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Production parameters of the therapeutic ^{105}Rh radionuclide using medium energy cyclotron

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Abstract. Production cross-sections of the therapeutic ^{105}Rh radionuclide from proton-induced reactions on natural palladium target were measured using stacked-foil activation technique combined with high resolution γ-ray spectrometry at the MC50 cyclotron of the Korea Institute of Radiological and Medical Sciences. Note that cyclotron production of the ^{105}Rh radionuclide from natural palladium target was measured here for the first time. Results are compared with the theoretical values obtained using the model codes TALYS and ALICE-IPPE. Thick target integral yields for the investigated ^{105}Rh radionuclide were deduced from the threshold energy to 40 MeV. Measured data of the ^{105}Rh radionuclide are important because of its potential applications in nuclear medicine and/or therapeutic purposes. Optimal production circumstances for the therapeutic ^{105}Rh radionuclide using a cyclotron are discussed elaborately.

Keywords. MC50 cyclotron; palladium target; ^{105}Rh radionuclide; integral yield; TALYS code; ALICE-IPPE code.

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1. Introduction

Radionuclides used in nuclear medicine are categorized into two principal types: diagnostics and therapeutics. Radionuclides that emit gamma-rays (γ) and positrons (β^+) with favourable physiochemical characteristics are used for diagnostic purposes. On the other hand, radionuclides that emit negatrons (β^-), alpha particles (α), and that have electron capture (EC) or isomeric transition (IT) decay leading to the emission of Auger electrons with favourable physiochemical characteristics are widely used for therapeutic purposes.

Clinical radionuclide therapy has so far been exclusively practiced using β^- emitting radionuclides. Based on various physical and chemical properties (half-life, average energy, intensity, mean range etc.), the β^- emitting radionuclides are again classified into

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three sub-groups: radionuclides frequently used for clinical purposes, radionuclides used in pre-clinical studies, and potential radionuclides that have yet to be investigated [1]. The radionuclide ^{105}Rh is considered as a low-energy β^- emitter, and is used in pre-clinical studies. It is a good candidate for giving therapy in small tumours ($d \cong$ 1–2 mm) [2] due to its physical properties ($T_{1/2}$ = 35.36 h, $E_{\beta^-\max}$ = 567.2 keV, I_{β^-} = 75%, weighted average of beta energy = 179.4 keV, and maximum range in soft tissue = 0.89 mm). Beside this, rhodium complexes are kinetically inert and are expected to be very stable *in vivo* [3]. Currently, large amount of high specific activity ^{105}Rh radionuclide is produced by nuclear reactors using an enriched ^{104}Ru target via the indirect ^{104}Ru(n, γ)^{105}Ru $\rightarrow$ ^{105}Rh processes. But, ^{105}Rh radionuclide produced via these processes is contaminated by high level of Ru impurity due to the complicated radiochemical separation method [1]. It is also possible to obtain very large quantities of ^{105}Rh as a fission product, if required. But the radiochemical work involved in the separation of the fission products is rather cumbersome. Alternatively, pure form of Rh-105 can be produced using medium energy cyclotrons through the proton and light charged particle irradiations on palladium targets.

Understanding the importance of therapeutic ^{105}Rh radionuclide, we investigated the ^{nat}Pd(p, x)^{105}Rh processes leading to the production parameters of ^{105}Rh radionuclide using an azimuthally field varying (AVF) MC-50 cyclotron at the Korea Institute of Radiological and Medical Sciences (KIRAMS). The integral yields of the investigated ^{105}Rh radionuclide were also deduced using the measured cross-sections and the electronic stopping power of natural palladium from 40 MeV down to its threshold energy.

2. Experimental method

The irradiation technique, the activity determination and the data evaluation procedures were similar to our previous works [4–8]. Some important features relevant to this work are discussed as follows. The well-established stacked-foil activation technique and a high-resolution γ-ray spectrometer were employed to determine the excitation function of the ^{nat}Pd(p, x)^{105}Rh processes. A highly pure (>99.99%) 50 μm thick Pd foil with a natural isotopic composition (1.02% ^{102}Pd, 11.14% ^{104}Pd, 22.33% ^{105}Pd, 27.33% ^{106}Pd, 26.46% ^{108}Pd and 11.72% ^{110}Pd) was used as the target for irradiation. Several foils of copper (>99.98% purity and 100 μm thickness), and aluminum (99.999% purity and 200 μm thickness) together with the Pd target foils were assembled in a stack. The Cu and the Al foils were used to monitor the beam intensity and to degrade the beam energy, respectively. The stacked foils were irradiated for 60 min by proton energy of 42.1 MeV with a beam current of about 100 nA from the external beam line of the MC-50 cyclotron at the KIRAMS. After the irradiation ($\sim$1 h) and an appropriate cooling time ($\sim$3 h), the γ-ray activity of the activated foils were measured using a γ-ray spectrometer. The spectrum analysis was done using the γ-ray vision 5.0 (EG&G Ortec) program. The photopeak efficiency curve of the γ-ray spectrometer was calibrated for the counting distances with a set of standard γ-ray point sources. The intensity of bombarding proton beam was determined using the monitor reactions, ^{27}Al(p, x)^{24}Na and ^{nat}Cu(p, xn)^{62}Zn [9], from the measured activities induced in monitor foils at the front position of the stack by

considering that the monitor foils were irradiated simultaneously and measured in the same counting geometry, and with the same HPGe detector calibrated by the above-mentioned standard point sources. Multiple monitor foils decrease the probability of introducing unknown systematic uncertainties during the activity determination. It was also considered that the loss of a proton flux was very small and very hard to deduce practically. The beam intensity was considered as constant to deduce cross-sections for each foil in the stack. The proton energy degradation along the stacked foils was calculated using the computer program SRIM-2003 [10]. The activation cross-sections for the $^{\text{nat}}\text{Pd}(\text{p}, x)^{105}\text{Rh}$ reaction were determined using the well-known activation formula [5,6]

$$\sigma(E_i) = \frac{\lambda C(E_i)}{\varepsilon(E_\gamma) I_\gamma \rho t \phi \cdot (1 - \text{e}^{-\lambda t_\text{m}})\, \text{e}^{-\lambda t_\text{c}} (1 - \text{e}^{-\lambda t_\text{i}})}, \tag{1}$$

where λ is the decay constant (s^{-1}), $C(E_i)$ is the net counts under the photopeak area at the ith sample, $\varepsilon(E_\gamma)$ is the detection efficiency of the HPGe detector, I_γ is the γ-ray intensity, ρ is the atomic density of the target (atoms/cm^3), t is the target foil thickness (cm), ϕ is the proton beam intensity ($\text{p} \cdot \text{s}^{-1}$), t_c is the cooling time (s), t_m is the counting time (s) and t_i is the irradiation time (s). The decay data of the radioactive products were taken from the NUDAT-2 database [11].

The uncertainty of the proton energy for each representing point was estimated from the uncertainty of the incident beam energy, the target thickness and the beam straggling. On the other hand, the uncertainty of cross-sections was estimated using the uncertainty propagation formula by considering the statistical uncertainty of the γ-ray counting ($\sim$10%), uncertainty in the monitor flux ($\sim$7%), uncertainty in the detector efficiency (2–3%), and uncertainty in the decay data ($\sim$1%). The overall uncertainties of the measured cross-sections were $\sim$13%.

3. Model calculations

Model calculations of nuclear reaction cross-sections are usually performed, if there is any lack of reference data and/or shows any discrepancy among various measurements. On the other hand, precisely measured experimental data are necessary to probe and improve the results of model calculations and/or to find the optimal parameters. In fact, experimental data and calculated ones from model codes could play a complimentary role for a complete understanding of the physical processes of nuclear reactions. Moreover, a model calculation allows us to extrapolate and predict the experimental data, and also ensure an internal consistency of the data. The measured data of the $^{\text{nat}}\text{Pd}(\text{p}, x)^{105}\text{Rh}$ processes were compared with the theoretical values obtained by the TALYS [12] and the ALICE-IPPE [13] codes for cross-validation. The TALYS-1.0 cross-sections presented in this work were calculated using the default parameter set of TALYS-1.0, and also cross-checked with the data available in the TENDL-2010 [14] database. On the other hand, ALICE-IPPE cross-sections presented in this work were taken from the MENDL-2P database [15]. However, a brief description of the model codes relevant to this work is available elsewhere [4–8].

4. Results and discussion

The long-lived radionuclide ^{105}Rh ($T_{1/2}$ = 35.36 h; β^- = 100%) has a short-lived metastable state ^{105m}Rh ($T_{1/2}$ = 40.0 s), which completely decays to the ground state by an isomeric transition (IT) process before the onset of our measurement. Therefore, the measured cross-sections are the sum of the cross-sections of the ground state and the metastable state of ^{105}Rh. The contributing direct channels for the formation of this radionuclide are ^{106}Pd(p, 2p)^{105}Rh ($E_{\text{thr}} = -9.34$ MeV), ^{108}Pd(p, α)^{105}Rh ($E_{\text{thr}} = 3.19$ MeV), ^{108}Pd(p, pt)^{105}Rh ($E_{\text{thr}} = -16.62$ MeV), ^{108}Pd(p, 2n2p)^{105}Rh ($E_{\text{thr}} = -25.11$ MeV), ^{110}Pd(p, 2nα)^{105}Rh ($E_{\text{thr}} = -11.8$ MeV) and ^{110}Pd(p, 2npt)^{105}Rh ($E_{\text{thr}} = -31.60$ MeV) within our investigated energy region. The radionuclide ^{105}Rh was identified using its strong and independent γ-line, E_γ = 318.9 keV (I_γ = 19.1%). We could not compare the present results with any previous measurements because of the lack of available literature data. The measured excitation function of this radionuclide formation is shown in figure 1 and compared with the value predicted by the TALYS [12] and the ALICE-IPPE [13] codes. The isotopic cross-sections estimated by the TALYS code explain that the first peak around 20 MeV is mostly from the contribution of the ^{108}Pd(p, x)^{105}Rh processes, and the increase in values from 30 MeV are due to the contributions from the ^{106}Pd(p, x)^{105}Rh and ^{110}Pd(p, x)^{105}Rh reactions. The shape of the present excitation function is similar to that predicted by both codes. However, the present absolute cross-sections around 20 MeV is systematically higher than those predicted by both the codes. The second peak around 40 MeV predicted by the ALICE-IPPE code could not be observed both in the TALYS code and in the present result, especially in absolute values. Although contribution of ^{105}Ru ($T_{1/2}$ = 4.44 h) radionuclide via β^- decay to the measured cross-sections of ^{105}Rh is energetically possible, we could not observe any characteristic γ-line (e.g., 724 keV (47.3%)) of ^{105}Ru in the complex γ-ray spectra. It is noted that, the theoretical cross-sections of the ^{nat}Pd(p, x)^{105}Ru reaction predicted by the TALYS and ALICE-IPPE codes are very low throughout the whole investigated energy region in this experiment. The possible reason for this deviation is the insufficient α emission process near the (p, α) threshold. ^{108}Pd(p, α)^{105}Rh exothermal reactions

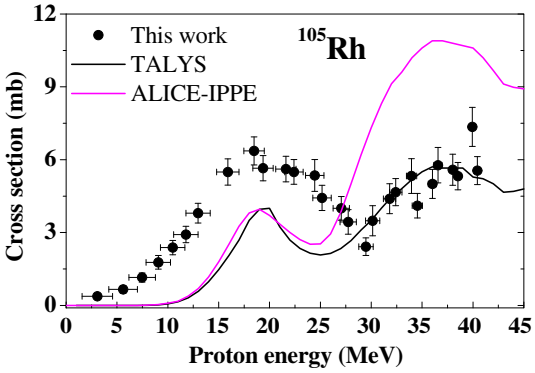

Figure 1. Excitation function for the ^{105}Rh radionuclide.

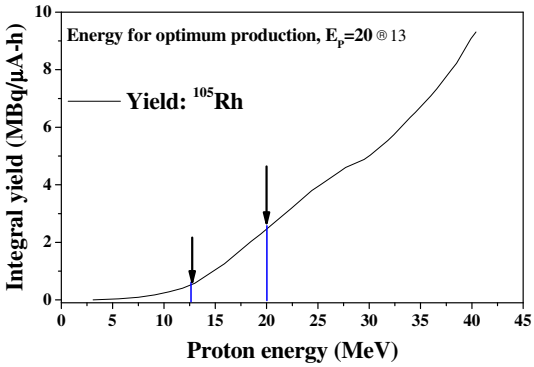

Figure 2. Integral yield for the ^{105}Rh radionuclide.

($Q > 0$) are supposed to make major contribution within the investigated energy region of this experiment.

5. Thick target yields

The thick target yields [9] for the investigated ^{105}Rh radionuclide were deduced using the measured cross-sections and electronic stopping power of ^{nat}Pd from threshold energy region to the initial proton energy region by taking into account that the total energy is absorbed in the target. A detailed explanation for the deduction of yield is available elsewhere [4–8]. The integral yield is expressed as MBq/μA·h. The analytical meaning of the thick target yields is the slope of the growing activity of the produced radionuclide vs. irradiation time at the beginning of the irradiation. The obtained thick target yields for the ^{105}Rh radionuclide are given in figure 2 as a function of proton energy. We cannot compare the present results with any directly measured thick target yield due to the unavailability of any literature data. It should be mentioned that our calculated integral yields can be used for the optimization of production yields of the corresponding radionuclide with minimum impurity contamination.

6. Conclusions

Production cross-sections of the ^{105}Rh radionuclide from the proton irradiations on natural palladium targets were measured using stacked-foil activation technique combined with high resolution γ-ray spectrometry in the energy range of 4–40 MeV with an overall uncertainty of 13%. The measured cross-sections of ^{nat}Pd(p, x)^{105}Rh were not well explained by the TALYS and ALICE-IPPE codes. As the decay properties of this radionuclide are suitable for therapeutic applications, the actual shape of the excitation function and absolute value should be confirmed by further measurements. The thick target yields derived from the measured cross-sections showed that the proton-induced reaction on a palladium target using low-energy ($E < 20$ MeV) cyclotron can be used for the production of ^{105}Rh, if one uses a ^{108}Pd-enriched target.

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