The Clinical Application of 18F-Fluoro-2'-Deoxyuridine to the Brain Tumor Patients

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In the previous issues of this report[1,2], we reported the possible usefulness of ^{18}F-fluoro-2'-deoxyuridine (^{18}FdUrd) as a brain tumor detecting agent for positron emission computed tomography from the view points of nucleic acid metabolism through the basic experiment using a rat brain tumor model. In this paper, the clinical application of ^{18}FdUrd to brain tumor patients are presented.

Materials and Method

Six brain tumor patients were studied; 3 were female and 3 were male, and the mean age was 33 years, ranging 15-45 years. The histological diagnosis were made based on the materials from autopsy, operation or stereotaxic biopsy; those were 2 glioblastoma multiforme, 1 embryonal cell carcinoma, 2 astrocytoma Grade II and 1 unknown. The last unknown case was strongly suspected of malignant glioma judged from X-ray CT and the clinical course.

4-8 mCi of ^{18}FdUrd was injected intravenously in each patients and a serial scannings were done every five minutes until 40 to 50 minutes. Then the additional one or two separate scannings were made. The images of PECT were obtained by ECAT II and differential absorption ratio (DAR) was calculated later.

Results

In three cases of malignant glioma and one unknown case, the clear images of brain tumor were visualized with high contrast on PECT (Fig. 1). DAR of the brain tumors were about 3-4 times as high as that of homolateral brain tissue in all 4 cases. In contrast, the positive images of brain tumor were not obtained in two cases of benign glioma and DAR in the tumor was similar to that of homolateral brain tissue (Fig. 3).

Discussion

Undoubtedly three-dimensional in vivo representation of nucleic acid

metabolism will give us an important information to manage the yet unbeatable foe for mankind – malignant neoplasms. ^{11}C-thymidine is a precursor of DNA synthesis and is natural to be expected as a good tracer of nucleic acid metabolism. However, the complicated and poorly efficient biosynthetic method makes the routine clinical use difficult of ^{11}C-thymidine.[3)]

On the other hand, fluorinated pyrimidines are known also to reflect the nucleic acid metabolism.[4)] Among the many ^{18}F-radiopharmaceuticals for neoplasms, we paid special attention to ^{18}FdUrd, since the tumor uptake of ^{18}FdUrd is higher than that of ^{18}F-5-fluorouracil or ^{18}F-fluorouridine.[5)] In our previous study, only the brain tumor image was turned up on autoradiography (ARG) by using ^{18}FdUrd, and the tissue sampling analysis revealed that the uptake of ^{18}FdUrd in the experimental brain tumor was about ten times higher than that of contralateral normal cortex.[1)] Also the multiple labeled autoradiographic investigation[6)] showed that the tumor image of ^{18}FdUrd was clearly different from that of 2-amino-1-^{14}C-isobutyric acid which manifests blood brain barrier impairment, but was rather similar to that of 2-^{14}C-thymidine.[2)] These results suggested that the accumulation of ^{18}FdUrd was thought to indicate mainly nucleic acid metabolism of the brain tumor and partly BBB dysfunction probably.

On the basis of the above mentioned basic investigation, the clinical application of ^{18}FdUrd was tried to human glioma patients using PECT. As a result, the ^{18}FdUrd brain tumor images were clearly distinct in four cases of maligant brain tumor, however, positive image of the tumor was not obtained in the two cases of benign glioma. In addition, DAR pattern showed distinct difference between benign and malignant gliomas; the latter was 3-4 times higher than the contralateral brain tissue, while the former remained indistinguishable from the normal brain tissue.

These results obtained through the clinical study of ^{18}FdUrd clearly demonstrate the useful characteristic of this new tracer to differentiate maligant gliomas from benign ones, although the number of patients was not many. Further study has to be performed including the evaluation of BBB impairment which may affects the accumulating pattern of ^{18}FdUrd, however, ^{18}FdUrd will be an interesting positron-emitting tracer for approaching brain tumor from the view points of nucleic acid metabolism.

Acknowledgement

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References

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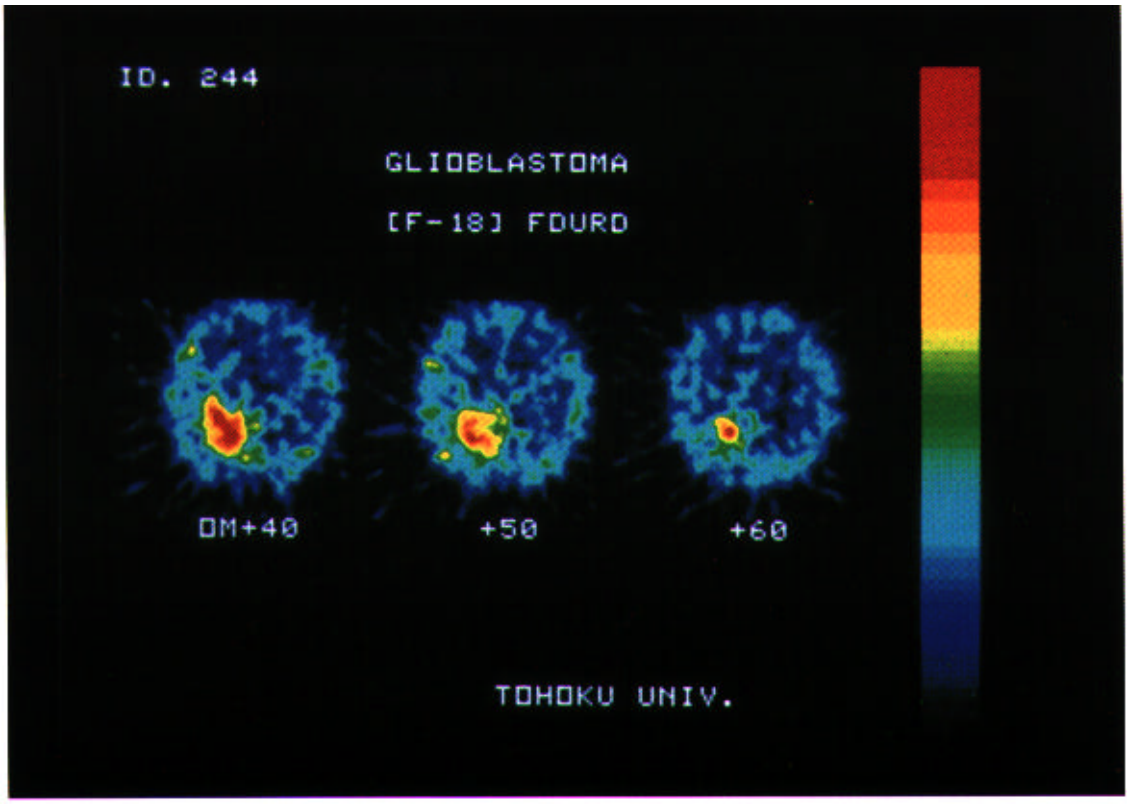

Fig. 1. A case of glioblastoma multiforme in left parietal region. Only the tumor image was visible on PECT using ^{18}FdUrd.

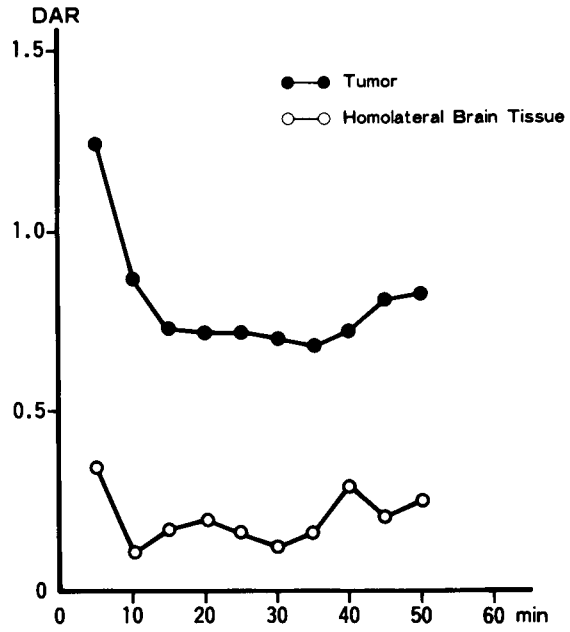

Fig. 2. DAR of ^{18}FdUrd in a case of malignant glioma. DAR in the tumor was about 3 times higher than that of homolateral brain tissue in every 5 minutes.

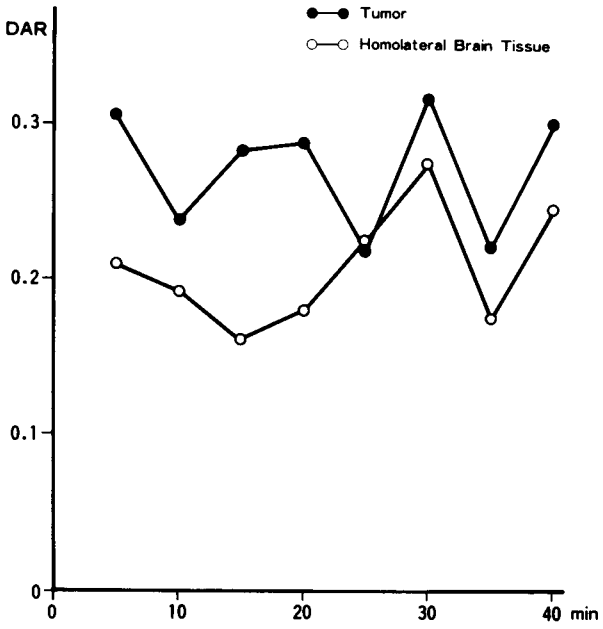

Fig. 3. DAR of ^{18}FdUrd in a case of benign glioma. DAR in the tumor did not show remarkable difference througout the study.