Accelerator-based synthesis of rhenium-186 that enables high spatial resolution imaging

S. Takeda,[*1] I. O. Umeda,[*1] M. Katsuragawa,[*1] A. Yagishita,[*1] A. Nambu,[*2] X. Yin,[*2] H. Haba,[*2] and T. Takahashi[*1]

Radiotheranostics is the integration of targeted radionuclide therapy with molecular imaging techniques such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT). The exponential growth of radiotheranostics in the field of oncology is due to its unique mechanism of action, which allows for the targeted elimination of tumor cells with minimal adverse effects. The radionuclides, used for diagnosis, emit β^+ particles in PET and γ rays in SPECT. In contrast, for cancer therapy, radionuclides that emit energetic α, β^-, and auger electron particles are utilized.

Rhenium radioactive isotopes are an attractive option for radiotheranostics, as they emit both particles suitable for targeted therapy and photons useful for diagnosis, and can aid in developing radiopharmaceuticals. Rhenium belongs to the same chemical family as technetium. Technetium-99m (^{99m}Tc) is the most widely used radionuclide in nuclear medicine imaging, due to its short half-life and favorable physical properties such as low radiation exposure to patients. Many ^{99m}Tc-labeled probes have been developed and are used clinically to diagnose of various diseases. Most of the ligands and chelation chemistry developed for technetium can be also applied to rhenium. ^{186}Re is typically produced through neutron irradiation in reactors in other countries, but production in Japan is challenging due to the difficulty of reactor production. Additionally, ^{186}Re produced in reactors includes a large amount of carrier Re as raw material. At the RIKEN RI Beam Factory, carrier-free ^{186}Re can be produced through proton and heavy ion-induced reactions of ^{186}W using the RIKEN AVF cyclotron. Our goal is to develop new radiotheranostics using ^{186}Re.[1,2]

^{186}Re emits gamma-rays at 137 keV, allowing visualization of biobehavior of ^{186}Re-labeled radiopharmaceuticals. However, the emission yield of 137 keV photons is as small as 9.4%. Therefore, high-sensitivity and high-resolution imaging have been challenging since the signals (137 keV photons) are prone to be contaminated by the continuum background constituted by scattering of high-energy gamma-rays caused by contamination of rhenium isotopes other than ^{186}Re. In our previous experiment, ^{186}Re was produced in the ^{186}W$(d,2n)^{186}$Re reaction using the 24-MeV d beam. We found that the byproduct of ^{184}Re significantly contributed to the contamination and caused significant degradation in imaging quality.

To improve imaging quality, it is essential to increase the radionuclidic purity of ^{186}Re. In this study, we produced ^{186}Re in the ^{186}W$(p,n)^{186}$Re reaction using the 14.8-MeV proton beam on target and successfully improved the radionuclidic purity of ^{186}Re from 94.43% to 99.56%.

A 19-MeV proton beam delivered from the RIKEN AVF cyclotron was degraded to 14.8 MeV through a Ta plate (192.6 μm) and irradiated onto a ^{186}WO$_3$ powder (isotope enrichment of ^{186}W: 99.79%; thickness: ∼200 mg/cm^2). After irradiation, ^{186}Re was purified by chemical separation.[3] 3 MBq of ^{186}Re in 200 μL of 0.01 M HCl was shipped to National Cancer Center Research Center for the imaging experiment.

We demonstrated the effectiveness of the purification for imaging using CdTe-DSD SPECT[4] (Fig. 1) developed by the IPMU team. CdTe-DSD SPECT is a novel small animal imaging system consisting of 8 modules of CdTe Double-sided Strip Detectors[5] and a multi-pinhole collimator made of tungsten. The detector has an energy resolution of 1–2 keV (FWHM) in 10–100 keV and 1.6% (FWHM) at 140 keV, which is around three times better than those of currently available high-grade semiconductor SPECT systems. An ultra-high spatial resolution of better than 350 μm is possible. Figure 2 compares phantom imaging results for ^{186}Re with a purity of 94.43% (left) and 99.56% (right). The image was noisy for lower purity because of the continuum background produced by ^{184}Re. On the other hand, the preferred image was obtained for high-purity ^{186}Re. This is a promising result, and we will proceed to in-vivo imaging with mice.

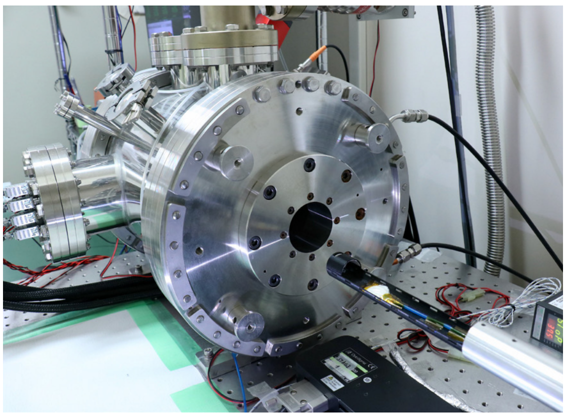

Fig. 1. CdTe-DSD SPECT viewed from the entrance window for small animals.

*1 Kavli Institute for the Physics and Mathematics of the Universe, University of Tokyo
*2 RIKEN Nishina Center

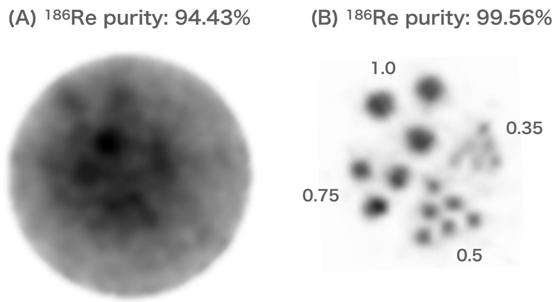

Fig. 2. The comparison of phantom imaging results for ^{186}Re with a radionuclidic purity of 94.43% (left) and 99.56% (right) taken with CdTe-DSD SPECT.

References

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