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Tracer Kinetic Modeling and Derivation of Time Activity Curves in Positron Emission Tomography in order to Enhance Accuracy in Cancerous Regions Diagnosis

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ABSTRACT: Positron Emission Tomography is one of the most efficient cancer diagnosis methods. In this method a radioactive (positron emitting) substance called Tracer is injected to the patient and the positron emission tomography scanner produces images by capturing the positrons emitted from the tracer existing inside the body. The qualified methods has mistaken in cancer diagnostics. In this paper, a mathematical method is used for diagnosis of cancerous region based on image obtained from positron emission tomography. A compartmental model based on ordinary differential equation is used for this reason. The fludeoxyglucose tracer which is one of most famous tracer for cancer diagnostic is used for modeling and the three compartments model is applied. To verify the applied mathematical methods, the experimental results of real case (positron emission tomography imaging of a mouse) is investigated and activity curve of tracer for different region of real case are plotted for diagnosis of cancerous tissue. The results indicated that reviewing time activity curves alongside positron emission tomography images can help enhancing the accuracy of cancer diagnosis.

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1- Introduction

In spite of decades of research and investigations on cancer biology and treatment, the capability in cancer diagnosis and treatment of cancer is highly limited due to complexity of tumors and expensive treatment and the adjunct risks of experimental methods. One of the most efficient and popular cancer diagnosis methods is positron emission tomography (PET) which is a non-invasive and in-vivo[1] method. In this method, the radioactive (positron emitting) substance called "Tracer" is injected into the patient's body and then the imaging starts and the PET scanner produces interpretable images for medics by absorbing the emitted positron from the body.

Fludeoxyglucose (FDG) is one of the commonest tracers used worldwide and the only one produced in Iran. FDG has the ability to penetrate in different tissues especially cancerous ones as it contains glucose and causes high glucose consuming tissues appear highlighted in PET images [1].

FDG is also highly soluble in water. Thus the organs in which water is concentrated, may be seen as highlighted zones also high density or high glucose consuming uncancerous organs [2,3]. In order to distinguish between cancerous and uncancerous glowing regions tracer, Time Activity Curves (TAC) can be used which shows the activity of tracer in the region of interest (ROI). Since the penetration of tracer differs in different tissues, different behavior of TACs in cancerous and uncancerous tissues can be seen regardless to the concentration of tracer in that tissue [4]. There are general methods to obtain TACs: 1- sampling and measuring tracer concentration which is inapplicable on humans due to its invasive and damaging nature. 2- Using dynamic PET image data. These images are not produced by commercial PET scanners and only can be obtained in scientific laboratory Scanners. 3- Using modelling and simulation methods which are used in this paper [5-8].

Kinetics of a substance in a biological system is its temporal and spatial distribution as a result of complex events such as blood cycling and material transfer to cells and metabolism with the goal to keep a certain amount of that substance in related system [7, 9]. Using the results of kinetic modeling by means of the compartmental models, the method predicts a better view of tracer concentration and penetration in different tissues and as a result improves cancer diagnosis methods. In the present study, compartmental modeling is used as the TAC derivation method and sampling and dynamic imaging are used as verification methods.

2- Materials and Method

In this investigation, a compartmental model having three inaccessible compartments model has been considered which is a common model used for FDG [6] (Fig. 1). Blood plasma is considered as the accessible compartment as the tracer is directly injected into it. Unknown parameters in inaccessible

1 Methods in which there is no need to extract sample via surgery in order to observe or study them and are applicable on living bodies.

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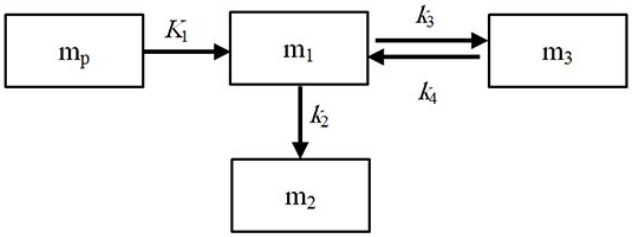

Figure 1. FDG compartmental model

pools are estimated using modeling and information from accessible pool.

The input function of the accessible compartment is a curve fitted to the tracer activity in blood plasma which is related to the tracer concentration. These data are obtained by measurement and gained from COMKAT official website [10]. Also, COMKAT is used to derive the TACs is a compartmental modeling. To verify the compartment modeling results, the experimental results on a 200g rat with injection dose of 5mCi F18-FDG are used. Three different regions in the rat body are studied which one of them is cancerous. The images of the sample are dynamic type obtained by a micro-PET scanner [10].

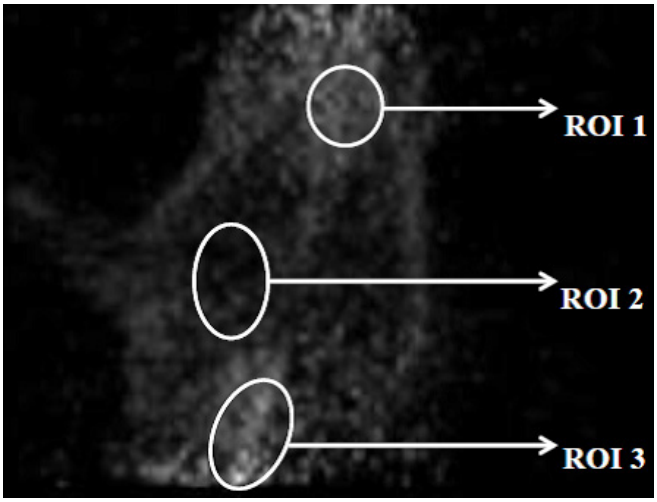

Figure 2. ROIs on sample [10]

3- Results and Discussion

In the present study, three ROIs from a rat body is studied (Fig. 2). Regions 1 and 3 are highlighted and we know that region 3 is cancerous and region 1 and 2 are normal.

The TACs are derived in these areas using the three compartmental modeling (Figs. 3 to 5). As it can be seen in Fig. 2, ROIs 1 and 3 are glowing on micro PET image. This means high tracer activity which is due to tracer concentration. The concentration of tracer in tissues is due to high glucose consumption in that tissue. In natural tissues the activity becomes constant after reaching a peak (Fig. 3), but in cancerous regions, the activity increases continuously (Fig. 5). As it can be seen from these figures, the use of TACs alongside PET images helps to distinguish accurately between cancerous and normal tissues.

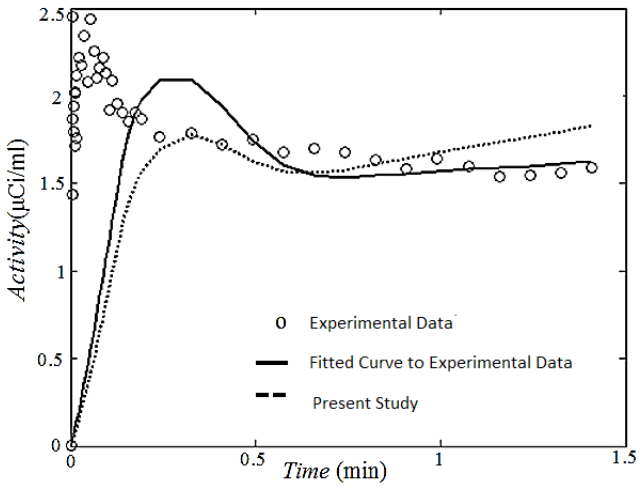

Figure 3. TAC in ROI 1

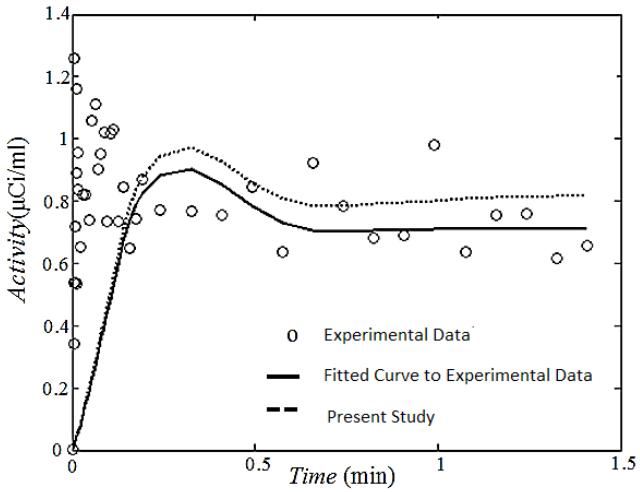

Figure 4. TAC in ROI 2

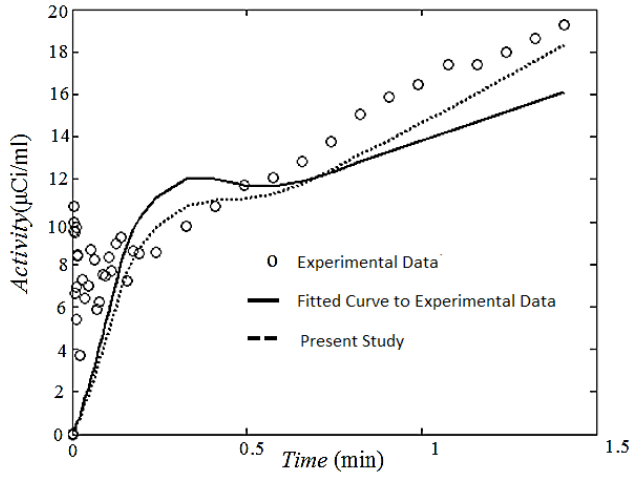

Figure 5. TAC in ROI 3

4- Conclusions

In the present study, the application of TACs derived using three compartmental modeling is investigated to distinguish between cancerous and normal tissues. The results indicated that tracer kinetic modeling can be considered as a supplementary method beside PET images to enhance the accuracy of diagnosis.

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