Estimation of the Productivity Isotope ^{67}Ga on Cyclotron C18 for Nuclear Medicine

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Abstract Theoretical calculations of the excitation functions for the reaction $^{67}\text{Zn}(p,n)^{67}\text{Ga}$ on natural and enriched zinc targets for the energy range from threshold up to 18 MeV are carried out using nuclear reaction models from program packages EMPIRE-3 and TALYS 1.4. The results of calculations are compared with available experimental data. The yields of gallium isotopes produced by the reaction $^{67}\text{Zn}(p,n)^{67}\text{Ga}$ on the proton beam of the cyclotron C18, IBA Belgium energy 18 MeV and current 30 μA are evaluated. Our calculations indicate that the yield of isotope ^{67}Ga in case of natural and enriched zinc targets are expected to be 23.6 MBq/ $\mu\text{A}\cdot\text{h}$ and 139 MBq/ $\mu\text{A}\cdot\text{h}$, respectively.

Keywords Nuclear Medicine, Diagnostic and Therapeutic Isotopes, Excitation Function, Isotopes Yields

1. Introduction

The study of nuclear reactions with intermediate or high energy protons is very important because it provides a basis for a wide range of technical applications. Particularly, using the reactions induced by intermediate energy protons, it is directly possible to produce radionuclides usable in the area of medicine and industry. In recent decades, the widespread use of diagnostic and therapeutic radioisotopes received. Depending of the type of radiation, the diagnostic isotopes are classified into two groups: β^+ -emitters (^{13}N , ^{15}O , ^{18}F , ^{62}Cu , ^{68}Ga , etc.) used in Positron Emission Tomography (PET), and γ -emitters (^{67}Ga , $^{99\text{m}}\text{Tc}$, ^{123}I , etc.) used in Single Photon Emission Computed Tomography (SPECT).

According to the information of World Health Organization (WHO) 8.2 million people worldwide died from cancer in 2012. More than 40 percent of deaths from cancer could be avoided in the case of early diagnosis. One of the methods for early diagnosis of cancer is a patient examination by SPECT.

The ^{67}Ga isotope is one of the main radionuclides produced on cyclotrons and used in clinical oncology for diagnostics of benign and malignant tumors.

The ^{67}Ga commonly is used in SPECT investigations as a trivalent citrate compound for nuclear medicine imaging, and it is a valuable agent in the detection and localization of certain neoplasms and inflammatory lesions. It is well known when ^{67}Ga is in the citrate form it is concentrated in many types of tumors, as well as non-malignant lesions. Although it is not a tumor-specific agent, it is used extensively for the localization of a variety of human malignant tumors and, due to its widespread application as a diagnostic tool in nuclear medicine. ^{67}Ga is one of the most widely employed cyclotron-produced radiopharmaceuticals.

In the radioisotope production procedure, the nuclear reaction data are mainly needed for respective optimization of production rates. This process involves a selection of the projectile energy range that will maximize the yield of produced isotopes and minimize the radioactive impurities. The total cross section of such production is also important in sphere of accelerator technology from the point of view of radiation protection safety. The calculations based on standard models for nuclear reactions can be helpful for determining the accuracy of various parameters for these models as well those evaluated from experimental measurements [1].

Figure 1. The decay scheme of ^{67}Ga

^{67}Ga with the half-life $T_{1/2} = 78.3$ h decays to stable ^{67}Zn by electron capture. The scheme of ^{67}Ga decay and its energetic characteristics are taken from Nudat 2.5 [2] and are

presented in the Fig. 1 and Table 1, respectively.

Table 1. Decay data of ^{67}Ga

Nuclide	Half-life	Decay mode (%)	E, keV	I _γ , %
^{67}Ga	78.3 h	EC (100)	93.31	38.81
			184.58	21.41
			300.2	16.64
			393.5	4.56

2. The Nuclear Reaction Cross-section Calculations

One of the main parameter at production of radioisotopes under proton beam is the specific activity which is the isotopes yield normalized to unit of beam current and unit of irradiation time – Bq/μA·h or Ci/μA·h.

In the case of thick target at calculation of specific activity one needs to consider the decrease of protons' energy as they pass through the target, and therefore integrate the cross sections over the entire energy range.

The saturated yield Y per unit current (Bq/μA) can be calculated using the following formula [8]:

$$Y = 6.24 \times 10^{12} \times \frac{N_A}{M} \int_{E_{out}}^{E_{in}} \frac{\sigma(E)}{S(E)} dE \quad (1)$$

where 6.24×10^{12} is the number of protons per second per μA, N_A is the Avogadro constant, M is the target atomic mass, $\sigma(E)$ is the reaction cross section (excitation function) as a function of energy expressed in mb and $S(E)$ is the target stopping power expressed in units $\text{MeV cm}^2 \text{g}^{-1}$.

The criterion in choosing of a nuclear reaction for the production of isotopes for medical uses is a high specific activity. Therefore, from the point of view of the specific activity we consider the production of ^{67}Ga isotope on natural and enriched zinc targets.

^{67}Ga is commonly produced by using enriched ^{68}Zn target through the nuclear reaction $^{68}\text{Zn}(p,2n)^{67}\text{Ga}$ in the proton energy range $E_p = 20\text{--}40$ MeV. The investigation on production ^{67}Ga through the reaction $^{68}\text{Zn}(p,2n)^{67}\text{Ga}$ was carried out in Korean Institute of Radiological and Medical Science (KIRAM) [3]. The solid enriched target ^{68}Zn was irradiated by 25 MeV proton beam. The average yield was 3 mCi/μA·h. In Institute of Nuclear Physics (INP) of Kazakhstan [4] the radioisotope ^{67}Ga for medical clinic using was obtained by reaction $^{68}\text{Zn}(p,2n)^{67}\text{Ga}$ applying proton beam with energy 30 MeV and current 50 μA. In this case the ^{67}Ga radioisotope yield in result of irradiation during 7 h was 282.5 mCi. Such method of production of the isotope ^{67}Ga applied also in Karlsruhe, Germany at proton beam energy 25 MeV [5]. To the issue of ^{67}Ga isotope production is also dedicated in the review of TRIUMF, Canada [6]. In the review is indicated the optimal proton energy range and integral yield for the production of Ga-67 ($E_p = 20\text{--}40$ MeV, yield is 4.5 mCi/μA). In the Ref [3–6] the target was made from enriched ^{68}Zn . In the Ref. [7] is considered the ^{67}Ga

production on the target made from natural Zn. The excitation function of the reaction $^{\text{nat}}\text{Zn}(p,xn)^{67}\text{Ga}$ has a single peak 135 mb at proton energy 20 MeV. For the yield of isotope ^{67}Ga produced on the target of natural zinc is provided the estimation of 30 mCi.

At the territory of A.I Alikhanyan National Laboratory the commercial proton cyclotron C18/18 IBA Belgium with energy 18 MeV and current 100 μA intended for routine production ^{18}F for PET is located. Up to now foreign preparations were used for SPECT examinations of patients in Armenia. We consider the possibility of ^{67}Ga isotope production through the reaction $^{67}\text{Zn}(p,n)^{67}\text{Ga}$ at external 18 MeV and 30 μA proton beam of the cyclotron C18/18 for to meet the needs in the isotope ^{67}Ga of clinics of Armenia and the region. For this purpose a study of the excitation function and the yield of the reaction $^{67}\text{Zn}(p,n)^{67}\text{Ga}$ on the targets made from natural and enriched zinc in the energy range of protons from the reaction threshold up to 18 MeV was performed.

In radioisotope production programmer, nuclear reaction data mainly needed for optimization of production routes. This process involves a selection of the projectile energy range that will maximize the yield of the product and minimize of the radioactive impurities.

The calculation of the yields of ^{67}Ga isotope in the reaction $^{67}\text{Zn}(p,2n)^{67}\text{Ga}$ allows to evaluate the efficiency of the production for both the natural and enriched targets.

Naturally occurring zinc is composed of 5 stable isotopes ^{64}Zn , ^{66}Zn , ^{67}Zn , ^{68}Zn , and ^{70}Zn .

In Table 2 the natural abundance of each isotope of zinc, all channels of reactions on each isotope of zinc and the thresholds for these reactions are listed. As seen from Table 2, due to the reactions threshold, the isotope ^{67}Ga could be produced on the proton beam of cyclotron C18 only on the isotopes ^{67}Zn and ^{68}Zn .

Table 2. Nuclear data of contributing reactions at natural zinc target

Natural target	Abundance, %	Contributing reactions	Threshold, MeV	Half-life
^{64}Zn	48.63	$^{64}\text{Zn}(p,n)^{64}\text{Ga}$	8.	2.9 min
		$^{64}\text{Zn}(p,2n)^{63}\text{Ga}$	18.6	32.4 s
^{66}Zn	27.90	$^{66}\text{Zn}(p,n)^{66}\text{Ga}$	6.	9.49 h
		$^{66}\text{Zn}(p,2n)^{65}\text{Ga}$	15.3	15.2 min
^{67}Zn	4.10	$^{67}\text{Zn}(p,n)^{67}\text{Ga}$	1.88	78.3 h
		$^{67}\text{Zn}(p,2n)^{66}\text{Ga}$	13.	9.49 h
^{68}Zn	18.75	$^{68}\text{Zn}(p,n)^{68}\text{Ga}$	3.75	67.71 min
		$^{68}\text{Zn}(p,2n)^{67}\text{Ga}$	12.15	78.3 h
^{70}Zn	0.62	$^{70}\text{Zn}(p,n)^{70}\text{Ga}$	1.45	21.14 min
		$^{70}\text{Zn}(p,2n)^{69}\text{Ga}$	9.2	Stable
		$^{70}\text{Zn}(p,3n)^{67}\text{Ga}$	33.9	78.3 h

In addition, from Table 2 can be seen, that accompanying unwanted products of the contributing reactions have short lifetimes compared with the lifetime of the ^{67}Ga . Consequently, their impurity in the final product is insignificant.

The calculation of the cross section for the reaction $^{nat}\text{Zn}(p,xn)^{67}\text{Ga}$ was performed by program TALYS 1.4 [9] and EMPIRE-3.1 [13]. In Fig. 2 the results of our calculation in which the natural abundance of each isotope and cross section of each channel of the reaction was taken into account together with the experimental data from Ref. [11] and Ref. [12] are shown. There is good agreement between the results of calculations for both models TALYS 1.4 and EMPIRE-3.1, and also with the given experimental data.

Figure 2. The cross section of the reaction $^{nat}\text{Zn}(p,xn)^{67}\text{Ga}$ calculated by TALYS 1.4 (red curve) and EMPIRE-3.1 [13] (blue curve). The open circles are the data of Ref. [11] and the crosses the data of Ref. [12]. The black curve is a polynomial fit to the data.

From Fig. 2 is seen that in case of target from natural zinc the best energy range for production of isotope ^{67}Ga on the cyclotron C18 is $E_p = 13\text{--}17$ MeV and maximum cross section in this range about 130 mb. This result is consistent with the data of Ref. [15] where the cross section at energy of 17.6 MeV is 131.6 mb.

For this energy range, the numerical calculations of the yields of ^{67}Ga production were performed by formula (1). The value $\sigma(E)$ of the cross sections was taken from the program TALYS 1.4 [9] and the value of stopping power $S(E)$ was obtained from SRIM [10]. The results of these calculations are shown in Fig. 3.

Figure 3. The dependence of Ga-67 production yield vs. proton energy on the natural zinc target

The calculations showed that the specific activity in case of target from natural zinc is $0.638 \text{ mCi}/\mu\text{A}\cdot\text{h}$ ($23.6 \text{ MBq}/\mu\text{A}\cdot\text{h}$). At irradiation during 2 hours by proton beam with energy 18 MeV and current $30 \mu\text{A}$ the yield of isotope ^{67}Ga is 38 mCi. Since the dose for one patient survey is 2 - 5 mCi the obtained yield is enough for inspection of about 8 patients.

From a commercial point of view, this method of production of ^{67}Ga isotope from natural zinc target is ineffective. Therefore, the reaction for the ^{67}Ga isotope production on enriched target of ^{67}Zn was studied.

The excitation function of the reaction $^{67}\text{Zn}(p,n)^{67}\text{Ga}$ for enriched target was calculated by means of programs TALYS 1.4 [9] and EMPIRE-3.1 [13].

The results of the calculations together with set of experimental data from IAEA Technical Reports [14] are shown in Fig. 4. It is seen from Fig. 4 that in a low energy range the calculation results by programs TALYS 1.4 [9] and EMPIRE-3.1 [13] are in good agreement with set of experimental data [14]. TALYS 1.4 and EMPIRE-3.1 codes predicted the maximum cross-section to be respectively 587.3 mb and 575.6 mb at the same 10 MeV energy. The effective energy range for ^{67}Ga production on the enriched zinc target is $E_p = 5\text{--}14$ MeV.

Figure 4. The comparison of the cross sections of reaction $^{67}\text{Zn}(p,n)^{67}\text{Ga}$ calculated by programs TALYS 1.4 (red curve) and EMPIRE-3.1 (blue curve). The set of experimental data is given from Ref. [14]

The specific activity for ^{67}Ga production was calculated on the base of formula (1) using data of programs TALYS 1.4 [9] and SRIM [10]. In case of enriched zinc target the special activity for isotope ^{67}Ga is $3.772 \text{ mCi}/\mu\text{A}\cdot\text{h}$ ($139 \text{ MBq}/\mu\text{A}\cdot\text{h}$), which agrees with the value $3 \text{ mCi}/\mu\text{A}\cdot\text{h}$ from Ref. [3].

The calculation results of the ^{67}Ga isotope's yield on enriched zinc target performed in the proton energy range with the maximum cross section are shown in Fig. 5.

Figure 5. The dependence of ^{67}Ga activity via incident proton energy on the enriched zinc target

The yield of isotope ^{67}Ga in case of irradiation of the enriched zinc target during 2 h by the proton beam with current 30 μA is 226 mCi. This amount of ^{67}Ga isotope is sufficient for diagnostic survey of more than 45 patients.

Taking into account the long half-life (78.3 hours) and the amount of the obtained isotope ^{67}Ga could be considered delivery the product to the clinics of the region.

3. Conclusions

New calculations on the excitation function of reactions $^{\text{nat}}\text{Zn}(p,xn)^{67}\text{Ga}$ and $^{67}\text{Zn}(p,n)^{67}\text{Ga}$ have been carried out using nuclear reaction models from TALYS 1.4 and EMPIRE-3.1. The yield of the reactions for the production of isotope ^{67}Ga on the natural and enriched targets of zinc was evaluated using program packages TALYS 1.4 and SRIM. It is shown that on the proton beam of the commercial cyclotron C18 with proton energy 18 MeV and current 30 μA using enriched target ^{67}Zn it is possible to produce ^{67}Ga isotope in amounts sufficient to meet the needs of the clinics of Armenia and countries of neighboring region.

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