HATAZAWA-1: Study of 4-borono-2-[^{18}F]-fluoro-phenylalanine PET to estimate ^{10}B concentration in tumors and normal organs in Boron Neutron Capture Therapy

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In boron neutron capture therapy (BNCT) for intractable cancer, the accurate estimation of ^{10}B tissue concentrations is important to predict effectiveness and to avoid adverse effects. The ^{10}B concentration in tumors and normal organs after loading with ^{10}B, however, has not been established in humans. [^{10}B]borono-phenylalanine (BPA) is one of the ^{10}B carrier to tumors in BNCT. 4-borono- 2-[^{18}F]-fluoro-phenylalanine (FBPA) is a PET agent to trace pharmacokinetics of BPA (Hanaoka K, et al., 2014). FBPA and BPA are transported into cells by L-type amino acid transporter 1 (LAT1) which is predominantly expressed on cancer cell membrane (Watabe T, et al., 2018). In this study, we performed FBPA PET in healthy volunteers and patients with brain tumors and estimated ^{10}B concentrations of normal organs and tumors.

In 6 healthy volunteers and patients with glioblastoma, whole-body FBPA PET were repeated 7 times during 1 h, and the mean FBPA distributions of 13 organs were measured. Based on the FBPA PET data, we estimated the changes in the ^{10}B concentrations of the organs when the injection of a therapeutic dose of ^{10}BPA–fructose complex (^{10}BPA–fr; 30 g, 500 mg/kg body weight) was assumed.

When the injection of a therapeutic dose of ^{10}BPA–fr was assumed, the estimated mean ^{10}B concentration in the kidney increased to 126.1 ± 24.2 ppm at 3 min after injection and then rapidly decreased to 30.9 ± 7.4 ppm at 53 min. The estimated mean ^{10}B concentration in the bladder gradually increased and reached 383.6 ± 214.7 ppm at 51 min. The mean ^{10}B concentration in the brain was estimated to be 7.6 ± 1.5 ppm at 57 min, and more than 30 ppm in glioblastoma.

FBPA PET has a potential to estimate ^{10}B concentration of tumors and normal organs before neutron irradiation of BNCT when several assumptions are validated in the future studies (Shimosegawa E, et al., 2016; Watabe T, et al., 2017; Romanov V, et al., 2020).

Synthesis of 4-borono-2-[^{18}F]fluoro-L-phenylalanine (FBPA) by employing [^{18}O]O_2-use [^{18}F]F_2 production system and [^{18}F]CH_3COOF as a labeling agent