

Wet chemistry processes utilized in development of $^{211}\text{Rn}/^{211}\text{At}$ generator for targeted alpha therapy

Y. Shin,^{*1} K. Kawasaki,^{*2} N. Yamada,^{*1}
K. Washiyama,^{*3} A. Yokoyama,^{*2} I. Nishinaka,^{*4} S. Yanou,^{*5} and H. Haba^{*5}

The short path length and high linear energy transfer of alpha particles are expected to facilitate targeted alpha therapy in tumor treatment. One of the promising nuclides among the various alpha emitters is ^{211}At , which has a half-life of 7.21 h. This nuclide attracts much attention because of its suitable half life and the expected chemical properties of the element, and this has motivated a large number of preclinical studies on At chemistry.¹⁻³⁾ As regards improvement of the ^{211}At availability, development of a 14.6-h ^{211}Rn generator, where ^{211}Rn is a parent nuclide of ^{211}At , can potentially provide nuclides in a wider range of locations distant from the accelerator facilities in which they are produced. However, At chemistry has not been well studied in relation to Rn decay and further knowledge is needed to control its behaviors in the required successive chemical processes.⁴⁾ The aim of this study was to investigate the wet chemistry processes of At so as to realize a $^{211}\text{Rn}/^{211}\text{At}$ generator that may facilitate a prevalent technology.

Radon-211 was produced through irradiation of a stack of Bi targets with 60-MeV $^7\text{Li}^{3+}$ beams from the Japan Atomic Energy Agency (JAEA) tandem accelerator via the $^{209}\text{Bi}(^7\text{Li}, 5n)^{211}\text{Rn}$ nuclear reaction. After the irradiation, the Bi target was dissolved in nitric acid solution and diluted with distilled water. Then, the produced ^{211}Rn was transferred to an organic phase, *i.e.*, dodecane, through solvent extraction. The trapped ^{211}Rn was then allowed to stand for over half a day to generate ^{211}At . Back-extraction of ^{211}At was performed using alcohol with an oxidizing agent.

In this study, to obtain the ^{211}At distribution ratios between the dodecane and ethanol (EtOH) solution with an oxidizing agent, the Bi target, which was irradiated at the RIKEN Azimuthally Variable Field (AVF) cyclotron, was delivered to Kanazawa University, dissolved in nitric acid, and diluted to a 1 M solution in acid concentration. The dodecane solution, into which At species were extracted from the nitric acid solution, was subjected to extraction experiments with and without an oxidization agent, *i.e.*,

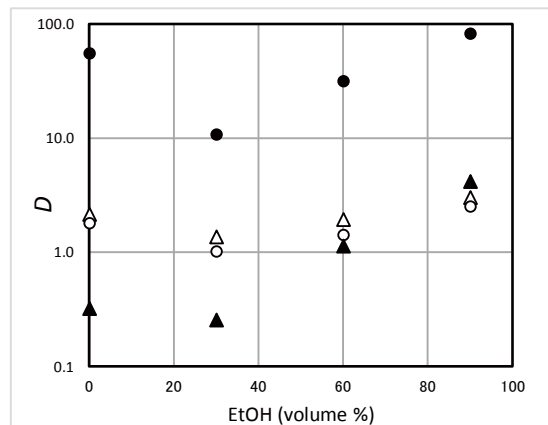


Fig. 1. Distribution values of ^{131}I (open symbols) and ^{211}At (closed symbols) for extraction with (circles) and without (triangles) an oxidizing agent.

N-Bromosuccinimide. The results were compared with those of the same experiments performed with a commercially available I-131 isotope.

After the back extraction to the EtOH solution, each phase was subjected to measurements with a liquid scintillation counter, to determine the back extraction distribution, D , of ^{211}At . Hence, we found that only At exhibit a notable effect of oxidation, as shown in Fig. 1. Here, the distributions were obtained from the ratios of the radioactivity in the EtOH solution to that in the dodecane. We also aimed to control the extraction behavior of the At from the nitric acid solution by using an ionic liquid with a crown ether. For the combination of 1-butyl-3-methylimidazolium Bis (trifluoromethanesulfonyl) imide and 18-crown-6, the extraction system was found to be promising because an extraction rate of up to 90% was attained at low acid concentrations.

References

- 1) F. Guérard, J-F. Gestin, M. W. Brechbiel, *Cancer Biother. Radiopharm.* **28**, 1 (2013).
- 2) D. S. Wilbur, *Nat. Chem.* **5**, 246 (2013).
- 3) M. R. Zalutsky, M. Pruszyński, *Curr. Radiopharm.* **4**, 177 (2011).
- 4) E. Maeda, A. Yokoyama, T. Taniguchi, K. Washiyama, I. Nishinaka, *J. Radioanal. Nucl. Chem.* **303**(2), 1465 (2015).

*1 Institute and College of Science and Engineering, Kanazawa University

*2 Graduate School of Natural Science and Technology, Kanazawa University

*3 Fukushima Global Medical Science Center, Fukushima Medical University

*4 Quantum Beam Science Research Directorate, National Institutes for Quantum and Radiological Science and Technology

*5 RIKEN Nishina Center