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Calculation of standardized uptake values (SUVs) and time activity curves (TACs) of mice in FDG-PET

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Abstract: Positron Emission Tomography (PET) with 18F-fluorodeoxyglucose (FDG) is an important imaging practice in cancer diagnosis, staging, treatment planning, and response assessment. Accurate interpretation of PET results requires an understanding of FDG uptake in organs. The time activity curve (TAC) and standardized uptake value (SUV) are the two common tools to measure tracer uptake in regions of interest. The TAC provides information on glucose consumption dynamics, while the SUV involves measuring the amount of tracer taken up by a specific region or volume of interest, and then adjusting the measurement by the amount of tracer injected and the subject's characteristics. In the current study, we measured the TACs and SUVs of the heart, brain, kidney, and muscle in ten mice injected with FDG over a period of 120 minutes. According to the TACs obtained in this study, the brain has a slower uptake than the other organs with a tendency to keep the FDG for a longer period of time. Also, the SUV of the brain showed a rising trend until the middle of the experiment with a sharp falloff afterwards. The pattern of the curves of the other three organs was almost the same. The findings of this study were in agreement with a similar study on humans and are explained by the metabolic activity and physiology of the organs studied.

Keywords: Positron Emission Tomography, PET, Time Activity Curve, TAC, standardized uptake value, SUV, Mice

1 Introduction

Positron Emission Tomography (PET) using the radiotracer ^{18}F-fluorodeoxyglucose (FDG) is a common nuclear medicine procedure that plays a crucial role in clinical oncology for cancer diagnosis, disease staging, treatment planning, and assessment of treatment response [1]. Understanding the physiological uptake of FDG is crucial for the accurate interpretation of a PET study. The accurate interpretation of the FDG accumulation in organs provides valuable insights into the function of these organs. It's also important to recognize that physiological FDG accumulation can sometimes resemble pathology in some organs.

One common tool used in analyzing PET images is the time activity curve (TAC). As the definition represents, the TAC provides quantitative information on the temporal dynamics of glucose consumption in organs. The shape of the TAC reflects the uptake and clearance kinetics of FDG, which in turn reflect the metabolic activity of the tissue.

Another approach for quantifying radiotracer accumulation in organs and studying its behavior within the body, which is more sophisticated than TAC, is the standardized uptake value (SUV). The SUV, which was first proposed in 1985 for oncological studies, is a semi-quantitative technique and commonly-used index for analyzing PET in clinical as well as preclinical practices. It measures tracer uptake in a region of interest (ROI) or voxel of interest and is normalized to the injected dose and a normalization factor based on the subject's characteristics [2]. Due to its versatility and independence from blood sampling, SUV is widely adopted as a straightforward method in clinical routine. Additionally, its ability to be used with a variety of PET radiotracers also makes it a desired technique for aiding in the diagnosis of diseases and tumor staging [3]. Furthermore, in cases where it is not easy to recognize abnormalities in organs, knowing about the SUV and uptake in normal tissue could help to identify abnormalities in organs.

To correctly interpret FDG-PET imaging, it is necessary to comprehend the variability of TACs and SUVs in organs. This information can be used for quantifying PET and extracting biokinetic data which are essential for performing dosimetry and assessing radiation risk. In the current study, we investigated the TACs and SUV values of mice's normal organs including the heart, brain, kidney, and muscle in nine time points over a 120-minute scanning period. We then compared the obtained curves with a similar study on humans to see the similarities.

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2 Materials and Methods

2.1 Animal Preparation

Our study cases were ten BALB/C mice (two male and eight female) aged between seven and eight weeks with an average weight of 15.25±2.24 grams. These mice were provided by the animal facility center of the Tehran University of Medical Sciences, Iran. They were maintained at a constant temperature of 23°C with ambient light-regulated to switch on and off respectively at 7 a.m. and 7 p.m. to provide a rhythmic lighting cycle. The mice had access to water and food ad libitum for three days before the PET scan. All experiments were carried out according to the local guidelines for the Care and Use of Animals.

2.2 PET Imaging

All animals fasted before FDG injection, with access only to water. For FDG injections and PET scans, the animals were warmed and anesthetized with intraperitoneal injections of a ketamine (80 mg/kg) and xylazine (10 mg/kg) mixture. In total, $\sim$ 12 MBq FDG (200 µL) was injected via the tail vein. The injected activity was determined by calculating the difference between the activity levels of the syringes before and after injection. Mice were imaged every 15 minutes from 3 to 120 minutes post-injection under general anesthesia during the scans. PET scans were carried out at the small-animal PET facility at Tehran university. Image reconstruction was performed using the OSEM algorithm with five iterations and four subsets. Since the imaging system did not include a CT scanner, reconstruction was performed with a first-order Chang's attenuation correction algorithm [4].

2.3 TAC Measurement

We used the AMIDE software to extract information from PET images [5]. First, the ROIs were drawn manually on the target organs and the counts were measured within each ROI. Using these counts and the imaging durations, we measured the activity in each organ of interest. The radiotracer concentrations in different organs (C_T) were determined based on the default voxel size ($0.78mm \times 0.78mm \times 1.07mm$) in the study. Putting all the steps above together, we could generate TACs for all organs.

2.4 SUV Measurement

We calculated SUVs according to the most prevalent SUV formula , which is expressed as[6]:

$$SUV = \frac{C_T(MBq/ml)}{A(MBq)/W(g)} \quad (1)$$

where C_T is the tracer activity concentration defined earlier, A is the decay-corrected amount of injected activity, and W represents the mice's body weight.

3 Results

In Figure 1, a PET scan of an exemplary mouse in AMIDE software is presented. The organ presented in red is the bladder of the animal which was taken 105 minutes after the injection of the FDG.

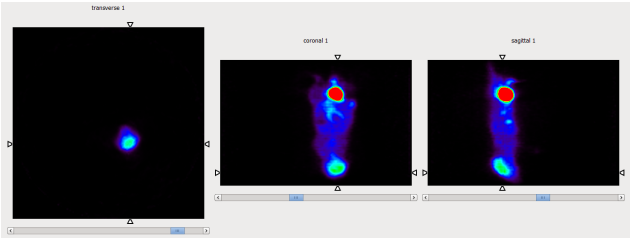

Fig. 1: FDG-PET image of a mouse in transverse, coronal, and sagittal views in AMIDE software

Figure 2 shows the FDG concentration (MBq per cc of administered activity) over time in four selected organs of ten mice. The figure illustrates that the activity concentrations in all organs, excluding the brain, rise rapidly to their maximum level within the first five minutes following activity administration. Subsequently, these organs release their activity immediately after it has reached their maximum concentration in the organ. In contrast, the brain represents a considerably delayed peak of activity concentration that persisted for a significant period of time. Based on these data, the optimal time point for brain scanning would be 30 minutes post-activity administration where the activity is at its peak value. Comparing the amount of activity uptake in all four organs, the kidney showed the maximum peak, followed by the brain and heart with muscle staying at the bottom of the list. At the end of the 120-minute study period, the kidney released more than 70% of its maximum uptake, followed by the heart, which released 65% of its maximum uptake. The brain and the muscle released almost 40% of their maximum uptake by the end of the study period.

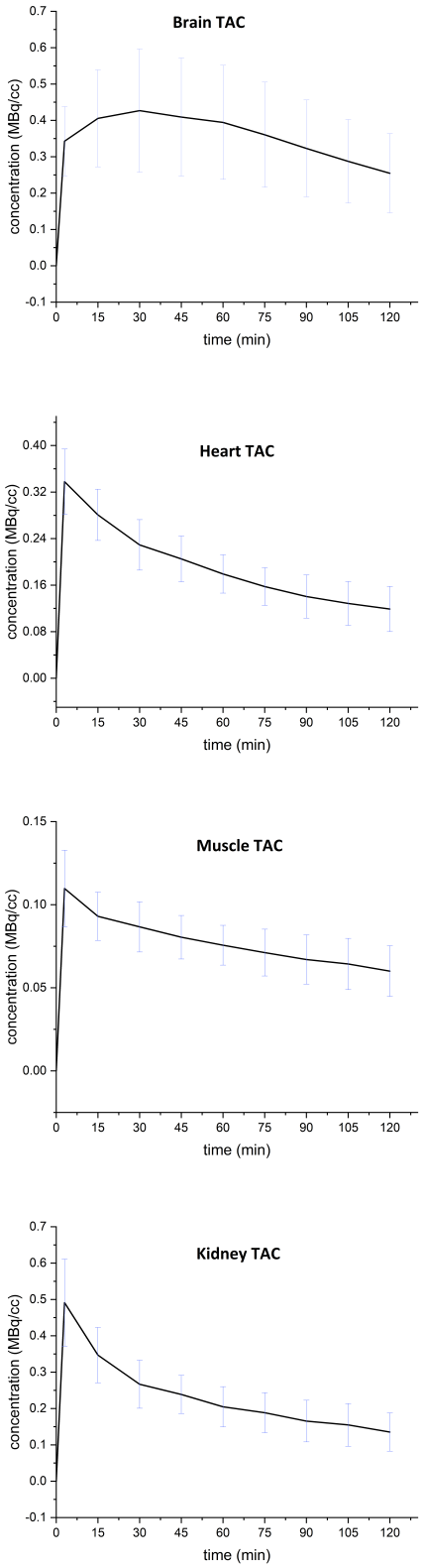

Fig. 2: TACs of the brain, heart, muscle, and kidney of mice over the 120-minute period following the injection of FDG

In Figure 3, the SUVs of all organs in an exemplary mouse are given over the study period. As it is observed, SUVs of the brain increased initially, then started to decrease. In the heart and the kidney, the SUV decreased from the first minutes of the study. The muscle showed the lowest SUVs throughout the study compared to the other organs with a slight increase over time.

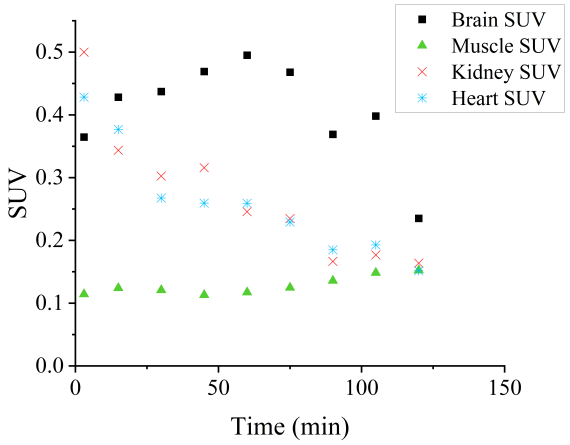

Fig. 3: SUVs of the brain, heart, muscle, and kidney of mice over the 120-minute period following the injection of FDG

4 Discussion

FDG is a widely used PET imaging tracer with a comprehensive and growing range of applications in diagnostic medicine. The study of the FDG uptake in biological organs is essential as it provides invaluable information regarding the diagnosis of diseases and assessment of the treatment process. Several studies indicate that measuring FDG uptake is valuable in distinguishing between cancerous and non-cancerous tumors, as well as in evaluating the effectiveness of cancer treatments [7, 8]. Animal models of human diseases, particularly mice, are commonly used research approaches that can help to understand disease processes and evaluate the effectiveness of potential therapies. Therefore, in the current study, we measured TACs and SUVs of FDG in four organs of mice and reported the kinetic of the radiotracer over 120-minute time following its administration.

According to our findings, after injecting the radiotracer intravenously, the tracer distribution in the body was not the same in all organs, showing the variability in the physiological uptake of the trace in the body organs. This observation is related to the fact that the consumption and washout of ra-

diotracer differ from one organ to another. The brain is the organ with the highest tendency to consume FDG, presenting a different form of the TAC compared to those of the other organs assessed in this study. This observation was consistent with previous studies on both mice and humans. For instance, a 2019 study by Sirnivasan et al. on the uptake of FDG in the heart wall, blood, brain, liver, stomach, small intestine, and kidney of humans [9] showed similar patterns as those we observed in our animal study. In both studies, the FDG slowly reached its maximum level and smoothly washed out from the brain, while in other organs the peak of the TAC appeared shortly after injection then the falling trend started immediately.

Comparing the organs' SUVs showed that the brain has a rising uptake over time. This is an expected observation as it has a high propensity to consume FDG as a source of energy. On the other side, the heart and kidney presented a decreasing trend in SUV values shortly after administration. One should bear in mind that the precision of SUVs is susceptible to various technical, biological, and physical factors, such as blood glucose level, image reconstruction technique, resolution of the image, and ROI definition accuracy [10, 11]. Therefore, making a direct comparison across similar studies may not be feasible. However, the trends of the SUVs in this study are explainable by the expected physiology of the organs studied.

In conclusion, our study of the behavior of the FDG in terms of TACs and SUVs is in good agreement with similar studies and is explainable by the physiology of the brain, heart, muscle, and kidney.

Our study, similar to other studies, has some limitations that could be addressed in future studies. The first limitation was the fairly large variation in mice weights in the current study, which led to different uptakes of FDG in similar organs of different mice imposing high SDs on the measurements. Secondly, the absence of structural information in our PET-only scans led to a significant inaccuracy in organ ROI delineation. Therefore, for future work, we propose a more comprehensive study of mice of similar sizes and weights scanned with a PET/CT or PET/MRI scanner.

Author Statement

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