A study on tumor boron dose evaluation using a pharmacokinetic model based on ^{18}F-BPA dynamic positron emission tomography (PET) Imaging in boron neutron capture therapy (BNCT)

Yasunori SHUTO[1,2] Satoshi NAKAMURA[3,7] Mihiro TAKEMORI[4] Hana ENDO[3,5] Naru YOSHIDA[6] Tetsu NAKAICHI[3] Shuka NISHINA[2,3] Yusaku KASAI[1,7]
Homare MURATA[1,7] Ai NAKAOKA[3] Tairo KASHIHARA[4] Mitsuko MASUTANI[8] Tomonori GOKA[1] Kimiteru ITO[9] Hiroshi IGAKI[2,4]

[1]Department of Radiological Technology, National Cancer Center Hospital [2]Department of Comprehensive Oncology, Nagasaki University Graduate School of Biomedical Sciences [3]Division of Radiation Safety and Quality Assurance, National Cancer Center Hospital[4] Department of Radiation Oncology, National Cancer Center Hospital [5]Department of Radiological Sciences, Komazawa University Graduate School [6]Department of Radiological Sciences, Tokyo Metropolitan University [7]Medical Physics Laboratory, Division of Health Science, Graduate School of Medicine, Osaka University [8]Department of Molecular and Genomic Biomedicine, Center for Bioinformatics and Molecular Medicine, Nagasaki University Graduate School of Biomedical Sciences[9] Department of Diagnostic Radiology, National Cancer Center Hospital

MEDICAL PHYSICS COMMUNITY INSPIRATION INNOVATION IMPACT
2026 JULY 19–22 VANCOUVER, BC
JOINT AAPM | COMP MEETING

ABSTRACT

Purpose: In BNCT, 18F-BPA-PET evaluates boron drug distribution for treatment eligibility, but is rarely incorporated into treatment planning. A key limitation is differences in drug administration protocols between PET and BNCT, which may weaken clinical outcome-to-dose associations. This study aimed to improve boron dose calculation in treatment planning by incorporating heterogeneous boron distribution using a voxel-wise pharmacokinetic model.
Methods: Dynamic 18F-BPA-PET from six head and neck cancer patients was voxelized (4 mm). A three-compartment model with an image-derived input function obtained from the carotid VOI was fitted in each tumoral voxel to derive rate constants (K1–k4). Model-estimated voxel-wise SUVs were compared with 1-h static PET SUVs after bolus injection using MAE and correlation coefficients. For clinical BNCT, tumoral voxel-wise boron concentrations under 2-h continuous infusion were estimated and used for boron dose calculations. Estimated boron concentrations were compared with values derived from 2-h static PET SUVs. Resulting doses were also compared with a conventional treatment planning method assuming a constant tumor-to-blood boron concentration ratio under a 1-h neutron irradiation using CICS-1. Blood boron concentration was set to 25 ppm after 2 h continuous infusion based on published pharmacokinetic data, and CBE was set to 4.0. Statistical analysis used the Wilcoxon signed-rank test.
Results: Estimated SUVs strongly correlated with 1-h static PET SUVs (r = 0.938), with a median MAE of 0.527. Estimated tumoral boron concentrations under 2-h continuous infusion differed from those derived from 2-h static PET SUVs ($p < 0.05$) but remained strongly correlated (r = 0.857). Median tumoral voxel-wise boron dose (5583 voxels) across six cases was 242.6 Gy-Eq for the conventional method and 102.4 Gy-Eq for the model ($p < 0.05$).
Conclusion: This voxel-wise pharmacokinetic approach enables protocol-consistent estimation of heterogeneous boron distribution for treatment planning. It may improve dose evaluation accuracy and support personalized BNCT.

CONTACT

Yasunori Shuto
National Cancer Center Hospital, Tokyo, Japan
5-1-1 Tsukiji, Chuo-ku, Tokyo, Japan
yshuto@ncc.go.jp
+81-3-3542-2511

INTRODUCTION

- Role of 18F-BPA-PET: Evaluates the biodistribution of boron drug (BPA) and is used to assess eligibility for BNCT
- PET imaging is rarely incorporated into BNCT treatment planning
- Drug administration protocols differ between PET imaging and BNCT treatment
- Treatment planning does not account for heterogeneous boron distribution
- These may weaken the association between dose and clinical outcomes

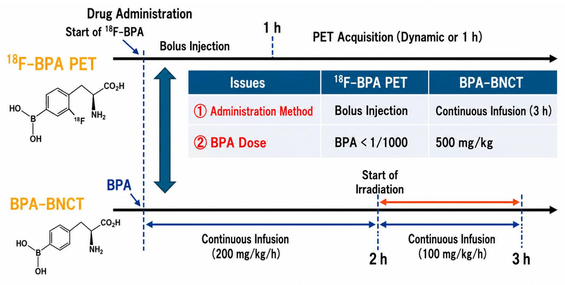


Fig.1 18F-BPA and BPA administration protocols

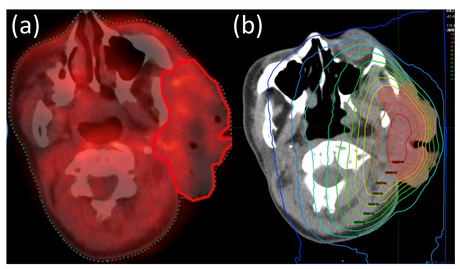


Fig.2 (a) Heterogeneous 18F-BPA distribution and
(b) dose calculation with assuming uniform BPA distribution

This study aimed to improve boron dose calculation in treatment planning by incorporating heterogeneous boron distribution using a voxel-wise pharmacokinetic model.

METHODS AND MATERIALS

- Patient : Six patients with head and neck cancer who underwent dynamic 18F-BPA-PET imaging (IRB : NCCH2017-091)

Incorporating drug distribution to dose calculation
☞ Establishing 3-compartment pharmacokinetic model
➡ Reduction of uncertainty due to differences in administration protocols

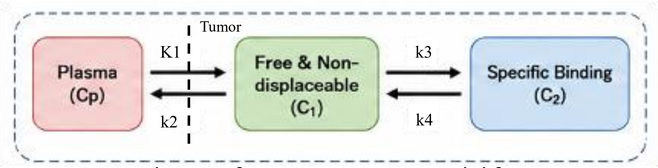


Fig. 3 Schema of 3-compartment model for 18F-BPA

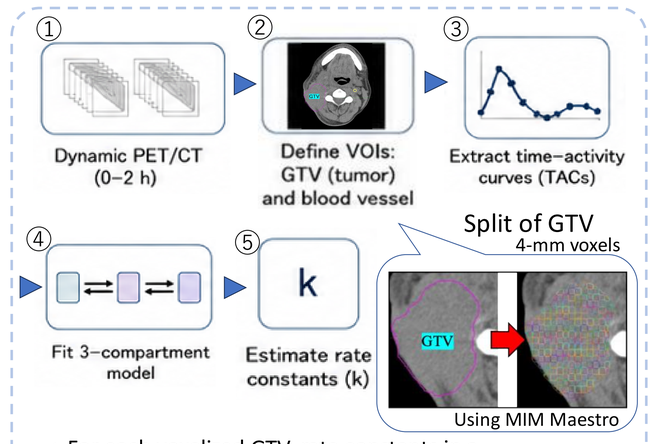
Model Equation

$$C_1 = (K1/(\alpha2-\alpha1))(k4-\alpha1)\exp(-\alpha1t)+(\alpha2-k4)\exp(-\alpha2t)) * Cp$$
$$C_2 = (K1k3/(\alpha2-\alpha1))(\exp(-\alpha1t)-\exp(-\alpha2t)) * Cp$$

- α_1 ,α_2: Hybrid rate constants representing the fast and slow kinetic components
- t: Time after tracer injection　* : convolution

To establish the model, rate constant k_i was derived from the fitting to the TAC in 18F-BPA PET imaging

Workflow for voxel-wise estimation of the rate constant *k* in the model
➡ Reduction of uncertainty due to heterogeneous boron distribution



- For each voxelized GTV, rate constants in a three-compartment pharmacokinetic model were derived.

Fig. 4 Schema of establishing voxel-wise pharmacokinetic model

Ⅰ.Comparison of model-estimated voxel-wise SUVs and 1h static PET SUVs

➡ Evaluation metrics : MAE and correlation coefficient

※MAE : Mean Absolute Error

$$MAE = \frac{\sum_{i=1}^{n} |y_i - x_i|}{n}$$

n: Number of data
y_i: Predicted value
x_i: Observed value

Ⅱ. Relative comparison of model-estimated SUVs under assuming 2-h continuous infusion and 1-h PET SUVs after bolus injection

The model-predicted SUVs for bolus FBPA administration and the predicted boron concentrations for continuous BPA infusion were each normalized to their respective maximum values and compared.

Ⅲ. Comparison dose calculation in GTV

Conventional method (uniform boron distribution)
vs. FBPA PET–based voxel-wise boron dose (bolus injection)
vs. BPA continuous infusion–based voxel-wise boron dose

Basic conditions

- 1h neutron beam irradiation using CICS-1 (BNCT system)
- Blood boron concentration (BBC): 25 ppm
- Compound biological effectiveness factor (CBE) : 4.0

● Conventional method (uniform boron distribution)

boron dose = T/B ratio × BBC × $D_{B,1ppm}$ × CBE

※ T/B ratio (Boron concentration ratio of tumor to blood) : 3.5

● FBPA PET–based voxel-wise boron dose (bolus injection)

boron dose = Normalization factor × SUV_{voxel} × BBC × $D_{B,1ppm}$ × CBE

※Normalization factor :
Conversion factor that sets the mean SUV of the carotid artery to a boron concentration of 25 ppm for each patient.

● BPA continuous infusion–based voxel-wise boron dose

boron dose = time-integrated boron concentration (1 - 2 h post-dose) × $D_{B,1ppm}$ × CBE

➡ The calculated boron doses were compared using the Wilcoxon signed-rank test.

RESULTS・DISCUSSION

Ⅰ.Comparison of model-estimated voxel-wise SUVs and 1h static PET SUVs

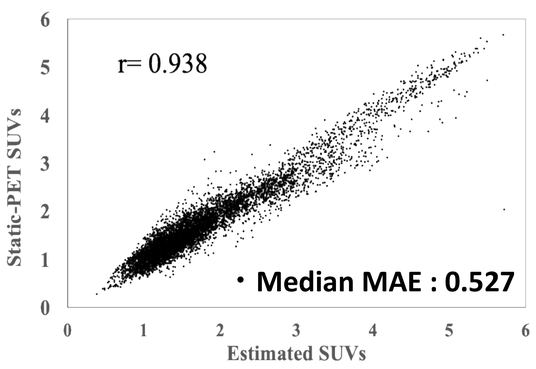


Fig.5 Scatter Plot of Static-PET and Model-Estimated SUVs in 18F-BPA PET images taken 1 h after bolus injection

Ⅱ. Relative comparison of model-estimated SUVs under assuming 2-h continuous infusion and 1-h PET SUVs after bolus injection

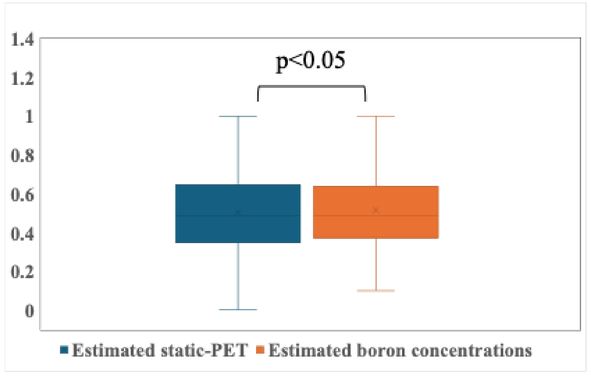
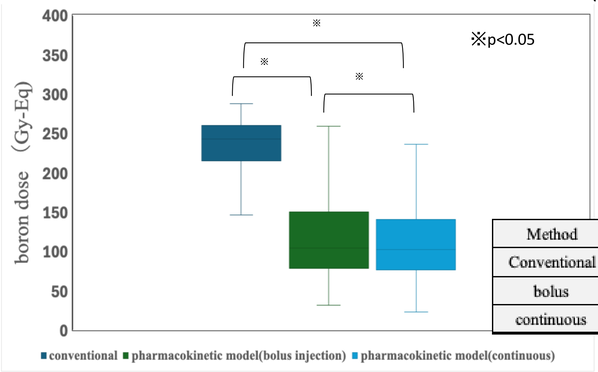


Fig6. Relative tumoral boron concentration comparison between the model-estimated SUV with continuous infusion and 1-h PET SUVs after bolus injection

Ⅲ. Comparison dose calculation in GTV

Conventional method (uniform boron distribution, blue)
vs. FBPA PET–based voxel-wise boron dose (bolus injection, green)
vs. BPA continuous infusion–based voxel-wise boron dose (light blue)



Method	Dose (Median) [Gy]
Conventional	242.6
bolus	104.6
continuous	102.4

Fig.7 GTV dose comparison between conventional method and pharmacokinetic method(bolus injection, continuous infusion)

- Validation of the derived rate constants by comparing model-estimated voxel-wise SUVs with 1-h static PET SUVs.
- Boron distribution may differ between bolus injection and continuous infusion. Accounting for this difference may improve the accuracy of boron dose calculations.
- Conventional dose calculations assuming a uniform boron distribution may overestimate the actual delivered dose.

CONCLUSIONS

This voxel-wise pharmacokinetic approach enables protocol-consistent estimation of heterogeneous boron distribution for treatment planning. It may improve dose evaluation accuracy and support personalized BNCT.

REFERENCES

1) Aihara T, et al. Otolaryngol 6:6 (2016)
2) Kivunoro H, et al. Appl. Radiat. Isot. 106: 189-194 (2015)
3) Kobayashi Y, et al. Appl. Radiat. Isot. 219: 111720 (2025)
4) Imahori Y, et al. Clinical Cancer Research Vol. 4, 1833-1 841(1998)
5) Ono K et al. Advances in Neutron Capture Therapy (2006)