Framework to Quantify the Metabolic Rate in the Heart using Monte Carlo Simulation and Compartmental Modeling

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Abstract

The Nuclear Medicine imaging using PET modality allows evaluating the physiological condition of the heart (i.e. heart disease, perfusion, cardiac stress, physics disorders, etc.), by the use of small amounts of radioactive material. While the visual information provided by PET image is quite important and today is heavily used by the specialists, it is clear that having quantitative values of the metabolism would help to determine the real condition of the myocardium, to get a more accurate diagnosis and to apply a better treatment. Thus, we developed a framework using different tools to simulate a real PET exam focused in the heart in order to analyze the metabolic exchange in this organ. This research produced realistic PET exams by using GATE platform that performs Monte Carlo simulations, together with an anthropomorphic phantom of the whole body called MASH. This study consisted of the modeling of a commercial PET scanner with BGO detectors, where the MASH's thorax was imaged by the scanner. In order to enhance the realism of the simulation, clinical data was considered, like the quantity of radiotracer (FDG) injected, time of acquisition, and number of frames along the time, among others. Next, the projections were reconstructed using STIR's algorithms. With the aim of obtaining a better quality of the volumes and to select the specific ROI, filtering and segmentation algorithms were applied, respectively. Finally, the heart metabolic analysis was performed using a mathematical model that seeks to describe and to quantify the level of consumption and exchange of glucose in the heart through a model with three compartments. The metabolic parameters obtained were: K_1=0.5690, k_2=0.2266, k_3=0.0718, and k_4=0.0243. It was evidenced that the process of metabolic quantification using compartmental modeling is significantly relevant because of its flexibility, noninvasiveness and reliability. Hereafter, we will apply this framework under real PET images.

1. Introduction

Clinically, it is known the importance for the specialist to have knowledge of the location and subsequently to detect functional and metabolic alterations in a particular area of the body, especially because they precede anatomical alterations [1, 2].

Thus, the role of the Nuclear Medicine is currently diagnostic, prognostic and control, with a very significant potential for therapeutic aspects in an attempt to cure diseases and some forms of cancer by radiotherapy [3, 4].

Due to the lack of computational tools and techniques to assess and study the dynamics of processes from images of Nuclear Medicine [4] is intended to contribute with new perspectives, new approaches and tools to assist, facilitate and improve the work of specialists.

This study aims to establish a procedure for quantifying and assessing the metabolism in the heart through well-controlled and non-invasive procedures.

2. Methods

Our work is constituted by a sequence of interrelated modules and steps which were implemented as part of the study such as: (a) Simulation and acquisition of 3D PET images; (b) Reconstruction of the simulated projections; (c) Filtering of 3D images; (d) Segmentation of 3D structures; and (e) Compartmental Modeling. The steps mentioned will be detailed below:

2.1. Simulation and acquisition of 3D PET images

The research no involves new experiments with animals or humans, since numerical phantoms were used. The simulation experiments were based on an anthropomorphic phantom called MASH [5] that is a representation of an adult man with a complete internal structure (organs, tissues, skeleton, and so on).

This investigation produced realistic PET exams by using the GATE (Geant4 Application for Tomographic Emission) platform that performs Monte Carlo simulations [6], together with the anthropomorphic phantom MASH of whole body [5]. We used the data

sheets and architecture manuals to model a commercial PET scanner with BGO detectors, where the thoracic part of the MASH phantom (that contains the heart) was coupling and imaging by the modeled scanner (Figure 1).

Total scan time was 48 min., divided into 8 frames with the following times: 1.417, 1.583, 2.083, 3.0, 3.750, 10.0, 28.0 and 48.0 min. The phantom had a resolution of 478×258 with each voxel having dimensions of 1.2 mm.

It was considered in the simulation a quantity of FDG injected (~ 10 mCi) used in clinical PET exams and, we assumed that about 10% of the amount of tracer injected into the patient reaches the region of interest (~ 1 mCi).

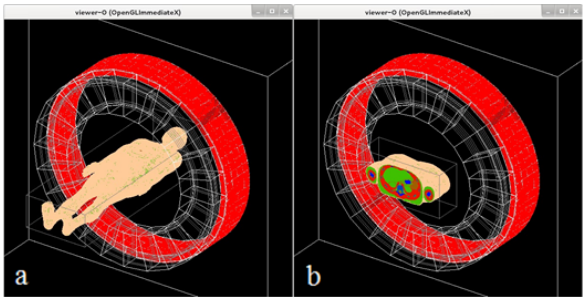

Figure 1. Simulation of the realistic PET exam with (a) full MASH phantom, and (b) the thoracic region of the MASH phantom within the modeled PET scanner.

With the total number of voxels used in the phantom (dorsal region) and the simulation time (collection), about 4% of the emitted photons were detected as part of the simulation process. Figure 2 shows the files obtained as result of the realistic simulation process using GATE: the projections and the sinograms, which were used in the reconstruction phase that we will detail in the next section.

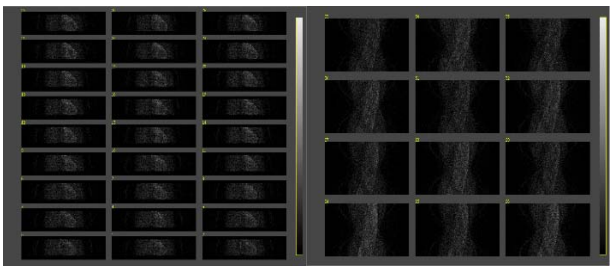

Figure 2. Output files from the realistic simulation process: projections (left), and sinograms (right).

2.2. Reconstruction of the simulated projections

The projections and/or sinograms were used in the reconstruction process [7] through analytic algorithms (FBP2D / FBP3D) and iterative algorithms (OSMAPOSL).

On one hand, the analytic methods are based on discrete implementations where the image estimate is directly calculated from the data. These methods sum the individual contributions to a spel (pixel or voxel) value from detected counts of all lines of response passing through this spel (pixel or voxel). On the other hand, the iterative methods have multiple parameters and incorporate the discrete nature of the data sampling through some statistical model of the data acquisition process. For this purpose, these methods apply a huge system of equations in order to approach an acceptable solution by a series of successively refined estimations. Importantly, attenuation correction and normalization steps were applied as part of the reconstruction process.

The two main differences between these two methods are the reduced processing time of the analytic methods and the superior noise suppression properties (remove undesirable artifacts) of the iterative methods. Figure 3 shows this process using the FBP3D algorithm.

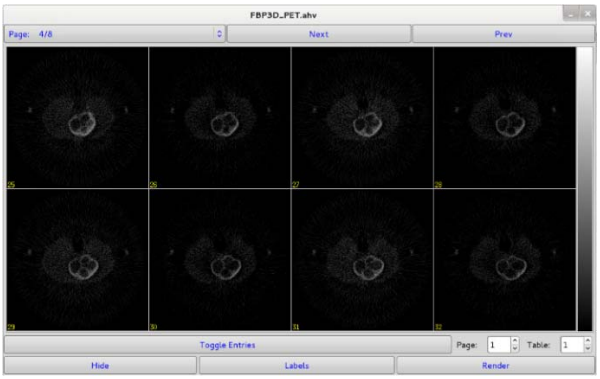

Figure 3. Reconstruction of the heart through the FBP3D algorithm and shown by XMedCon.

2.3. Filtering of 3D images

As known, the PET images are corrupted by Poisson noise that is dependent of the signal [8].

The filtering process in this study used the Anscombe/ Wiener filter, which allows the reduction of undesirable noise generated in the acquisition process.

First, we applied the Anscombe transform [9] that allows to change the Poisson noise of a digital image that is signal dependent into a noise approximately independent of the signal, additive, Gaussian, with zero mean and unit variance [8]. Then we applied the Wiener filter [10], over the noise that became approximately independent of the signal and it was described by a Gaussian distribution, in order to reduce the Gaussian noise. Afterwards, we applied the Inverse Anscombe transform for highlighting the interest structures of the filtered image. Figure 4 shows the effect of filtering step applied to the heart volume.

2.4. Segmentation of 3D structures

The segmentation process applied in this work is based on the concept of Fuzzy Connectedness (FC) method using the approach of dynamic weights [11].

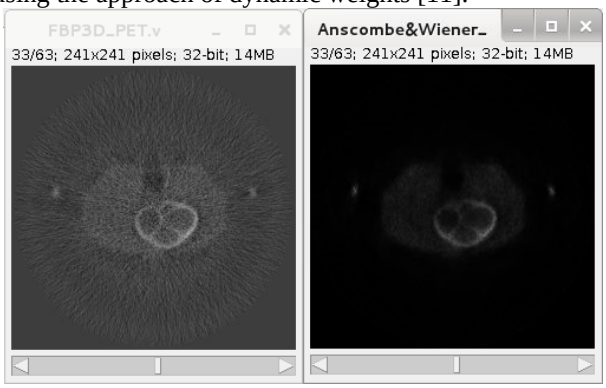

Figure 4. Filtering process using the 3D Anscombe and Wiener approach using Java/Eclipse and ImageJ.

One of the fundamental concepts of the FC method is the factor of Affinity. Based on the concept of affinity, it is possible to find a connectivity between any two spels (pixel or voxel), c and d. If $p_{c,d} = \langle s_1, s_2, \ldots, s_N \rangle$ is one path between c and d, where s_i is N spels adjacent to each other pairs, the affinity of this path is given by:

$$\mu_K(p_{c,d}) = \min_{1<i<N}(\mu_k(s_{i-1}, s_i)) \quad (1)$$

Thus, the selection of the higher affinity will be the best representation of the global connectivity. Therefore, assuming that $p_{c,d}$ is a set of all paths p, the global connectivity between c and d is defined as:

$$\mu_K(c,d) = max_{p \in P_{c,d}}(min_{1<i<N}(\mu_k(s_{i-1}, s_i))) \quad (2)$$

Figure 5 shows the segmentation process. It is possible to note that we selected a seed that belongs to the ROI in order to segment the 3D heart structure.

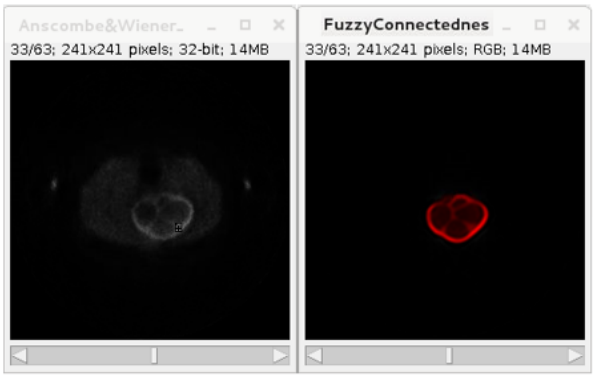

Figure 5. Segmentation process based on the concept of FC method using the approach of dynamic weights.

2.5. Compartmental modeling

Compartment models are often used to describe the exchange of material in several physiological processes such as studies of metabolic systems. A compartmental system is made up of two or more compartments, each compartment exchange material with another following certain rules [12].

There are several authors that have used the Compartmental Model approach [13, 14], but their studies performed invasive procedures such as blood sample and/or biopsy of the ROI as method to obtain the activity curves. Therefore, we used image-processing techniques directly from the images in order to obtain the activity curves that were used as excitation functions of the model.

This study used a model with three compartments as shown in Figure 6 (top on the right), where: C_p is the concentration of tracer in the blood plasma; C_1 and C_2 are the concentration of tracer in the tissue (myocardium): K_1 to k_4 correspond to the parameters that regulate the model.

The compartmental system of three compartments is modeled by a set of ordinary differential equations, each equation describing the time rate of change of amount of material in a particular compartment. However, this type of mathematical models need information along the time (the plasma time activity curve PTAC, as well as the tissue time activity curve TTAC) in order to calculate the constants that represent the exchange of material between the compartments.

Both PTAC and TTAC were loaded into the mathematical model as excitation function. These information permitted to estimate the metabolic constants K_1 to k_4.

In Figure 6, both activity curves were obtained directly from the 3D images using the blood region and the myocardium region, respectively.

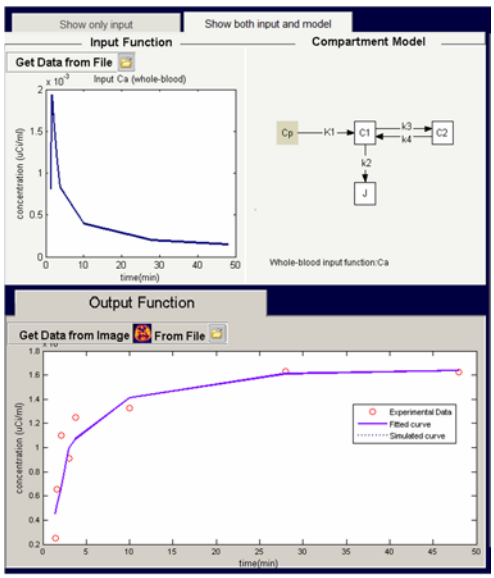

Figure 6. Input activity curve (top on the left),

Compartment model with three compartments (top on the right) and, Tissue Activity Curve (on the bottom).

3. Results

Finally, the heart metabolic analysis was performed through the mathematical model that seeks to describe and to quantify the level of consumption and exchange of glucose in the heart through a model with three compartments. The metabolic parameters obtained were: K_1=0.5690, k_2=0.2266, k_3=0.0718, and k_4=0.0243.
Additional simulations were used in order to repeat the whole process of obtaining metabolic constants. In all cases, similar values to those indicated were obtained. The differences in the calculation of metabolic constants were due to the use of Monte Carlo simulations.

4. Conclusion

The estimation method of the metabolic constant was well defined and implemented. It has advantageous points respect to traditional processes of metabolism rate, such as:
(1) The activity curves from PET images, as functions of excitation of the mathematical model, are obtained by non-invasive procedures using image processing techniques. That means we did not need to use any invasive procedure in patients such as surgery and blood analysis.
(2) As the activity curves are obtained directly from the PET images, it is possible to evaluate and/or compare various sub-regions that belong to the chosen organ or ROI. Thereby, it is possible to compare a healthy region with a neighbor region that shows some abnormality sign.

The process of metabolic quantification using compartmental modeling is significantly relevant because of its flexibility, noninvasiveness and reliability.

In order to provide more accuracy to our methodology for the estimation of metabolism, will be used real 3D PET images in future tests.

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