Evaluation of

4-Borono-2-[18F]Fluoro-L-Phenylalanine-Fructose as a Probe for BNCT in Glioma-Bearing Rat Model.

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Abstract

L-p-Boronophenylalanine (BPA) has been applied as a potential boron carrier for the treatment of malignant glioma in clinical boron neutron capture therapy (BNCT) since 1994. To provide the pharmacokinetics of BPA for clinical use of BNCT in Taiwan,4-borono-2-(18)F-fluoro-L-phenylalanine-fructose ((18)F-FBPA-Fr) was synthesized and the biologic characteristics of this radiotracer in glioma-bearing rats were investigated. METHODS: Radiolabeled (18)F-F(2) was produced via the (20)Ne(d,alpha)(18)Freaction, and (18)F-acetyl hypofluorite ((18)F-AcOF) was generated by passing (18)F-F(2) through a column filled with tightly packed KOAc/HOAc powder. The effluent containing (18)F-AcOF was bubbled into BPA in trifluoroacetic acid, then purified byhigh-performance liquid chromatography, and further composited with fructose to afford (18)F-FBPA-Fr. Male Fischer 344 rats bearing F98 glioma in the left brain were used for biologic studies. The biodistribution of BPA-Fr and (18)F-FBPA-Fr was determined, and the microautoradiography and PET imaging of (18)F-FBPA-Fr were performed, on the 13th day after tumor inoculation. RESULTS: The radiochemical purity of (18)F-FBPA-Fr was >97% and the radiochemical yield of (18)F-FBPA-Fr was 20%-25%. In glioma-bearing rats, the accumulation ratios of B-10 for glioma-to-normal brain were 2.05, 1.86, 1.24, and 1.10 at 0.5, 1, 2, and 4 h, respectively, after administration of 43 mg BPA-Fr via the tail vein. The accumulation ratios of (18)F-FBPA-Fr for glioma-to-normal brain were 3.45, 3.13, 2.61, and 2.02, whereas the tumor-to-heart blood ratios were 1.72, 2.61, 2.00, and 1.93, respectively, for the same time points. The uptake characteristics of BPA-Fr and (18)F-FBPA-Fr in F98 glioma were similar with a maximum at 1 h after the drugs' administration. The results obtained from the biodistribution studies indicated that 0.5-1 h after BPA-Fr injection would be the optimal time for BNCT. Biodistribution, PET images, and brain microautoradiography of (18)F-FBPA-Fr all confirmed this finding. CONCLUSION: (18)F-FBPA-Fr showed specific tumor uptake in F98 glioma-bearing rats and could be used as a probe for BPA-Fr in BNCT. This

study provides useful information for the future clinical applicationof BNCT in brain tumor therapy.