Improved Treatment of Malignant Glioma with Clinical Use of a Newly Developed PET Molecular Imaging Probe [methyl-11c]-4`-thiothimidine (4DST) to Measure DNA Synthesis Rate

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Introduction

PET molecular imaging is now known as an inevitable clinical tool for the treatment of malignant brain tumors. PET amino acid probes such as 11C-methionine (MET) are considered as one of most appropriate probes for clinical use. MET-PET, however, is not almighty and has several cautious points. It may over-estimates tumor malignancy in oligodendroglioma, because of the influence of vascular bed. It may not clearly differentiate low grade tumor and inflammatory disease. Recently we developed [methyl-11C]4`-thiothimidine (4DST) as a radiotracer for DNA synthesis. We evaluated the utility of 4DST-PET in comparison to MET-PET.

Methods

56 patients were enrolled in this study; 48 patients with glioma, 5 metastatic brain tumor, 1 malignant lymphoma, mutiple sclerosis, and craniopharyngioma. All subjects underwent 4DST and MET-PET within a week. Regional uptake of tracers in static condition (40-60 min and 20-25 min after injection for 4DST and MET, respectively) was expressed as tumor/normal ratio for MET, and SUV in 4DST-PET.

Results

1) 4DST-PET images were almost identical to MET-PET images in astrocytic tumors before treatments (figure1). This result suggested the validity of 4DST-PET in preoperative diagnosis of astrocytic tumors. Threshold of malignancy is 1.0 (SUV) in 4DST-PET images.
2) 4DST-PET could distinguish between oligodendroglioma and anaplastic oligodendroglioma clearly. Furthermore, 4DST uptake was far less than 1.0 (SUV) in a case of multiple sclerosis. These results suggested that 4DST-PET image showed cell proliferation precisely and could complement the area that cannot be clarified with MET-PET(Figure 2).
3) 4DST was uptook in to malignant glioma even without BBB disruption. This fact suggeted that this probe can cross intact BBB through nucleoside transpiorter on vessel wall and cell wall (figure 3).
4) The effectiveness of radiation or chemotherapy was clearly demonstrated by the decreased uptake of 4DST, instantly after the treatment (Figure 4).

Figure 1

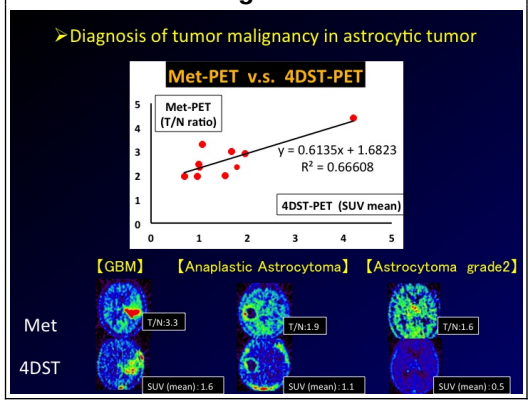


Figure 2

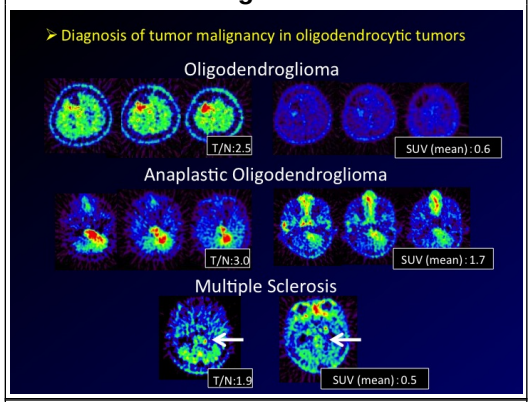


Figure 3

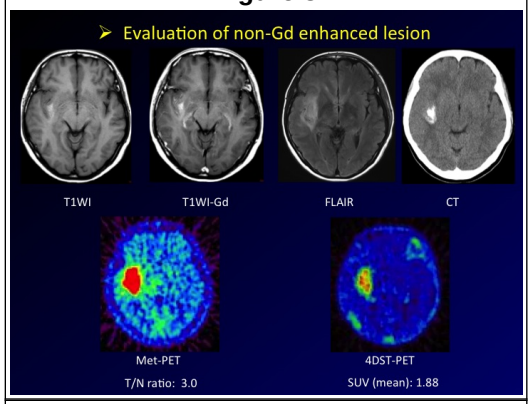
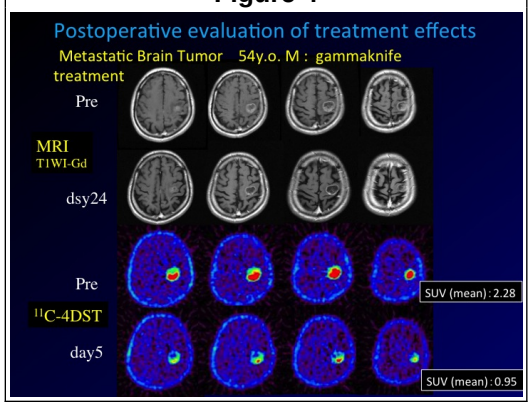


Figure 4



Conclusions

The utility and validity of 4DST-PET were demonstrated in our initial clinical trial for malignant brain tumors. As 4DST-PET may reflect cell proliferation rates more clearly than MET-PET, it has great potential as a PET molecular imaging probe for the management of malignant brain tumors.

Learning Objectives

to learn how a newly developed molecular imaging contribute to the treatment of malignant glioma.

References

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