Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

Polymeric Titanium Oxychloride Sorbent for $^{188}W/^{188}Re$ Nuclide Pair Separation

Le Van So[a]; C. D. Nguyen[b]; P. Pellegrini[a]; V. C. Bui[b]
[a] Radiopharmaceutical Research Institute, Australian Nuclear Science & Technology Organisation, Menai NSW, Australia [b] Nuclear Medicine Department, ChoRay Hospital, VN

To cite this Article So, Le Van , Nguyen, C. D. , Pellegrini, P. and Bui, V. C.(2009) 'Polymeric Titanium Oxychloride Sorbent for $^{188}W/^{188}Re$ Nuclide Pair Separation', Separation Science and Technology, 44: 5, 1074 — 1098
To link to this Article: DOI: 10.1080/01496390902728819
URL: http://dx.doi.org/10.1080/01496390902728819

Separation Science and Technology, 44: 1074–1098, 2009

ISSN: 0149-6395 print/1520-5754 online
DOI: 10.1080/01496390902728819

Taylor & Francis
Taylor & Francis Group

Polymeric Titanium Oxychloride Sorbent for $^{188}W/^{188}Re$ Nuclide Pair Separation

Le Van So,[1] C. D. Nguyen,[2] P. Pellegrini,[1] and V. C. Bui[2]
[1]Radiopharmaceutical Research Institute, Australian Nuclear Science & Technology Organisation, Menai NSW, Australia
[2]Nuclear Medicine Department, ChoRay Hospital, VN

Abstract: The chemical synthesis conditions ($TiCl_4$: iPrOH reagent ratio and reaction temperature scheme) were optimized for the preparation of polymeric titanium oxychloride sorbent which met the requirements for clinically useful $^{188}W/^{188}Re$ generator production, such as high W-adsorption capacity, high ^{188}Re-elution yield, low ^{188}W-breakthrough, and good mechanical stability. This polymeric material was formed by polycondensation of titanium-oxychloride units, the chemical formula of which was supposed as $[OTiO\ (Ti_{40}\ Cl_{80}\ (OH)_{80}\ (TiO_2)_{95}.60H_2O)\ OTiO]_n$. The effect of the W-content of tungstate solution on the WO_4^{2-} ion adsorption (with minimizing the poly-tungstate ion adsorption) and its covalent bonding with the Ti metal atoms in the polymeric matrix were justified with respect to the optimal W-adsorption conditions for the preparation of a useful $^{188}W/^{188}Re$ generator column. The high W-adsorption capacity of about 515.6 mg W/g sorbent and ^{188}Re elution yield of higher than 85% were achieved. The large difference in the distribution ratio values found for alumina and polymeric titanium oxychloride sorbent in 0.005% NaCl solution ($D_{W,\ Re\text{-}188} = 50$ and $D_{W,\ Re\text{-}188} = 1.0$, respectively) offered an advantage for the preparation of a consecutive-elution based ^{188}Re generator system which combined both ^{188}Re elution and ^{188}Re concentrating processes in one portable system. This generator system is of a tandem column type which consists of a polymeric titanium oxychloride sorbent coupled to an alumina column. This system gave a ^{188}Re concentration factor of approximately 10. The overall ^{188}Re yield achieved from this system was >80%. ^{188}W isotope and elemental

Received 8 August 2008; accepted 3 November 2008.

Address correspondence to Le Van So, Radiopharmaceutical Research Institute, Australian Nuclear Science & Technology Organisation, New Illawarra Road, Lucas Heights, P.M.B. 1, Menai NSW 2234, Australia. Tel.: +61 2 97179725. E-mail: slv@ansto.gov.au

tungsten breakthrough were not detected in its ^{188}Re eluate. This system thus offers a potential application for clinically useful ^{188}Re production using low specific radioactivity ^{188}W (around 500 mCi/g) producible in a medium neutron flux reactor.

Keywords: Concentration of ^{188}Re-perrhenate solution, high tungsten adsorption capacity sorbent, inorganic polymer, ^{188}Re generator, titanium-dioxide

INTRODUCTION

The ^{188}W nuclide is a β^- emitter ($T_{1/2} = 69.4$ d), its daughter nuclide ^{188}Re ($T_{1/2} = 16.94$ h, $E_{mean,\ \beta-} = 763$ KeV with 99.9% intensity, mean β^- dose: 0.762 MeV/Bq-s). The useful half-life and β^- radiation energy and the convenient labeling process (adaptable from ^{99m}Tc radiopharmaceuticals) make this radioisotope of great interest for radiotherapeutic application. ^{188}Re is produced from a ^{188}W/^{188}Re generator in which ^{188}W is produced using the double neutron capture reaction ^{186}W (nn, γ) ^{188}W. The ^{188}W parent nuclide currently produced in a high neutron flux ($>10^{15}$ $n \cdot cm^{-2} \cdot s^{-1}$) reactor accessible in only a handful of countries in the world (8–13) has ^{188}W specific radioactivity of 5–10 Ci/g W. This specific activity is effectively used only for a ^{188}Re generator, in which a sorbent of W-adsorption capacity higher than 150 mg W/g sorbent is applied (7, 8, 13, 16, 28). Today the alumina based ^{188}Re generators are commercially available. This type of ^{188}Re generator has a low ^{188}W radioactivity (from 250 mCi to 1.0 Ci ^{188}W for each generator unit) due to the moderate W-adsorption capacity of alumina (around 150 mg W/g alumina) (8–16). Consequently, a ^{188}Re solution of rather limited ^{188}Re concentration (around 100 mCi ^{188}Re/mL) is also produced from this type of ^{188}Re generator. So, the complex automated ^{188}Re concentrating systems coupled with this generator are needed to enhance the ^{188}Re concentration to a value of from 0.5 Ci to 1.0 Ci ^{188}Re per mL (14, 15, 23–27), which can be useful for targeting radiotherapeutic application. However, this production route may cause a problem of cost-ineffective ^{188}Re production due to the high cost of the complex automation system. Despite the enhanced ^{188}Re concentration improved by the automated concentrating system, both the cost-ineffectiveness and the shortage in ^{188}W/^{188}Re generator producers as mentioned above may disadvantageously affect the wide application of the ^{188}Re radionuclide. To increase the clinically useful ^{188}Re generator availability for the increased demand of its radiotherapeutic application, the ^{188}W/^{188}Re generator production from lower specific radioactivity ^{188}W solution producible in the medium neutron flux ($>2.10^{14}$ $n \cdot cm^{-2} \cdot s^{-1}$) reactors operated in many countries should be

promoted. For this purpose, the availability of the sorbents with much higher ^{188}W-adsorption capacity (compared to the alumina which is currently used for ^{188}Re generator) for an alternative ^{188}Re generator production route should be anticipated. Moreover, the requirement of high ^{188}Re-concentration solution applicable for targeting radiopharmaceutical preparation could also be fulfilled with a rather compact generator system using a sorbent of high ^{188}W-content (or high W-adsorption capacity). Some approaches were investigated years ago to increase the generator radioactivity based on the generator columns of higher W-content. Hydroxyapatite, the hydrous oxides of zirconium, titanium, manganese, tin (IV), and cerium, silica gel, the AG 1-X12 anion and AG 50 W-X12 cation exchange resins and activated charcoal were studied for W-adsorption and ^{188}Re elution (1–3, 8). Unfortunately, all these materials showed an unimproved W-adsorption capacity compared to alumina. Some developments involved the assessment of columns based on zirconium- or titanium-tungstate gels and chloride functional zirconium-silica sorbents (17–22). All these sorbents contained a higher W-content compared to alumina, but still gave, to some extent, lower ^{188}Re elution performance. A polymeric zirconium compound (PZC) has recently been investigated for ^{188}Re and ^{99m}Tc generator column packing (4, 5, 6). This material showed a high adsorption capacity for both tungstate and molybdate ions. The PZC sorbent based ^{188}Re and ^{99m}Tc generators were also prepared and gave clinically applicable ^{188}Re and ^{99m}Tc eluates, respectively. However, the approx. 7 mL 0.9% NaCl solution needed to elute ^{188}Re-perrhenate from the one gram weight PZC column (4) is still far from the goal of using low specific radioactivity ^{188}W for clinically useful ^{188}Re generator production. Therefore this area requires further development of new sorbents with high W-adsorption capacity and desired ^{188}Re-elution properties for the preparation of a high radioactivity ^{188}W/^{188}Re generator capable of producing a ^{188}Re solution of high ^{188}Re-concentration. As a contribution to this further development, an investigation into the use of polymeric titanium-oxychloride (PTC) material (a member of the polymeric tetravalent metal oxychloride compound group like PZC material) as a sorbent for ^{188}Re generators is presented in this paper.

EXPERIMENTAL

Materials and Reagents

$TiCl_4$, $Na_2WO_4 \cdot 2H_2O$ and isopropyl alcohol (iPrOH) of "Reagent" grade were supplied by Merck. All other chemicals used for experiments

were of analytical grade.^{188}W solution was supplied by RIAR (Russia) and alumina-A adsorbent by ICN Biomedicals (Germany).

Radioactivity Measurement, Radionuclide Calibration, and Elemental Analysis

The radioactivity of ^{188}W and ^{188}Re radioisotopes was calibrated using a CAPINTEC Dose calibrator. Radioactivity measurement and radionuclide identification were carried out at the 155.04 keV and 290.67 keV photonpeaks for ^{188}Re and ^{188}W, respectively, using an ORTEC gamma-ray spectrometer coupled with a high purity Ge detector. The gamma ray energy and radioactivity calibration of this analyzer system was performed using a ^{152}Eu radioisotope solution standard. Generator elution profiles were recorded using a HPLC radioisotope detector coupled with an analyzer supported by LAURA computer software. The determination of tungsten concentration in the solution was carried out by photocolorimetry at the 398 nm wavelength with colored tungsten (V)-thiocyanate complex formed by reduction of tungsten (VI) to the five-valence state with titanium (III) chloride.

Preparation, Characterization, and Properties of PTC Sorbent

PTC sorbent was synthesized from iPrOH and $TiCl_4$ under strictly controlled conditions. Different reaction temperature schemes and $TiCl_4$: iPrOH reagent ratios were applied in order to optimize the synthesis of the PTC sorbent product suitable for the ^{188}Re generator preparation.

In one synthesis series, variable $TiCl_4$: iPrOH reactant ratios were applied, but the reaction temperature scheme 93°C → 112°C → 125°C remained unchanged (see Table 1). This synthesis series was performed in order to find out the suitable reactant ratio for the PTC material preparation, as follows: A given amount of $TiCl_4$ was carefully added to different amounts of iPrOH. The temperature of the reaction mixture was 93°C at the end of the $TiCl_4$ reactant addition. This solution became viscous after keeping the solution at this temperature for 4 hours using a thermostat. Then the temperature of this viscous solution was increased to 112°C by more intensively heating the reaction mixture. At this time a water-soluble PTC gel (the intermediate precursor) was very quickly formed. By further heating the reaction mixture to 125°C, the water-insoluble, solid PTC material of particle sizes of 0.10 mm to 0.01 mm was slowly formed. Keeping the temperature of reaction mixture at 125°C for 45 minutes made the formation of solid PTC material

Table 1. Synthesis conditions (variable ratio of reactants) and W-adsorption characteristics of the PTC material

Synthesis number	$TiCl_4$ Weight (g)	Volume of iPrOH (mL)	Reaction temperature scheme	Particle size of PTC material (mm)	Swelling in H_2O (% volume)	W-adsorption capacity (mgW/g PTC)*	^{188}Re elution yield (%)**	W-break through (%)***
S-1	40.7	40	93°C→112°C→125°C	0.1–0.001	220.4	485.2	88.1	0.01
S-2	40.7	80	93°C→112°C→125°C	0.1–0.001	26.3	515.1	90.4	0.02
S-3	40.7	100	93°C→112°C→125°C	0.15–0.001	29.6	518.2	94.3	0.03

*The W-adsorption capacity of PTC material was investigated with the 25.6 mg W/mL tungstate solution of pH = 7 at 50°C for 45 minute adsorption time (pH of post-adsorption solution was pH = 4.5). The 0.75 g PTC samples and the tungstate solutions of 431.25 mg W tungsten-content (corresponding to 575 mg W/g PTC) were used for W-adsorption experimentals.

**3 mL 0.9% NaCl solution was used for the ^{188}Re elution from ^{188}W-contained PTC columns. ^{188}Re elution yield (%) = (Total ^{188}Re activity in 3 mL eluate/Total ^{188}Re activity in the ^{188}W-contained PTC column) × 100.

***W-breakthrough (%) = (Total W-content in 3 mL ^{188}Re-eluate/Total W-content of PTC column) × 100.

complete. This solid PTC material was used for further evaluation with respect to its applicability for ^{188}Re generator preparation.

In another synthesis series, different reaction temperature schemes were applied, while the $TiCl_4$: iPrOH reactant ratio remained unchanged at the value of 40.7 g $TiCl_4$: 80 mL iPrOH (see Table 2). The 93°C → 112°C → 125°C, 93°C → 112°C → 140°C and 93°C → 112°C → 160°C reaction temperature schemes were applied. The synthesis procedure was the same as mentioned above, except the heating temperature at the final stage of synthesis for solid PTC particle formation. This synthesis series was to investigate the effect of reaction temperature on the properties of the PTC material. The obtained materials were used for further evaluation with respect to its applicability for ^{188}Re generator preparation as mentioned above.

Investigation on the chemical composition, structure, and physicochemical properties of the PTC sorbent was carried out as follows. Ti content of the sorbents was analyzed gravimetrically by ignition of the sorbent samples at 1200°C for two hours. TiO_2 weight was measured and the Ti content calculated. The carbon, hydrogen, and oxygen elemental content of PTC sorbent samples were determined by thermal decomposition of the sorbents on a PerkinElmer 2400 II Elemental Analyzer instrument. The chlorine content of the sorbent was analyzed by thermal decomposition of sorbent samples. The decomposed product, HCl, was trapped in an alkaline solution and the Cl^- content was determined by ion chromatography. Thermal analysis of the sorbent samples was carried out on MB-7H derivatographer instrument with N_2 gas flow rate of 50 mL/min and a heating rate of 10°C/min. Potentiometric titrations of PTC sorbent samples were carried out with 0.1 g PTC sorbent samples in 60 mL 0.1 M NaCl solution. The titration solution was 0.1 M NaOH.

Investigation on the W Adsorption and ^{188}Re Elution

15 mL radioactive tungstate solution (containing around 5–10 mCi ^{188}W radioactivity) of 25.6 mg W/mL concentration (pH = 7) was added to the PTC samples of 0.75 g weight which were then gently shaken in a water bath at 50°C for 45 minutes. The samples were then left to stand and a portion of the clear supernatant solution was taken out to measure the ^{188}W radioactivity (for the W-adsorption capacity calculation) and then the remaining solution was decanted to get the solid sorbent portion. This solid ^{188}W-contained PTC sample was packed in an 8 mL glass column and washed with 50 mL water followed by 10 mL 0.9% NaCl solution. The first ^{188}Re elution was started after 120 hours of equilibration time and an elution was conducted every 3 days with 3 mL 0.9% NaCl

Table 2. Effect of reaction temperature schemes on the performance of the PTC material

Synthesis number	$TiCl_4$ weight (g)	Volume of iPrOH (mL)	Reaction temperature scheme	Particle size of PTC material (mm)	Swelling in H_2O (% volume)	W-adsorption capacity (mgW/g PTC)**	^{188}Re elution yield (%)***	W-break through (%)****
S-4*	40.7	80	93°C→112°C→125°C	0.1–0.001	26.1	512.3	91.2	0.02
S-5	40.7	80	93°C→112°C→140°C	0.08–0.001	18.2	215.3	70.5	0.02
S-6	40.7	80	93°C→112°C→160°C	0.08–0.001	10.3	160.5	64.3	0.01

*The reaction condition was the same as used for the synthesis number S-2 in Table 1.

**The W-adsorption capacity of PTC material was investigated with the 25.6 mg W/mL tungstate solution of pH = 7 at 50°C for 45 minute adsorption time (Post-adsorption solution was pH = 4.5). The 0.75 g PTC samples and the tungstate solutions of 431.25 mg W tungsten-content (corresponding to 575 mg W/g PTC) were used for W-adsorption experiments.

***3 mL 0.9% NaCl solution was used for the ^{188}Re elution from ^{188}W-contained PTC columns. ^{188}Re elution yield (%) = (Total ^{188}Re activity in 3 mL eluate/Total ^{188}Re activity in the ^{188}W-contained PTC column) × 100.

****W-breakthrough (%) = (Total W-content in 3 mL ^{188}Re-eluate/Total W-content of PTC column) × 100.

solution. The ^{188}Re elution yield and W-breakthrough were determined for each elution.

The effect of the W-content of tungstate solution on the W-adsorption capacity and ^{188}Re elution performance (^{188}Re elution yield and W-breakthrough) was investigated as follows. The variable volumes (corresponding to variable W-contents) of the radioactive tungstate solution (containing around 1 mCi ^{188}W radioactivity) of 25.6 mg W/mL concentration (pH = 7) were added to PTC samples of 0.2 g weight, then gently shaken in a water bath at 50°C for 45 minutes. The samples were then left to stand and a portion of the clear supernatant solution was taken out to measure the ^{188}W radioactivity for the W-adsorption capacity calculation and then the remaining solution was decanted to get the solid sorbent portion which was then packed onto a 2 mL glass column. These ^{188}W-contained PTC columns were washed with 5 mL water followed by 5 mL 0.9% NaCl solution. After this step, the first ^{188}Re elution was started after 113 hours of equilibration time (100% of maximum equilibrium ^{188}Re radioactivity achievable at $t_{max} = 113.3$ hours maximum equilibrium time for ^{188}W-^{188}Re decay process) and an elution was conducted every 3 days with 1 mL 0.9% NaCl solution.

The above procedure was also used to investigate the effect of the adsorption time on the ^{188}W adsorption and ^{188}Re elution when the variable adsorption times from 35 to 60 minutes were applied.

Consecutive Elution Based ^{188}Re Generator using PTC Sorbent Column

The distribution ratio ($D_{W,\ Re\text{-}188}$) of ^{188}Re-perrhenate ions in the variable concentration NaCl solutions for alumina and for non-radioactive tungsten-saturated PTC (W-PTC) sorbents were investigated using the method described in our previous paper [30]. Before the start of $D_{W,\ Re\text{-}188}$ measurement, the sorbents were chemically treated as follows: Alumina was first conditioned with 0.1 M HCl solution and washed with water until pH = 5. Then it was dried at 80°C for two hours and the 0.75 g portions were weighed into the vials used for the $D_{W,\ Re\text{-}188}$ measurement. PTC samples were treated as follows: 15 mL non-radioactive sodium-tungstate solution of 25.6 mg W/mL concentration (pH = 7) were added to the PTC samples of 0.75 g weight. The total W-content of tungstate solution was 431.25 mg W, corresponding to 575 mg W per 1 g PTC sample. This mixture was then gently shaken in a water bath at 50°C for 45 minutes. The sorbent samples were then filtered and washed to pH = 5 with the relevant NaCl solution. Then the samples were collected into the vials for the $D_{W,Re\text{-}188}$ determination. Based on the obtained result of the $D_{W,\ Re\text{-}188}$ study, a tandem column system was

designed for eluting and concentrating the ^{188}Re eluate. The investigation of the ^{188}Re eluting-concentrating process was carried out by eluting ^{188}Re from the ^{188}W-contained PTC (^{188}W-PTC) column with 0.005% NaCl solution and then this eluate was passed through a small alumina column where all the $^{188}ReO_4^-$ was retained. Then the $^{188}ReO_4^-$ was eluted with a small volume of physiological 0.9% NaCl solution from the alumina column to enhance the ^{188}Re concentration in its eluate.

RESULT AND DISCUSSION

Synthesis and Characterization of PTC Material

The PTC material appearance varied from light yellow-brown to dark brown in color. The color of PTC materials became darker when the temperature at the final stage of the synthesis process for solid PTC particle formation was higher. Its appearance changed to white when soaked in water. It swelled well in water and was hydrolyzed to give an acidic solution while the solid PTC material matrix remained insoluble. As seen in Table 1, an increase in the iPrOH: $TiCl_4$ reactant ratio brought about a higher degree of swelling of sorbent particles in aqueous solution. This may improve the diffusion of the tungstate ions into the solid matrix of the PTC materials during the adsorption process. However, the swelling gave rise to a decrease in the mechanical stability of the solid PTC particles. So, the PTC material of moderate swelling, which was obtained at synthesis number S-2 (see Table 1), was preferable.

In Table 2, the investigation result of the effect of reaction temperature schemes on the performance of the PTC material was presented. The increasing reaction temperature at the final stage of solid PTC material formation caused a shrinking of PTC particle. The swelling of the PTC in water was strongly reduced from 26.1% to 10.3%, when the temperature at the final stage of the synthesis process changed from 125°C to 160°C (see Table 2). Consequently, the PTC particles became smaller and the W-adsorption capacity and ^{188}Re elution yield was significantly reduceds, however, the ^{188}W breakthrough changed to a smaller extent. Based on the results obtained in Tables 1 and 2 , it was stated that the W-adsorption capacity and ^{188}Re elution yield of the PTC material were more strongly affected by the reaction temperature than by the the iPrOH: $TiCl_4$ reactant ratio applied for the synthesis.

For the purpose of the $^{188}W/^{188}$Re generator preparation, the PTC sorbent of high W-adsorption capacity and high ^{188}Re elution yield, as well as the low W-breakthrough and good mechanical stability should be preferable. It is obvious that the PTC material from the synthesis

number S-2 and/or S-4 as shown in Tables 1 and 2 met all requirements listed above. So, the synthesis number S-2 was chosen for the preparation of the PTC sorbent applicable for the $^{188}W/^{188}Re$ generator technology. This PTC sorbent material is mentioned in all further studies of the following sections as a PTC-sorb sorbent.

Characterization of PTC-Sorb Sorbent

The PTC-sorb sorbent was prepared with the reaction conditions of the synthesis number S-2 described above (Table 1). The synthesis condition and the main adsorption-elution properties of the PTC-sorb sorbent are summarized in Table 3. As for the adsorption experiments, to avoid the additional adsorption of poly-tungstate ions onto the PTC-sorb (which might cause a variable W-adsorption capacity as discussed in the following section based on the saturation-characteristics of the plateau on the W-adsorption vs. W-content curve in the range of from 575 to 675 mg W of the tungstate solution shown in Fig. 2.) the following optimal conditions was applied. These conditions are found in the Tables 1–3.

The results of the chemical and thermal analysis of the PTC-sorb sorbent were shown in Table 4. As shown in Fig. 1, 34.14% weight loss below 202°C was attributed to HCl released from the PTC-sorb sorbent. This HCl amount corresponded to a chlorine content of 18.965% weight of the PTC-sorb. The HCl released from the PTC-sorb can be explained based on the 110°C boiling point of an azeotropic solution of HCl at 760 mm Hg pressure. In the range of from 202°C to 500°C, the crystalline water loss was followed by the structural water loss. The loss of structural water at a higher temperature than 353.6°C might cause a considerable change in the PTC-sorb structure. This supposition was based on the presence of a well-defined exothermic peak at 427.7°C on the DTA curve of Fig. 1. This exothermic peak was attributed to a crystalline phase transformation following the structural water decomposition. The similar structural water decomposition-followed-by a crystalline phase change process was also observed for the thermal decomposition of several polymeric inorganic ion exchangers (33). This possible crystalline-phase transformation in the PTC-sorb was proposed based on the anatase-rutile structural transformation of titanium dioxide powders at the 455°C exothermic peak reported in the literature (31) and on the similarity in chemical composition between the thermally decomposed PTC-sorb and titanium-dioxide. Based on the chemical and thermal analysis results (Table 4), the molecular formula of PTC-sorb was proposed as follows:

$$[OTiO(Ti_{40}Cl_{80}(OH)_{80}(TiO_2)_{95}.60H_2O)OTiO]n.$$

Table 3. Synthesis condition and adsorption-elution characteristics of the PTC-sorb sorbent

Sorbent	$TiCl_4$ weight (g)	Volume of iPrOH (mL)	Reaction temperature scheme	Particle size of PTC-sorb (mm)	Swelling in H_2O (% volume)	Tungsten adsorption capacity (mgW/g PTC-sorb)*	^{188}Re elution yield (%)**	W- break-through (%)***
PTC-sorb	40.7	80	93°C→112°C→125°C	0.1–0.001	26.2 ± 0.6	515.6 ± 0.8	91.1 ± 1.1	<0.02

*The W-adsorption capacity of PTC-sorb sorbent was investigated with the 25.6 mg W/mL tungstate solution of pH = 7 at 50°C for 45 minute adsorption time (pH of post-adsorption solution was pH = 4.5). The 0.75 g PTC-sorb samples and the tungstate solutions of 431.25 mg W tungsten-content (corresponding to 575 mg W/g PTC-sorb) were used for W-adsorption experiments.

**3 mL 0.9% NaCl solution was used for the ^{188}Re elution from ^{188}W-contained PTC-sorb columns. ^{188}Re elution yield (%) = (Total ^{188}Re activity in 3 mL eluate/Total ^{188}Re activity in the ^{188}W-contained PTC-sorb column) × 100.

***W-breakthrough (%) = (Total W-content in 3 mL ^{188}Re-eluate/Total W-content of PTC-sorb column) × 100.

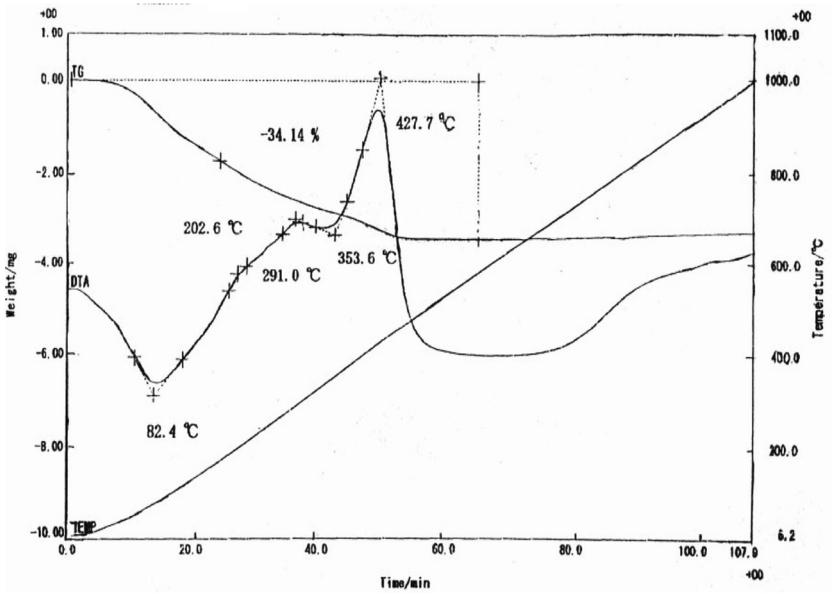
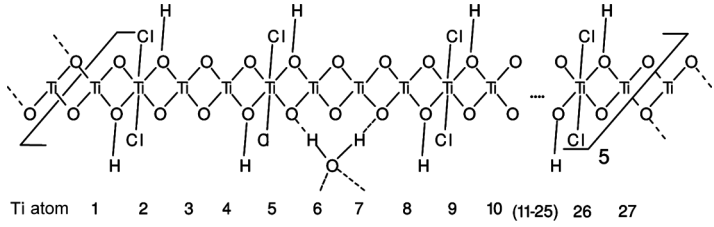


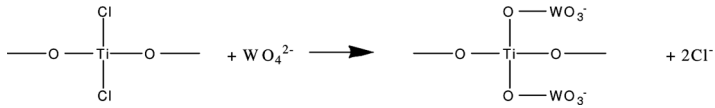
Figure 1. Typical thermoanalysis of PTC-sorb sorbent.

Bonding of atoms in a unit of this formula is expected as below.



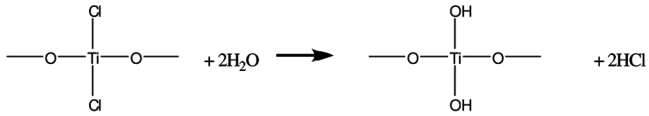
The molecular mass of the PTC-sorb molecular unit is 4939.56. The chlorine content is 5.35 millimol Cl/g PTC-sorb. It is assumed that the adsorption of the tungsten on the PTC-sorb involves the replacement of chloride ions by tungstate ions. Supposing that the tungstate ions adsorbed on PTC in the form of WO_4^{2-}, and one mole of WO_4^{2-} ion replacing two moles of Cl^- ion in PTC-sorb, an adsorption capacity of 491.8 mg W/g PTC-sorb should be expected. This value was comparable to the experimental W-adsorption capacity of 515.6 mg W/g PTC-sorb as shown in Table 3. The 23.8 mg W/g PTC-sorb difference (corresponding to about 5% of experimental value) between the calculated and

experimental results might be attributed to the inherent possible polymerization of tungstate ions in acidic solution (32), which is discussed in the following sections. The strong adsorption of the tungsten on the PTC-sorb was attributed to the covalent bond formation between the tungstate ion and the Ti metal atoms in the polymeric matrix. The W adsorption reaction can be assumed as follows.

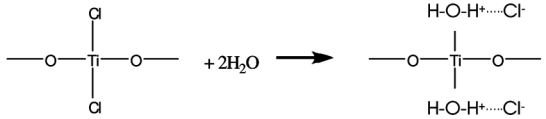


The PTC-sorb was hydrolyzed, but not dissolved, in aqueous solution and gave an acidic solution of pH = 1.4 in water. The hydrolysis reactions of the PTC-sorb sorbent can be described with two following reactions:

Hydrolysis reaction 1

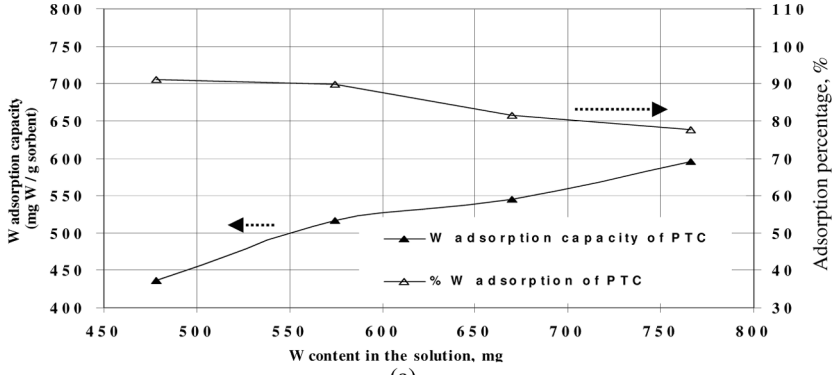


Hydrolysis reaction 2

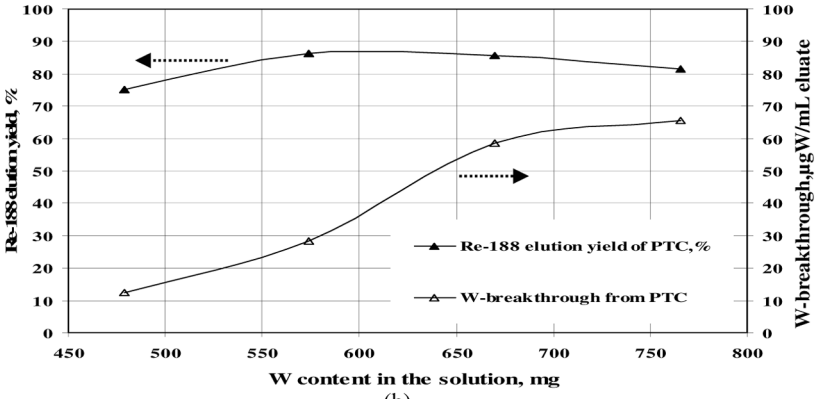


The potentiometric titration of the HCl contents released from the two above-mentioned hydrolysis reactions showed a value of 5.35 meq OH^-/g PTC-sorb at pH = 11, corresponding to 5.35 meq H^+ decomposed per gram

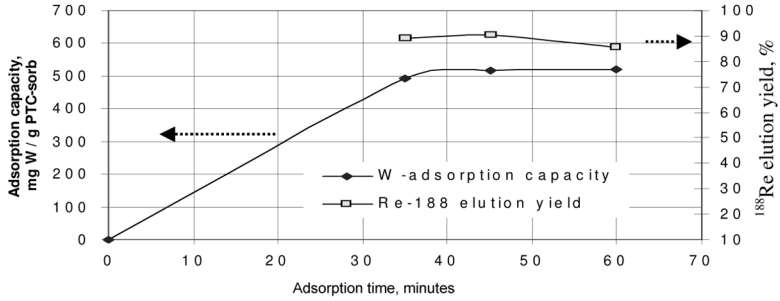
Figure 2. Effect of the W-content of tungstate solution on the W-adsorption capacity of the PTC-sorb sorbent (a) and on the ^{188}Re elution yield and W-breakthrough of ^{188}Re eluate (b) and W-adsorption of the PTC-sorb sorbent and corresponding ^{188}Re elution yield vs. adsorption time (c). (The values on the abscissa in Figs. 2a and 2b were referred to 1 gram PTC-sorb. For the adsorption experiments a and b, the 25.6 mg W/mL tungstate solution of pH = 7 at 50°C was used; pH of post-adsorption solution was 4.5; 45 minute adsorption time was applied; 0.2 g PTC-sorb samples were used; Adsorption percentage (%) = 100 × [W-adsorption capacity/W-content of solution]. For experiment c, the adsorption conditions were the same as in experiments a and b, except the adsorption time was variable. For the ^{188}Re nuclide elution process, ^{188}Re was eluted from the ^{188}W-PTC-sorb column with 1 mL 0.9% NaCl solution; ^{188}Re elution yield (%) = (Total ^{188}Re activity in 1 mL eluate/Total ^{188}Re activity in the ^{188}W-contained PTC-sorb column) × 100.)



(a)



(b)



(c)

Figure 2. Continued.

PTC-sorb. It was assumed that a free HCl amount (4.35 meq), which was completely released from the hydrolysis reaction 1, was easily neutralized up to pH = 7 and then the further neutralization of 1.0 meq H^+(for hydrogen-bonding proton in hydrolysis reaction 2) was to some extent weaker,

Table 4. Chemical composition of the PTC-sorb sorbent

Element and compound	Cl	H	Ti	O	H_2O
Content (% weight)	18.965	0.535	43.870	29.33	7.300
Atomic ratio	0.584	0.584	1.0	2.001	0.443

followed in the range of from pH = 7 to pH = 11. As seen in the hydrolysis reactions 1 and 2, total H^+ amount of 5.35 meq H^+/g PTC-sorb achieved above corresponded to 5.35 meq Cl^-/g PTC-sorb. This Cl^- content value agreed with the chlorine content of PTC-sorb which was found in the thermal analysis mentioned above. This result also confirmed the above proposed molecular formula for the PTC-sorb sorbent. The correspondence between the NaOH quantity added for potentiometric titration of the PTC-sorb up to pH = 11 and the chlorine content of PTC-sorb meant that the potentiometric titration result can be used for the calculation of W-adsorption capacity of the PTC-sorb sorbent. This W-adsorption capacity calculation was based on the stoichiometric equation $-[TiO_2Cl_2]-+WO_4^{2-}=-[TiO_2\,WO_4]-+2Cl^-$, which was deduced from the W-adsorption reaction described above.

W Adsorption and ^{188}Re Elution Performance of PTC-Sorb Sorbent

The effect of the W-content of the ^{188}W-contained tungstate solution on the W-adsorption capacity and on the ^{188}Re-elution performance of the PTC-sorb was investigated. The results presented in Fig. 2 revealed the fact that the W-adsorption capacity of the PTC-sorb and the W-breakthrough from the ^{188}W-contained PTC-sorb (^{188}W-PTC-sorb) column increased with the increasing W-content of the tungstate solution used for the adsorption in the range of from 675 to 775 mg W (per g PTC-sorb). This increase could be attributed to an additional non-covalent adsorption of poly-tungstate ions, which could form in the acidic solution. This weakly adsorbed poly-tungstate quantity was considered to be a reason of higher W-breakthrough from PTC-sorb columns of higher tungstate loading as experienced in this work. Moreover, this adsorbed poly-tungstate content may block the pathway of ^{188}Re perrhenate ion out-diffusion and cause the lower ^{188}Re elution yield as shown in Fig. 2b. However, the solution of lower W-content in the range of lower than 575 mg W resulted in an unsaturated adsorption of tungsten on the PTC-sorb. As a result of this process, some free and active (–TiOH) groups of high anion-affinity were left on the PTC-sorb surface. These active

groups might cause an increased retention of both ReO_4^- and WO_4^{2-} ion, thus reducing the ^{188}Re elution yield and W-breakthrough in the ^{188}Re eluate as found in Fig. 2b. To avoid an additional adsorption of poly-tungstate ions onto the PTC-sorb, the W-adsorption process should be carried out with a tungstate solution of 25.6 mg W/mL concentration (pH = 7) containing 575 mg W-content (referred to 1 g PTC-sorb). This justification was based on the saturation-characteristics of the plateau on the W-adsorption curve in the range of from 575 to 675 mg W-content of the tungstate solution as shown in Fig. 2. The plateau of the adsorption curve might suggest saturation in the WO_4^{2-} adsorption prior to the start of poly-tungstate ions adsorption. In this range of WO_4^{2-} adsorption, about 90% of the W-content of the tungstate solution was adsorbed by the PTC-sorb sorbent. This adsorption condition was considered to be optimal to give PTC-sorb columns the best performance for W adsorption and ^{188}Re elution.

The W-adsorption capacity and ^{188}Re elution of the PTC-sorb sorbent vs. adsorption time were shown in Fig. 2c. The W-adsorption capacity reached nearly constant value of around 515 mg W/g PTC-sorb after 35 minutes of reaction. The increase of the reaction time to 60 minutes might cause a slight decrease in the ^{188}Re elution yield which was around 90% for the 45 minute reaction time. The slight variation in the W-adsorption capacities and ^{188}Re elution yields found at the reaction times longer than 45 minutes was not considered significant. So, the time of $\geq$45 minutes was chosen as an adequate period for the complete W adsorption onto the PTC-sorb sorbent.

Single Column Based ^{188}Re Generator using PTC-Sorb Sorbent Column

Figure 3 shows the ^{188}Re elution profiles of the $^{188}W/^{188}Re$ generator in which 1 g weight PTC-sorb column was used. As seen, an elution volume of around 4 mL 0.9% NaCl solution was adequate to achieve more than 85%^{188}Re radioactivity from this size $^{188}W/^{188}Re$ generator column.

The improved elution profile, with the reduced ^{188}Re eluate volume (approx. 4 mL) in comparison to the 7 mL volume achieved with PZC (4) and alumina (8–11, 16) based generators has allowed for a more compact generator design using high specific radioactivity ^{188}W solution. This may eliminate the ^{188}Re concentrating process (14, 15, 23–27) which is currently used together with the commercially available single alumina column based ^{188}Re generators. This type of generator uses a high specific radioactivity ^{188}W solution which is available only from the high neutron flux reactors at Oak Ridge National Laboratory (USA) and the Research Instititute of Atomic Reactors (Russia). Despite the PTC-sorb

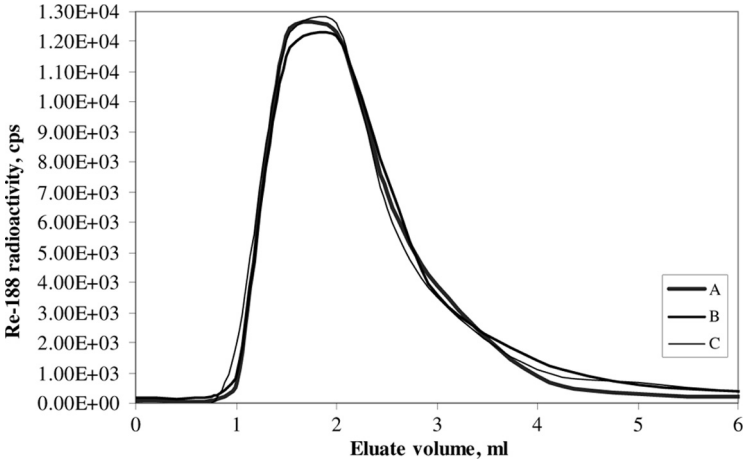


Figure 3. ^{188}Re elution of the ^{188}W/^{188}Re generator containing ^{188}W-PTC-sorb column The ^{188}Re elution profiles of three ^{188}W/^{188}Re generators (around 5 mCi ^{188}W each) which contained 1.0 g weight PTC-sorb column each (A, B and C generator contained 492.2 mg W, 515.1 mg W and 521.2 mg W adsorbed on the PTC-sorb column, respectively). 0.9% NaCl solution was used for the ^{188}Re elution from ^{188}W-contained PTC-sorb columns. ^{188}Re elution yield (%) = (Total ^{188}Re activity in 4 mL eluate/Total ^{188}Re activity in the ^{188}W-contained PTC-sorb column) × 100. (W-adsorption for ^{188}W-PTC-sorb column was performed at 50°C for 45 minutes with the radioactive tungstate solution (around 5 mCi ^{188}W activity) of 25.6 mg W/mL concentration and pH = 7; pH of post-adsorption solution was 4.5. The 1 g PTC-sorb and the tungstate solutions of 575 mg W tungsten-content were used.)

sorbent having a significantly improved adsorption-elution performance with a smaller volume elution, its application for the production of a single column based ^{188}Re generator using rather low specific radioactivity ^{188}W solution is still not too promising. Further investigation on more elution properties of the PTC-sorb sorbent was conducted and are discussed in the following section, which outlines its capability for high specific volume ^{188}Re generator production while maintaining a high value of tungsten adsorption capacity.

Consecutive Elution Based ^{188}Re Generator System

Despite the high W-adsorption capacity of the PTC-sorb sorbent and its good ^{188}Re-elution properties, an eluate of insufficient ^{188}Re concentration was normally obtained from the PTC-sorb column containing low

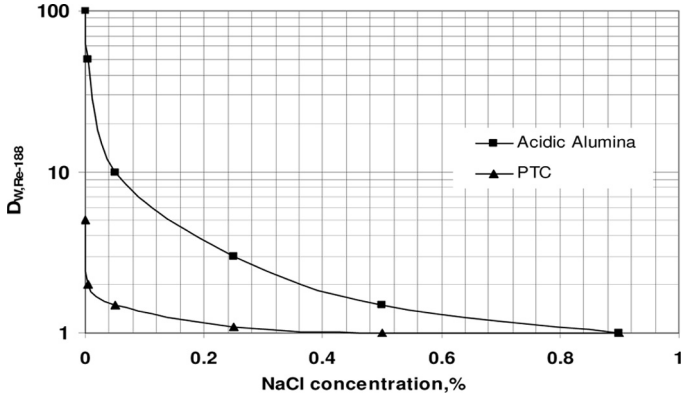


Figure 4. Distribution ratio of ^{188}Re-perrhenate ions for the alumina and PTC-sorb sorbent in the different NaCl solutions at pH = 5.

specific activity ^{188}W (^{188}W-PTC-sorb column). So, the elution of the ^{188}W-PTC-sorb column should be followed by concentrating the ^{188}Re eluate. To facilitate the use of this elution-followed-by concentrating procedure, the combination of both elution and concentrating processes in one generator system is a technical option to be developed.

To support this development, the distribution ratio ($D_{W,Re-188}$) of $^{188}ReO_4^-$ ions for different sorbents was measured and the obtained results are presented in Fig. 4. As shown, the big difference in the $D_{W,Re-188}$ values of alumina and PTC-sorb sorbent was found in a NaCl solution of concentration less than 0.005%.

Making use of this finding and the advantage of high W-adsorption capacity of the PTC-sorb sorbent, the design of a clinically useful compact ^{188}Re-generator based on the concept of consecutive-elutions from a combined PTC-alumina column system was developed. The operation of this generator system, which combined both elution and concentrating processes in one system, is as follows: ^{188}Re-eluate eluted from the ^{188}W-PTC-sorb column with a 0.005% NaCl solution was continuously passed through a small alumina column, where all ^{188}Re- perrhenate was retained. Then, in the consecutive elution step, ^{188}Re- perrhenate was eluted from the alumina column with a smaller volume of 0.9% NaCl solution. A typical result of these studies is presented in Table 5 and Fig. 5.

A schematic prototype of the 100 mCi ^{188}W/^{188}Re generator system is shown in Fig. 6. A final eluate of ten times larger ^{188}Re concentration (^{188}Re concentration factor = 10) was achieved. More than 20 elutions (1 per week) were successfully performed with ^{188}Re elution yields of around 85% and ^{188}W breakthrough of lower than 0.001%.

Table 5. Elution performance of the consecutive elution based $^{188}W/^{188}Re$ generator system composed of a ^{188}W-PTC-sorb column coupled with ^{188}Re concentrating alumina column (see picture at the right corner of Fig.5 to identify the elution profiles)

First elution from the ^{188}W-PTC-sorb column (*)with 0.005% NaCl solution eluant				
0.005% NaCl solution volume (mL)	^{188}Re radioactivity eluted from the ^{188}W-PTC-sorb column (mCi)**	^{188}Re radioactivity retained on the ^{188}Re-concentrating alumina column (mCi)**	^{188}Re elution yield of the ^{188}W-PTC-sorb column (%)	^{188}W- breakthrough in the ^{188}Re eluate (%)
3	95.5 ± 0.4	95.5 ± 0.4	91.0 ± 0.3	<0.001
Second elution from the alumina column with 0.9% NaCl solution eluant				
0.9% NaCl solution volume (mL)	^{188}Re radioactivity eluted from the ^{188}Re-concentrating alumina column (mCi)*	^{188}Re elution yield of the ^{188}Re-concentrating alumina column (%)**	^{188}Re-concentration factor	^{188}W-breakthrough in the eluate (%)
3	89.3 ± 0.5	85.0 ± 0.2	10	<0.001

*^{188}W-PTC-sorb column: 6.0 g PTC-sorb sorbent containing 3.0 g elemental tungsten of 105.0 mCi ^{188}W radioactivity (105.0 mCi ^{188}Re in equlibrium). ^{188}W-PTC-sorb column preparation was performed with the W-adsorption condition described in the footnotes of Fig. 3 with an up-scale of 1 g weight PTC-sorb column to 6 g weight PTC-sorb column.

**All these parameters were calculated based on the ^{188}Re radioactivity calibrated at $t = 0$ (at generator loading time point).

***Percentage of ^{188}Re-radioactivity in the ^{188}W-PTC-sorb column.

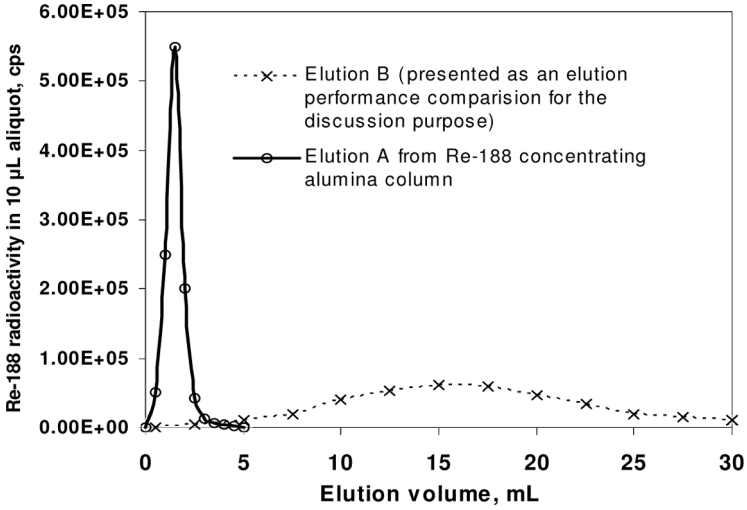


Figure 5. ^{188}Re-elution profiles of a consecutive elution based ^{188}W/^{188}Re generator system composed of a 6 gram weight ^{188}W-PTC-sorb column coupled with a 1.5 gram weight ^{188}Re concentrating alumina column. The design and specification of this generator system are found in Fig. 6 and Table 5, respectively. Elution A: ^{188}Re elution profile recorded at position A (see Fig. 6b) from the ^{188}Re-concentrating alumina column in the second elution step for enhancing the^{188}Re concentration. Elution B: ^{188}Re elution profile recorded at position B (see Fig. 6b) using an optional elution mode (eluting ^{188}Re with 0.9% NaCl solution from ^{188}W-PTC-sorb column without coupling with the alumina column).

The protocol of ^{188}Re elution from this generator was as follows: 30 mL of 0.005% NaCl solution (vial 5) was passed through the ^{188}W-PTC-sorb column into a waste container 8 via valve 4 with the pump in operation. Subsequently, the pump was stopped and the valve 4 set to open for the connection of the alumina column and the 0.9% NaCl solution (via 6). The ^{188}Re was eluted from the alumina column with an evacuated collection vial (vial 7) providing the impetus for elution. After the ^{188}Re was collected, with the pump operating, and the valve reconnecting vial 5 to the ^{188}W-PTC-sorb column, 10 mL of 0.005% NaCl solution was pumped through both ^{188}W-PTC-sorb and alumina columns into the waste container 8. Further elutions using the same procedure can be performed after the generator was allowed to equilibrate for 113 hours.

This consecutive-elution based ^{188}Re generator system offers a potential application for clinically useful ^{188}Re production using low specific radioactivity ^{188}W produced in rather low power research reactors. As a predictable example of the up-scale of the generator system shown in Fig. 6, a 1.5 Ci ^{188}W generator could be prepared using low specific radioactivity ^{188}W (from

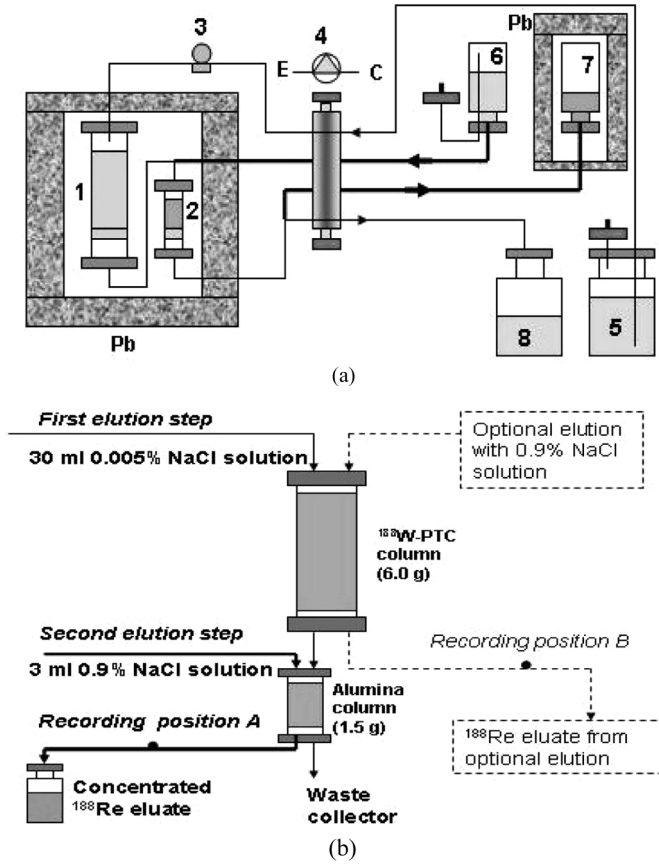


Figure 6. Consecutive elution based $^{188}W/^{188}Re$ generator system composed of a ^{188}W-PTC-sorb column coupled with the ^{188}Re concentrating alumina column a: Practical design of an operational generator system 1. ^{188}W- PTC-sorb column; 2. Alumina column; 3. Mini peristatic pump; 4. Selection valve with E open and C close positions; 5. 0.005% NaCl solution; 6. 0.9% NaCl solution; 7. Evacuated vial for ^{188}Re eluate; 8. Waste container, Pb is lead shielding container for radiation protection. b: Flow diagram of generator.

0.5 Ci/g to 0.78 Ci/g achievable from an 50–100 days irradiation time using the 2.3×10^{14} n · cm^{-2} · s^{-1} neutron flux OPAL reactor ($\Phi_{th}/\ \Phi_{epi} = 44$) with 99.79% enriched ^{186}W target; referring to the 703 mCi/g ^{188}W specific radioactivity produced in ORNL (USA) reactor of 2.8×10^{14} n · cm^{-2} · s^{-1} neutron flux).The standard process of nuclear reaction yield calculation for $^{186}W(n\ n,\gamma)^{188}W$ reaction was applied with the thermal cross-section and resonance integral of the ^{186}W and ^{187}W nuclides available from references

(8,29). The above planned generator could provide 3 mL eluate of 500 mCi/mL ^{188}Re-concentration for direct application in targeting-radiopharmaceutical preparations. It is notable that the high radioactivity of a generator may cause a more serious radiolysis problem which results in a significant amount of free active radicals in the solution surrounding the PTC sorbent in the column and could reduce the ^{188}Re elution yield as experienced in many studies of ^{99m}Tc and/or ^{188}Re generator preparation (10, 16, 28, 6). Obviously, the expertise in the routine production of high radioactivity ^{99m}Tc generators will be valuable in working towards a system with radioactivity as large as the 1.5 Ci ^{188}W generator planned above.

CONCLUSION

The PTC-sorb sorbent for the preparation of chromatographic ^{188}Re generator was successfully synthesized and its chemical composition and molecular structure determined. The chemical synthesis condition was optimized for preparation of PTC-sorb sorbent which met the requirements of clinically useful ^{188}W/^{188}Re generator production, such as high W-adsorption capacity, high ^{188}Re elution yield, low ^{188}W-breakthrough, and good mechanical stability. A tungstate ion adsorption mechanism was proposed based on the molecular structure and hydrolysis behavior of the PTC-sorb sorbent. The W adsorption of the PTC-sorb in different tungstate solutions and the ^{188}Re elution from the^{188}W-PTC-sorb column were investigated. The W-adsorption capacities of about 515 mg W/g PTC-sorb and ^{188}Re elution yield higher than 80% were also achieved with the PTC-sorb sorbent. Effect of the W-content of tungstate solution on the WO_4^{2-} ion adsorption and its covalent bonding with the Ti metal atoms in the PTC polymeric matrix were justified with respect to the optimal W-adsorption conditions for the preparation of a useful ^{188}W-PTC-sorb generator column. The consecutive-elution based ^{188}Re generator system combining both elution and concentration processes in one system was developed. This system offers a potential application for the clinically useful ^{88}Re production using low specific radioactivity ^{188}W (500 mCi/g) producible in a medium flux reactor. A ^{188}W generator of more than 1.5 Ci ^{188}W-radioactivity was designed to provide 3 mL eluate of 500 mCi/mL ^{188}Re-concentration for labeling specific ligands used in targeting endoradiotherapy.

ACKNOWLEDGMENT

The authors would like to thank the International Atomic Energy Agency, Australian Nuclear Science and Technology, and Vinatom's

NRI for the financial support of this project. The authors also wish to acknowledge their thanks to Mrs. Hien P.T. Do for her discussion and support.

REFERENCES

1. Lewis, R. E. (1966) Production of 70-day Tungsten-188 and Development of a 17 hour Rhenium-188 radioisotope generator. *J.Nucl. Med.*, *7*: 804.
2. Hayes, R. L. (1966) Rhenium-188 as a possible dianostic agent. Oak Ridge Associated Universities, Medical Division Report, ORAU 101: 74.
3. Monroy-Guzman, F.; Badillo-Almaraz, V.E.; Flores De La Torre, J.A.; Cosgrove, J.; Knapp, F.F. (2007) Hydroxyapatite-Based Mo-99/Tc-99 m and W-188/Re-188 Generator Systems. *Proceeding of the International Symposium on Trends in Radiopharmaceuticals, ISTR-2005, IAEA*, Vienna, Austria, Vol.1: 333–348.
4. Matsuoka, H.; Hashimoto, K.; Hishinuma, Y.; Ishikawa, K.; Terunuma, H.; Tatenuma, K.; Uchida, S. (2005) Application of PZC to W-188/Re-188 generators. *J. Nucl. Radiochem. Sciences*, *6*: 189.
5. Tanase, M.; Tatenuma, K.; Ishikawa, K.; Nishino, M.; Hasegawa, Y. (1997) A ^{99m}Tc generator using a new inorganic polymer adsorbent for (n, γ) Mo-99. *Appl. Radiat. Isot.*, *48*: 607.
6. Le, V.S. (2006) Procedures for the production of poly-zirconium-compound (PZC) based chromatographic ^{99m}Tc generator to be available for clinical application. *Proceedings of the Workshop on the Utilization of Research Reactors*, 12–16 January, 2004, Serpong, Jakarta, Indonesia, Japan Atomic Energy Agency, JAEA – Conf—2006-00: 229–256.
7. Mikheev, N.B.; Popovich, V.B.; Rumer, I.A. (1972) Re-188 Generator. *Isotopenpraxis*, *8*: 248.
8. Knapp, F.F.; Mirzadeh, S. (1992) Reactor capabilities for production of Tungsten-188 for the Tungsten-188/Rhenium-188 generator system. Oak Ridge National Laboratories, Report ORNL/TM-12222: 6.
9. Lisic, E.C.; Callahan, A.P.; Mirzadeh, S.; Knapp, F.F. (1992) The "tandem" W-188/Re-188 perrhenate/perrhenic acid generator system. *Radioact. Radiochem.*, *3*: 42.
10. Knapp, F.F.; Lisic, E.C.; Mirzadeh, S.; Callahan, A.P. (1993) W-188 /carrier-free Re-188 perrhenic acid generator system, U.S. Patent 5,186,913.
11. Knapp, F.F.; Lisic, E.C.; Mirzadeh, S.; Callahan, A.P. (1994) W-188/carrier-free Re-188 perrhenic acid generator system, U.S. Patent 5,275,802.
12. Kamioki, H.; Mirzadeh, S.; Lambrecht, R.M. (1994) W-188/Re-188 generator for biomedical applications, *Radiochim. Acta*, *65*: 39.
13. Knapp, F.F.; Callahan, A.P.; Beets, A.L. (1994) Processing of Reactor-produced W-188 for Fabrication of Clinical Scale Alumina-based W-188/Re-188 Generators. *Appl. Radiat. Isot.*, *45*: 1123.
14. Knapp, F.F.; Beets, A.L.; Mirzadeh, S.; Guhlke, S. (1998) Use of a new tandem cation/anion exchange system with clinical-scale generators provides

high specific volume solutions of Tc-99 m and Re-188. IAEA-TECDOC-1029: 419.
15. Guhlke, S.; Beets, A.L.; BIERSACK, H.-J.; Knapp, F.F. (1997) Elution of Re-188 from W-188/Re-188 generators with salts of weak acids permits efficient concentration to low volumes using a new tandem cation/anion exchange system, Annual meeting of the society of nuclear medicine. San Antonio, Texas, June 1–6, 1997. *J. Nucl. Med.*, *38*: 125.
16. Mikolajczak, R.; Zuchlinska, M.; Pawlak, D. (2006) Optimized alumina column for preparation of W-188/Re-188 generator. *7th International Symposium on Technetium in Chemistry and Nuclear Medicine TE.C. NU.M.-2006,* Italy.
17. Ehrhardt, G.J.; Ketring, A.R.; Turpin, T.A. (1987) An improved W-188/Re-188 generator for radio-therapeutic applications. *J.Nucl. Med.*, *28*: 656.
18. Ehrhardt, G.J.; Ketring, A.R.; Liang, Q. (1987) Improved W-188/Re-188 zirconium-tungstate gel radioisotope generator chemistry. *Radioact. Radiochem.*, *3*: 38.
19. Dadachov, M.S.; Lambrecht, R.M. (1995) W-188/Re-188 gel generator based on metal tungstates. *J. Radioanal. Nucl. Chem. Lett.*, *200*: 211.
20. Dadachov, M.S.; Le, V.S.; Lambrecht, R.M.; Dadachova, E. (2002) Development of a titanium tungstate-based W-188/Re-188 gel generator using tungsten of natural isotopic abundance. *Appl.Radiat.Isot.*, *57*: 641.
21. Le, V.S.; Lambrecht, R.M. (2000) Development of a Gel-type W-188/Re-188 generator using titanium-tungstate containing W-188 as a column packing. *Proceedings of Third Symposium on Nuclear Physics and Techniques*, Science and Technology Publisher, Hanoi.
22. Le, V.S. (2003) Preparation of titanium-tungsate gel based W-188/Re-188 generator. *Proceedings of Fifth Symposium on Nuclear Physics and Techniques*, Science and Technology Publisher, Hanoi.
23. Guhlke, S.; Beets, A.L.; Oetjin, K.; Mirzadeh, S.; Biersack, H.J.; Knapp, F.F. (2000) Simple new method for effective concentration of Re-188 solutions from alumina-based W-188/Re-188 generator. *J. Nucl. Med.*, *41*: 1271.
24. Mushtaq, A. (2003) Preparation of high specific-volume solutions of Tc-99 m and Re-188. *Appl.Radiat. Isot.*, *58*: 309.
25. Jackel, B.; Cripps, R.; Guntay, S.; Bruchertseifer, H. (2005) Development of semi-automated System for the preparation of Re-188 aqueous solution of high and reproducible activity concentrations. *Appl.Radiat. Isot.*, *63*: 299.
26. Luo, T.-Y.; Lo, A.-R.; Hsieh, B.-T.; Lin,W.-J. (2007) A design for automatic preparation of highly concentrated (Re-188)-perrhenate solutions. *Appl. Radiat. Isot.*, *65*: 21.
27. Novotny, D.; Wagner, G. (2007) Automation in generator technology. IAEA's Oordination Research Program, Third Meeting on *Development of Generator Technologies for Therapeutic Nuclides*, 8–12 Ctober, 2007, Daejon, Korea.
28. Kuznetsov, R.; Tarasov, V.; Romanov, Y. (2007) Development of Tungsten-188 production technology. IAEA's Oordination Research Program, Third

Meeting on *Development of Generator Technologies for Therapeutic Nuclides*, 8–12 October, 2007, Daejon, Korea.
29. Parrington, J.R.; Knox, H.D.; Breneman, S.L.; Baum, E.M.; Feiner, F. (1996) *Nuclides and Isotopes;* 15th Ed., Lockheed Martin, GE Nuclear Energy: USA.
30. Le, V.S.; Morcos, N. (2008) New SPE column packing material, retention assessment method and its application for the radionuclide chromatographic separation. *J. Radioanal. Nucl. Chem.*, *277* (3): 651.
31. De Farias, R.F.; E Silva, C.C.; Restivo, T. G. (2005) Thermal study of the anatase-rutile structural transitions in sol-gel synthesized titanium-oxide powders. *J. Serb. Chem. Soc.*, *70* (4): 675.
32. Cotton, F.A.; Wilkinson, G.; Murillo, C.A.; Bochmann, M. (1999) *Advanced Inorganic Chemistry;* 6th Ed., John Wiley & Sons, Inc.
33. Zsinka, L.; Szirtes, L.; Le, V.S.; Poko, Z. (1978) Thermoanalytical investigation of crystalline cerium Phosphate. *J. Thermal Anal.*, *14*: 245.