Evaluation of Improved Production Methods and Supply of no-carrier added Lu-177

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1. Introduction

Lutetium-177 (^{177}Lu, $t_{1/2}$ = 6.7 d) is increasing in demand as an important therapeutic radionuclide for targeted radiotherapy in nuclear medicine because of its high theranostic potential. ^{177}Lu emits β^- particles ($E_{\beta,max}$ = 498 keV) with a soft tissue penetration range of less than 3 mm and γ-rays (E_γ = 208 keV (11.0%) and 113 keV (6.4%)) suitable for imaging with a detector.

^{177}Lu can be produced in high yield by the ^{176}Lu(n,γ)^{177}Lu reaction. However, this production method has a limitation in that carrier ^{176}Lu are mixed and by-products ^{177m}Lu with a long half-life ($t_{1/2}$ = 160 d) are produced. In this respect, no-carrier added (nca) ^{177}Lu has high specific activity and high radionuclide purity without long-lived radionuclide impurity, making them particularly useful for radioimmunotherpy. The nca ^{177}Lu can be produced by the ^{176}Yb(n,γ)^{177}Yb → ^{177}Lu reaction by irradiating neutrons to an enriched $^{176}Yb_2O_3$ target. The critical process is the radiochemical separation of nca ^{177}Lu from macroscopic amount of Yb target with adjacent atomic number.

As the demand of lanthanide nuclides (including ^{177}Lu) increases, numerous researchers have devoted themselves to developing faster and more efficient separation techniques. In particular, the separation technology based on ion exchange to improve selectivity have been developed. In ion exchange technology, generally, α-HIBA and NH_4^+ is used as a complexing agent and a separating ion, respectively. However, P.S. Balasubramanian reported that ^{177}Lu was separated from neutron-irradiated ytterbium using a cation exchange resin (Dowex-50X8, 200-400 mesh) with α-HIBA and Zn^{2+} ion as a separating ion.

KAERI has conducted to get a high purified ^{177}Lu from neutron-irradiated ytterbium targets. Better elution conditions than traditional methods for separating lanthanum elements have been secured. Based on this, separation was made possible under the reduced column length. These results provide the advantage of reducing waste and, above all, shortening the separation times.

The produced isotopes were supplied to five institutions to secure the purity and labeling yields.

2. Experiments

In the conventional method for purification, ^{177}Lu was recovered by serially connecting three 2 ml Sep-pak filled with cation exchange resin. HIBA was removed by washing 3 times each with 10 ml of 0.1 M HCl and 1 M HCl. When ^{177}Lu in the column was recovered with 9M HCl, the yield was about 60%. The improved method linked one 1 ml Sep-pak packed with cation exchange resin. When ^{177}Lu was eluted, 0.2M HCl was co-inject to the purification column to obtain ^{177}Lu. HIBA was removed by washing once with 0.1M HCl and 10ml of 1M HCl. Finally, ^{177}Lu was recovered with 9M HCl and its yield was about 90%. The purification time was also reduced from 3 hours to 1 hour, which is shown in Fig. 1.

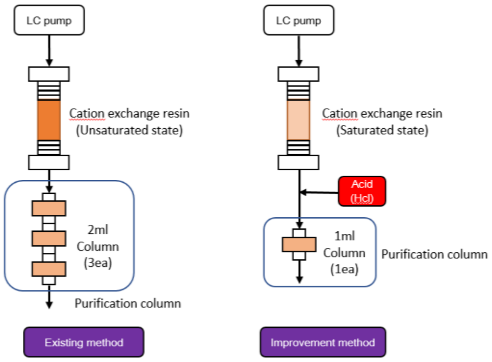

Fig. 1. Comparison of existing and improved method

Based on these experiments, large-scale (> 1Ci) equipment was designed. It will be divided into 4 section; LC pump section (part A), separation column section (part B), valve section (part C), and purification section (part D). This configuration is for rapid replacement in preparation for malfunction of each part. (Fig. 2)

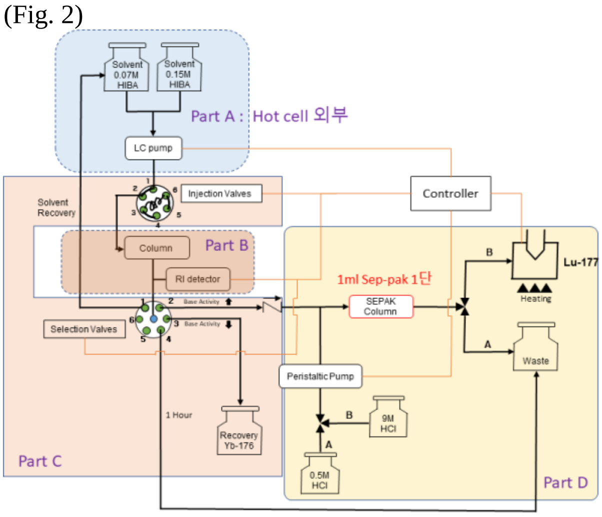

Fig. 2. The concept of a no-carrier added Lu-177 production equipment

3. Evaluation of Isotope Supplies

The spectrums of the HPGe show the radionuclide purity of the n.c.a ^{177}Lu like below Fig. 3. Before purification, the characteristic peak of the Yb series was identified (blue). After purification, it was confirmed that the characteristic peak of Yb was removed (red). As a result, it was confirmed that pure acid no-carrier added ^{177}Lu was produced.

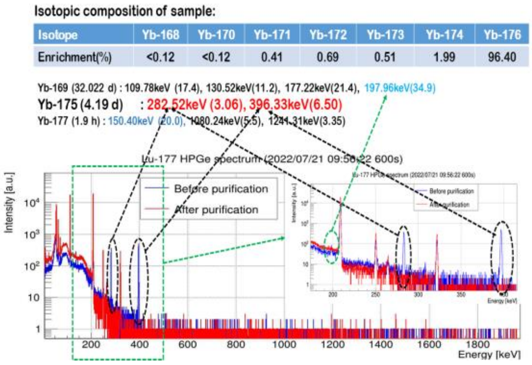

Fig. 3. HPGe semiconductor detector spectra of Lu-177 before and after separation

4. Conclusion

The improved methods for producing n.c.a ^{177}Lu could reduce processing time within 4hrs. Base on basic experiments and separation technologies, more than 1Ci of handling equipment is currently being manufactured. In the fall of 2023, n.c.a ^{177}Lu will be produced using the developed equipment.

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