DEVELOPMENT OF NEW METHODS FOR PRODUCTION OF MEDICAL RADIONUCLIDES AT THE RADIOISOTOPE COMPLEX RIC-80

V.N. Panteleev, A.E. Barzakh, L.Kh. Batist, D.V. Fedorov, V.S. Ivanov, S.A. Krotov, P.L. Molkanov, S.Yu. Orlov, M.D. Seliverstov, Yu.M. Volkov

1. Introduction

The development of nuclear physics experimental methods combined with the use of high current cyclotrons and very sensitive detectors provide very good opportunities for a completely new direction in medical diagnostics and therapies of various diseases. The nuclear medicine technologies used for diagnostics and therapy are based on the employment of artificially produced radioactive isotopes with specific properties. In this paper, the new installation RIC-80 (radioactive isotopes at cyclotron C-80) [1, 2] is shortly discussed, which is being constructed presently at the beam of a new C-80 cyclotron [3]. The RIC-80 project includes the construction of three target stations, one of them is the station coupled with a mass-separator. It is planned to produce the most widely used medical radioisotopes. These are $^{64, 67}$Cu, ^{68}Ge, ^{82}Sr, ^{111}In, ^{123,124}I, $^{223, 224}$Ra, and others, which are under discussion at present as perspective radionuclides for diagnostics and therapy. The mass-separator method will make it possible to produce very pure beams of some radioisotopes.

In this paper, the results on the development of a new method [4] of a high temperature separation of radioisotopes ^{82}Sr and ^{67}Cu and others from different kind of target materials are presented. The production of radionuclides that decay with emission of positrons, allowing their use for positron emission tomography (PET), is very important for diagnostics of different diseases. The isotope-generator ^{82}Sr, which is utilized for PET diagnostics of heart and brain diseases, is one of the most needed radionuclides for PET diagnostics over the world.

The radioisotope ^{67}Cu is regarded now as one of very promising radionuclides for the cancer therapy using monoclonal antibodies. A high demand in radiopharmaceuticals on the base of ^{67}Cu requires new efficient methods for its production, which are actively developed at accelerators.

2. The RIC-80 istallation

The main parameters of the new built C-80 cyclotron are the following: the proton beam energy can be varied in the interval 40–80 MeV, and the beam intensity is planned to be up to 200 μA. The cyclotron is intended mainly for production of a wide spectrum of medical radionuclides for diagnostics and therapy. A photograph of the C-80 external beam line with three proton beam lines to the target stations is presented in Fig. 1. The proton beam line is directed from the ground floor to the cellar, where it can be deflected and focused to one of three target stations. The mass-separator with its target station [2] will allow for production of separated beams of medical radionuclides of a high purity implanted into the corresponding collectors from which they can be easily extracted. The target stations will be equipped with special devices to transfer the highly radioactive targets into protection containers, so that they can be transported safely to special storage places, or to hot cells for the after-treatment and corresponding preparations for pharmaceutics. As it was pointed out previously, the C-80 gives a possibility to obtain sources of a high activity practically for a whole list of radionuclides produced at accelerators.

Fig. 1. Cyclotron C-80 (ground floor) with three proton beam lines to the target stations (in the cellar)

3. ^{82}Sr production and extraction from RbCl target material

In the experimental tests for production of ^{82}Sr, the powder of RbCl was used as a target material. The radionuclide ^{82}Sr with a half-live $T_{1/2}$ = 25.55 days is a generator for its daughter isotope ^{82}Rb ($T_{1/2}$ = 1.25 min), which is widely used in PET diagnostics. For separation of the target material and the produced strontium isotopes, a new developed high temperature method was utilized [4].

After irradiation by a 1-GeV proton beam at the PNPI synchrocyclotron, the RbCl powder was placed into a vessel manufactured from stainless steel, which was put into a Ta–W oven heated by direct current. The powder was heated slowly in a high vacuum to a temperature of 900 °C to be evaporated into a separate volume specially constructed to minimize losses of the irradiated material in the process of its evaporation. At that temperature, the process of complete evaporation of the target material of one gram mass takes about one hour. To control the evaporation process, the γ spectrum of the vessel with the irradiated RbCl was measured at regular intervals [5]. Additionally, after each heating the vessel was weighed to control the mass of the evaporated material. In Figures 2 and 3 a part of γ spectra of the irradiated sample of rubidium chlorine is presented. They were measured with a high purity germanium detector. The γ line of the energy 552 keV belongs to the decay of ^{83}Rb with the half-life 86.2 days and its decreasing indicates the efficiency of the target material evaporation. The γ line of the energy 776 keV belongs to the decay of ^{82}Rb with the half-life 1.27 min, which is the daughter isotope of ^{82}Sr, and its decreasing indicates the strontium radionuclide evaporation. In Figure 2, the spectrum of the vessel with the irradiated RbCl before heating is shown by squares. The spectrum after one hour vessel heating at a temperature of 500 °C is shown by circles. In Figure 3, the spectra after heating at a temperature 500 °C (*red dots*) and at a temperature 900 °C (*green dots*) are compared.

As one can see in Fig. 2, heating of the irradiated sample at a temperature 500 °C for one hour does not give any effect on the target material evaporation. The same result was obtained by weighing the sample before and after its heating at 500 °C. At the same time, Fig. 3 shows that after the vessel with the RbCl was heated up to 900 °C, the target material was evaporated completely with almost hundred percent conservation of strontium. The fact of complete evaporation of the irradiated target material was confirmed by weighing the sample before and after its heating at 900 °C. Finally, the conserved radioactive Sr atoms can be evaporated from the vessel at a higher temperature, or it can be washed out by a small amount of an acid solution.

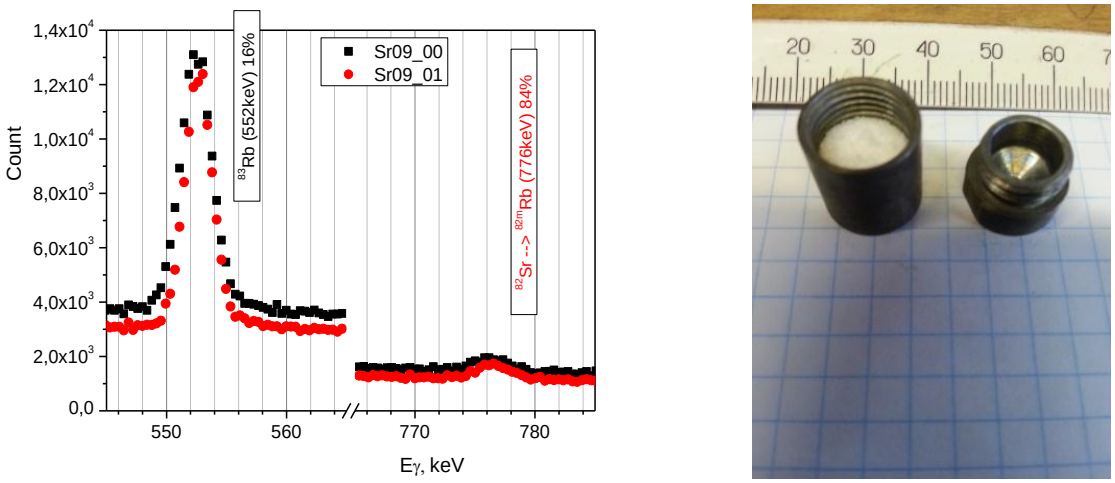

Fig. 2. *On the left* – the spectrum of the vessel with the irradiated RbCl before heating is shown by *squares*; the spectrum after one hour vessel heating at a temperature 500 °C is shown by *circles*. *On the right* – the vessel with the irradiated RbCl powder after one hour vessel heating at a temperature 500 °C is shown [5]. The RbCl white powder is seen in the vessel

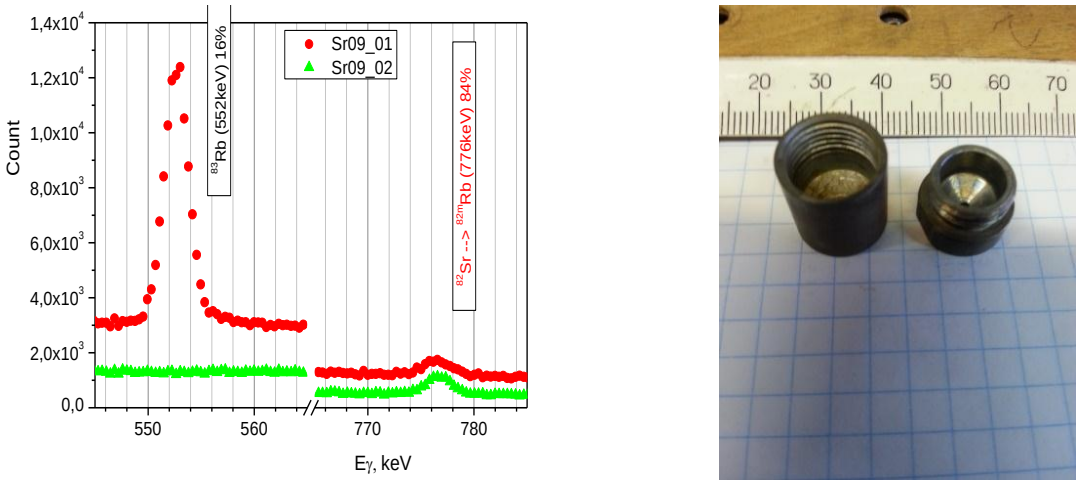

Fig. 3. *On the left* – the spectrum of the vessel with the irradiated RbCl after its heating at a temperature 500 °C (*red dots*) and the spectrum after one hour vessel heating at a temperature 900 °C (*green gots*). *On the right* – the vessel after one hour heating at a temperature 900 °C [5]. It is seen that practically all RbCl powder was evaporate

Therefore, as one can see in Figs. 2 and 3, the separation of strontium isotopes can be performed in a few stages of evaporation of the target material and the produced species by heating the target in a high vacuum at different temperatures. To separate strontium from the rubidium chloride target, the target heating was started at a low temperature 500–900 °C to evaporate the target material RbCl which is considerably higher volatile than strontium atoms. After that, strontium was selectively extracted by washing of internal vessel volume with the HCl solution. Another way of extraction of strontium was to use the niobium or tantalum vessel, which was heated up to 1 700 °C after the target material was evaporated at 900 °C. The evaporated strontium atoms were directed to the collector cooled by floating water. The carried out experiments have demonstrated the efficiency of the target material separation higher than 99.9%. The efficiency of the strontium radionuclide extraction was about 95%.

4. Experiment description and results of ^{67}Cu and other radionuclide extraction from irradiated target materials

In the experimental tests for production of ^{67}Cu, natural metallic Zn was used as a target material. The radionuclide ^{67}Cu with a half-live 2.57 days is considered as a very perspective radioisotope for therapy of some kinds of malignant tumours. For separation of the target material and the produced ^{67}Cu radionuclide, the new so called "dry" high temperature method, similar to the one of strontium isotope extraction was utilized. After irradiation by the 1-GeV proton beam at the PNPI synchrocyclotron, metallic zinc was placed into a vessel manufactured from tantalum, which was put into a Ta–W oven heated by direct current. In a high vacuum, the irradiated zinc was heated slowly up to the temperature 700 °C to be evaporated into a separate volume specially constructed to minimize losses of the irradiated material in the process of its evaporation. The process of complete evaporation of the target material of one gram mass (at the temperature of 700 °C) took about one hour. To control the evaporation process, the γ spectrum of the vessel with the irradiated zinc was measured before and after the heating process. Additionally, the vessel after its heating was weighed to control the mass of the evaporated material. In Figures 4a and 4b, a part of the γ spectra of the irradiated sample of zinc is presented [6]. The γ line of the energy 1 115 keV belongs to the decay of ^{65}Zn with a half-life 244.3 days, and its disappearance indicates the efficiency of the target material evaporation. The fact of complete evaporation of the irradiated zinc target material was confirmed by weighing the sample before and after its heating at 700 °C. The γ line of the energy185 keV belongs to the decay of ^{67}Cu ($T_{1/2}$ = 2.57 days), which is the produced required radioisotope. The spectrum of the vessel with the irradiated Zn before heating is shown in Fig. 4a by *blue dots*. The spectrum after one hour vessel heating at a temperature 700 °C is shown by *red dots*.

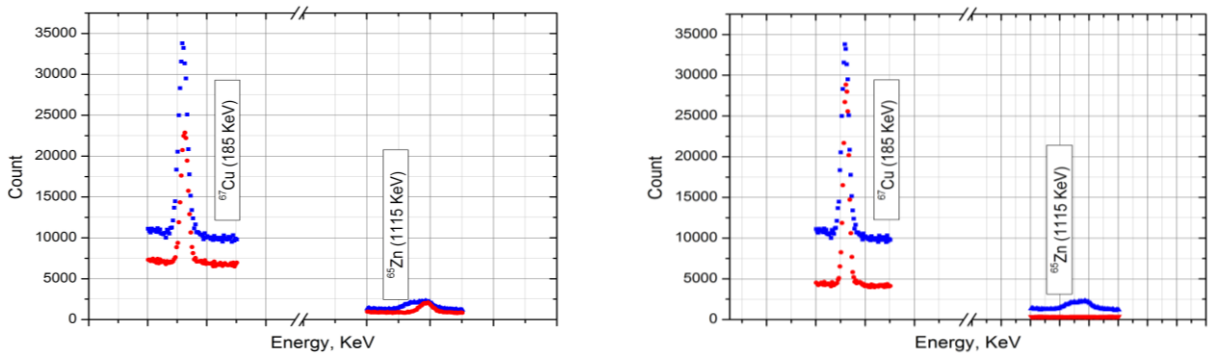

Fig. 4. The spectrum of the vessel with the irradiated Zn before heating is shown by *blue dots*; the spectrum after one hour vessel heating at a temperature 700 °C is shown by *red dots* (a). The spectrum of the evaporated copper atoms collected at the cold finger cooled by floating water after the vessel heating at a temperature 1 460 °C for two hours is shown by *red dots*; for comparison, the spectrum of the vessel with the irradiated Zn before heating is shown by *blue dots* (b)

As one can see, after heating the target material was completely evaporated. It was confirmed by weighing the vessel before and after heating as well. At the same time, the radioactive atoms of copper, having considerably higher boiling point (2 562 °C), remained in the vessel. Also, the presence of the γ line of the energy 1 120 keV of ^{46}Sc ($T_{1/2}$ = 83.8 days) at the spectrum measured after the target material evaporation (Fig. 4a) demonstrates that atoms of scandium which is a rather hard volatile element (boiling point at 2 830 °C) do not evaporate from the target vessel at a temperature of 700 °C. The spectrum of the evaporated copper atoms collected at the cold finger cooled by floating water after heating the vessel at a temperature 1 460 °C for two hours is shown in Fig. 4b by *red dots*. For comparison, the spectrum of the vessel with the irradiated Zn before heating is also shown (*blue dots*). Therefore, as one can see in Figs. 4a and 4b, for separation of the copper radionuclides and the zinc target material, there should be two stages: the first one is slow evaporation of the target material at a temperature about 700 °C; and the second one is evaporation of the produced copper species by heating the target at a temperature 1 460 °C. The first

experiments carried out demonstrated the efficiency of the target material separation better than 99%. The efficiency of the copper radionuclide extraction and collection was about 90%.

In Figure 5, a slightly different part of the γ spectrum of the irradiated sample of zinc is presented. The γ lines of the energy 1 115 and 1 120 keV belong as in the previous spectra to the decay of ^{65}Zn and ^{46}Sc, whereas the γ lines of the energy 1 039 and 1 099 keV are from the decay of ^{66}Cu, which is a daughter isotope of ^{66}Ni, and from the decay of ^{59}Fe. The irradiated Zn spectrum is shown before heating (*blue dots*) and after two hours heating at a temperature 700 °C (*red dots*). As one can see in Fig. 6, the target material (zinc) was fully evaporated from the heated vessel. The fact of complete evaporation of the irradiated zinc target material was confirmed by weighing the sample before and after its heating. At the same time, the radioactive atoms of Ni, Fe, and Sc, having considerably higher boiling points than the target material (Ni – 2 562 °C, Fe – 2 861 °C, Sc – 2 830 °C), remained in the vessel. The boiling point of the target material Zn is 907 °C. These measurements demonstrate that separation of the target material and the produced radioisotope may be very efficient, if the target material and the produced species have considerably different boiling points. This method of separation of the target material, when the required nuclides do not escape from the target vessel can be used only for production of relatively long-lived radionuclides, as the process of evaporation of the target material may take some hours.

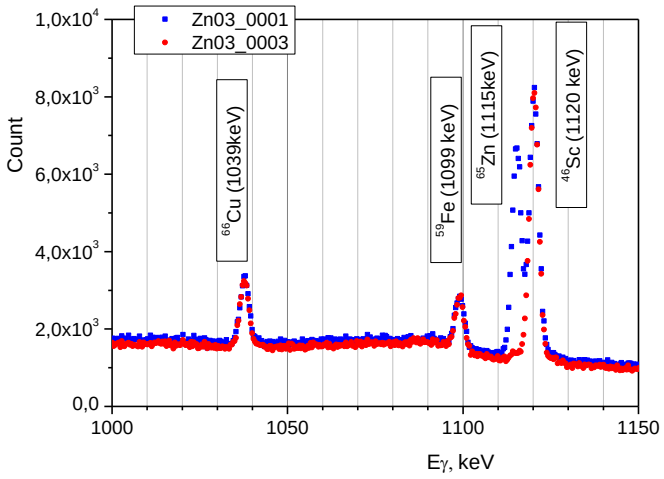

Fig. 5. The irradiated Zn spectrum before heating (*blue dots*) and after two hours heating at a temperature 700 °C (*red dots*)

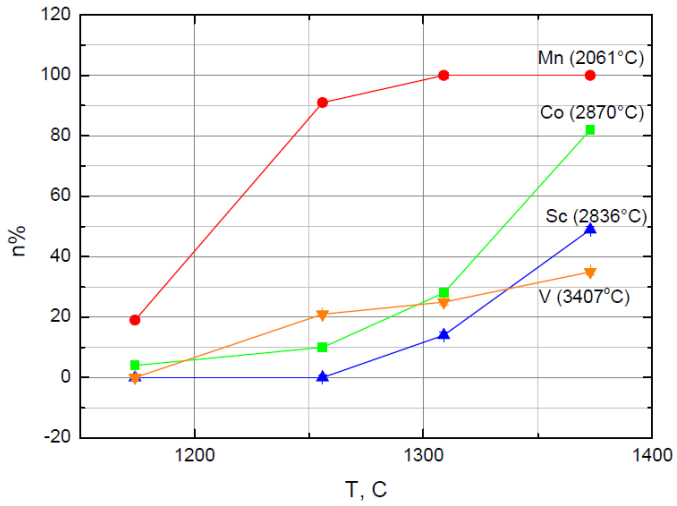

Fig. 6. The evaporated fractions of different radionuclides produced by nuclear reactions in the copper target material and evaporated from it at different temperatures [6]. In the right side in brackets, the boiling points of the evaporated species are presented

Similar experiments were carried out with copper as irradiated target material [6]. A metallic copper sample of natural abundance was heated slowly in the tantalum capsule up to the temperature of 1 500 °C. The mass of the evaporated target material was controlled by weighing the sample after each step of its heating. The evaporated amount of the radioactive species was controlled by measurements of their γ-lines integral counts after each step of heating at the defined temperature. In Figute 6, the fractions of atoms of different radioactive isotopes produced by nuclear reactions in the copper target material and evaporated from it at different temperatures are shown. The evaporated fraction is given by the following equation:

$$n = [(N_1 - N_2)/N_1] \cdot 100\%,$$

where N_1 is the appropriate γ-line integral count before heating; N_2 is the same γ-line integral count after heating at the defined temperature.

As one can see in Fig. 6, the evaporated fraction of the radionuclides produced in the measured temperature interval is in good correlation with their boiling point. This makes it possible to rather effectively separate the radionuclides having considerably different boiling points, for example, to separate the radionuclide Mn from Sc or from V.

5. Conclusion

At PNPI, a high current cyclotron C-80 with the energy of extracted proton beam of 40–80 MeV and the current up to 200 μA has been put into operation lately. One of the main goals of C-80 is production of a large number of medical radio nuclides for diagnostics and therapy. At the present time, the construction of the radioisotope complex RIC-80 at the beam of C-80 is carried out. A peculiarity of the proposed radioisotope facility is the use of the mass-separator with the target-ion source device as one of three target stations for on-line and semi on-line production of a high purity separated radio isotopes. An important part of the work was devoted to the developments of targets for the new project RIC-80. The tested target materials will be used to manufacture real target prototypes for the RIC-80 radioisotope complex. The R@D of new high temperature methods of separation of the produced radionuclides ^{82}Sr and ^{67}Cu from the rubidium and zinc irradiated targets was carried out. As it was demonstrated, the new developed high temperature method can be expanded for production of other medical radionuclides. The following stage of the work will be construction of the target unit prototype with the amount of the target material of 40–60 g, which is required for effective medical radionuclide production at the RIC-80.

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