Journal of Pre-Clinical and Clinical Research, 2016, Vol 10, No 1, 60-62
www.jpccr.eu

SHORT COMMUNICATION

Using PET/CT imaging performance to qualify ^{18}F-Fluorodeoxy- glucose (FDG) uptake in common carp (*Cyprinus carpio*)

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Zaheri- Abdehvand S, Csipkés R, Forgács A, Trencsényi G, Garai I, Komlósi I. Using PET/CT imaging performance to qualify ^{18}F-Fluorodeoxy-glucose (FDG) uptake in common carp (*Cyprinus carpio*). J Pre-Clin Clin Res. 2016; 10(1): 60–62. doi: 10.5604/18982395.1208191

Abstract

Introduction. Positron Emission Tomography (PET) is a non-invasive diagnostic tool that provides tomographic images and measures quantitative parameters of cell viability and metabolic activity of tissues. The most important used tracer in PET is an 18-F-Fluorodeoxy-glucose (FDG)**,** the glucose molecule of which is labeled with a radiotracer and allows measurement and mapping of tissue glucose uptake. There are many studies in PET/CT which rely on some mammalian species, and recently on fish.

Objective. The aim of this survey by using FDG-PET/CT are to optimize and determine FDG uptake in fish, in this case, common carp (*Cyprinus carpio*) using three treatments: Basic fish meal, Vita Pulvis and Probiotics s with two replications were used. Sphere Volume of interest (VOI) were drawn hand for the all organs, and standard uptake value (SUV) means were calculated.

Results. The SUV mean for glucose uptake in the liver and gastrointestinal tract of fish were more similar to those of humans than rats or mice. SUV mean in fish fed by Probiotics ss in the major organ were less than those fed by Vita Pulvis and basic fish meal. The results present the opportunity to focus on studies of metabolism and screening for the effects of nutrients on body development.

Key words

FDG PET, CT, glucose metabolism

INTRODUCTION

Fish are rapidly becoming the best models as an alternative to other vertebrate models because of their low cost and ease of culture and short term of the reproductive cycle. Since 1910, many fish species have been confirmed as animal research models [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12] and different fish species have already have been studied. Fish models provide the opportunity for a substantial increase in the scale of experimental research, compared to rodents, enabling large-scale behavioural and genetic screenings and rapid study of the effects of pharmacological and genetic perturbations during development [12], and as promising replacement animals for mammals in carcinogenesis research [13]. Positron Emission Tomography (PET) is a non-invasive diagnostic tool that provides tomographic images and measures quantitative parameters of cell viability and metabolic activity of tissues [14]. The combination of positron emission tomography (PET) and computed tomography (CT) is a new method for studying functional and metabolic assessment of tissues used in neurology, cardiology and oncology [15]. PET is capable of detecting areas of metabolic activity using radio-labelled molecular probes with specific uptake rates. To date, 2-Dioxie-2-[^{18}F]-Fluoro-D-glucose (FDG) has been one of the most clinically employed positron-emitting tracers by virtue of its utility in assessing glucose metabolism in a variety of tissues [16], while CT provides anatomic and morphologic information (size, shape, density of lesions) but provides little physiologic insight into tissues [15]. The FDG is a glucose analogue that allows measurement and mapping of tissue glucose uptake [17]. FDG, like glucose, enters the cells and is phosphorylated by hexokinase to FDG-6-phosphate, but unlike glucose, it is not further metabolized and thus remains in the cell [18, 19]. In normal tissues, FDG uptake peaks in the heart, liver and kidneys shortly after administration [20]. The retention of the tracer is calculated as SUV (standard uptake value), the most widely used unit of measurement of the metabolic rate of glucose uptake [18, 20]. SUVs provide highly reproducible parameters of cellular glucose metabolism, allowing for accurate comparison among PET studies [17]. Growth in fish is regulated by hormones, including growth hormone [21, 22], which is strongly influenced by the nutritional status of the fish [23]. It is widely accepted that nutrition has major health implications [24] and effects on growth performance in fish [25].

OBJECTIVE

Because FDG-PET/CT is a relatively new method in fish, the aims of this study were to use this technique to compare FDG uptake regarding the use of different supplementary diets

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Received: 22 September 2015; accepted: 29 April 2016

in experimental common carp (*Cyprinus carpio*), in order to determine how nutrients affect the assessment of glucose uptake, and to develop the PET/CT imaging protocol in fish.

MATERIALS AND METHODS

Common carp (*Cyprinus carpio*) were subjected to each of three treatments: Basic fish meal, Vita Pulvis and Probiotics with two replications were used. The average weights of six experimental fish were 1,240.5 ± 80.81 g with 34.95 ± 1.99 cm standard lengths. All fish were obtained from the fish culture research laboratory of the Faculty of Agricultural and Food Sciences and Environmental Management at the University of Debrecen, which is equipped with a recirculating tank system. All fish were retained in recirculation 300-L tanks at 23±2 °C Turing the natural day light period, with aeration. Water quality parameters were checked weekly with pH 8.5–9.5, nitrites and ammonia=0, Nitrates > 50 ppm. Each fish was placed in a 30-L tray and immobiliser with 20 drops of Clove Oil (Naturol, Hungary), and transported from their holding tank to the PET/CT Centre and fasted for 48 hours before imaging. Upon arrival, the fish were sedated with 10 more drops of Clove oil. During this time, the anesthesia was kept at stage III/1 (Light anesthesia), defined by total loss of muscle tone, responds to deep pressure and loss of spinal reflex [26]. A 3^7–$3{,}5^7$ Bq fixed dose of FDG was injected intravenously into the caudal vein; residual activity was also measured. There was a 40 min interval between tracer administration and PET registration. After the post-injection time the fish were scanned with combined human PET/CT (Mediso AnyScan CP, Hungary). The Fish were out of the water for 7–8 min per scan in total, and recovered by being replaced in fresh water for further experiments.

The spiral CT parameters were 120kV, 100mA and (slice thickness, 2.5mm, pitch 1). PET scans were obtained by using 3D acquisition mode, and PET data were attenuation corrected based on the CT data [13]. All obtained PET images were reconstructed using 3D OSEM reconstruction, according to the manifacturer's default protocol with time of flight compensation (3 iteration, 4 subsets) in a matrix size of 144×144 and a voxel of 4×4×4 mm. All images of PET/CT were evaluated specifically using InterView Fusion Medical Imaging Software. Shere Volume of interest (VOI) were drawn by hand for the organs (heart, liver, brain, muscle, gastrointestinal and kidney), and the mean standard uptake values (SUV) were calculated. Average SUV and standard error of the 2 measurements were also calculated. The final values were compared with the normal human, mice and rat uptake values (Reference for standard values).

RESULTS

Result of FDG-PET/CT image showed that the control fish with colour-coded areas, which reflected the FDG uptake rates, with red as the highest uptake to the lowest in yellow, green and blue (Fig. 1). VOI SUV means and standard errors of fish fed with different supplementary diets were listed according to the time point (Fig. 2), which shows the SUVs of fish as a control group in the heart, liver and brain were higher than other groups. The SUV means of the control group in kidney and muscle were slightly similar to group

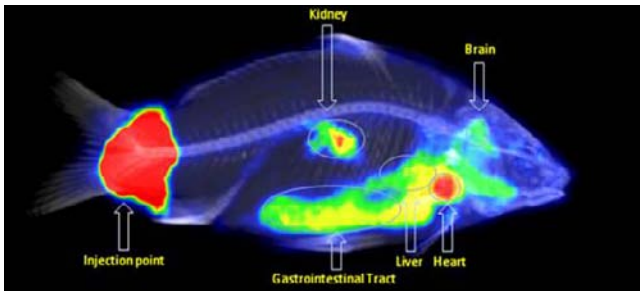

Figure 1. Demonstrative FDG-PET/CT image of a Control fish and the localization of the organs

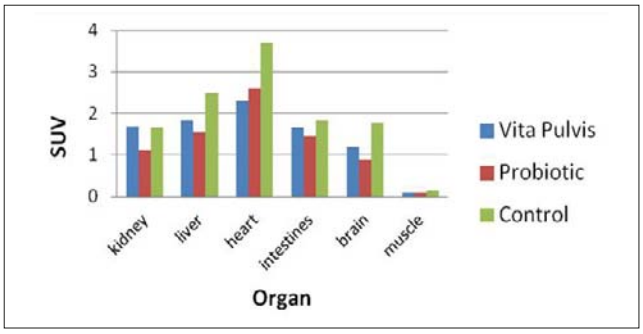

Figure 2. The comparison of the standard uptake value (SUV) mean for the following VOIs for all fish fed with different supplementary diets: heart, liver, brain, dorsal musculature, gastrointestinal and kidney

of fish fed with Vita Pulvis supplementary diets, whereas it was moderately different in fish fed with Probiotics. Fish fed with Probiotics supplementary diets showed SUVs in all organs, expect the heart, which was less than in the other groups. Comparison of the diet groups demonstrated that fish fed with basic fish meal (Control) and Vita Pulvis can have a slight effect on glucose uptake, and consequently on growth performance than fish fed with Probiotics which enhanced the digestion of feeds in the fish.

All fish were combined into a single group and compared with to human and other mammalian species, like the rat and mouse (Fig. 3). There were no differences SUV in liver, heart and gastrointestinal tract, whereas big differences in brain, muscle and kidney were found between fish and humans. In the presented study, comparison of the SUVs between fish and other mammalian species, rat and mouse, showed differences in all fish organs. In the liver, kidney and gastrointestinal tract, measurable uptakes were higher than

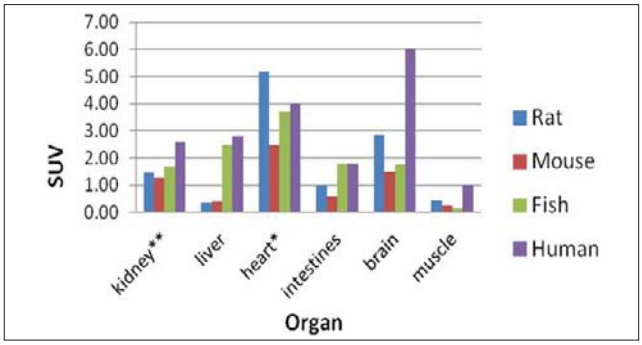

Figure 3. The comparison standard uptake values (SUV) mean of fish with human, rat and mice for the following VOIs for all fish fed with different supplementary diets: heart, liver, brain, muscle, gastrointestinal and kidney
* Human heart SUV mean, Kaneta et al. 2006
** Human Kidney SUV mean, Ye et al. 2019

those in rats and mice, while in brain, the uptakes were lower than in rats and slightly higher than in mice.

The results in the comparison of SUVs in the heart of fish, rats and mice showed that there were big differences between them, the heart SUV in fish was lower than in rats, but higher than in mice. On the other hand, these results showed that there were no differences in SUVs in muscle, while in rats these values are higher than fish and mice. In comparison, kidney SUVs results showed slight differences between fish and other mammals**.** It is Important that the pattern of FDG uptake in fish is determined and used as a reference for interpreting studies of metabolism and screening for the effects of nutrients and environmental parameters on body development. Additionally, the use of fish as an animal model for the screening of environmental carcinogen factors would be enhanced by this technology. Browning *et al.* [13], demonstrated that omnivorous and herbivorous fish are much more suitable as a model species for use with FDG-PET/CT than carnivorous Fish. Because of this evidence, the common carp (*Cyprinus carpio*) was chosen as one of the largest omnivorous fish.

DISCUSSION

The presented study proved that the use of fish offers a possible alternative model, which has more similarity to human than mammalian models with some parameters, such as cell-specific rates of glucose uptake. It also revealed that there was no significantly different organ system (brain, liver, kidney, gastrointestinal tract and muscle) when comparing FDG uptake in fish vs. humans; however, the current study basically showed big differences in some organs, such as the brain and muscles. Similar to the results obtained by Browning [13], the results for comparing human SUVs to those of mice and rats, showed high differentiation in all organs; all fish also showed unexpectedly high SUVs in the tail muscle region, which was caused by movement of the animal after injection, or failure in arterial delivery of the pharmaceuticals from the injection site. The presented study suggests the suitability of the FDG-PET/CT technique for using fish as a model animal in future studies in different aspects of biology, medicine and other sciences, as well as the efficiency of different supplementary diets on the internal organs and their activity during the growing time of fish.

Acknowledgements

The authors wish to thank Éva Csorvási for providing the experimental fish and We also sincerely acknowledge the field staffs of PET-CT Centre at the Department of Nuclear Medicine of the Medical and Health Centre at Debrecen University.

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