Imaging of Gastrin-Releasing Peptide Receptor-Expressing Prostate Tumor using a ^{68}Ga-Labeled Bombesin Analog

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1. Introduction

Prostate cancer is the most common non-cutaneous malignancy among American men, and it is the second leading cause of cancer death in men in the United States [1]. Because prostate carcinoma cells do not use glucose notably more than normal cells, the most widely used ^{18}F-FDG does not play a prominent role in the diagnosis and staging of prostate cancer; an overall sensitivity of only 57% on a per-patient basis on staging or restaging for 244 prostate cancer patients was reported [2, 3]. Although ^{18}F-choline is considered to be the standard diagnostic imaging tool for the clinical assessment of recurrent prostate cancer in Europe, it is not specific for cancer cells. Therefore, in this study, we describe the imaging efficacy of ^{68}Ga labeled bombesin analog to facilitate earlier and more accurate diagnosis and treatment of GRPR-expressing prostate tumors.

2. Methods and Results

2.1 Preparation of ^{68}Ga-labeled bombesin derivative

Our previous study demonstrated the targeting and therapeutic efficacy of ^{177}Lu-DOTA-gluBBN for the treatment of GRPR-expressing prostate tumors [4]. In this study, the DOTA-gluBBN was labeled with ^{68}Ga which was purified and concentrated using NaCl-based 68Ga eluate concentration method [5].

As shown in Fig. 1, the purified and concentrated ^{68}Ga was labeled with DOTA-gluBBN by high radiochemical purity (>98%).

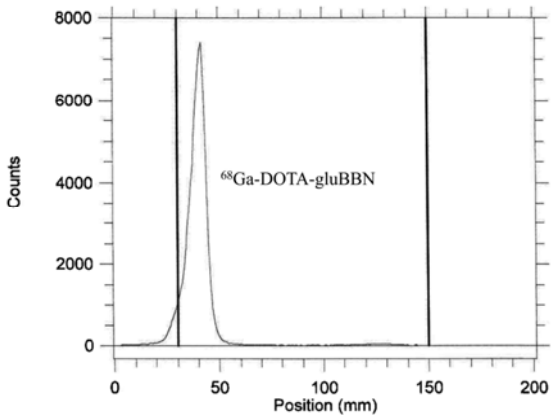
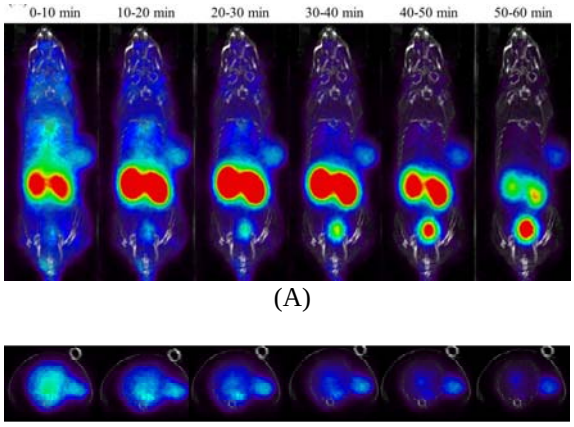


Fig. 1 Typical iTLC profiles of ^{68}Ga-labeled DOTA-gluBBN.

2.2 Imaging study of ^{68}Ga-DOTA-gluBBN

Nude mice bearing subcutaneous PC-3 tumor xenografts next to the right shoulder were scanned to 60 min post injection and serial PET-CT images were acquired (Fig. 2). PC-3 tumors were clearly visualized in all images. In addition, ^{68}Ga-DOTA-gluBBN was rapidly excreted from the blood pool to the urinary bladder through the kidneys, and the highest radioactivity was observed in the urinary bladder at 50 to 60 min post-injection.

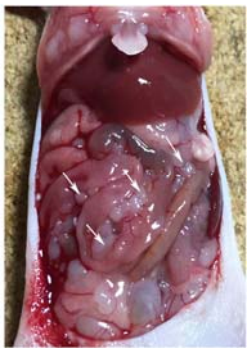


(A)

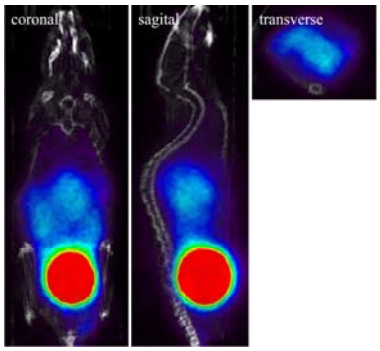
(B)

Fig. 2 Series of coronal (A) and transverse (B) images from subcutaneously PC-3 xenografted nude mice.

The imaging efficacy of ^{68}Ga-DOTA-gluBBN was evaluated in the PC-3- peritoneal metastasized model. As shown in Fig. 3(A), intraperitoneal-injected PC-3 prostate cancer cells were diffusely metastasized into the whole peritoneal cavity, and were primarily localized in the peritoneal wall, pancreas, and mesentery. In Fig. 3(B), the radioactivity was also distributed diffusely in the whole peritoneal cavity similar to the gross observation in Fig. 3(A).



(A)



(B)

Fig. 3 Gross observation of peritoneal metastasized PC-3 prostate tumors (A) and PET images of the mice using ^{68}Ga-DOTA-gluBBN (B).

2.3 Ex vivo autoradiography

Dark radioactivity was imaged in the subcutaneously xenografted tumor as well as the peritoneal metastasized PC-3 tumor, and the uptake of ^{68}Ga-DOTA-gluBBN in S.C.- and I.P.- induced PC-3 tumors were confirmed. In addition, the uptake was blocked by co-administration of DOTA-gluBBN, indicating GRPR-specific uptake.

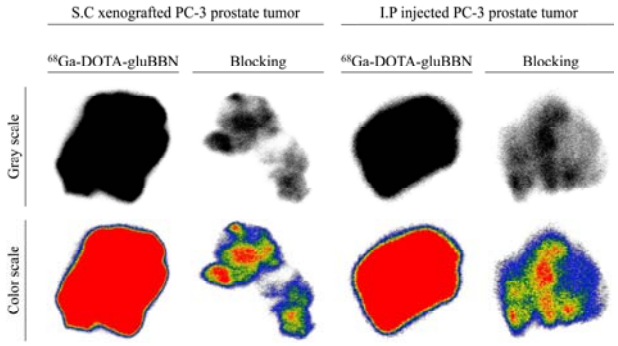


Fig. 4 Ex vivo autoradiography of subcutaneously and intraperitoneally injected PC-3 prostate tumors using ^{68}Ga-DOTA-gluBBN

3. Conclusions

These results suggest that ^{68}Ga-labeled bombesin derivative has promising characteristics as a novel nuclear medicine, especially for the imaging of GRPR over-expressing prostate tumors.

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