

Comparative Study on Tumor Accumulation of 18F-Labeled Deoxy-Aldohexoses

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Introduction

Increased glycolysis is one of the most important characteristics of the cancer cells. Therefore, positron labeled sugars are thought to be good tracers for cancer detection. We reported that (F-18)-2-deoxy-2-fluoro-D-glucose (^{18}F -FDG) and (F-18)-2-deoxy-2-fluoro-D-mannose (^{18}F -FDM) were excellent cancer diagnostic agent.¹⁾ In this study, we have newly synthesized a series of (F-18)-deoxy-aldohexoses and compared the degree of tumor accumulation in the transplanted hepatoma bearing rats.

Materials and Methods

(F-18)-deoxy-aldohexoses were synthesized by the analogous method to ^{18}F -FDG synthesis. Details will be described in other paper.²⁾ The radiopharmaceuticals, which were tested in this study, were (F-18)-2-deoxy-2-fluoro-D-glucose (^{18}F -FDG), (F-18)-2-deoxy-2-fluoro-D-mannose (^{18}F -FDM), (F-18)-2-deoxy-2-fluoro-D-galactose (^{18}F -FDGal), (F-18)-2-deoxy-2-fluoro-D-altrose (^{18}F -FDA), and (F-18)-2-deoxy-2-fluoro-L-glucose (L- ^{18}F -FDG). The chemical structures of these compounds were shown in Fig. 1.

Male Donryu rats (weighing 140-160 g) were used for tissue distribution study. Transplantable hepatoma cells (AH109A), which were maintained through ascitic path, were subcutaneously injected into rats and were grown. When tumor size reached 1 cm in diameter, the experiments were made. Ten microcuries of each compound was intravenously injected into rats through lateral tail vein. The rats were killed by neck dislocation at 10, 30, 60, and 120 min after injection. The organs and tumor were removed, blotted, weighed and the radioactivities were counted by NaI well scintillation counter. Tumor and tissue uptakes were expressed as % injected dose/g of tissue.

Results and Discussion

Figure 2 was a tissue distribution curve of ^{18}F -FDG in AH109A bearing rats. Each point was a mean of 6-7 animals. The tumor uptake of ^{18}F -FDG was very high, formed a nearly plateau after 30 min and followed by gradual increase up

to 120 min. On the other hand, uptakes of liver, kidney, and pancreas were relatively lower than that of tumor and followed by rapid wash out of the radioactivity, in spite of high glucose metabolism in these organs. Blood clearance was also very rapid.

Figure 3 showed distribution of ^{18}F -FDM. The tumor uptake of ^{18}F -FDM was as high as that of ^{18}F -FDG. The distribution pattern of organs were nearly the same as that of ^{18}F -FDG, although the uptakes in brain and small intestine were lower than ^{18}F -FDG.

Figure 4 showed the distribution of ^{18}F -FDGal. The uptakes pattern of ^{18}F -FDGal was very different from the first two agents. The liver uptake was very high, peaking at 30 min (10% dose/g) and maintained same level of activity up to 120 min. The uptake pattern of other organs were essentially the same as that of the liver, although the peak uptake levels were extremely lower than that of the liver. This showed that ^{18}F -FDG was trapped and maintained in each organ and tumor. However, the tumor uptake was low, giving 0.7% dose/g at 60 min.

Figure 5 showed the distribution of ^{18}F -FDA. The agent was rapidly cleared away from all organs containing tumor tissue.

Figure 6 showed the distribution of L- ^{18}F -FDG. The agent was rapidly excreted from kidney and all the other tissues. The tumor uptake was very low.

Table 1 showed the tumor uptakes at 60 min and tumor-to-normal tissue ratios. Tumor uptakes of ^{18}F -FDG and ^{18}F -FDM were very high (2.65% dose/g) and tumor-to-liver, kidney, and blood ratios were also high. Thus, these two agents were thought to be good tracers for cancer detection, especially for the detection of cancers located in abdomen. On the other hand, other agents were not available for cancer detection, although ^{18}F -FDGal could be used for liver imaging.³⁾

Conclusion

(1) ^{18}F -FDG and ^{18}F -FDM were the best agent for cancer detection among ^{18}F -deoxy aldohexoses which we tested. (2) Not only normal tissue but also tumor tissue did not utilize ^{18}F -FDA and L- ^{18}F -FDG, which were deoxy form of non physiological sugars.

References

- 1) Fukuda H. et al., Eur. J. Nucl. Med. 7 (1982) 294.
- 2) Tada et al., (in preparation).
- 3) Fukuda H. et al., CYRIC Annual Report (1982).

Table 1. Tumor uptake and tumor-to-tissue ratios of ^{18}F -deoxy aldohexoses

Radiopharmaceuticals	Tumor uptake (% dose/g)	Tumor/Liver	Tumor/Blood
^{18}F -FDG	2.65 ± 0.61	18.9	22.1
^{18}F -FDM	2.65 ± 0.81	9.14	29.4
^{18}F -FDGal	0.70 ± 0.10	0.09	4.37
^{18}F -FDA	0.50 ± 0.08	0.99	1.43
L- ^{18}F -FDG	0.27 ± 0.07	1.07	1.00

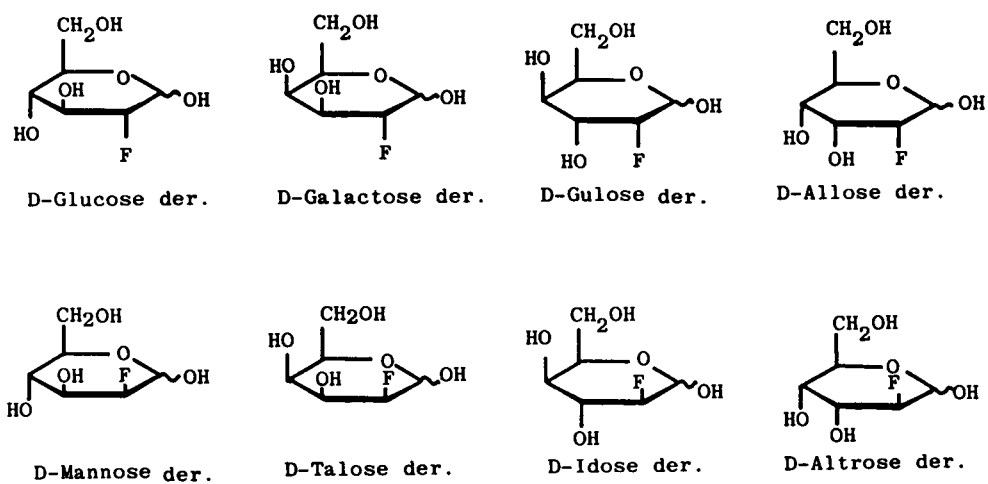


Fig. 1. Fluorinated 2-deoxy aldohexoses

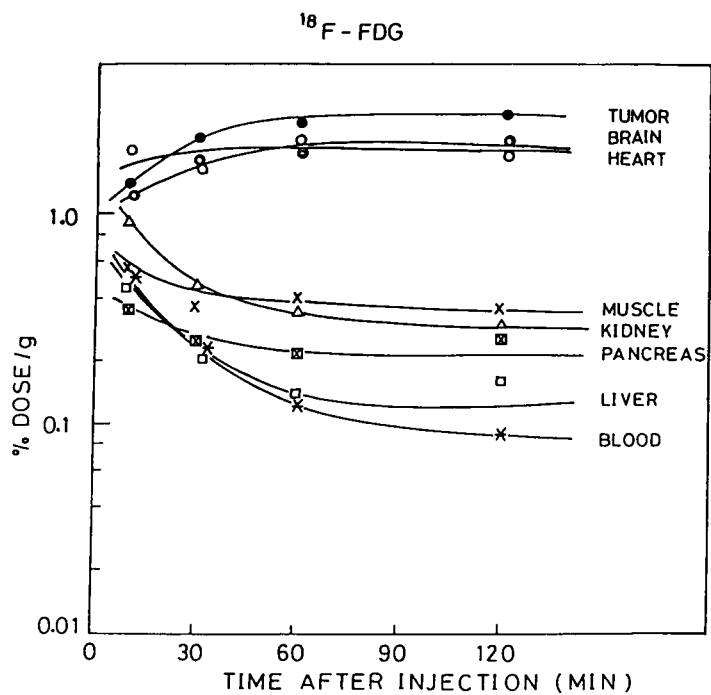


Fig. 2. Tissue distribution curve of ^{18}F -FDG in hepatoma (AH109A) bearing rats

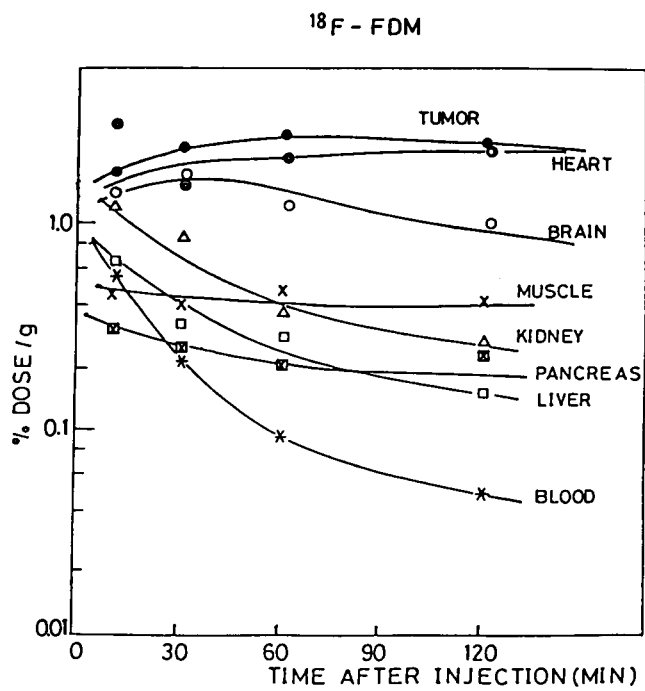


Fig. 3. Tissue distribution curve of ^{18}F -FDM in hepatoma (AH109A) bearing rats

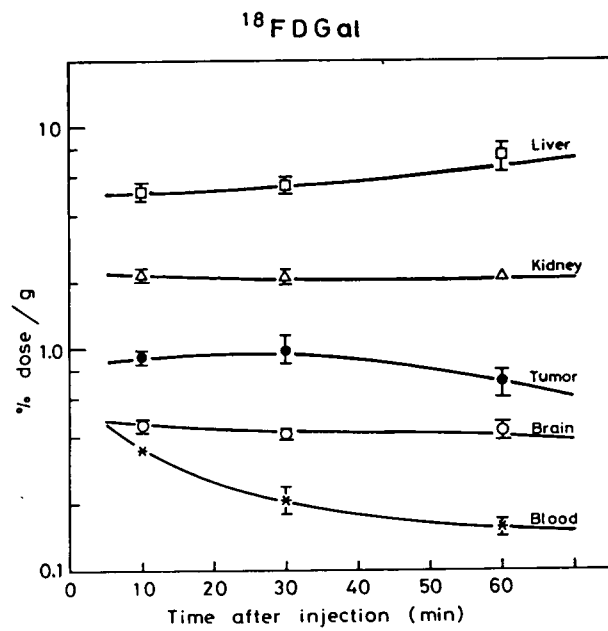


Fig. 4. Tissue distribution curve of $^{18}\text{F-FDGal}$ in hepatoma (AH109A) bearing rats

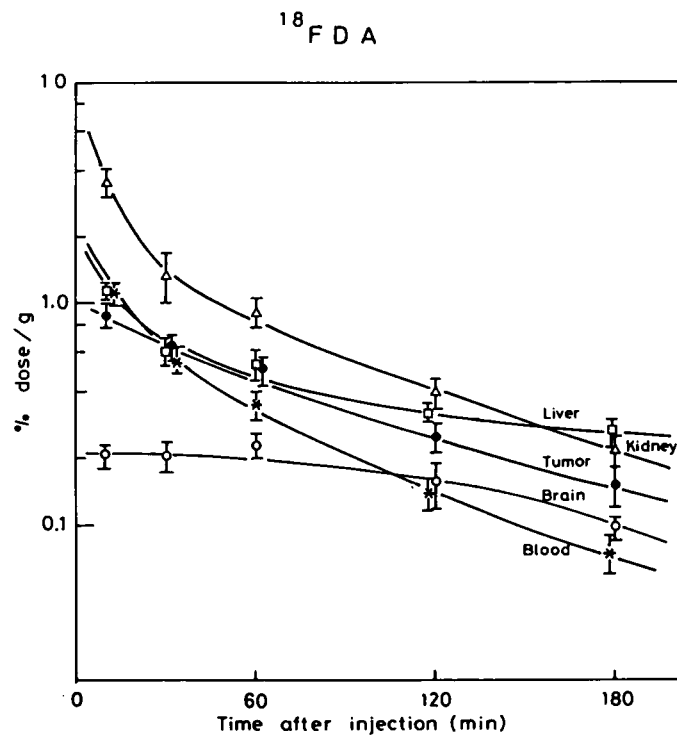


Fig. 5. Tissue distribution curve of $^{18}\text{F-FDA}$ in hepatoma (AH109A) bearing rats

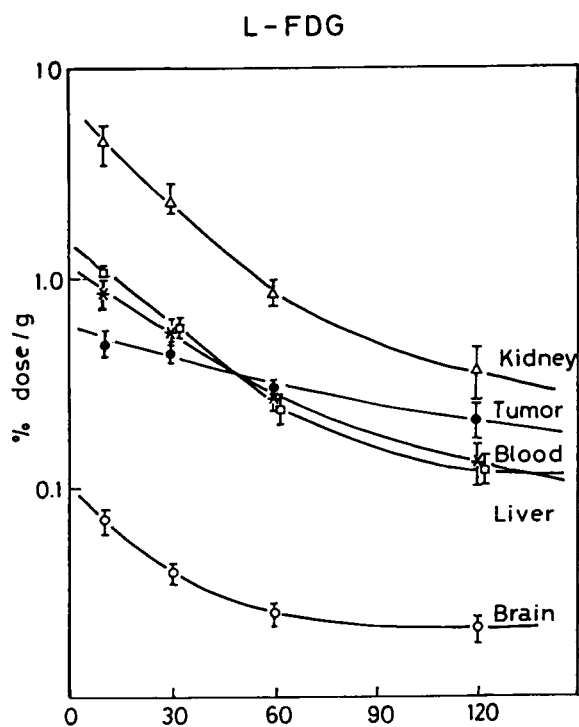


Fig. 6. Tissue distribution curve of L-¹⁸F-FDG in hepatoma (AH109A) bearing rats