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III. 8 An Experimental Study for Diagnosis of Orbital Tumor by Positron CT using  $^{18}\text{F}$  Fluorodeoxyuridine in Animal Studies

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Introduction

Most common and frequent orbital disease, orbital malignant tumor and inflammatory pseudotumor could not to be differentiated each other only by means of routine examinations, and pathological examinations were most helpful. However, it is most desirable to have a possible diagnosis of these lesions prior to either biopsy or surgery. We have reported possibility of differential diagnosis between them using positron CT imaging with  $^{18}\text{F}$  Fluorodeoxyglucose as a tracer<sup>1,2)</sup> in experimental orbital affection. One of  $^{18}\text{F}$  labeled pyrimidines,  $^{18}\text{F}$ -5-Fluoro-2'-deoxyuridine ( $^{18}\text{F}$ -FdUrd) was also reported to be a suitable tracer for detecting tumors in the brain by positron CT.<sup>3,4)</sup> We studied  $^{18}\text{F}$ -FdUrd uptakes in the tumors and aseptic inflammation in rats. We also tried to differentiate malignant tumors from experimental aseptic inflammation in rabbit orbit by positron CT with  $^{18}\text{F}$ -FdUrd.

Materials and Methods

Radiopharmaceuticals:  $^{18}\text{F}$ -FdUrd were synthesized by the methods reported by Ishiwata et al.<sup>5)</sup> with high radiochemical purity of over 96%.

Tissue distribution study: Sixteen Donryu rats with mean weight of 150g were used. AH109A ascitic hepatoma cells were inoculated subcutaneously on the right side of the back in each rat. Seven days after the inoculation, croton oil was injected subcutaneously on the other side of the back in each rat to induce an aseptic inflammatory lesion. Three days after the croton oil injection the experiment was performed. The rats were killed at 10, 30, 60, and 120 minutes after the intravenous injection of  $^{18}\text{F}$ -FdUrd. Tissues were obtained, weighted, and radioactivities were measured. The uptakes were expressed as % dose/g.

Positron CT radioautogram study: Experimental papillary adenocarcinoma VX-2 were transplanted to three rabbits. Tumor cells were injected into the retrobulbar space of two rabbits as reported previously.<sup>1,2)</sup> A tumor mass with 0.5×0.5×0.5mm in size was inoculated into the subchoroidal space in eye ball of a rabbit.<sup>6)</sup> Rabbits with orbital or intraocular tumors (20×20×20mm) were used.

Aseptic inflammation in the orbit was induced by retrobulbar injection of 0.1 ml croton oil. Positron CT and radioautogram study were done on the 4th day of the treatment, when the rabbit showed prominent exophthalmos. All rabbits were anesthetized with pentobarbital and settled on the positron CT bed for examination. A transmission scan was performed with  $^{68}\text{Ge}/^{68}\text{Ga}$  ring source. Immediately after the injection of 4-9mCi  $^{18}\text{F}$ -FdUrd, emission scans were performed. Each data sampling time was set 300 seconds. Immediately after the ECAT scan, that was 60 minutes after  $^{18}\text{F}$ -FdUrd injection, the rabbit with intraocular tumor-bearing rabbit was killed and decapitated. The head was frozen and section 40 micrometer in thickness were made. X-ray films contacted with the sections were exposed for 24 hours in  $-30^{\circ}\text{C}$  and developed.

#### Results and Discussion

Distribution of  $^{18}\text{F}$ -FdUrd radioactivity in tissues of rats bearing AH109A tumor and inflammation is indicated in Fig. 1. Liver, AH109A tumor and bone showed the highest uptake of  $^{18}\text{F}$ -FdUrd: Radioactivity of the tumor is approximately 2 times higher than that of inflammation during the course of the examination. The brain and lacrimal gland showed very low radioactivity.

Fig. 2 shows positron CT scan images of a rabbit with intraocular tumors. Fig. 3 shows the histopathological picture and radioautogram of the same tumor shown in Fig. 2. The  $^{18}\text{F}$ -FdUrd in the tumors in both eyes and the cranial bone showed high radioactivity. The highest uptake of  $^{18}\text{F}$ -FdUrd in the bone is due to accumulation of free  $^{18}\text{F}$  anion.<sup>3,5)</sup>

Fig. 4 is the positron-CT images of the rabbit head with aseptic inflammation in the orbit. Orbital inflammation and normal orbit are indicated by a single arrow and double arrow respectively. There is slight differences between them.

In conclusion,  $^{18}\text{F}$ -FdUrd would be a useful tracer to differentiate malignant tumors from inflammatory pseudotumors in humans by positron CT.

#### References

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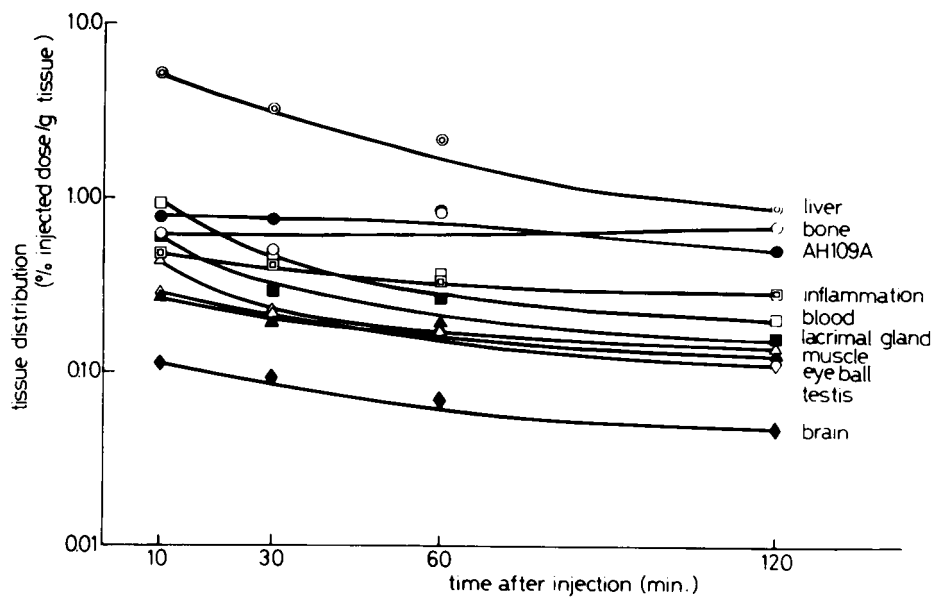


Fig. 1. Tissue distribution of  $^{18}\text{F}$ -FdUrd in AH109A and inflammation-bearing rat. Uptakes are expressed as the % dose / g tissue.

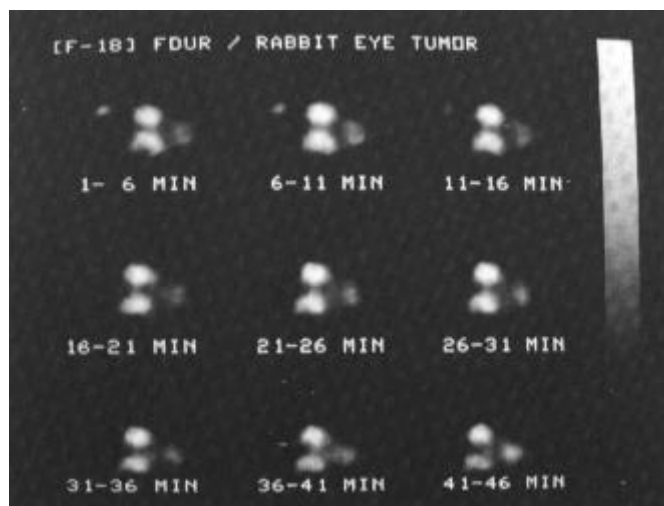


Fig. 2. Positron CT images of a rabbit with intraocular tumors.

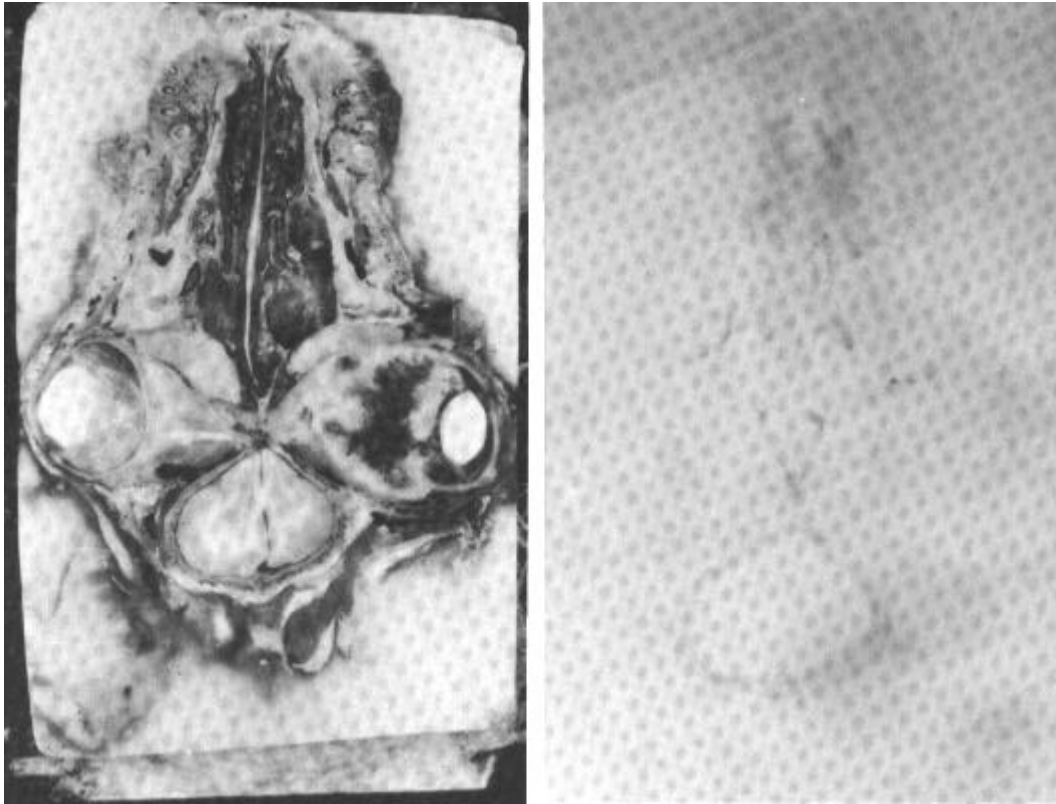


Fig. 3. Photogram and autoradiogram of the identical section of tumor-bearing rabbit shown in Fig. 2.

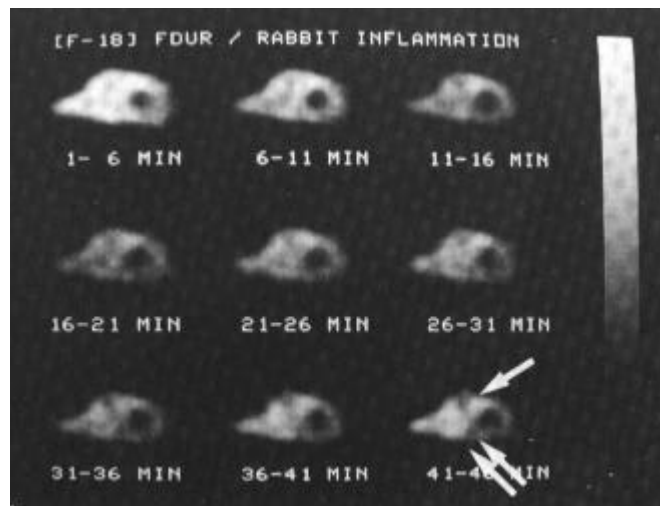


Fig. 4. Positron CT images of a rabbit with aseptic inflammation in the orbit.