the SUVMean all the voxels in a certain region or volume are taken into account. The SUVMax has a low inter and intra observer variability but a high technical statistical variation. The SUVMean on the other hand has a lower technical variation but a higher inter and intra observer variability, since the borders of the volume are a determining factor of the result.
The SUVPeak is introduced as a “best of both worlds” parameter, it calculates the voxels in a limited volume around the voxel with the maximum value.

When comparing images of the same patient acquired at different moments in time, a certain degree of variability of the SUV parameters is unavoidable, such as patient preparation, biological variability and technical variability. Limiting the variations and standardizing the process as much as possible is therefore essential. The goal is to control and minimize the inter and intra observer variability as well as the technical variability between images as much as possible. Studies shown that limiting the variation in image reconstruction, uptake time and scanner characteristics can limit the effect of technical variability to less than 10% of the SUV [4, 5, 6].
Knowledge of the significance of the difference between intra-patient quantifications parameters, when the images are acquired with the same scanner and software reconstruction, is crucial to provide a reliable interpretation of the data. In this study we present a method to estimate the standard deviation of the SUV parameters on different SUV parameters and lesion sizes of images acquired with the

same scanner and reconstructed with the same method. The basics of the method is that one PET acquisition is divided into a number of time-frames and that the variation between the SUV quantification of the separate time-frames is used to estimate the standard deviation of the total acquisition. The proposed method determines the standard deviation of SUV parameters such that the relevance of technical statistical SUV changes in clinical practice can be established in the context of other fluctuations. The variation that we quantify in this paper adds to other technical, biological and physical factors affecting the quantification of FDG PET images, as for example listed in [4]. In our method the biological factors, variations in blood glucose, contrast factors and paravenous administration of FDG are not included. Furthermore, because we use a single acquisition and we only later split it in subsets and reconstruct them with the same software, the possible variability in PET calibration, synchronization, image and scan reconstruction parameters is not present. We quantify the variability of the SUV parameters between subsets of images derived from the same acquisition and reconstructed in the same way. In comparison with test-retest method, our framework compares images with less variable conditions and we focus on the impact of the reconstruction on images from the same subset. With this method we want to quantify a degree of technical variability that is scanner- and reconstruction-specific and that might have a relative larger impact in images with small lesions, low photon counts and/or high noise.
The method is described, validated and applied on a 150 s acquisition of the image quality phantom with a foreground to background activity ratio of 10:1 as example of application. The values and standard deviations of the SUVMax, SUVMean and SUVpeak of the several spheres in the phantom are presented and discussed.

Our method gives insight in the variation of the several SUV parameters and can be used routinely on a specific scanner-reconstruction software combination to give an insight in the technical variation of a determined SUV quantification. Knowledge about the technical variation of the parameter enables a sharper definition on whether a change is significant or not.

Material and methods

Image acquisition and reconstruction

A NEMA NU2–2007 image quality phantom was imaged on a Philips Gemini TF PET/CT system (Philips Healthcare, Andover, MA). PET reconstructions were made using scanner's default ordered subset expectation maximization (OSEM) reconstruction algorithm with 33 subsets, 3 iterations, matrix size of 144 × 144, and voxels of 4 × 4 × 4 mm. No Gaussian filter was applied. The reconstruction corrected for geometrical response and detector efficiency (normalization), random coincidences, scatter, and attenuation. Data were stored in list-mode, to be able to reconstruct different acquisition times. All list-mode reconstructions were decay-corrected to the start time of the acquisition.

The phantom acquisitions were made according to the requirements for the EANM/EARL FDG-PET/CT accreditation [7]. The phantom was composed by a fillable torso compartment acting as background, by a cylindrical insert in the centre of the torso compartment and by 6 fillable spheres of different diameters (10 mm, 13 mm, 17 mm, 22 mm, 28 mm and 37 mm) placed around the central insert. The fillable torso compartment and the spheres have been filled with a solution of water and F^{18}-FDG. At the starting moment of the scan the activity concentration was 2.10 MBq/ml in the torso background compartment and 20.04 MBq/ml in the spheres, resulting in a sphere to background ratio of 9.6:1 (aim is 10:1). [8]

The original dataset was acquired with 150 s frame duration. The total acquisition time was 10 minutes. An attenuation corrected reconstruction was performed at different reconstruction lengths, varying from 4 s to 30 s, generating as many images as possible per subset, without using the same coincidences by varying the starting time of the reconstruction. For example, for the first subset (4 s reconstruction length), the first image was reconstructed using the coincidences recorded between 0 and 4 seconds, the second image by using the coincidences recorded between 5 and 8 seconds and so on, varying the starting moment of the reconstruction, generating a total of 37 images. The longest frame length was 30 s, generating a subset of 5 images. A total of 14 subsets was generated, of respectively 4s, 6s, 8s, 10s, 12s, 15s, 17s, 19s, 20s, 22s, 24s 26s, 28s and 30s acquisition length. The Philips reconstruction software automatically corrected each reconstruction for the decay of F^{18} (half-life of 109.7 minutes [9]), compensating the time difference between the start of the study and the start of the reconstruction by using an opportune scaling factor.

Image analysis

The datasets were analysed using a Python 3.7.0 script (default, Jun 28 2018, 08:04:48) [MSC v.1912 64 bit (AMD64)]. Different SUV parameters were calculated in each image of the subsets:

- SUVMax 2D: the maximum in the central 2D plane of each sphere. The algorithm fitted the sphere, found its central plane, and then found the maximum voxel value in this 2D central plane.
- SUVMax 3D: maximum of the complete sphere. The algorithm fitted the sphere and found the maximum voxel value in the 3D volume;
- SUVMean 2D: the average value in the central 2D plane of each sphere. The algorithm fitted the sphere, found its central plane and calculated the average value of this 2D central plane.
- SUVMean 3D: the average value of each 3D sphere. The algorithm fitted the sphere and calculated the average value of the 3D volume. The SUVMean 2D and 3D were calculated considering the complete 2D central plane or 3D volume, respectively, without using thresholding techniques based on pixel values or on a percentage of the maximum value.
- SUVPeak: the average value within a 1 cm^3 sphere centred in the maximum value of the sphere [10]. The algorithm fitted the sphere, found the maximum voxel value in the 3D volume, used this voxel as the centre of a spherical Region of Interest (ROI) of 1 cm^3 and calculated the average value within the sphere.

The SUV values were calculated per each image in a subset. The SUV values population has been tested for normality with a Kolmogorov-Smirnov test and all subsets matched the characteristics of a normal distribution. The SUV parameters of the different images in a subset were averaged and their standard deviation was calculated. The coefficient of variation of the SUV parameters was calculated as the standard deviation divided by their average value multiplied by 100.

In our measurements we can assume a random sampling model, with no correlations, for independent and identically distributed random measurements. The different subsets do not differ in activity nor voxel dimensions and the quantification of the SUV parameters has been done by using the same ROI dimension. We can therefore describe the ratio of the standard deviations SD of two independent repetitions of PET measurements as:

$$\frac{SD1}{SD2} = \left(\frac{RL1}{RL2}\right)^{-\frac{1}{2}} \tag{1}$$

With SD1 and SD2 being the standard deviations and RL1 and RL2 being the reconstruction lengths. [5]. By using the measured variation of the SUV values in a subset as SD1 and the length of the reconstruction of the specific subset as RL1, it is possible to estimate the variation SD2 between repetitions of scans at the total acquisition time RL2=150 s.

Since we divided our acquisition into 14 different subsets, we could calculate 14 different estimations of the SD2, using the described method above. We validated our method by testing whether the value of the estimated SD2 was independent of the acquisition length of the images in the subset. The results were tested to verify if is a significant difference between the spheres was present. The population of two adjacent spheres (10 mm and 13 mm, 13 mm and 17 mm, 17 mm and 22 mm, 22 mm and 28 mm, 28 mm and 37 mm) were tested by using a two-sample t-test assuming unequal variances with a significance level alpha=0.05.

Results

The method that we describe in this paper for estimating the variation of SUV parameters between PET images includes three main steps:

- acquisition of a dataset of a specific length
- generation and reconstruction of subsets
- estimation of the variation in the original dataset by using the subsets, according to Formula 1.

As an example for this method we used a 150 s acquisition for the original dataset, then we divided it in 14 subsets and estimated the SUV parameters. The aimed foreground to backgroud activity ratio was 10:1.

The SUVMax 2D and 3D, the SUVMean 2D and 3D and the SUVPeak were calculated for the 6 spheres in each image of a subset. Their values were averaged and their standard deviation was estimated. In this way it was possible to plot the recovery curves based on each parameter, with their standard deviation, for each reconstruction length. The results are shown in Fig. 1 for the 4 s, 15 s an 30 s subsets.

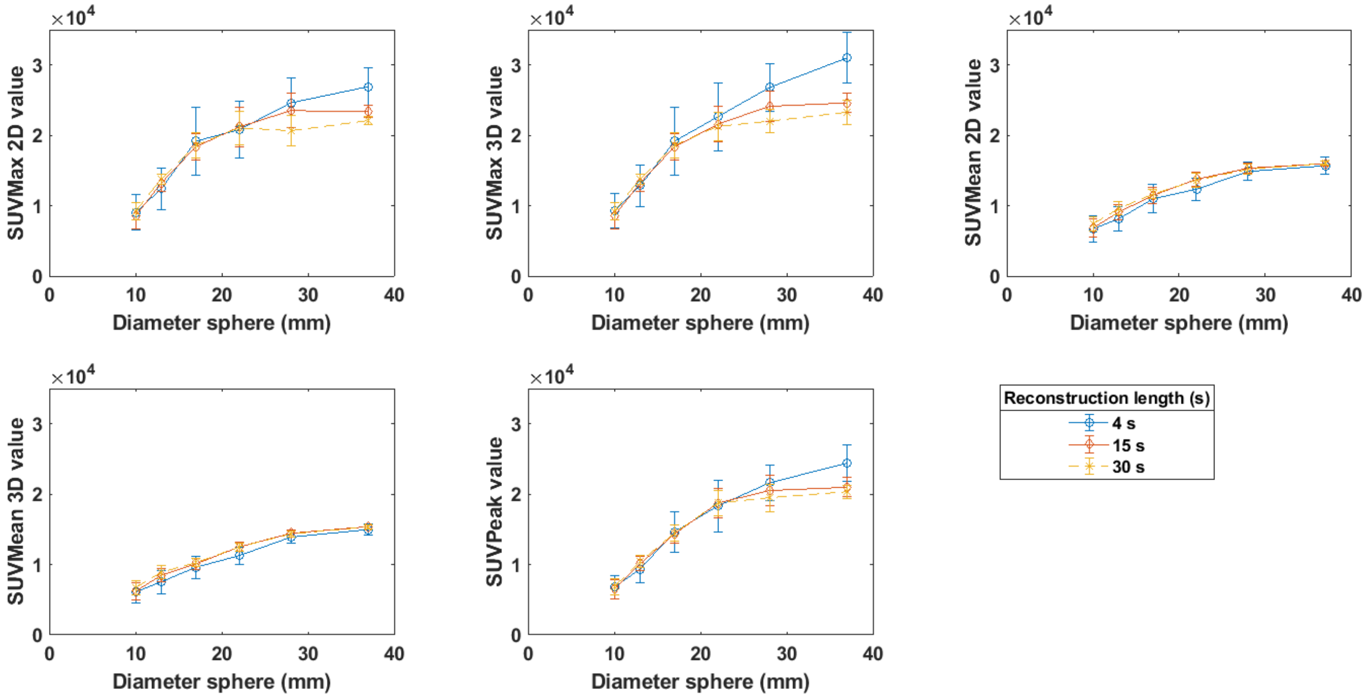

Fig.1: SUVMax 2D and 3D, SUVMean 2D and 3D and SUVPeak for spheres with different volume for 4s, 15 s and 30 s reconstruction lengths.

For the larger spheres, for the SUVMax and the SUVPeak parameters, the shorter acquisition lengths tend to have a higher average value, as shown for the three representative datasets in Fig.1.

Fig. 2 to 6 show the variation of the measured SUV parameters. The coefficient of variation of the SUV is plotted as a function of the reconstruction length for the different spheres. We show the results for the spheres with 10 mm and 37 mm diameter as representative results.

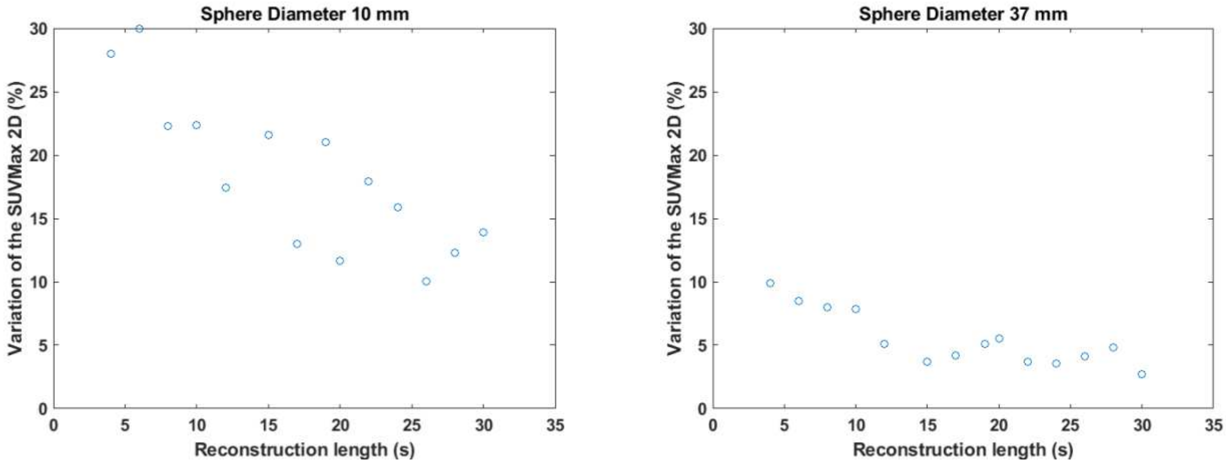

Fig.2: Coefficient of variation of the SUVMax 2D as a function of the reconstruction length.

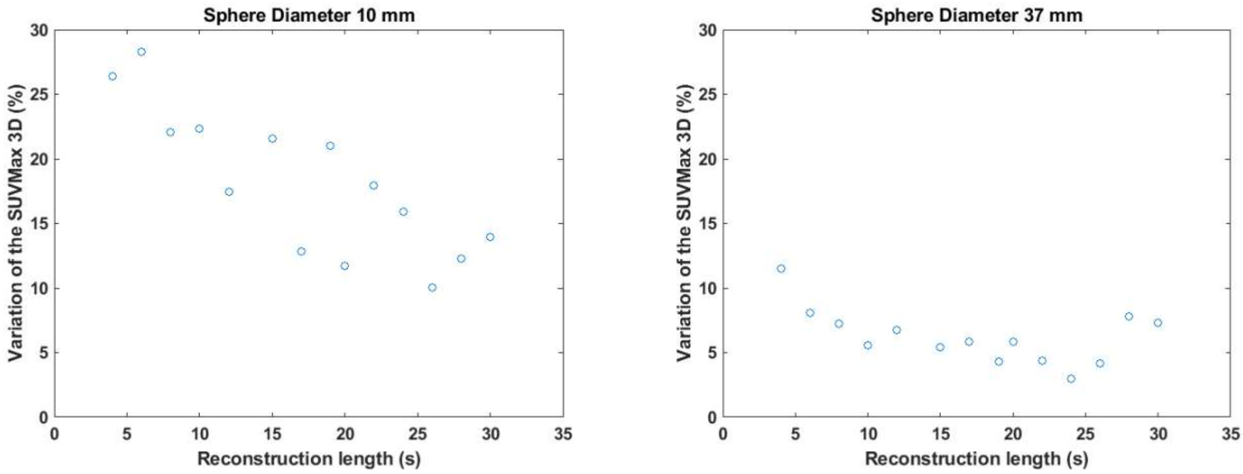

Fig.3: Coefficient of variation of the SUVMax 3D as a function of the reconstruction length.

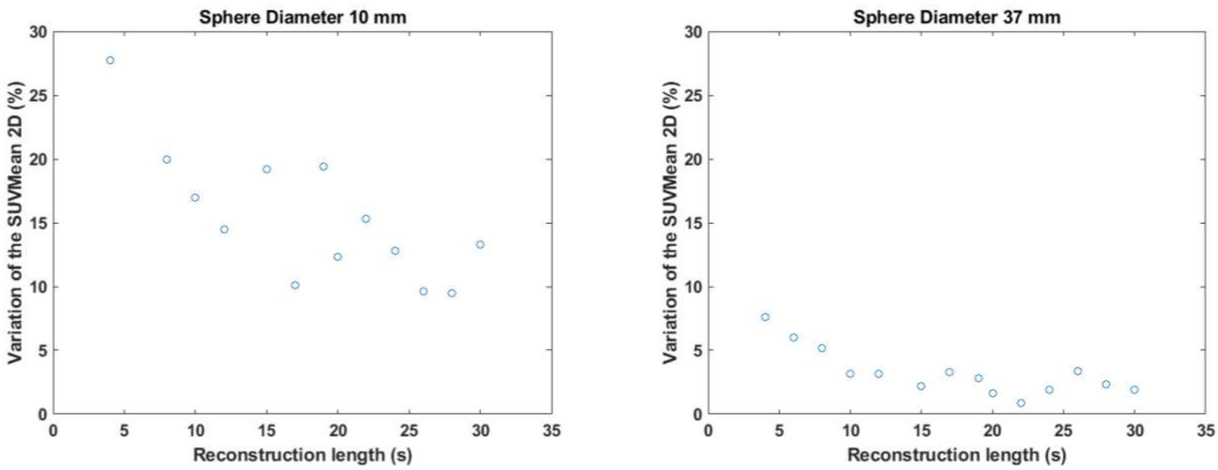

Fig.4: Coefficient of variation of the SUVMean 2D as a function of the reconstruction length.

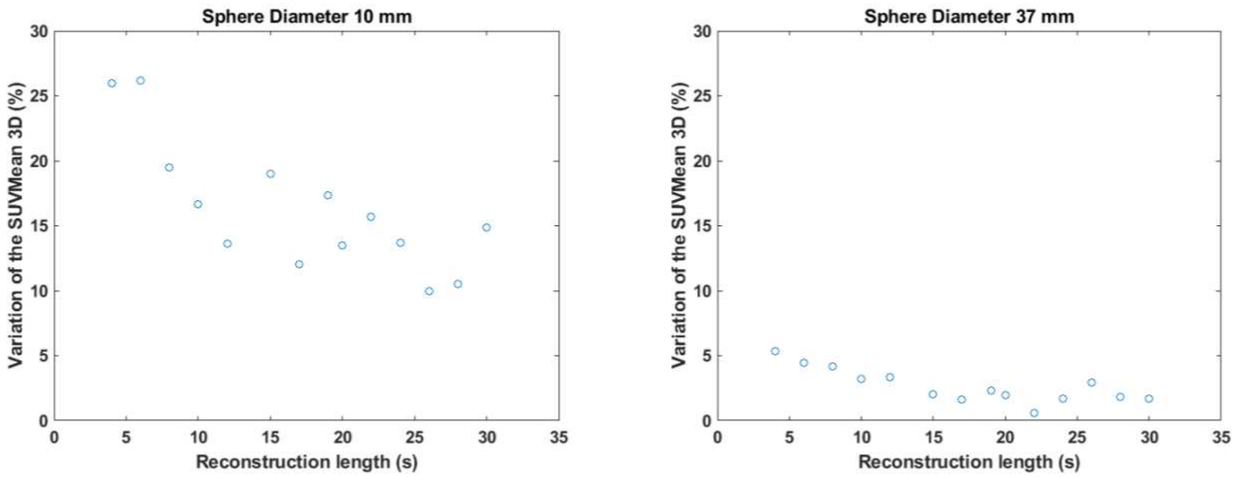

Fig.5: Coefficient of variation of the SUVMean 3D as a function of the reconstruction length.

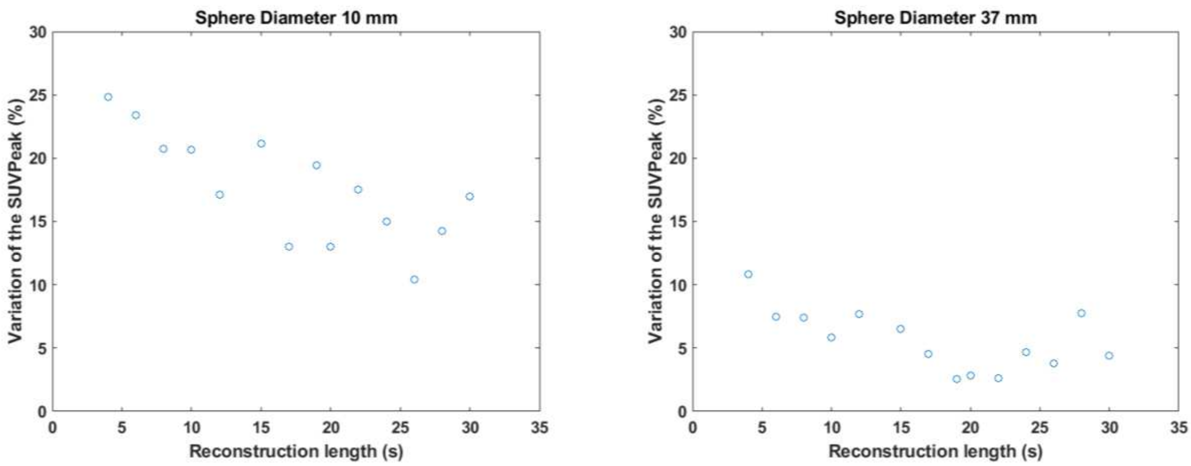

Fig.6: Coefficient of variation of the SUVPeak as a function of the reconstruction length.

One of the goals of the methodology described in this article is to estimate the expected estimated SD of the SUV parameters at a given acquisition length. In order to test the validity of the method Formula 1 was applied to derive the expected SD (*SD2*) at reconstruction length 150 s (*RL2*=150 s) from the SD of the subsets (*SD1*) at different reconstruction lengths (*RL1*) according to:

$$SD2 = SD1\left(\frac{RL1}{RL2}\right)^{\frac{1}{2}} \qquad (2)$$

This formula was used to calculate the estimated SD of the SUV at reconstruction length *SD2*=150 s using each subset of the dataset. The estimated SD (*SD2*) of the SUVMax2D and 3D, SUVMean2D and 3D and SUVPeak at 150 s reconstruction length has been estimated for spheres of different diameters. The average estimated SD is summarized in Table 1. The difference between estimated SD of the SUV parameters for different spheres has been tested with a t-test. The spheres reporting a significant difference between them (p value t-test<0.05) are underlined and in bold in Tab.1.

	d_{sphere}=10mm	d_{sphere}=13mm	d_{sphere}=17mm	d_{sphere}=22mm	d_{sphere}=28mm	d_{sphere}=37 mm
Est. SD SUVMax 2D	***5.6±1.1%***	***3.8±1.2%***	3.4±0.8%	3.3±0.7%	***2.9±0.9%***	***1.6±0.3%***
Est. SD SUVMax 3D	***5.5±1.1%***	***3.8±1.2%***	3.4±0.8%	3.1±0.7%	***2.6±0.6%***	***1.9±0.6%***
Est. SD SUVMean 2D	***5.0±1.0%***	***3.7±1.1%***	***2.8±0.5%***	***2.2±0.4%***	***1.7±0.4%***	***0.9±0.3%***
Est. SD SUVMean 3D	***5.0±0.9%***	***3.6±0.9%***	***2.5±0.6%***	***1.6±0.3%***	***1.3±0.3%***	***0.8±0.2%***
Est. SD SUVPeak	***5.5±1.1%***	***3.6±0.8%***	***2.8±0.6%***	2.9±0.7%	2.8±0.8%	***1.7±0.6%***

Tab.1: Average estimated SD for SUV Max, Mean and Peak for different spheres.

The data were statistically analysed to verify if the difference between the estimated SD of the SUV parameters was significant between spheres (same parameter, different sphere diameter, so difference between columns in Tab.1) and between SUV parameters (different SUV parameter, same sphere diameter, so difference between rows in Tab.1).

Concerning the differences between spheres, we report that the difference between the estimated SD of the SUV parameters of the sphere with d=10 mm and d=13 mm and with d=28 mm and d=37 mm is significant for SUVMax, Mean and Peak. For SUVPeak, the difference between the estimated SD of

the sphere with d=13 mm and d=17 mm is also significant. The difference between estimated SD of the SUVMean 2D and 3D is significant between each sphere diameter.
Concerning the differences between SUV parameters, we report no significant difference between the estimated SD of the SUV parameters of the two smaller spheres (d=10, 13 mm). The values of the SUVMean 3D are significantly lower than the values of the SUVMax 2D, 3D and SUVPeak for the four larger spheres (d=17, 22, 28, 37 mm). The SUVPeak significantly differs from SUVMax 2D and 3D for d=17 mm and for SUVMean 2D and 3D for d=22, 28, 37 mm.

Discussion

This study describe a methodology to estimate the standard deviation of different SUV parameters and lesion sizes of images acquired with the same scanner and reconstructed with the same method. This method divides the total acquisition into subsets at different timeframes and estimates the standard deviation of the total acquisition using the standard deviation between the timeframes. The method was tested on a 150 s acquisition with a foreground to background activity ratio of 10:1. The article shows how subsets of an original scan can be used to estimate the variation between images at different reconstruction lengths. The measured results were compared with their estimation calculated according to a formula proposed in [5]. The measured data are generally in accordance with the estimation performed by used the other subsets and Formula 1. Because of this we could use the available measured variations to estimate the expected variation at reconstruction length 150 s.

In Fig. 1 the calculated values of the SUV parameters are shown for all spheres and for all acquisition lengths of the timeframes in the subset. We report higher average SUV values for shorter acquisition lengths. This can be explained by the fact that at shorter acquisition lengths, when the images are noisier, the chance is bigger that a single voxel or group of voxels will have a higher value due to the a higher statistical variation. This effect occurs with the SUVMax and the SUVPeak, but not at the SUVMean where all the voxels in the regions are used for the calculation.

Fig. 2 to 6 show the coefficient of variation of the SUV parameters as a function of the reconstruction length for the different spheres. This test can provide an expectation of the variation for noisier images (images with high standard deviation between voxels) or for small lesions. In our case we observe that the variation is higher for shorter reconstruction lengths, suggesting that the contribution of the technical variation might be higher, for example, for images acquired with a shorter acquisition time or with a low counts emitter. The higher variation at shorter reconstruction lengths reaches values up to 30%, in our case, for the sphere with 10 mm diameter. This suggests that, when performing quantification of PET images on small lesion, the effect of the technical variability evaluated with this method might not be negligible when compared with the variation used for diagnostical purposes. Our method might also be used to define the minimal required acquisition length: when the technical statistical variation of the SUV has become negligible to the test-retest variation, a longer acquisition time might not add value.

In Table 1 we report the result of the estimated standard deviation of the SUV quantifications. We report significant differences in variation for different sphere dimensions. The difference is always significant for each SUV parameter for the smallest (diameter of 10 mm) and the largest (diameter of 37 mm) sphere. The difference is significant between all spheres for the SUVMean. The values are typically ranging from 5% to 1%, for the 10 mm sphere to the 37 mm. We notice that this is in accordance with the range reported for simulated data [11]. The maximum expected variation between images, for any estimated parameter, did not exceed the 6% for the smallest object (sphere of diameter 10 mm) and the 2% for the largest object (sphere of diameter 37 mm) for an acquisition length of 150 s. This provides an indication of the contribution of the technical variation when the same scanner is used, with equal reconstruction length and activity, and can be compared with the variation measured in FDG PET test-retest studies reporting a typical variation of approximately 10% [14, 15, 16]. In our study the variation is smaller due the fact that we do not have to deal with other factors, as for example repositioning of the patient or phantom and reinjection of the activity, as in test-retest studies.

Nevertheless, it is important to notice that the value of the estimated standard deviation calculated for our scanner and reconstruction method is not directly translatable to other centres. The variability in the calculation of SUV parameters inhibits the direct comparison of these values. [17] Other factors introducing variation of the technical components are reconstruction protocols, analysis methods and scan duration, and their influence is too prominent for a direct comparison of the absolute values of the variation. [18] A simple method as the one described in this article can be routinely implemented to identify the contribution of the technical variation between PET images, in order to take into account of it during quantifications and comparisons of images for diagnostic purposes.

The SUV parameters (Max, Mean and Peak) presents some significant differences for the same sphere diameter. For what concerns the smaller spheres (d=10, 13 mm), the averaging step introduced in the calculation of SUVMean and Peak does not provide a significant difference in SD in our measurements, suggesting that the variation in quantification of SUV for small lesions does not decrease compared with the use of SUV Max. For larger lesions the difference between the variation in SUV Mean 3D and SUV Peak is significant. This suggests that the dimension of the ROI used for the averaging has a crucial effect on the SUV quantification and that a too large ROI might flatten the results. Our definition of SUVMean was based on the knowledge of the objects that were measured because the ROI was defined as a sphere of diameter equal to the diameter of the imaged sphere. This is not always possible during the analysis of images for diagnosis purposes. In that case another definition of SUVMean must be used and the variation between measurements might be expected to increase [10, 12, 13]. Other factors present in clinical practice, as glucose blood levels, velocity of FDG uptake in the lesions or weight recording can increase the SUV variation in diagnostic images of patients. [19, 20, 21]

Another method to estimate the variation between images would be to acquire a dataset with long acquisition time in comparison with the acquisition time used for diagnostic and generate subsets of the long acquisition. This could be a more direct way to measure the variation, possibly less susceptible to low photon statistics as we report in images reconstructed with a short reconstruction length. A similar approach has been shown in [5] for SUVMax and Mean for reconstruction length of 5 minutes with variation between 11.2% to 1.2% depending on the filter, type of acquisition (2D or 3D) and parameter (Max or Mean) used.

For this study we worked with a foreground to background activity ratio of 10:1. In order to further verify the method with other uptakes it would be possible to repeat the study with other ratio's, as for example 5:1 and 2.5:1. Furthermore, the acquisitions could be repeated after a certain amount of hours in order to analyse the variation with other levels of noise. As previously discussed, a higher coefficient of variation is to be expected for noisier images.

Conclusion

In this study we present a method to estimate the standard deviation of different SUV parameters. We used the method to estimate the standard deviation of different SUV parameters for different lesion sizes of images acquired with the same scanner and reconstructed with the same method. The method shows that the variation of SUVMax, SUVMean and SUVPeak varies as a function of the dimension of the objects in the imaged phantom and ranges between 5 and 6% for the smallest sphere (diameter of 10 mm) and between 0.9 and 2% for the largest sphere (diameter of 37 mm). The coefficient of variation reaches values up to 30% for shorter acquisition lengths, suggesting that the variation might become not negligible for noisier images with low counts. The difference between SUV parameters (Max, Mean and Peak) was not significant for the smaller spheres.

The variation in SUVMean 3D was significantly lower for the larger spheres in comparison with the variation of the other parameters. Our method can be used routinely to provide insight into the variation of a SUV quantification between images acquired with the same scanner and reconstruction parameter.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author.

Key words

Standard Uptake Value, PET quantification, variation in Standard Uptake Value

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Contributions

The authors read and approved the final manuscript.

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Ethics declarations

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Figures

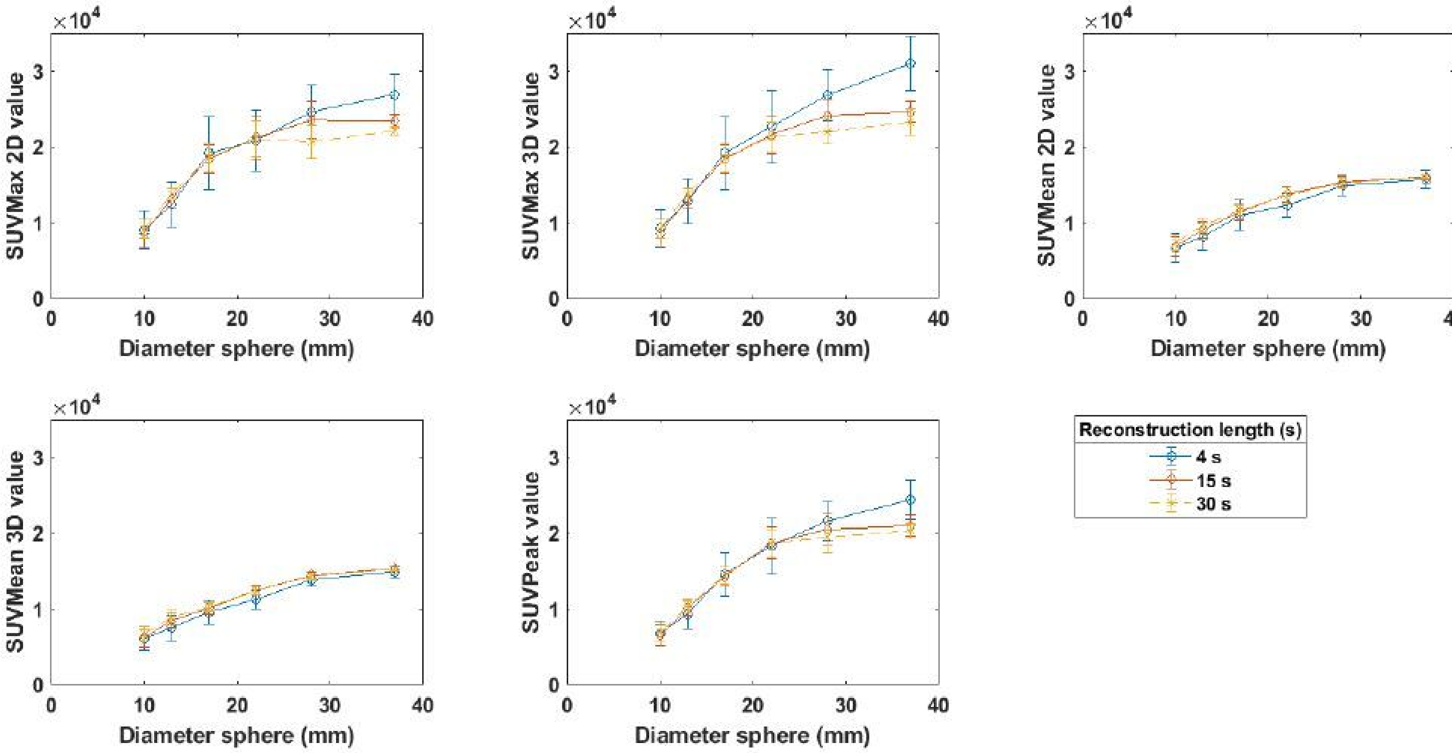

Figure 1

SUVMax 2D and 3D, SUVMean 2D and 3D and SUVPeak for spheres with different volume for 215 4s, 15 s and 30 s reconstruction lengths.

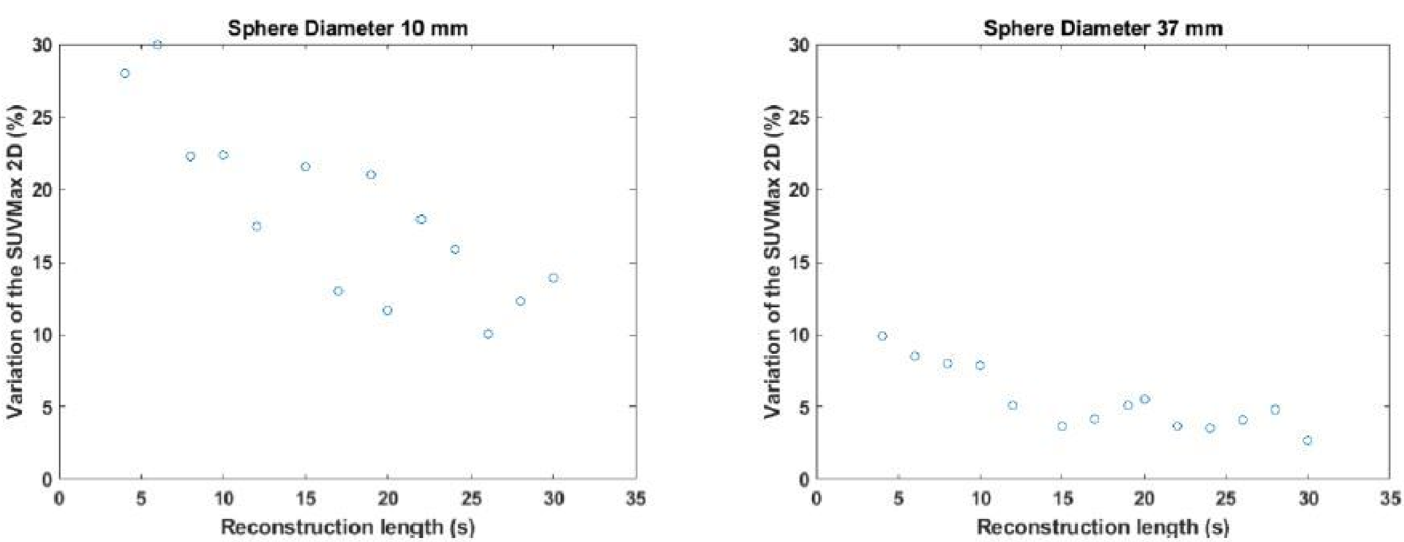

Figure 2

Coefficient of variation of the SUVMax 2D as a function of the reconstruction length.

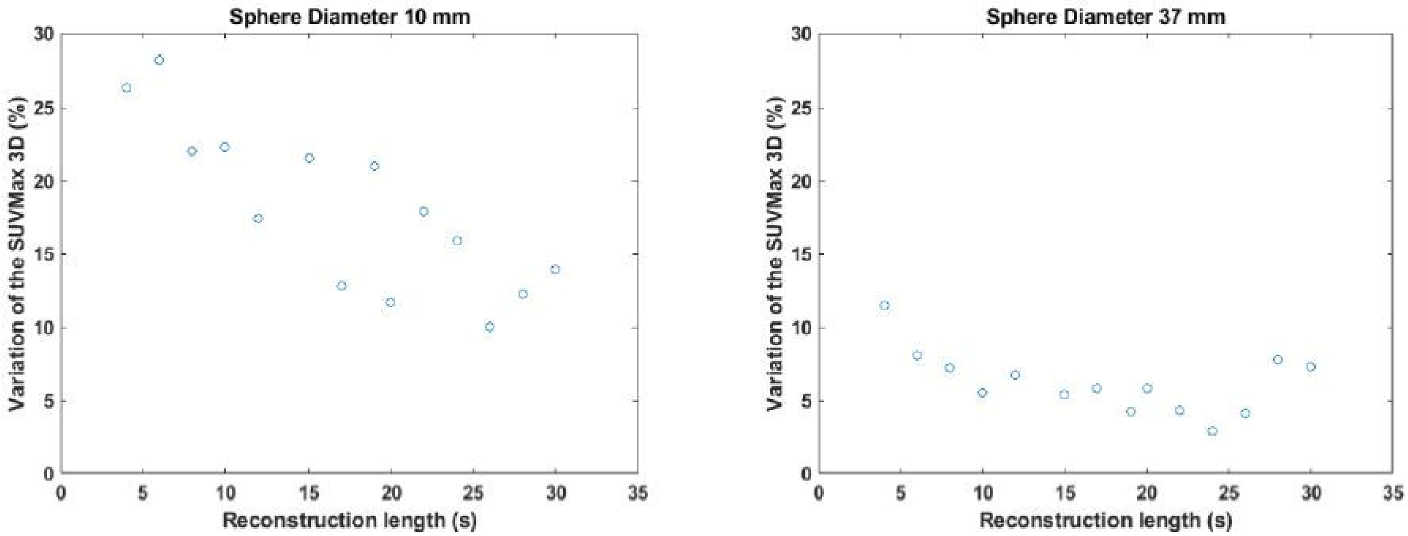

Figure 3

Coefficient of variation of the SUVMax 3D as a function of the reconstruction length.

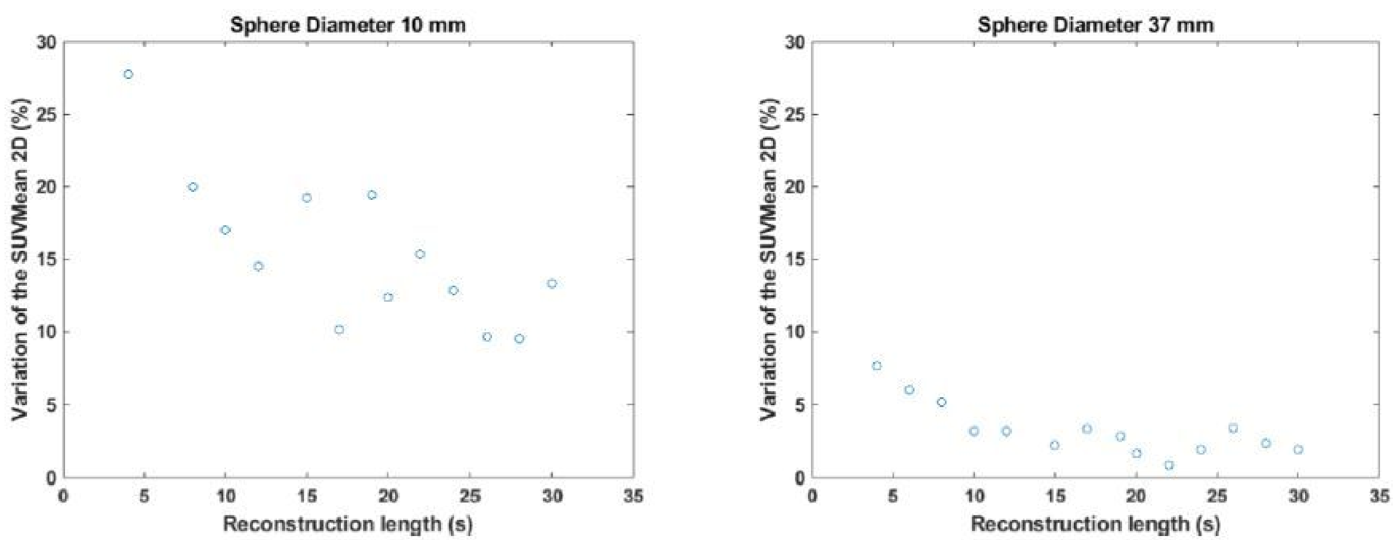

Figure 4

Coefficient of variation of the SUVMean 2D as a function of the reconstruction length.

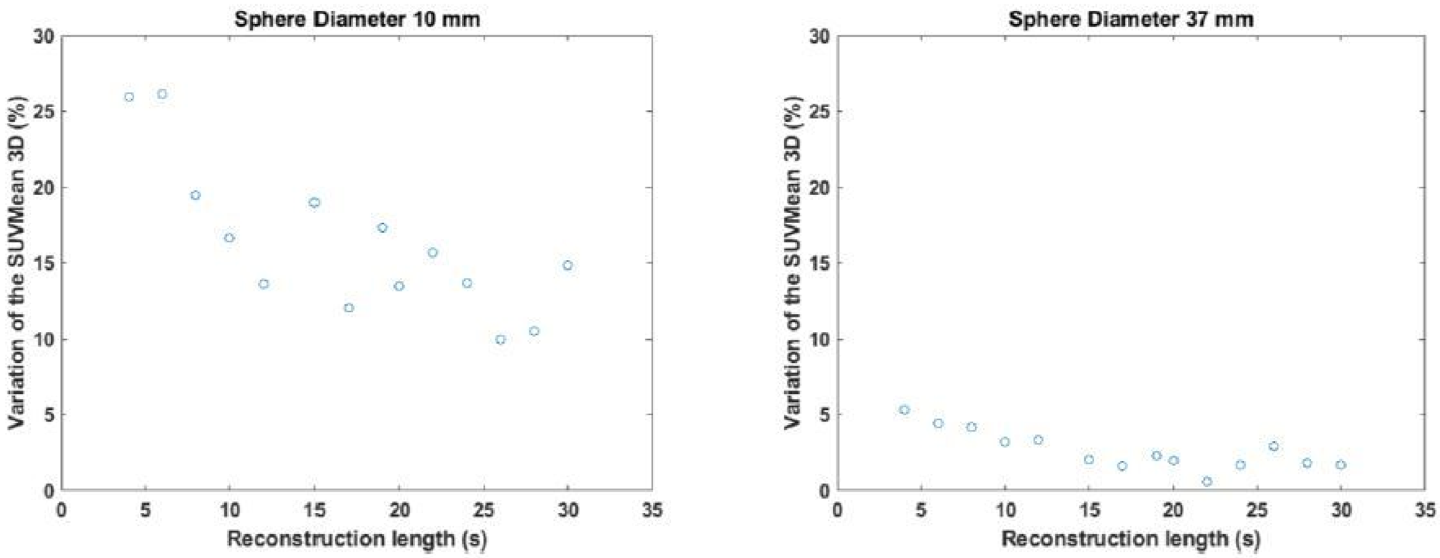

Figure 5

Coefficient of variation of the SUVMean 3D as a function of the reconstruction length.

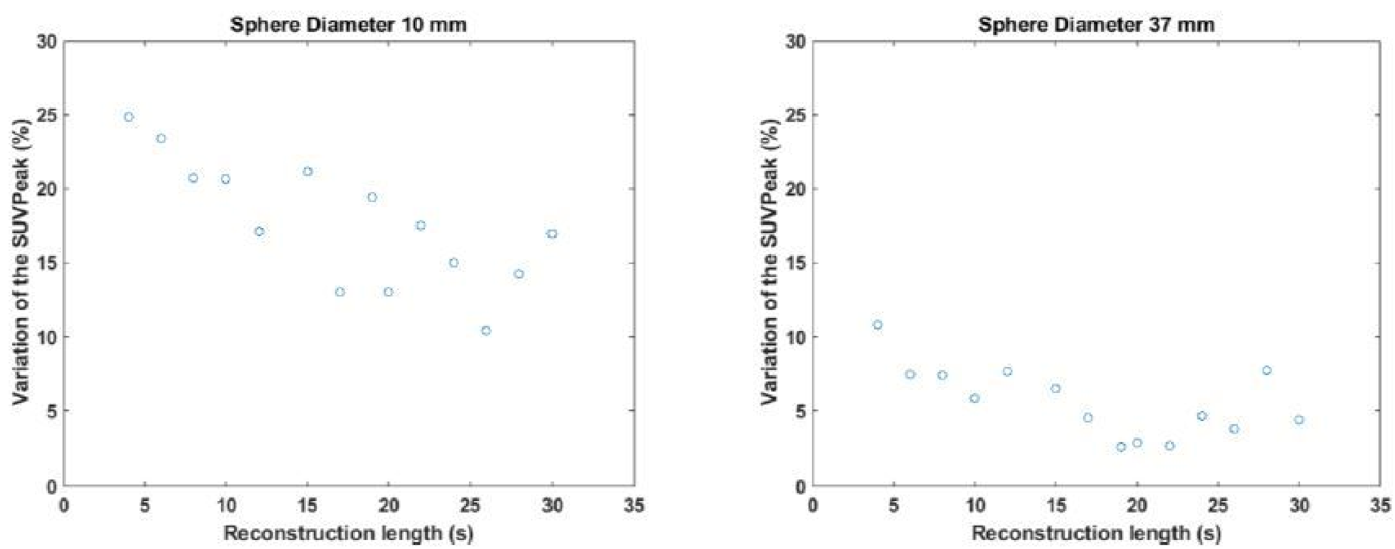

Figure 6

Coefficient of variation of the SUVPeak as a function of the reconstruction length.