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Study of high specific activity production of ^{186g}Re at cyclotron C18 /18 by ^{186}W(p,n) reaction

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Abstract. Theoretical investigations of production of ^{186g}Re radionuclide at low energy proton cyclotron C18/18 are performed. Different models from the TALYS 1.9 and EMPIRE 3.2 codes as well as ACSELAM library were used to calculate the nuclear excitation function and yield of ^{186g}Re production in ^{186}W(p,n) nuclear reaction. The excitation functions of proton-induced reactions are compared with available experimental data. Possible impurities from the accompanying reactions to the production of ^{186g}Re are estimated in the proton energy range up to 18 MeV accessible for cyclotron C18/18 located at the A. Alikhanyan National Science Laboratory (Yerevan Physics Institute).

Keywords: cyclotron C18/18, isotope production, No-Carrier-Added form, excitation function

1. Introduction

Radioisotopes play an important role in nuclear medicine and represent powerful tools for imaging and therapy. The radionuclide ^{186g} Re is currently used in cancer diagnostics, palliative therapy, metabolic radiotherapy, monoclonal antibodies, bone cancer pain relief, treatment of rheumatoid arthritis and prostate cancer. The ^{186g} Re radionuclide is a short-range β^- emitter ($< 4.5mm$ in tissue). It has been proposed for Radio-Immuno-Therapy (RIT) due to its relatively short half-life, energetic beta particles, gamma photon imaging and chemical properties similar to technetium ($T_{1/2}$ = 3.7 day, $E_\beta = 1.07MeV$ and $0.933MeV$, main $E_\gamma = 137keV$). The suitable 3.7-day half-life allows sufficient time for the synthesis and shipment of potential radiopharmaceuticals. At the same time, the $137keV$ gamma radiations are convenient for the use in diagnostic purposes.

Traditionally, ^{186g} Re is produced using neutron beams from the nuclear reactors via neutron capture reaction $^{185}\mathrm{Re}(n,\gamma)^{186}\mathrm{Re}$. The production of ^{186g} Re in nuclear reactors is not in No-Carrier-Added (NCA) form and the specific activity is too low for the use in targeted radiotherapy.

The production of this radionuclide in NCA form, i.e., in high specific activity, which is the main pre-requisite for the production of isotopes for medical use, can be carried out by charged particles in cyclotrons [1, 2]. In this case, the nucleus produced in a final state differs from that in a target, which greatly facilitates its radiochemical separation.

The main objective of this work is to investigate the production feasibility of ^{186g} Re on ^{186}W target by proton induced nuclear reaction at the low energy cyclotrons (up to 18 MeV) using the nuclear codes TALYS 1.9 [3] and EMPIRE 3.2 [4]. Note that there are large discrepancies between experimental data from different measurements concerning the excitation function of the reaction $^{186}W(p,n)^{186}$ Re [2, 9-12, 14].

2. Production and Physical Characteristics

^{186}Re has two isomeric states. The ground state ^{186g}Re $(T_{1/2} = 3.72 day)$ with a 1^- spin and a long-lived metastable state ^{186m}Re$(T_{1/2} = 2\times10^5\, y)$ with about $150 keV$ higher energy level from the ground state and having 8^+ spin. The characteristics of these two states as well as their decay schemes are presented in Table 1 and in Fig. 1, respectively.

Nuclei	Spin	Half-life	Threshold, MeV	Intensity, (%)	E_γ, keV
^{186g}Re	1^-	3.72 d	1.36	92.5 (β^-) 7.5 (EC)	137.2 (9.47 %) 122.6 (0.6 %)
^{186m}Re	8^+	2x10^5 y	1.52	90 (IT) 10 (β^-)	40.4 (5 %) 59 (17.8 %)

Table 1. Characteristics of ^{186m,g}Re states

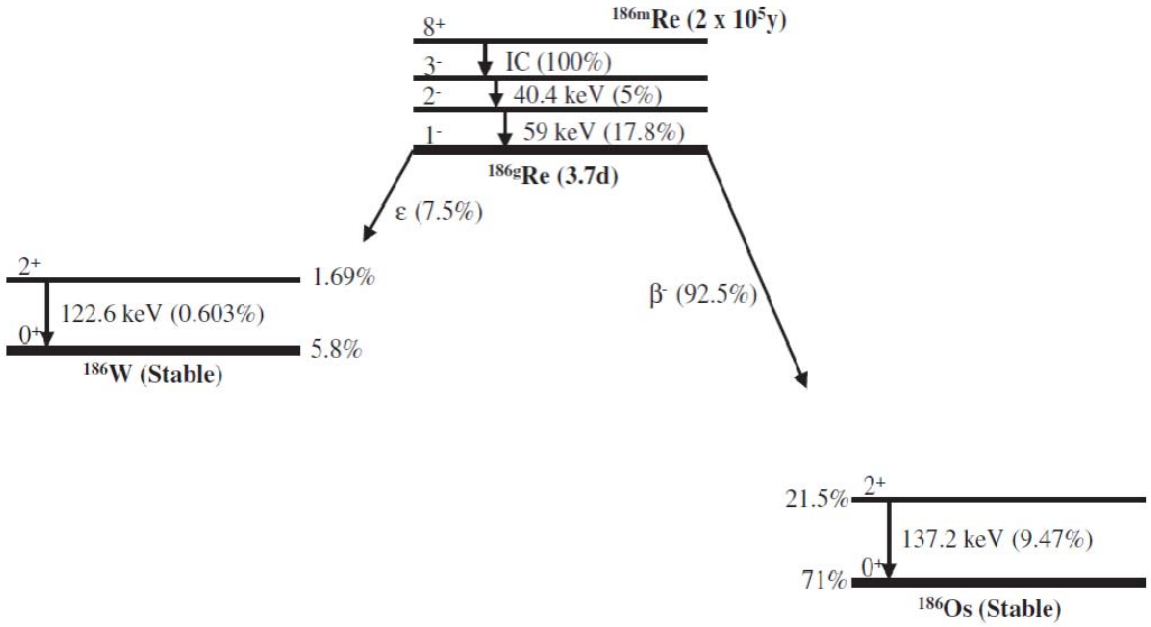

Fig. 1. The decay scheme of ^{186}Re [5]

The required thickness of the tungsten target has been calculated using the SRIM (Stopping and Range of Ions in Matter) code [7]. The calculations showed that for complete absorption of the proton energy $(18 MeV)$ the tungsten target thickness should be about $450 \mu m$ (see Fig. 2).

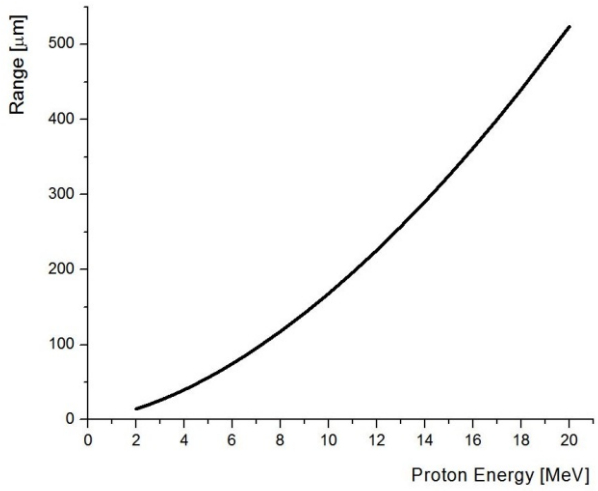

Fig. 2. Range of protons in tungsten target calculated by SRIM code

The required thickness of the tungsten target has been calculated using the SRIM (Stopping and Range of Ions in Matter) code [7]. The calculations showed that for complete absorption of the proton energy $(18MeV)$ the tungsten target thickness should be about $450\mu m$ (see Fig. 2).

To select the best irradiation conditions for optimization of the isotope production and simultaneously estimation obtained impurities scientists spend a lot of time and efforts for the experimental determination of the reaction cross-sections and isotope yield. For practical application is suggested the method based on comparison of available experimental data with calculations of excitation functions by different models of TALYS 1.9 and EMPIRE 3.2 nuclear codes. As a result of this procedure, a theoretical model is chosen that best describes the entire set of experimental data. Further, the yield of the activity of the investigated isotope, as well as the estimation of undesirable impurities is made through the chosen model.

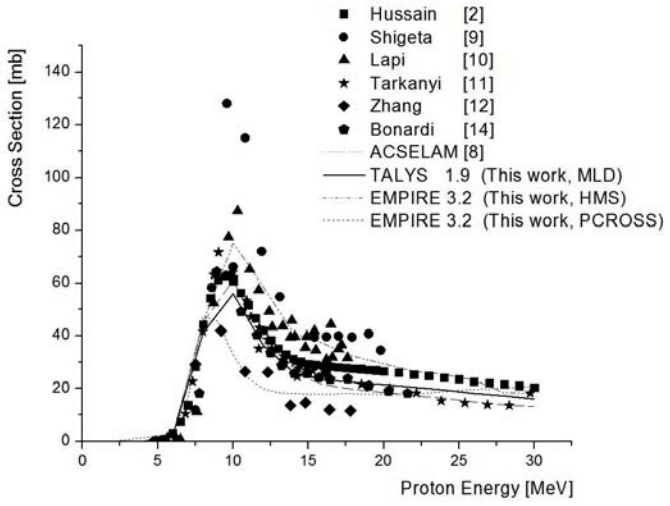

Fig. 3. Comparison of calculated excitation functions with experimental data for ^{186}W(p,n)^{186}Re reaction [2, 9-12, 14]

3. Nuclear model calculations

In order to estimate the level of undesirable impurities and determine the optimum energy range of incident protons for the production of the ^{186g}Re isotope the excitation function of the reactions $^{186}W(p,xn)$ have been calculated by TALYS 1.9 and EMPIRE 3.2 nuclear codes as well as ACSELAM library [8].

TALYS-1.9 allows choosing a level density model per nuclide considered in the reaction. The excitation functions by TALYS 1.9 code have been performed taking into account 3 phenomenological level density models and 3 options for microscopic level densities. The calculations by EMPIRE 3.2 code are performed using exciton model PCROSS and Hybrid Monte-Carlo Simulation (HMS).

The results of these calculations by TALYS 1.9 and EMPIRE 3.2 nuclear codes with the available experimental data [2, 6, 8-12, 14] are presented in Fig. 3.

As seen from Fig. 3, the results of theoretical calculations performed by different codes are consistent. In case of using the ACSELAM library the peak is shifted to a lower energy region. However, there are significant discrepancies between the data from different measurements, especially in the region of intermediate energies where the discrepancy achieves up to 3 times [9]. The best agreement with the experimental data was shown by TALYS 1.9 program using the Microscopic Level Densities (MLD) model based on temperature dependent Hartree–Fock–Bogolyubov (HFB) estimations using the Gogny force.

Based on the results of calculations on excitation functions, the optimum region of proton beam for the production of ^{186g}Re isotope is $5-17MeV$.

From the viewpoint of the production of isotopes for medicine, the relative yield of isotopes is of considerable interest. The calculation of integral yield of ^{186g}Re has been done by MLD model TALYS 1.9 code. The results of this calculation with IAEA recommended data [13] and experimental data [9, 14, 15] is depicted in Fig. 4. Data from Ref. [14] is consistent with both TALYS 1.9 calculations and IAEA recommended value. A significant excess of ^{186g}Re yield from Ref. [9] is because the measured excitation function in this case is about 3 times higher than that from the other measurements (see Fig. 3).

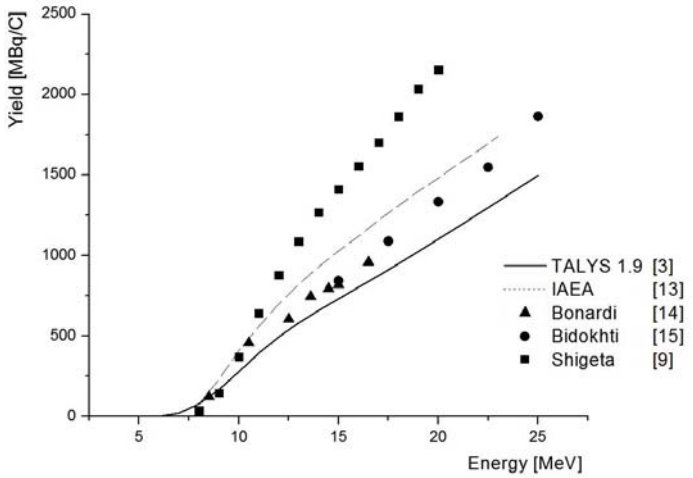

Fig. 4. Comparison of integral yield of ^{186g}Re isotope calculated by TALYS 1.9 code [2], IAEA recommended values [13] and experimental data [9, 14, 15]

The production of therapeutic isotope ^{186g}Re is accompanied by undesired long-lived ^{186m}Re. The level of impurity of ^{186g}Re was estimated by TALYS 1.9 code calculating the yields for the ground (Y_g) and metastable (Y_m) states respectively. The ratio Y_m / Y_g is found to be $1.63 \cdot 10^{-8}$. Thus, the amount of activity of ^{186m}Re formed along with ^{186g}Re is negligibly small.

The production yield can be calculated by the following equation:

$$Y \equiv \frac{N_A H}{M} I\left(1-e^{-\lambda t}\right) \int_{E_1}^{E_2} \left(\frac{dE}{d(\rho x)}\right)^{-1} \sigma(E) dE, \quad (1)$$

where Y is the activity (in Becquerel) of the product, N_A is the Avogadro number, H is the isotope abundance of the target nuclide, M is the mass number of the target element, $\sigma(E)$ is the cross-section at energy E, I is the projectile current, $dE/d(\rho x)$ is the stopping power, λ is the decay constant of the product and t t is the time of irradiation. E_1 and E_2 are the lower and upper boundaries of the energy region of isotopes production, respectively. Consequently, an increase of the isotopes production yield can be achieved by both increasing the duration of irradiation, the current and energy of the beam (see Eq. (1)).

The production of ^{186g}Re through the reaction $^{186}W(p,n)^{186}$Re during the irradiation of enriched tungsten by a proton beam is accompanied by formation of ^{185}Re and ^{184m,g}Re isotopes. In the Table 2, the thresholds for these accompanying reactions and half-lives of corresponding radionuclide are listed.

Product	Half life	Reaction	Threshold, MeV
^{184g}Re	38d	^{186}W(p,3n)	15.294
^{184m}Re	169 d	^{186}W(p,3n)	15.399
^{185}Re	Stable	^{186}W(p,2n)	7.582

Table 2. The thresholds for several accompanying reactions and half-lives of corresponding radionuclide

The presence of stable ^{185}Re in the final product leads to a decrease of specific activity. As follows from Table 2, the maximum energy of the proton beam should be limited to 15.5MeV in order to ensure the radionuclide purity of the therapeutic isotope ^{186g}Re (avoid the mixture from ^{184m,g}Re isotopes). This energy limit corresponds to the thickness of tungsten target about 325μm (see Fig.2).

It should be noted, that to reduce the amount of undesirable impurities from other isotopes of tungsten, the degree of enrichment of ^{186}W must be very high. A lower enrichment would lead to lower yield for ^{186g}Re, which in its turn would result in lower specific activity.

4. Conclusions

The model calculations using the TALYS 1.9 and EMPIRE 3.2 nuclear codes lead to the recommended sets of data, which should be useful for optimizing the available methods for the production of the medical intended radionuclide ^{186g}Re at low energy cyclotrons. The best

description of existing experimental data is achieved with the calculations performed by the TALYS 1.9 code using the MLD model. It is shown that the production of a therapeutic ^{186g}Re isotope on cyclotron $C18/18$ is possible. To obtain high radionuclide purity of the final product, the proton beam energy should be below $15.5MeV$. The $^{186}W(p,n)^{186}$Re reaction using an enriched target provides a method for producing ^{186g}Re in NCA form. In order to obtain the ^{186g}Re isotope on commercial scale a target with highly enriched level, high beam currents and long duration times for irradiation are necessary.

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