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Application of PZC to $^{188}W/^{188}Re$ Generators

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Applicability of newly developed PZC (poly zirconium compound) to an adsorbent for a $^{188}W/^{188}Re$ generator system was investigated for long term. The PZC generator gave reproducible ^{188}Re elution yields (60−75%) with 0.03% of ^{188}W parent breakthrough during 154 days corresponding to twice of the half-life of ^{188}W (69.4 d). Furthermore, the labeling yields of hydroxyethyliden diphosphonic acid and mercaptoacetyltriglycine with ^{188}Re eluted from the PZC column were high enough and there was no significant different with the results using ^{188}Re eluted from the alumina system. The $^{188}W/^{188}Re$ generator prepared by PZC indicated a good performance for the practical use.

1. Introduction

Rhenium-188 ($T_{1/2}$ = 17.0 h) is an attractive radionuclide for radiotherapy and can be obtained at carrier-free levels from β-decay of the long-lived ^{188}W (69.4 d) produced by the double neutron capture of ^{186}W in a reactor.[1, 2] The $^{188}W/^{188}Re$ generators are of particular interest,[3] since ^{188}Re can be produced repeatedly at a low cost during a long period for the synthesis of labeled compounds. However, the relatively large volume of 0.9% NaCl are required for the elution of ^{188}Re from traditional alumina-based $^{188}W/^{188}Re$ generators because the parent ^{188}W is produced in a relatively low specific activity by the double neutron capture reaction of ^{186}W with the low cross sections. Therefore, methods for concentration of ^{188}Re solution from alumina-based $^{188}W/^{188}Re$ generators have developed by a tandem cation-anion column system[4] or by a single anion exchange column system.[5, 6]

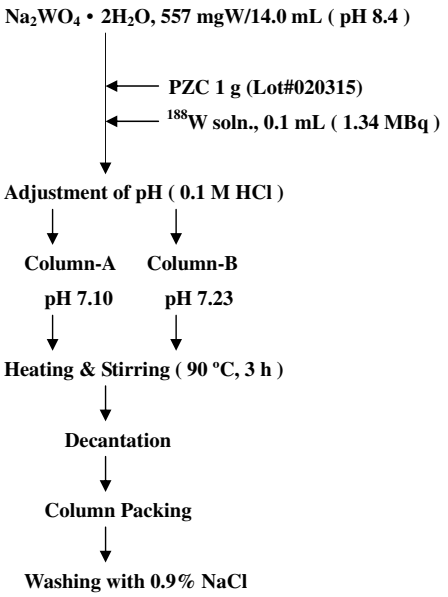
On the other hand, newly developed poly zirconium compound (PZC)[7] as the adsorbent of ^{99}Mo has more than 100 times higher adsorption capacity of molybdenum than alumina. PZC enables to prepare a more compact $^{99}Mo/^{99m}Tc$ generator than alumina. Development of compact $^{99}Mo/^{99m}Tc$ generators by using PZC has been progressed in the project of FNCA (Forum for Nuclear Cooperation in Asia).[8] In this study, applicability of PZC to an adsorbent for a $^{188}W/^{188}Re$ generator system- the adsorption behavior of ^{188}W was investigated for long term (about 5 months). Labeling yields of hydroxyethylidene diphosphonic acid (HEDP) and mercaptoacetyltriglycine (MAG3) with ^{188}Re obtained from the PZC-based generators were compared with those with ^{188}Re obtained from alumina-based generators.

2. Experimental

PZC was synthesized through the thermal condensation reaction between $ZrCl_4$ and isopropyl alcohol (PrOH) according to the procedure of Tanase et al.[7] Two different lots of PZC which have 483 and 526 mg W/g PZC of the maximum adsorption capacity of W were used in this study.

2.1. Production of ^{188}W.[2] Tungusten-188 was produced by the double neutron capture reaction of ^{186}W. The target material was 99.79% enriched $^{186}WO_3$ (ISOTEC Inc., USA or Euriso-top, France). The target (25−50 mg) in a quartz ampoule was irradiated for 26−52 days in JMTR (thermal neutron flux, 2.7×10^{14} $cm^{-2}\cdot s^{-1}$). The irradiated target was allowed to stand for more than 4 weeks for decay of ^{187}W (23.72 h). The irradiated target was dissolved in 2 M NaOH with heating. The specific activity of ^{188}W was 5~13 MBq/mgWO_3 at the end of bombardment.

2.2. Preparation of $^{188}W/^{188}Re$ generators by using PZC. Preparation of $^{188}W/^{188}Re$ generators based on PZC was shown in the Scheme 1. $Na_2WO_4\cdot 2H_2O$ which corresponds to the maximum adsorption capacity of W to 1 g of PZC, PZC and the ^{188}W solution (1.3−4.1 MBq) were added and pH was adjusted to about 7 with 0.1 M HCl. The solution was heated to 90 ˚C for 3 hours with occasional stirring. After eliminating the fine powdered PZC by decantation, the PZC adsorbed ^{188}W was packed to a glass column. The PZC column (8 mm$\phi \times$ 24−32 mm) was then washed with normal saline. Rhenium-188 was eluted with normal saline after the radioequilibrium between ^{188}W and ^{188}Re had almost reached. The radioactivity of ^{188}Re was determined by γ-ray spectroscopy using a calibrated HPGe detector.



Scheme 1. Preparation of $^{188}W/^{188}Re$ generators based on PZC.

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The $^{188}W/^{188}Re$ alumina generator was prepared as described in the literature.[3]

2.3. Preparation of ^{188}Re-HEDP and ^{188}Re-MAG3. ^{188}Re-HEDP [9]: HEDP was purchased from Kishida Chemical Co., Japan. To an HEDP aqueous solution (35.8 mg/280 μL), distilled water (504 μL), *l*-ascorbic acid (4.56 mg), 1 M HCl (336 μL), 400 μL of a ^{188}Re solution from the generators (PZC and alumina), and 120 μL of a stannous chloride solution (3.80 mg/mL of $SnCl_2 \cdot 2H_2O$/0.6 M HCl) were added. The reaction mixture was allowed to react in boiling water for 30 min. The final pH of the reaction mixture was 0.7. Radiochemical yield of ^{188}Re-HEDP was determined silica gel TLC (Merck No. 5735/acetone) and paper chromatography (Whatman No. 1/0.9% NaCl). The distribution of ^{188}Re in TLC and PC was measured with a radioanalytic imaging system (AMBIS-100).

^{188}Re-MAG3[10]: To 0.55 mg of S-Bz-MAG3, 450 μL of 0.1 M HCl and 450 μL of a freshly prepared $SnCl_2 \cdot 2H_2O$ in 0.1 M citrate-buffer (pH = 5) (6 mg / mL of $SnCl_2 \cdot 2H_2O$) were added. The reaction mixture was vigorously stirred by ultrasonic waves and 300 μL of a ^{188}Re solution from the generators was added. After stirring the solution by vortex, the mixture in a closed vial was allowed to react in boiling water for 30 min. The mixture was cooled on ice for 5–10 min. The final pH of the reaction mixture was 2.4. After the solution was filtered through a 0.22 μm filter, radiochemical yields of ^{188}Re-MAG3 were determined by HPLC (Hypersil BDS-5C18, 4.6 × 150 mm, Chemco Science Co., Japan) using 4% EtOH - 0.01 M phosphate buffer (pH = 7) at 1 mL/min of a flow rate. The liquid chromatograph used was a Waters 2690 separations module equipped with a Waters 996 photodiode array detector and a radio-HPLC detector (Packard Radiomatic 515TR).

3. Results and Discussion

3.1. Adsorption yield of ^{188}W to the PZC column. After an non-adsorbed ^{188}W was removed by the decantation and washing the column with 0.9% NaCl, adsorption yield of ^{188}W to the PZC column was determined. Adsorption yield of ^{188}W to PZC was 70–95% and was almost the same as that of ^{99}Mo.[8]

3.2. Elution behavior of ^{188}Re from the PZC generator. Elution profile of ^{188}Re from the PZC generator with 0.9% NaCl solution was investigated 12 days to 154 days after the column preparation, as shown in Figure 1. More than 90% of ^{188}Re was eluted from the PZC generator in the first 4 mL of the effluents, however no ^{188}Re was eluted from the alumina-based generator in the first few milliliters (the volume depends on column size). It is due to the fact that ^{188}W distributed uniformly in the PZC column whereas ^{188}W adsorbed on the top of alumina column. Furthermore, the elution profile was reproducible for 154 days after the column preparation. The flow rate of generators was influenced by the conditions of column preparation and was different ranging from 0.4 to 2.4 mL/min. However, the difference of the flow rate of generators in this range did not influence the elution profile of ^{188}Re.

Figure 2 shows the elution yields of ^{188}Re from the PZC generators. Though the elution yield of ^{188}Re decreased gradually from 75% with increasing elapsed time, it was 56–60% even after 154 days. Decrease of the elution yield with increasing

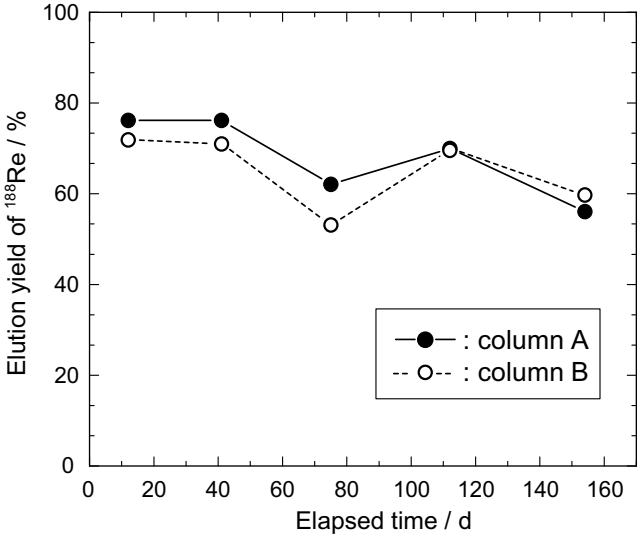

Figure 2. Elution yield of ^{188}Re.

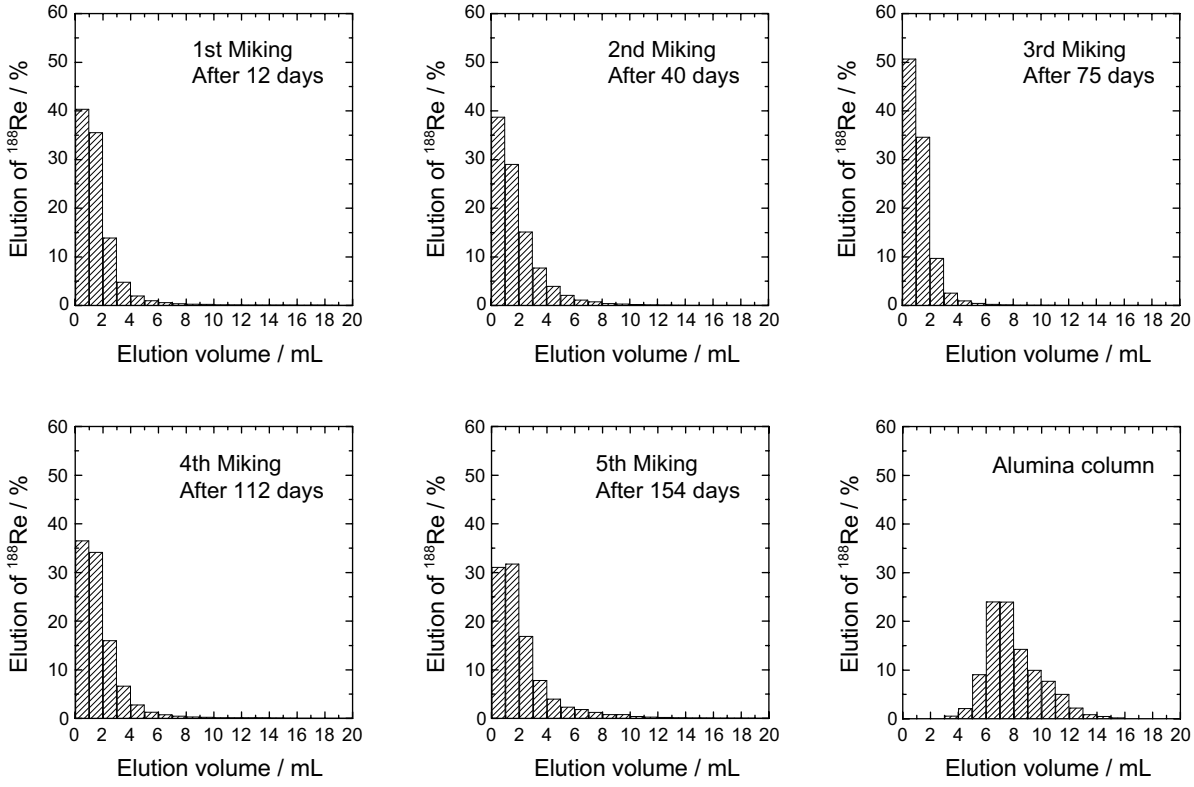

Figure 1. Elution behavior of ^{188}Re from the PZC generator (PZC column: 8 mmϕ × 32 mm, alumina column: 10 mmϕ × 60 mm).

elapsed time was also observed for $^{99}Mo/^{99m}Tc$ PZC generators.[7] And, the same phenomenon was also observed for the alumina based $^{188}W/^{188}Re$ generator systems.[5, 11] The elution yield of ^{188}Re from the alumina generator decreased gradually from 80% to 64% within 3 months.[5]

3.3. Breakthrough of ^{188}W. Breakthrough of ^{188}W was defined as the ratio of ^{188}W radioactivity to ^{188}Re radioactivity in the ^{188}Re effluents. The radioactivity of ^{188}W in the ^{188}Re effluent at the 3rd milking (27 days after the column preparation) was determined by extrapolation of the radioactivity of the daughter ^{188}Re after decaying the initial ^{188}Re, as shown in Figure 3. The breakthrough of ^{188}W was 0.03% and two times higher than ^{99}Mo breakthrough of Radiopharmaceuticals Low Limit of Japan (0.015%). However, the ^{188}W breakthrough can be reduced by using an alumina column as the second column.[12]

3.4. Labeling of HEDP and MAG3 with ^{188}Re. Labeling of HEDP and MAG3 with ^{188}Re eluted from the PZC generator and the alumina-based generator was investigated. The labeling yield of ^{188}Re-HEDP and ^{188}Re-MAG3 was more than 90%, respectively. There are no significant different in the labeling yield of ^{188}Re-HEDP and ^{188}Re-MAG3 prepared with different ^{188}Re source.

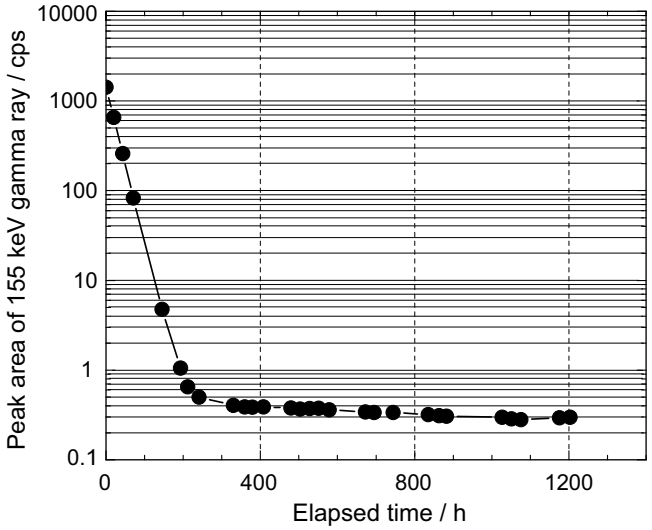

Figure 3. Determination of ^{188}W breakthrough in the ^{188}Re effluent.

4. Conclusion

The adsorption yield of ^{188}W to PZC was 70–95%. More than 90% of ^{188}Re was eluted in the first 4 mL. The ^{188}Re elution yields were 60–75% during 154 days corresponding to twice of the half-life of ^{188}W (69.4 d). The parent ^{188}W breakthrough was 0.03% by measuring γ-rays of the daughter ^{188}Re. And, the labeling yields of HEDP and MAG3 with ^{188}Re eluted from the PZC column were high enough and equal to the results using ^{188}Re eluted from the alumina system. The $^{188}W/^{188}Re$ PZC generator prepared with a low radioactivity (a few MBq) of ^{188}W indicated a good performance for the practical use. However, further investigation on various kinds of characteristics which might be affected by higher radioactivity of ^{188}W is needed.

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