COMPARISON OF Cu-67 PRODUCTION AT CYCLOTRON AND ELECTRON ACCELERATOR*

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Abstract

The isotope Cu-67 is considered as one of the most perspective for application in radioimmunotherapy. At the same time, available methods for its production on the base of cyclotrons and high-flux reactors do not meet potential need of clinical nuclear medicine. The report contains the fundamentals of the Cu-67 generation under high-energy bremsstrahlung through the reaction $^{68}Zn(\gamma,p)^{67}Cu$. Study and optimisation of the Cu-67 yield were conducted by means of computer simulation. The dependence of specific activity of the Cu-67 and side-products in the target of natural zinc from electron energy in the range of 30…45,MeV has been obtained in the experiment. Comparative analysis of different methods for Cu-67 manufacturing is carried out.

INTRODUCTION

Cu-67 is the mean β-emitter, which permits its efficient use for acting upon tumors up to 4 mm in size [1]. The advantages of this isotope also include the presence of relatively weak gamma-lines of energy applicable for gamma-camera visualization, and also, the optimum half-life period $T_{1/2}$=61.83 h.

Cu-67 can be obtained in different reactions (see Table 1). As it can be seen from the tabulated data, the photonuclear reaction cross section is by order of magnitude higher than the corresponding value for the (n,p) channel, and is within the limits typical of the reactions on protons. At the same time, the photonuclear method appears more attractive in view of a relatively low cost of electron accelerators and their low running expenses in comparison with heavy particle accelerators, and also in view of a considerably lower ecological hazard as opposed to nuclear reactors.

Table 1: Main reactions of Cu-67 production

Particle	Reaction	Cross-section σ,mb
p	$^{68}Zn(p,2p)^{67}Cu$	**6** (E_p=30…85,MeV)
		24.8 (E_p=130…425,MeV)
	$^{70}Zn(p,\alpha)^{67}Cu$	**15** (E_p=16MeV)
α	$^{64}Ni(\alpha,p)^{67}Cu$	**34** (E_α=22MeV)
n	$^{67}Zn(n,p)^{67}Cu$	**1.07**
e→γ	$^{68}Zn(\gamma,p)^{67}Cu$	**11** (E_γ=22MeV)

The conceptual feasibility of Cu-67 production at the electron accelerator has been known long enough [2]. Later on, a few more studies were performed in this direction [3,4]. Their common peculiarity was the absence of both the analysis and the optimization of the structure of output devices of the accelerator (exit window, bremsstrahlung converter, target) in order to obtain the highest gross and specific activities of the Cu-67 isotope with due regard for the real beam parameters and the absorbed radiation power in the device elements. In this respect, the computer simulation appears the most efficient method of optimization.

The present communication reports the results from studies and optimization of the Cu-67 yield during exposure of natural zinc targets to a high energy bremsstrahlung. A comparative analysis of different production techniques of the isotope was carried out.

COMPUTER SIMULATION OF PHOTONUCLEAR Cu-67 GENERATION

The radiation processes, including radiation energy losses in a substance, are well simulated with the use of the Monte-Carlo-based program system PENELOPE [5]. To provide also the studies of photonuclear reactions, additional modules as well as the data on reaction excitation functions were introduced into the basic system package [6]. This approach has made it possible to compute simultaneously the isotope product yield and the absorbed radiation power in the constructional elements.

Figure 1 shows the simulation data on the spatial distribution of Cu-67 nuclei generated in the semi-infinite natural zinc target under the action of bremsstrahlung photons.

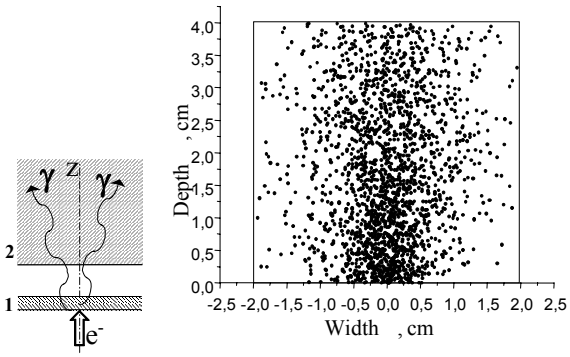

Figure 1: Distribution of Cu-67 nuclei in the zinc target (electron energy is 30 MeV). 1 – bremsstrahlung converter, 2 – Zn target.

It can be seen that the distribution occupies a great volume and is essentially nonuniform. So, the isotope product yield is dependent on the target size and the target position in the bremsstrahlung flux.

The simulation data have also demonstrated that with an increasing electron energy from 30 MeV up to 45 MeV the Cu-67 yield in the cylindrical natural zinc target, 2x2 cm in size, increases by three times [7]. The mentioned target size appears optimum for photonuclear

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production of Cu-67 from the standpoint of the gross-specific activity ratio.

To optimize the structure of the output devices with due regard for the absorbed radiation power in their elements, the variant presented in Fig. 2 was studied. In the given case, the converter presented a set of plates (Ta, 1 mm each) separated by cooling water layers (1 mm).

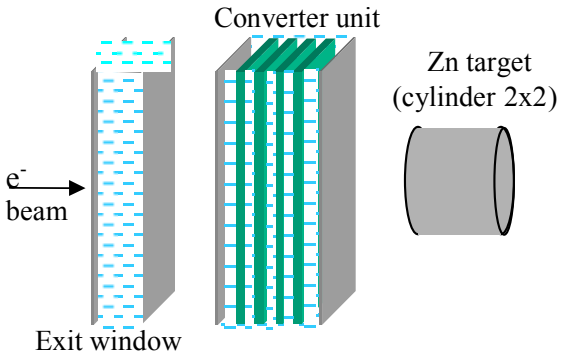

Figure 2: Schematic of output devices with a plate converter.

Figure 3 shows the results of simulation for the absorbed power in both the converter and the target, and also the data on the Cu-67 activity generated in the target for 24 hours of exposure to the electron beam with an average current of 200 μA at an energy of 40 MeV, with the beam profile corresponding to the conditions of the Linac KUT-30 [8].

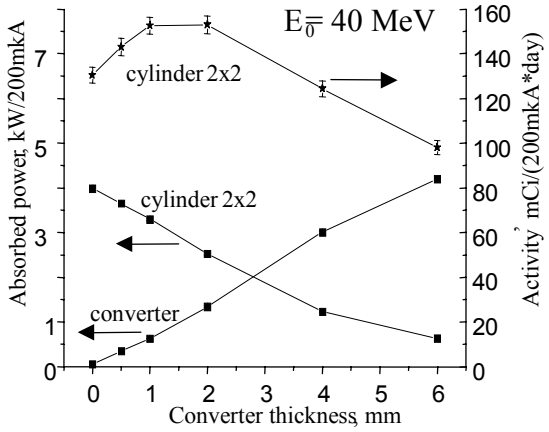

Figure 3: Absorbed power in the Ta converter and the Zn target, as well as the Cu-67 yield as functions of the converter thickness.

It can be seen that the radiation heating power of the target can be controlled by varying the quantity of plates in the converter, lowering in this way the heating power to the acceptable value. However, in this case the yield of Cu-67 is also reduced.

EXPERIMENTAL STUDIES ON THE YIELDS OF Cu-67 AND IMPURITIES

The simulation data given in the previous section were restricted to the consideration of only the photonuclear channel with emission of only one particle – proton or neutron – from the excited nucleus. However, with a rise in the photon energy there may open the channels with emission of two or more particles. In other words, the increase in the electron energy along with an increase in the isotope product yield may lead to the increase in the yield of undesirable radionuclides-impurities. The additional channels of their generation can also be created by photoneutrons, which are generated in the converter together with the bremsstrahlung. Thus, in natural zinc irradiated at the electron accelerator, the isotope Cu-67 can be generated in two channels

^{68}Zn(18.8%)(γ,p)+^{67}Zn(4.1%)(n,p) → **^{67}Cu**(61.83H) .

Simultaneously, other stable zinc isotopes give rise to a number of by-product radionuclides such as

^{64}Zn(48.6%)(γ,2n) → **^{62}Zn**(9.26H) → ^{62}Cu(9.74M) → ^{62}Ni(Stab.);

^{66}Zn(27.9%)(γ,n)+^{67}Zn(4.1%)(γ,2n)+^{64}Zn(48.6%)(n,γ) → ^{65}**Zn**(243.2D) → ^{65}Cu(Stab.);

^{70}Zn(0.6%)(γ,n)+^{68}Zn(18.8%)(n,γ)+^{70}Zn(0.6%)(γ,p) → ^{69}Cu(2.85M) → **^{69m}Zn**(13.76H) → ^{69}Zn(57.M) → ^{69}Ga(Stab.).

The terms in brackets stand for the abundance (in percentage, for stable isotopes) and the half-life period (for unstable isotopes).

In view of the complexity of the mentioned processes, it appears reasonable to investigate them by experiment. Such investigations were conducted at the upgraded accelerator LU-40m [9] with the use of a specially devised output device (Fig. 4). As it can be seen, its structure is close to the one considered at simulation (see Fig. 2).

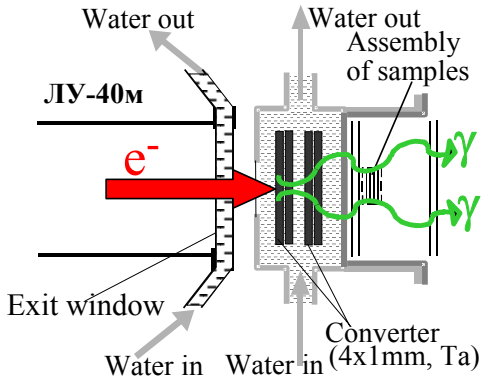

Figure 4: Activation circuit scheme of experimental Zn targets.

The targets were made as discs, 6 mm in diameter. There were located in a special duralumin case strictly along the center line of the target device, which was coincident with the axis of the electron beam. The results of γ-spectrometric analysis of the irradiated targets are presented in Table 2.

Table 2: Specific yield of radionuclides in the Zn target

Electron energy, MeV		**35**	**41**	**45**
Isotope	**$T_{1/2}$**	**Specific yield, mCi/g*200μA*day**		
Cu^{67}	62 h	7,684	10,33	14,18
Zn^{65}	244 d	2,194	2,510	2,513
Zn^{69m}	13,7 h	2,723	3,205	4,220
Zn^{62}	9,2 h	28,91	37,74	69,34

CONCLUSION

As the data given in Table 3 indicate, the use of the electron accelerator with the real parameters provides the better conditions of Cu-67 generation in regard to the total yield of the isotope product, the relative level and composition of radionuclides-impurities (the table omits the technologies that provide a lower Cu-67 yield – e.g. see refs. [11-13]). In this case, the impurities are predominantly the zinc isotopes, which can be got rid of by the known radiochemical procedures. According to the available data, the activity of Cu-64 by the end of irradiation may three times exceed the activity of Cu-67 [3]. This being substantially lower than in the reactions on protons.

It should be also mentioned that the results presented for the photonuclear method refer to the natural zinc target. It appears more expedient to use the material enriched in the Zn-68 isotope. In this case, the yield of Cu-67 increases still more by a factor of 5. Besides, the channels of generation of the majority of the impurities mentioned in the table get eliminated. At the same time, in view of a rather high cost of enriched zinc, there arises the necessity of target recovery after each extraction of Cu-67. The disadvantage of the photonuclear method is the necessity of treatment the target of substantial mass at its relatively low specific activity (~ 10 mCi/g).

Table 3: Comparative characteristics of Cu-67 production methods

Installation, parameters	**Target characteristics**	**Cu-67 production rate**	**Main admixture**	**Relative admixture activity, $A_{ad.}/A_{Cu-67}$**
Cyclotron PSI; 67MeV, 70 μA [10]	$Zn_{nat.}$ 5.6 g	66.2 mCi/day	Cu-64 Zn-62 Zn-65 Zn-69m Ga-67 Ni-57	36.4 57.1 0.78 0.56 3.4 0.18
Proton Linac BLIP; 193 MeV, 43 μA [1]	$ZnO_{nat.}$ 40 g	64.1 mCi/day	Cu-61 Cu-64	6.7 10.6
Electron Linac KIPT; 41MeV,200μA experiment	$Zn_{nat.}$ 95.4 mg	10.33mCi/g·day	Zn-62 Zn-65 Zn-69m	4.7 0.17 0.3
Electron Linac KIPT; 40MeV,200μA simulation	$Zn_{nat.}$ 45 g (cylinder 2x2 cm)	113.2 mCi/day		

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