Dynamic PET Imaging of Whole Body Glucose Distribution after Oral Administration of [18F]-fluoro-deoxy-glucose

IV. 1. Dynamic PET Imaging of Whole Body Glucose Distribution after Oral Administration of [^{18}F]-fluoro-deoxy-glucose

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Introduction

[^{18}F]-labeled-2-deoxy-2-fluoro-D-glucose (FDG) is a positron-emitting analogue of glucose and has been used for investigating pathophysiology of the brain, heart and other organs in vivo in human. So far, its usage has been confined to through the intravenous route only as it was thought that its structural complexity might pose some prohibition to intestinal absorption. Uptake of sugar from intestinal lumen is an active process, which requires sodium dependent glucose transporter, SGLUT1. However, the SGLUT1 has been known to be specific for the structure of pyranose ring with hydroxy group at the second position[1]. FDG is hardly to be a substrate for this enzyme because it has fluorine at this position. Therefore intestinal uptake of FDG seemed quite unlikely. However, Martinez et al first tried the oral FDG administration as an alternative method for brain imaging[2]. Their study suggested the possibility of FDG absorption from the small intestine. The intestinal absorption is often matter of interest in clinical situations such as malabsorption syndromes and extensive intestinal surgery. Practical PET tracer is necessary to quantitative glucose uptake from the intestine. Recent advance in PET technology has promoted whole body imaging using sequential movement of PET coach. We attempted to image dynamic change of whole body FDG distribution after its oral administration. The process of alimentary uptake and transfer of glucose from blood to tissue has been successfully visualized.

Method and Materials

Six normal volunteers (mean age 28.6 years) were studied with a multi-ring tomography, SET-2400 (Shimadzu, Japan) in three-dimensional data acquisition mode. Dynamic whole-body imaging was performed every 2 minutes from pelvis to head after oral intake of ^{18}FDG (37 MBq). The image acquisition continued up to 90 minutes and image analysis was performed. The analysis was to calculate the tracer accumulation changes in each organ to the total FDG intake doses (fraction % of intake dose, %ID) and to try the mono exponential fittings to evaluate the mean passage time (T1/2) after setting the ROI in the

organs.

Result

Figure 1 shows the time-related changes in whole body ^{18}FDG distribution. ^{18}FDG passed through the stomach and disappeared from the alimentary tract. Following FDG accumulation was observed to the liver and the brain. Figure 2 shows the time-related %ID changes for the stomach, the small intestine, liver and the brain. The T1/2 for the stomach and for the small intestine were 18.3 (+/-4.0) and 59.3 (+/- 4.8) minutes respectively. The accumulation to the brain was observed after 30 min of oral intake and showed a gradual increase up to the end of measurement.

Discussion

Three subtypes of glucose transporter has been reported which contribute the sugar absorption from the small intestine i.e. SGLT1, GLUT2 and GLUT5[3]. The SGLUT1 and GLUT5 locate at the luminal side and the GLUT2 locates at the visceral side of intestinal epithelium. This specific location of glucose transport system is observed in both small intestine and kidney for glucose absorption or reabsorption. SGLT1 plays an active role for the glucose absorption from the small intestinal lumen to the epithelium. It is specific for the structure of pyranose ring with hydroxy radical at the second-position[4]. FDG dose not match the aforementioned structure as it has fluorine at the second position (deoxy-glucose). GLUT5 is specific for the lactate absorption and no significant affinity to the deoxyglucose[5,6]. GLUT2 has an affinity to FDG, however locates at the visceral side of the epithelium and transform from the epithelium to the portal vein[7,8].

So FDG cannot be assimilated from the lumen to the blood following the previous established mechanism. However, Our image has clearly shown the absorption of FDG and its distribution to the various organs, even to the brain. There are two possibilities to explain our images. The one possibility is the SGLUT1's structural requirement to glucose analogue is not so strict in human. The affinity of SGLUT1 to the 2-deoxy glucose has varied according to the animal spices[1], then that to the FDG might be varied. The other possibility is some alternative carrier of FDG absorption. Halaihel et al has reported the heterogeneity of glucose transport system in pig intestine[9]. We also assume that similar heterogeneity of glucose absorption system not only existing the pig but also human. Substantially, this recent heterogeneity mode of glucose transport not only clarifies our imaging finding but also advocate its usage through oral ingestion in various scanning protocol with PET. We did not analyze the plasma to identify the radioactive component is FDG. A possible explanation of FDG uptake from intestine is its metabolism by intestinal bacteria. Free 18F-fluorine, when released from FDG, may enter into circulation. However, fluorine ions are known to accumulate in the bones strongly and do not cross the blood-brain

barrier, which was not our case.

Even Though the FDG absorption mechanism is still not clear, most possible FDG absorption will be the same mechanism of glucose absorption. FDG has the steady Km value for the glucose transporter, and then the quantitative visualization of FDG using PET will be quite useful to evaluate the glucose absorption ability in case of the malabsorption syndrome and the extensive intestinal surgery. Our procedure also can be used to evaluate the natural glucose absorption related to the other organs.

References

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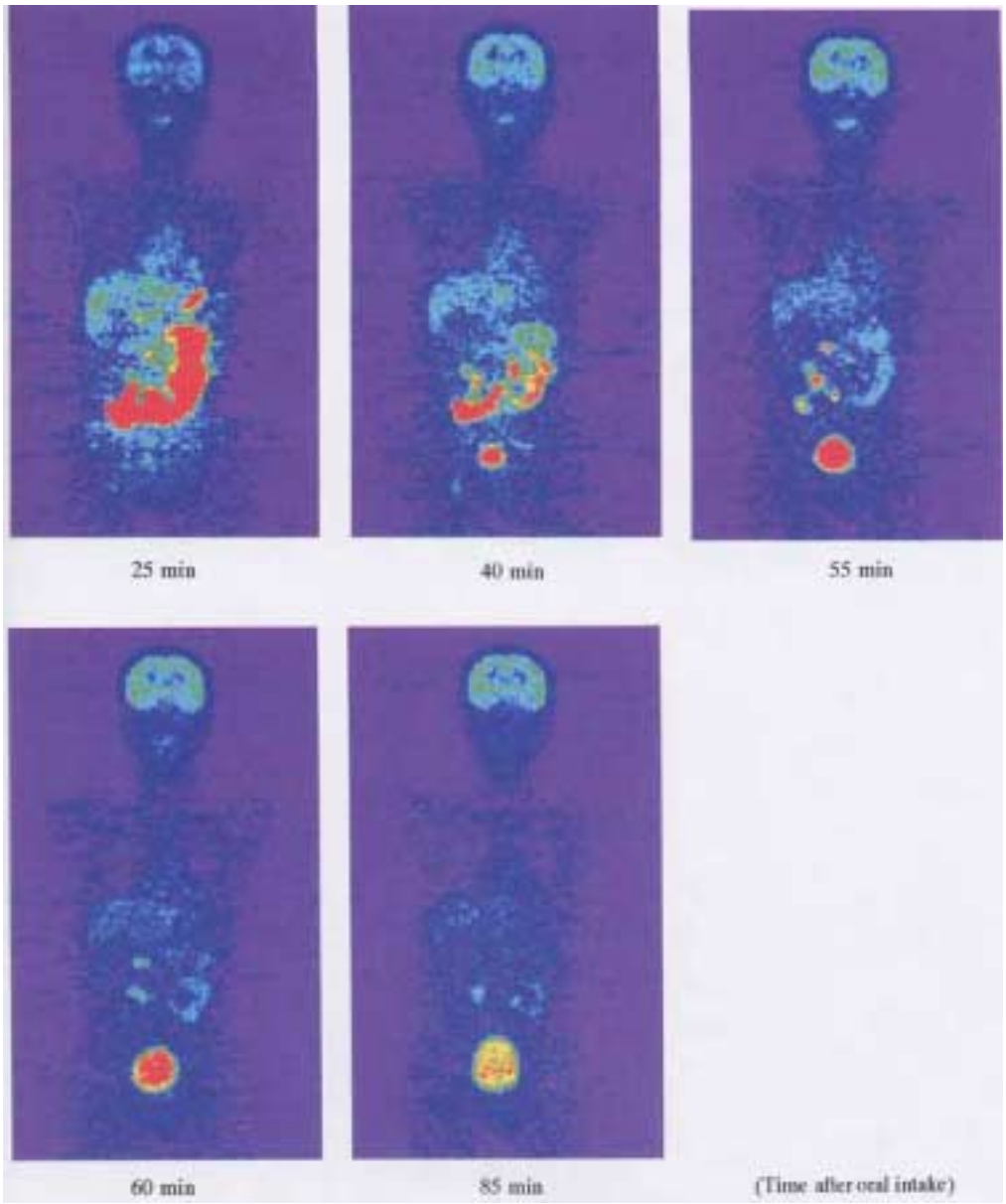

Figure 1. Time course whole body image of oral intake FDG. The whole body image was obtained every 15min. FDG elimination from the abdomen and gradual accumulation to the brain is clearly observed.

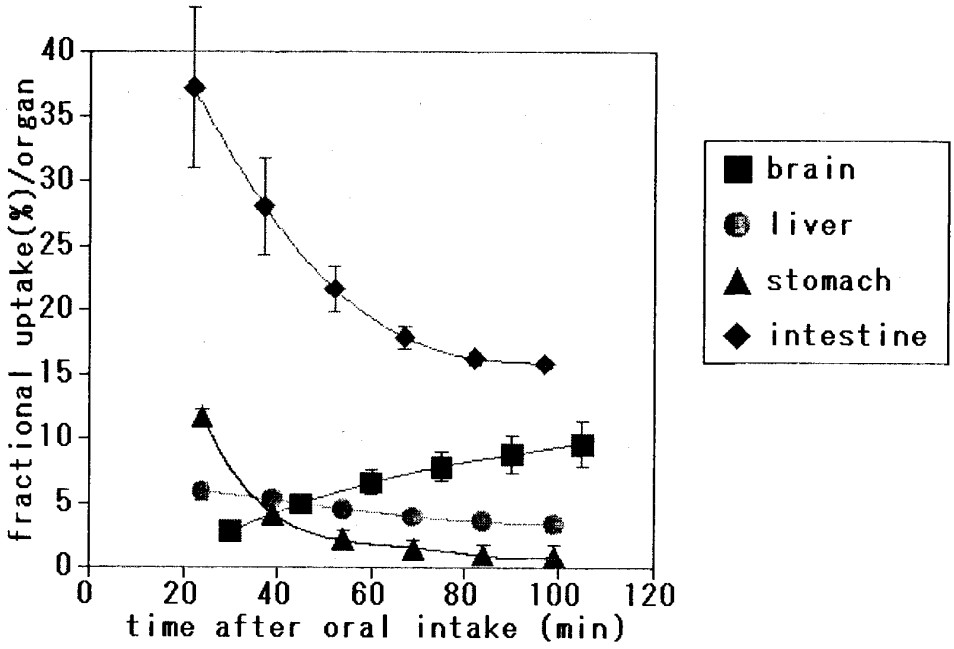

Figure 2. Time activity curve in every organ. The transverse axis shows time after oral intake and the vertical axis shows the fractional uptake. The stomach and intestinal activity decrease rapidly. The brain activity increases gradually.