Selective complexation and a 3D printer device for separation and purification of medical radioactive metal ions from target metals

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Radioactive metals such as ^{68}Ga and ^{89}Zr have been used and studied as probes for positron emission tomography (PET). In the synthesis of probes, it is essential to efficiently and rapidly separate and purify radioactive metal ions from the target metal produced by a cyclotron. In our laboratory, we have established a method for the separation and purification of ^{68}Ga from ^{nat}Zn by means of charge polarity conversion and cation exchange through selective complexation using the difference in complexation constants with organic ligands.[1] We have achieved high speed and automated preparation using a 3D-printer-fabricated flow system.[2] In this study, we examine the separation and purification of ^{89}Zr, which is expected to be used as a PET diagnostic agent, as well as of ^{68}Ga and ^{89}Y, which are its raw material.

Ethylenediaminetetraacetic acid (EDTA) was used as an organic ligand. EDTA complexes with various metal ions, but the charge polarity can be controlled by adjusting the pH value of the matrix solution as the complexation constants differ for each metal. In particular, at pH 0.5, Zr exists as a Zr-EDTA complex and Y as a cation.

A disposable separation and purification flow device with a volume of 10 mL, which is 10 times larger than that of conventional devices,[2] was fabricated using a 3D printer for actual field use. The device used in this study was fabricated with UV curable resin using a liquid crystal display type printer. A cation exchange resin (Dowex® 50 W × 8 100–200 mesh, 2.0 g) was loaded in the device to adsorb Y^{3+} present as a cation in the sample, and Zr-EDTA and Y were separated. The solutions used for sample loading and recovering Y were, respectively, 0.3 M HNO_3 and 6 M HCl and flowed at 1.0 mL/min. The Zr-EDTA was recovered as Zr^{4+} through oxidative decomposition using a UV lamp incorporated in the device.

First, the device was used to evaluate the separation of a stable isotope metal sample (50 μg Zr/L + 10 gZn/L with 1 mM EDTA in 0.3 M HNO_3). ICP-MS (iCAP^{TM} RQ, Thermo Scientific^{TM}) was used for the evaluation. After 10 mL of a stable isotope metal sample was introduced into the device, Zr and Y were perfectly separated, and the target Zr was quantitatively recovered in 25 min.

Next, we evaluated the separation and purification using a radioisotope metal solution (2.3 MBq ^{89}Zr/L + 0.2 g^{89}Y/L with 1 mM EDTA in 0.3 M HNO_3, byproduct of the ^{89}Zr, ^{88}Y as a tracer). ^{89}Zr was produced in the ^{89}Y$(d, 2n)^{89}$Zr reaction at the RIKEN AVF cyclotron. A semiconductor radiation detection and pulse-height analysis system (GMX-25190-P, SEIKO EG&G ORTEC) were used for the evaluation. The γ-ray spectra of a radioisotope metal, ^{89}Zr recovery, ^{89}Y recovery, and wash solutions are presented in Fig. 1. More than 93% of ^{89}Zr was observed in the Zr recovery solution even though the observed tracer ^{88}Y was less than the limits of detection (LOD). The LOD for ^{88}Y corresponds to 1 mg^{89}Y/L under the present condition. Further, more than 99% of ^{89}Y was observed in the Y recovery solution. Thus, the present system can well separate Zr and Y into recovery solutions. Rapid and highly efficient separation and purification of radioisotope metal ions was achieved by a disposable device fabricated using a 3D printer. High throughput (10 mL/treatment) was achieved, and sufficient performance was demonstrated for the synthesis of the PET diagnosis probe.

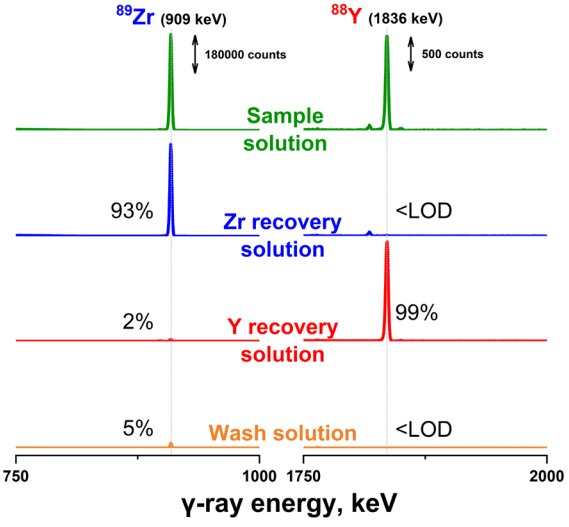

Fig. 1. γ-ray spectra of various solutions measured by a semiconductor detector and pulse-height analysis system (the scales are same for all the panels.).

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