Production of ^{88}Y for gamma-ray emission imaging

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Radioimmunotherapy (RIT) is an internal radiation therapy that uses radiolabeled drugs, in particular particularly in monoclonal antibodies (mAbs) or peptides. ^{90}Y emits highly cytotoxic β^- ray and is thus a promising radionuclide for use in RIT. However, ^{90}Y cannot be readily imaged by nuclear medicine imaging modalities, because ^{90}Y is a pure β^- emitter.[1] On the other hand, ^{86}Y emits β^+ rays, which can be detected by PET.[1-3] In addition, ^{86}Y-labeled drugs (mAbs or peptides) display identical biodistributions to ^{90}Y-labeled drugs because ^{86}Y is chemically identical to ^{90}Y.[1] Therefore, in recent years, ^{86}Y has attracted attention as an attractive surrogate for studying ^{90}Y-labeled drugs. However, the physical half-life of ^{86}Y ($T_{1/2}$ = 14.7 h) is shorter compared to that of ^{90}Y ($T_{1/2}$ = 64.1 h), and thus, it is not suitable as a surrogate for investigating serial biodistribution of RIT drugs with long biological half-lives, such as mAb, which remain circulating in vivo for weeks.[4] A chemically identical surrogate with a longer half-life is desirable for development phases of ^{90}Y-labeled drugs.

^{88}Y is chemically identical to ^{90}Y and has a long half-life of $T_{1/2}$ = 106.6 d. Moreover, ^{88}Y emits γ rays with energies of 898 and 1836 keV, which can be detected using semiconductor Compton cameras through gamma-ray emission imaging (GREI).[5] Therefore, the imaging of ^{88}Y-labeled drugs with GREI has the potential ability to investigate the serial biodistribution of ^{90}Y-labeled drugs with a long biological half-life, in particular, in preclinical studies. The final purpose of our study is to develop an imaging method for ^{88}Y-labeled drugs through GREI. In this study, we produced ^{88}Y for the GREI experiment.

^{88}Y was produced by the ^{nat}Sr(d,x)^{88}Y reactions. To prepare a ^{nat}SrO pellet target with a diameter of 10 mm, approximately 400 mg of $^{nat}SrCO_3$ (Wako Pure Chemical Industries, Ltd., chemical purity: 99.99%) was heated for 2 h at 1000˚C and pressed at 1.6 t. The pellet was covered with a 10-μm Al foil (chemical purity: 99.999%). The target was irradiated with a 24-MeV deuteron beam supplied from the RIKEN AVF cyclotron. The irradiation was performed for 5 h at a beam current of approximately 1.5 particle μA.

Thirty-nine days after the irradiations, ^{88}Y was chemically isolated from the ^{nat}SrO target by extraction chromatography using Ln-resin (Eichrom Technologies, Inc., particle size: 50-100 μm) filled in a Muromac column (Muromachi Technos Co., Ltd., internal diameter: 5 mm, height: 50 mm). The Ln-resin column was washed in advance with 3 mL of water, 10 mL of 10 M HNO_3, and then 4 mL of water, and was pre-equilibrated with 2 mL of 1 M HNO_3. The irradiated ^{nat}SrO target was dissolved in 1 M HCl and evaporated to dryness on a hot plate and under a heat lamp. The residue was dissolved in 5 mL of 1 M HNO_3, and was evaporated to dryness. Subsequently, the residue was dissolved in 5 mL of water and 2 mL of 1 M HNO_3, and was evaporated to dryness. Then, the residue was dissolved in 2 mL of 1 M HNO_3 and loaded onto the Ln-resin column. The resin was then washed with 16 mL of 1 M HNO_3. ^{88}Y was eluted from the resin with 10 mL of 10 M HNO_3. The eluted solution was heated to dryness, and 2 M HCl was added to the residue.

The γ-ray spectrum of the final purified product is shown in Fig. 1. Approximately 10 MBq of ^{88}Y was obtained. The radiochemical yield of ^{88}Y in the chemical isolation process was approximately 80%. In the next experiment, we plan to synthesize ^{88}Y-labeled drugs and try to visualize their biodistirbution using GREI.

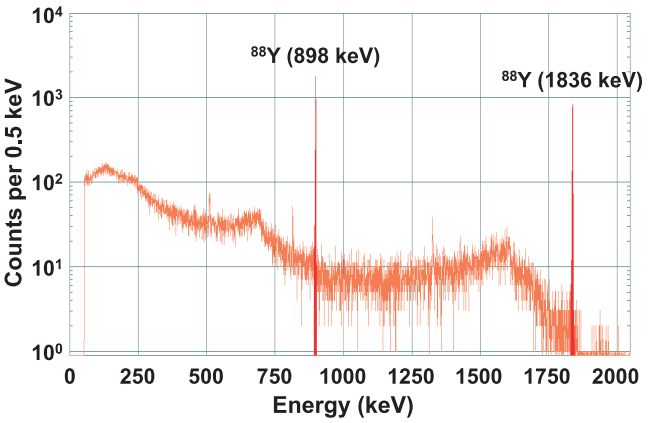

Fig. 1. Gamma-ray spectrum of ^{88}Y after the chemical isolation.

References

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