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Development of a 4D Digital Phantom for Tracer Kinetic Modeling and Analysis of Dynamic Perfusion PET and SPECT Simulation Studies

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Abstract

The goal is to develop a 4D digital perfusion cardiac-torso (PCAT) phantom, a tracer kinetic extension of the XCAT phantom, by modeling the time activity curves (TACs) of individual organ regions in the phantom for dynamic perfusion PET and SPECT simulation studies. The PCAT phantom is based on a generalized compartmental model, which accepts the blood input function, multiple series or parallel compartments, the bidirectional rate constants between the compartments, the blood volume in the tissue, the extraction curves, and other properties of a specific tracer. Based on the kinetic differential equations of the compartmental model, the TACs of the targeted organ regions were determined. For a specific time point, a voxelized anatomical realistic phantom, which with or without the cardiac and respiratory motions, was generated and the activity concentrations in the organ regions were assigned according to the corresponding TACs. According to the dynamic scanning protocol, multiple phantoms at different acquisition time points, which could have uniform or non-uniform time intervals, were generated. When combining the dynamic phantoms with realistic projection simulator, realistic dynamic projection data could be generated by easily adopting to various scanning protocols and imaging systems. With the availability of the “known truth”, the activity map of the targeted organ regions, the TACs, the estimated rate constants and other kinetic parameters, from the projection data and the reconstructed images could be quantitatively evaluated. We demonstrate the usefulness of the 4D PCAT phantom in initial simulation studies in dynamic myocardial perfusion PET imaging with different tracers. The PCAT phantom was found to be an important bridge between the creation of TACs and the generation of simulated projection data. It is a useful simulation tool to study different kinetic analysis methods, acquisition protocols, reconstruction methods, and imaging parameter settings.

I. Introduction

Tracer kinetic techniques have been increasingly employed in many medical modalities, especially in PET and SPECT, and recently in CT and MRI to measure the functional and physiological properties of the organs of interest with the given tracer. For cardiac PET and SPECT studies, one of the primary goals of performing dynamic studies is to quantify the myocardial blood flow. The extended cardiac-torso (XCAT) phantom [1] is widely used in the simulation studies of medical imaging research of different modalities, especially in SPECT and PET studies [2–6]. Realistic human anatomic structure and cardiac and respiratory motion are modeled and fully adjustable through parameter files. In this project, we aim to develop a 4D digital perfusion cardiac-torso (PCAT) phantom, a tracer kinetic extension of the XCAT phantom, by modeling the time activity curves (TACs) of individual tissue regions in the phantom for dynamic PET and SPECT simulation studies. By combining the PCAT phantom with projection simulator and reconstruction method, the main benefits of performing this realistic simulation are (1) the simulated projection and reconstructed image data are anatomically and physiologically realistic as compared to those found in clinical studies, and (2) the “known truth” of the parameters of the kinetic models, such as the TACs, the rate constants, and the activity map of the targeted tissue regions, are available for quantitatively evaluation of the protocols, image reconstruction and kinetics analysis methods employed.

II. Methods

A. TACs from Generalized Compartmental Model

The PCAT phantom was based on a generalized compartmental model as shown in Fig. 2, which included an arterial blood compartment and up to four tissue organ compartments connected in series or parallel with interconnected bi-directional rate constants. It allowed modeling the blood input function, and adjustable parameters, including the bidirectional rate constants between the compartments, the blood volume in the tissue, the extraction curves, and other required tracer properties.

Here we used a sample kinetics model of a myocardial perfusion tracer as an illustration. For a general two-tissue-compartmental model of myocardial perfusion with myocardial compartment constituted of two sub-compartments as shown in Fig. 3.

The kinetic equations [7] could be summarized as:

$$C_m(t) = \frac{K_1 k_2}{k_2 + k_3} e^{-(k_2 + k_3)t} \otimes C_a(t) + \frac{K_1 k_3}{k_2 + k_3} \int_0^t C_a(\tau) d\tau, \quad (1)$$

and

$$C_{PET}(t) = V_B C_{LV}(t) + (1 - V_B) C_m(t), \quad (2)$$

where $K_1, k_2, k_3 > 0$ and $k_4 = 0$. C_a and C_m are the concentrations of the tracer in the arterial blood and the myocardium compartments. C_{LV} and C_{PET} are the measured concentrations of

the tracer in the blood pool and the myocardium. C_a can be obtained from metabolic corrected C_{LV} . V_B is the blood volume fraction in tissue with a real number between 0 and 1. Based on the kinetic differential equations of the compartmental model with the required corrections (decay, extraction, and metabolites), the TACs of the targeted tissue regions were calculated through publicly available compartment modeling tools (e.g. *Comkat* [8] was used in current implementation) and custom-built program and script for interfacing with PCAT phantom.

B. Voxelized PCAT phantoms at different time points

For each specific time point, the activity and attenuation maps of a voxelized human anatomical realistic 3D PCAT phantom, in which the cardiac and respiratory motions could be switch on or off, were generated as shown in Fig. 4. In the activity map, the regions of the tissue organs were assigned to the specific activity levels according to the calculated TACs. In the attenuation map, the regions of the tissue organs were assigned to specific attenuation coefficients according to the tissue types. According to the dynamic scanning protocol, multiple 3D PCAT phantoms were generated at multiple acquisition time points were generated and the time intervals could be uniform, non-uniform, or arbitrary assigned.

C. Projection Data Simulation and Image Reconstruction

When combining the dynamic phantoms with realistic projection simulator, realistic dynamic projection data could be generated by adapting to various scanning protocols and imaging systems. We used the combined SimSET 2.9 and GATE 3 Monte Carlo simulation program [9] to generate projections of the human torso of PCAT phantom. The geometry of the simulated PET system was based on GE RX PET scanner, consists of 24 rings and 630 crystals per ring as in Fig. 5(a). Sinogram was rebinned using single-slice rebinning method as shown in Fig 5(b) then a 3D OS-EM reconstruction method using modified STIR (Software for Tomographic Image Reconstruction) [10] with attenuation correction using the attenuation map averaged over motion cycle was applied. The reconstructed image size as shown in Fig. 5(c) was 128 by 128 by 47 voxels with isotropic voxel size of 3.27mm.

III. Sample Simulation Results and Discussions

To demonstrate the capability of the PCAT phantom, we simulated a series of dynamic PET studies using the PCAT phantom with three different tracers, which were ^{83}Rb , ^{13}N -ammonia, and ^{18}F -Flurpiridaz. These tracers have different compartmental models (one tissue-compartment and two tissue compartment models) and quite different rate constants and parameters.

For ^{83}Rb simulation study, one tissue-compartment model (Fig. 6(a)) was used and the TACs were generated based on the typical K_1 , k_2 and V_B . The input function was measured from a 8-minutes ^{83}Rb patient study. The values of the kinetic parameters were obtained from the same patient study, with $K_1=0.413$, $k_2=0.08$, and $V_B=0.477$. The activity samples measured of the arterial (left ventricle blood pool) and the myocardial regions measured from a patient study were plotted in the Fig. 6(b) as red and blue crosses correspondingly. The spline-fitted TAC of the measured samples of the arterial region was plotted as the red

curve. Based on the given kinetic parameters from the patient study, the TAC of the myocardial region were calculated and plotted as the blue curve. As illustrated in Fig 6(b), the calculated myocardial TAC was reasonably fitted with the measured data samples, especially near the time interval near the peak. Further investigation is needed to identify the cause of the significant depart of the calculated and measured data towards the time interval beyond 4 minutes.

For ^{13}N -ammonia PET simulation study, two tissue-compartment model (Fig. 7(a)) was used and the TACs were generated based on the typical K_1 , k_2 , k_3 , and V_B . The input function of ^{13}N -ammonia study was measured from a patient 20-minutes study. The values of the kinetic parameters were obtained from the same patient study, with $K_1=0.580$, $k_2=0.080$, $k_3=0.020$, and $V_B=0.324$. The activity samples measured of the arterial (left ventricle blood pool) and the myocardial regions measured from a patient study were plotted in the Fig. 7(b) as red and blue crosses correspondingly. The spline-fitted TAC of the measured samples of the arterial region was plotted as the red curve. Based on the given kinetic parameters from the patient study, the TAC of the myocardial region were calculated and plotted as the blue curve. As illustrated in Fig 7(b), the calculated myocardial TAC was reasonably fitted with the measured data samples, over the whole 20 minutes time interval.

For ^{18}F -Flurpiridaz PET simulation study, two tissue-compartment model (Fig. 8(a)) was used and the TACs were generated based on the typical K_1 , k_2 , k_3 , and V_B . The input function of ^{18}F -Flurpiridaz study was extracted from a figure in a porcine 20-minutes study [11]. The values of the kinetic parameters were based on the average values from a study of fourteen pigs, with $K_1=0.56$, $k_2=0.07$, $k_3=0.0099$, and $V_B=0.38$. The measured activity samples of the arterial (left ventricle blood pool) and the myocardial regions extracted from the pig study were plotted in the Fig. 8(b) as red and blue crosses correspondingly. The spline-fitted TAC of the measured samples of the arterial region was plotted as the red curve. Based on the given kinetic parameters, the TAC of the myocardial region were calculated and plotted as the blue curve. As illustrated in Fig 8(b), the calculated myocardial TAC was reasonably fitted with the measured data samples, for the later stage of the experiment, time interval over 4 minutes. The calculated TAC was significantly difference from the measured data at the time interval near the peak. One of the possible explanation is that average kinetic constants were used which might be significant from the actual constants of the specific study.

As depicted in Fig. 9, we demonstrated the capability of the PCAT phantom. When combining with projection simulator and reconstruction method, realistic dynamic phantoms of various PET tracers, rate constants, and models, and the corresponding PET image sequences at specific time points and at the noise level similar to the one in typical clinical studies were generated.

IV. Conclusion

The 4D dynamic PCAT phantom was found to be an important bridge between the creation of TACs of specific agent in a subject and the generation of simulated PET or SPECT projection data which can be used subsequently to generation PET or SPECT images with

known “truth”. It is a useful simulation tool to study different kinetic analysis methods, protocols, reconstruction methods, instrumentation settings and the properties of new tracers.

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Fig. 1.
(a) The anatomically and physiologically motion realistic 4D XCAT whole-body and (b) heart phantoms with the cardiac beating motion at end-systolic and end-diastolic phases.

Fig. 2.
Generalized compartmental model

Fig. 3.

A sample two tissue-compartmental model of a myocardial perfusion tracer

Fig. 4. Activity (left) and attenuation (right) maps of PCAT phantom with no cardiac and respiratory motions

C. Projection Data Simulation and Image Reconstruction

Fig. 5.

(a) Geometry of the PET system used; (b) Sinogram of the generated PET data; (c) Reconstructed PET image.

Fig. 6.
 (a) The employed one tissue-compartment model, and (b) the plot of the generated TACs in ^{82}Rb PET simulation with the measured data samples from a patient study.

(a)

(b)

Fig. 7.

(a) The employed two tissue-compartment model, and (b) the plot of the generated TACs in ^{13}N -ammonia PET simulation with the measured data samples from a patient study.

(a)

(b)

Fig. 8.

(a) The two tissue-compartment model used, and (b) the plot of the generated TACs in ^{18}F -Flurpiridaz PET simulation with the measured data samples from a porcine study.

Fig. 9. Sample generated phantoms (left column) and simulated PET image sequence (right column) ($t=0.65$, 1.05 and 7.0 min) of a dynamic PCAT simulation with ^{83}Rb PET tracer.