Quantitative accuracy of PET/CT for image-based kinetic analysis

Youngho Seo,^{a)} Boon-Keng Teo, Mohiuddin Hadi, Carole Schreck,
Stephen L. Bacharach, and Bruce H. Hasegawa
*Center for Molecular and Functional Imaging, Department of Radiology and Biomedical Imaging,
University of California, San Francisco, California 94143-0946*

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Accuracy in quantification of activity concentrations (e.g., in Bq/ml) is essential for compartment modeling and kinetic analysis of dynamic reconstructed PET images. Dynamic PET data can be acquired in list-mode, and often are preferred over frame mode acquisitions due to the flexibility of reformatting the list-mode data into different dynamic image sequences after the acquisition is complete. However, most PET data are acquired as static frames. It therefore is important to evaluate the quantitative accuracy of list-mode or dynamic PET acquisitions prior to their use for clinical or research applications. The quantitative accuracy of list-mode acquisitions obtained with a Siemens Biograph 16 PET/CT scanner at our institution was evaluated; the image data were acquired from an anthropomorphic phantom (Data Spectrum, Hillsborough, NC) filled with an aqueous solution of ^{18}F -fluorodeoxyglucose (FDG). PET data were acquired with the phantom for the following three different configurations: (1) with nonradioactive water in the body compartment and aqueous solution of ^{18}F -FDG in only a fillable cylindrical insert to simulate the first several seconds of highly concentrated radioactivity within the field of view such as that in major venous or pulmonary vessels or in the cardiac ventricles, (2) with radioactivity throughout the entire body compartment and imaged with 3 min static frames and 12 min in list-mode that was reformatted into four 3-min frames, and (3) with radioactivity throughout the body compartment and imaged in list-mode and reformatted into sequential time frames having durations of 3, 10, 20, 30, 50, and 67 s, respectively (i.e., total of 180 s). All measured concentration values were compared against values acquired from static images or against the actual activity concentrations calculated from the calibrated activities dispensed into the phantom corrected for physical decay of ^{18}F . These analyses demonstrated that the count rate limitation is minimal or negligible as long as there is no more than 370–440 MBq (10–12 mCi) activity entirely within the axial FOV and that list-mode acquisition yields accurate quantitation of activity concentrations over a clinically realistic range of activities. In addition, reformatting a single list-mode acquisition into frames of different durations retains quantitative accuracy with respect to static frame data and compared to the known radionuclide concentration in the phantom. Within these constraints, the list-mode data acquired with the Biograph 16 PET/CT system are quantitatively accurate for image-based kinetic analysis. © 2008 American Association of Physicists in Medicine. [DOI: [10.1118/1.2937439](https://doi.org/10.1118/1.2937439)]

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I. INTRODUCTION

Positron emission tomography (PET) is known as a quantitative radionuclide imaging modality.¹ However, the clinical use of quantitative information from PET has been mostly limited to the standardized uptake value (SUV),² where the measured activity is normalized by the administered activity and body mass. For experimental studies, more sophisticated quantification methods using compartmental modeling combined with kinetic analysis have been used and validated as a method to derive actual metabolic rates in tissues³ with radiopharmaceuticals such as ^{18}F -fluorodeoxyglucose (FDG).

Recently, there has been considerable effort expended on obtaining arterial input functions from image-based techniques^{4,5} to avoid the invasiveness and complexity of direct arterial blood or arterialized venous blood sampling. However, measuring the arterial input function using image-based kinetic analysis requires the PET data to be acquired

either dynamically or in list-mode so that the time-dependent input function can be extracted from the overall PET acquisition. The list-mode acquisition option is generally allowed as a research package on modern gamma cameras and PET scanners; however, the access and use of the list-mode acquisition option may require a special research agreement with a scanner manufacturer. Thus, the measurement of the arterial input function from PET requires accurate measurements of activity concentrations (Bq/ml) in the arterial compartment for the following situations: (A) at high count rates immediately following tracer administration, (B) during dynamic or list-mode acquisitions where accuracy comparable to that of sequential acquisition of static frame-mode data must be achieved, and (C) reformatting list-mode data into dynamic frames in different durations and at different time points. In this report, the quantitative accuracy of activity

FIG. 1. The anthropomorphic phantom with a fillable cylindrical (left). The custom cylindrical phantom (right). The shaded areas in both photographs are where activities were present for the first configuration of the experiment.

concentrations measured for the above conditions was evaluated using a modern PET/CT scanner (Siemens Biograph 16) at UCSF.

II. METHODS AND MATERIALS

All measurements performed in this study were obtained with a Biograph 16 PET/CT system (Siemens Medical Solutions, Malvern, PA) with a 16-slice CT subsystem and a PET subsystem with lutetium oxyorthosilicate (LSO) detectors with the Hi-Rez option. With the Hi-Rez option, LSO crystals have smaller x - y dimensions (4×4 mm) than those (6.45×6.45 mm) without this option in the same size detector block, which yields improved spatial resolution.⁶ The Biograph acquires data only in a 3D acquisition mode, and also allows list-mode PET acquisitions. All data were reconstructed using an iterative ordered subsets expectation maximization (two iterations, eight subsets) algorithm with 2D Fourier-rebinning (FORE+2D-OSEM) provided by the manufacturer. PET data were acquired from an anthropomorphic phantom (Data Spectrum, Hillsborough, NC) filled with an aqueous solution of ^{18}F -FDG, representing whole body distribution of the radionuclide. For high count-rate measurements, a custom cylindrical phantom (190 mm diameter and 127 mm height in the fillable region) was also used in addition to the anthropomorphic phantom.

The PET data were acquired in three configurations to simulate different distributions of radioactivity and different protocols for acquiring a dynamic sequence of image data. The first configuration was designed to test high count-rate acquisitions, using the anthropomorphic phantom with non-radioactive water in the whole-body compartment and an aqueous solution of ^{18}F -FDG in a fillable cylindrical insert (i.e., a spine insert without the bone material) [Fig. 1(a)]. This phantom configuration simulates the first several seconds of highly concentrated radioactivity within the field of view such as that in the large venous or pulmonary vessels, or in the cardiac ventricles. In order to compare this to typical situations in which activity is dispersed, the custom cylindrical phantom (190 mm diameter) was used in addition to the anthropomorphic phantom with the small fillable cylindrical insert. This custom cylindrical phantom was filled with a uniform aqueous solution of ^{18}F -FDG having a similar total activity to that used for the anthropomorphic phantom measurements [Fig. 1(b)]. For these two phantom measurements, the absolute total activities in the field of view would be similar, but the cylindrical insert in the anthropomorphic

phantom contains a highly concentrated activity, at an activity concentration 30 times that in the cylindrical phantom in the non-high-count-rate configuration. The data were acquired for 3 min each using static acquisition modes for the two phantoms at three different locations in relation to the longitudinal central axis of the field of view, that is, the center of the field of view (CFOV). Three locations were as follows: The longitudinal central axis of the cylindrical insert or the cylindrical phantom at (A) the CFOV, (B) 117 mm offset from the CFOV, and (C) 210 mm offset from the CFOV on the same axial plane. This entire measurement sequence for both phantoms was repeated seven times over approximately 390 min (3.55 physical half-lives of ^{18}F) while the activity physically decayed to simulate the activity levels encountered during both initial and later phases of dynamic acquisition, corresponding to activity levels from 700 MBq (19 mCi) to 54 MBq (1.5 mCi), respectively, in the field of view (FOV).

The second configuration used a uniform concentration of radioactivity throughout the entire body compartment of the anthropomorphic phantom without the cylindrical insert. The data were acquired for 12 min using list-mode followed by a 3 min static acquisition, with the list-mode data later reformatted into a dynamic sequence of four 3 min time frames. This sequence was repeated at six times over approximately 315 min (2.87 physical half-lives of ^{18}F) to simulate a range of realistic activity levels (i.e., from 550 MBq or 15 mCi to 85 MBq or 2.3 mCi in the FOV).

The third configuration used the same anthropomorphic phantom (i.e., uniform concentration of radioactivity throughout the entire body compartment without the cylindrical insert) as in the second configuration. The data were acquired with a 3 min list-mode acquisition at an activity concentration of approximately 43 kBq/ml (approximately 315 MBq or 8.5 mCi in the FOV) at one time point. In order to evaluate quantitative accuracy in different durations when the data are acquired in list-mode and reformatted into a set of durations, the list-mode PET data then were replayed into sequential frames covering the durations from 0 to 3, 3 to 13, 13 to 33, 33 to 63, 63 to 113, and 113 to 180 s (i.e., 3, 10, 20, 30, 50, and 67 s durations, respectively) for analysis.

For each phantom configuration prior to the imaging study, the phantom filled with ^{18}F -FDG was agitated so that the concentration of the radionuclide would be uniform. ^{18}F concentrations from the reconstructed PET images were measured by calculating a mean value of activity concentrations in a cylindrical volume-of-interest (VOI) placed within the uniform compartment (for all configurations) of the anthropomorphic phantom not involving the cylindrical insert or the cylindrical phantom or within the cylindrical insert (for the first configuration). The measured concentrations of ^{18}F -FDG first were measured and compared for list-mode and static image sequences, and then against the known activity concentrations that were expected to be true values at each time point assuming the physical decay of ^{18}F from the initial calibrated values. For the second configuration, the

FIG. 2. (a) Measured vs true activity concentrations to test high count rate situations of PET acquisitions using an anthropomorphic phantom with a cylindrical insert (left). (b) Measured vs true activity concentrations to test high count rate situations of PET acquisitions using a cylindrical phantom (right).

agreement between the measured and known concentrations then was assessed using linear regression analysis.

III. RESULTS

Measured concentrations are plotted against known concentrations [Figs. 2(a) and 2(b)] for the anthropomorphic and cylindrical phantoms in the first configuration. In these two phantoms, the measured concentration values start deviating significantly from the true values when the total activity within the FOV exceeds 370 to 444 MBq (10 to 12 mCi). The deviations were greater when the highly concentrated radioactivity is offset from the CFOV [117 and 210 mm offsets from CFOV in Fig. 2(a)] in the anthropomorphic phantom where all radioactivity is concentrated within the cylindrical insert; the deviations from the true values are consistent regardless of the locations of the cylindrical phantom [Fig. 2(b)]. This discrepancy is likely due to the difference in the amount of radioactivity observed by a single detector block for the uniform versus highly concentrated radioactivity distributions in these two phantoms.

Similarly, Fig. 3 shows measured activity concentrations from the second phantom configuration to compare activity concentration values obtained from static and list-mode acquisitions. For the range of concentrations evaluated in this experiment, there is a linear correlation with a slope close to unity between measured and true concentrations for both list-mode and static acquisitions. Correlation coefficients (R) for both acquisition modes are over 0.99. The concentration values from list-mode PET acquisitions were consistent with the values from static PET.

Finally, the standard deviation of the measured activity concentrations from the third phantom configuration with the list-mode acquisition that was reformatted to simulate fast dynamic acquisitions (i.e., sequential frames covering 3, 10, 20, 30, 50, and 67 s durations) was within 1% of the mean value, demonstrating the quantitative accuracy of reformatted list-mode data.

IV. DISCUSSION

In our experimental measurements, the case where the activity concentration is varying with time was not addressed. For example, when reformatting list-mode data into 30 s frames, if the count rate has changed considerably during that period of time, then the random and dead-time correction factors could be incorrect. If the peak count rate during this time period is much greater than the average, then the computations for randoms and dead-time correction factors could be inaccurate if they are based on the average values. This error is particularly prominent for dead-time corrections dealing with high count-rate situations when they are calculated from the singles rates. A test to show this time-varying effect would require a dynamic phantom in which radioactivity distribution would change over time, which is a subject of our future study. Our results are mainly related to the count-rate performance of a specific scanner

FIG. 3. Measured vs true activity concentrations for realistic activity concentrations to compare values from static and list-mode acquisitions using an anthropomorphic phantom.

(Siemens Biograph 16). For other scanners, system-specific count-rate performance should be investigated carefully before deriving any comparison to our results.

Also, although an iterative algorithm such as FORE +2D-OSEM used for our data is generally considered acceptable for quantitative measurements of PET data, it is still a topic of investigation to compare an analytic reconstruction method with iterative techniques.^{7,8} In this report, such a comparison study was not performed.

V. CONCLUSION

For quantitative dynamic PET studies with the Siemens Biograph 16 PET/CT scanner, (A) the count rate limitation is minimal or negligible as long as there is no more than 370–440 MBq (or 10–12 mCi) activity entirely within the axial FOV (Fig. 2), which is consistent with previous measurements using the NEMA NU 2–2001 standard for the same scanner.⁹ In most F-18 studies (e.g., FDG and FLT), a slow infusion of the tracer instead of fast bolus administration can be used to reduce this potential problem. When the radioactivity within the detector field of view exceeds the foregoing limit, both the amount and the spatial distribution of the radioactivity within the object affect the quantitative accuracy of activity concentrations measured by the scanner. (B) As shown in Fig. 3, list-mode acquisition produces activity concentration values that agree with values obtained with frame mode acquisition, and against the known activity values in the phantom, for all ranges of activity levels and phantom geometric configurations tested. (C) For a single list-mode acquisition, reformatting into different time intervals and/or frame durations still yields comparable quantitative accuracy.

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^aElectronic mail: youngcho.seo@radiology.ucsf.edu

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