

Title	Evaluation of the total distribution volume of 18F-FBPA in normal tissues of healthy volunteers by non-compartmental kinetic modeling
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論文内容の要旨  
Synopsis of Thesis

氏名 Name	Romanov Victor
論文題名 Title	Evaluation of the total distribution volume of $^{18}\text{F}$ -FBPA in normal tissues of healthy volunteers by non-compartmental kinetic modeling (非コンパートメントモデルによる健康人の正常組織における $^{18}\text{F}$ -FBPAの総分布容積の評価)
論文内容の要旨	
<p>[目的(Purpose)]</p> <p>Boron neutron capture therapy (BNCT) is a radiation therapy method for cancer treatment. In BNCT, <math>^{10}\text{B}</math> 4-borono-L-phenylalanine (<math>^{10}\text{B}</math>-BPA) is commonly used as a boron carrier. <math>^{10}\text{B}</math>-BPA is taken up by both tumor and normal cells, so it is necessary to know boron (<math>^{10}\text{B}</math>) concentration not only in tumor cells but also in normal tissues surrounding the tumor to avoid adverse effects. <math>^{18}\text{F}</math> labeled <math>^{10}\text{B}</math>-BPA (<math>^{18}\text{F}</math>-FBPA) PET has been employed to estimate <math>^{10}\text{B}</math> concentration in BNCT with <math>^{10}\text{B}</math>-BPA.</p> <p>The purpose of the current study was to evaluate the total distribution volume (<math>V_t</math>) of <math>^{18}\text{F}</math>-FBPA in normal organs of healthy volunteers using three non-compartmental, tracer reversible-binding graphical models and to estimate boron concentration in normal organs for the therapeutic dose of <math>^{10}\text{B}</math>-BPA using obtained <math>V_t</math> values.</p>	
<p>[方法ならびに成績(Methods/Results)]</p> <p><math>^{18}\text{F}</math>-FBPA was prepared by direct fluorination of <math>^{10}\text{B}</math>-BPA using the F-1 synthesizer. Six healthy volunteers (4 males and 2 females, ages 21 – 56 yrs, BW 48 – 66 kg) were injected with <math>^{18}\text{F}</math>-FBPA (3–5 MBq/kg), and 7 PET scans followed by a CT scan were performed subsequently. <math>^{18}\text{F}</math>-FBPA radioactivity in whole blood and plasma was measured before, and eight times after the injection. <math>^{18}\text{F}</math>-FBPA metabolites were measured at 20 and 50 minutes after the injection. PET images were analyzed by PMOD software. Twelve volumetric regions of interest including the brain, heart, right lung, spleen, liver, parotid salivary glands, esophagus, stomach, pancreas, intestines, and bone marrow were drawn manually for each subject and analyzed with the Logan plot and two Ichise multilinear analyses (MA1 and MA2). The better model was defined by several goodness-of-fit parameters and residual distribution. After <math>V_t</math> values had been derived, boron concentration was estimated in ppm for the <math>^{10}\text{B}</math>-BPA-fructose (<math>^{10}\text{B}</math>-BPA-fr) dose 30 g/l and 2 h post-injection using <math>V_t</math> and interpolated plasma activity data.</p> <p>The Ichise MA2 model showed the best fit among all models. The highest average <math>V_t</math> value was observed in the pancreas, followed by liver, parotid glands, esophagus, stomach, heart, bone marrow, intestines, spleen, brain, and lung in descending order. Estimated boron concentration for <math>^{10}\text{B}</math>-BPA-fr had the highest value in the pancreas (<math>14.0 \pm 1.9</math> ppm 1 h after, and <math>5.7 \pm 1.7</math> ppm 2 h after the <math>^{18}\text{F}</math>-FBPA administration) and the lowest value in the right lung (<math>2.4 \pm 0.3</math> ppm 1 h, and <math>1.0 \pm 0.3</math> ppm 2 h post-injection).</p>	
<p>[総括(Conclusion)]</p> <p>The <math>^{10}\text{B}</math> concentration in normal tissues was best estimated using <math>V_t</math> values of <math>^{18}\text{F}</math>-FBPA with the Ichise multilinear analysis 2 (MA2).</p>	

## 論文審査の結果の要旨及び担当者

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## 論文審査の結果の要旨

本論文の研究では研究者が6人の健康人のフルオロボロノフェニルアラニン (FBPA) PETデータを解析し、生体内でホウ素濃度を測定した。

FBPAの薬物動態分析パラメーターとして総分布量 ( $V_t$ ) を使用し、正常臓器を囲む12の手動で描かれた関心領域におけるFBPAの集積を解析した。

正確な $V_t$ 値を得るために、3つの非コンパートメントグラフィカルモデル (Loganプロット、Ichise MA1、およびMA2モデル) を利用し、いくつかの適合度パラメーターで比較した。

より良いモデルを選択した後 $V_t$ 値を計算し、その $V_t$ 値及び血漿におけるFBPA濃度を使い、最終的に中性子捕捉療法の実験で一般的に使われているボロノフェニルアラニン (BPA) の薬用量30 g下の健康人の正常組織におけるホウ素濃度を測定した。

本研究で提案された方法では、正常臓器のホウ素濃度をBNCTの前に複数の時点で測定できるという。

本論文は学位に値すると考える。