

TARGET DEVELOPMENT FOR MEDICAL RADIONUCLIDES Cu-67 AND Sr-82 PRODUCTION

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

NRC “Kurchatov Institute”, PNPI, Gatchina, Russia

Abstract. At PNPI NRC KI (Petersburg Nuclear Physics Institute of National Research Center “Kurchatov Institute”), a high current cyclotron C-80 has been put into operation recently. External proton beam of the energy of 70 MeV and intensity of 100 μ A has been obtained. Presently, the work is being carried out to obtain the planned beam parameters: the energy up to 80 MeV and the current up to 200 μ A. The main goal of the C-80 is the production of medical radionuclides for diagnostics and therapy. One of the cyclotron beams is intended for the treatment of ophthalmologic diseases by irradiation of malignant eye formation. The radioisotope complex RIC-80 (Radioactive Isotopes at cyclotron C-80) which is constructed at the beam of C-80 will allow us to obtain sources of high activity practically for the whole list of radionuclides produced at accelerators. An essential peculiarity of the RIC-80 is the use of an on-line mass-separator connected to one of the target stations that will allow the production of separated radionuclides of high purity. The target prototypes intended for the production of different radionuclides at the RIC-80 target stations are being studied and developed. The results of different target material tests for the production of ^{67}Cu , ^{82}Sr and other radioisotopes are presented. A new method of a high-temperature separation of the target materials and produced radioactive isotopes has been discussed.

Key words: Production of medical radionuclides, gamma spectrometry, radioisotopes of a high purity

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1. INTRODUCTION

Developments of nuclear physics experimental methods, combined with the utilization of high current cyclotrons and very sensitive detectors, give a very good possibility for a completely new direction in medical diagnostics and therapies for different diseases. The nuclear medicine technologies used for diagnostics and therapy are based on the employment of artificially-produced radioactive isotopes with specific properties [1]. In this paper, the new installation RIC-80 (Radioactive Isotopes at cyclotron C-80) [2,3] is briefly discussed. It is being constructed presently at the beam of a new C-80 cyclotron [4]. 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 widely used medical radioisotopes. These include $^{64,67}\text{Cu}$, ^{68}Ge , ^{82}Sr , ^{111}In , $^{123,124}\text{I}$, $^{223,224}\text{Ra}$ and others, which are at present under discussion as perspectives for diagnostics and therapy. The mass-separator method will give the possibility for the production of very pure beams of some radioisotopes.

In this paper, the results on the development of a new method [5] of a high-temperature separation of radioisotopes ^{82}Sr and ^{67}Cu and others from different kinds of target materials are presented. The production of radionuclides that decay with emission of positrons,

allowing their use for PET (Positron Emission Tomography), is very important for the diagnostics of different diseases. ^{82}Sr -generator, which is utilized for PET diagnostics of heart and brain diseases, is one of the most needed radionuclides for PET diagnostics over the world.

Radioisotope ^{67}Cu is one of the most promising radionuclides for cancer therapy using monoclonal antibodies. A high demand for ^{67}Cu -based radiopharmaceuticals requires new efficient methods for its production, which are actively developed using accelerators.

2. THE RIC-80 INSTALLATION

The main parameters of the newly built C-80 [3] cyclotron are the following: the proton beam energy can be varied from 40 to 80 MeV and the beam intensity can reach 200 μ A. The cyclotron is intended mainly for the 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 on one of the three target stations. The mass-separator with its target station [2] will allow for the production of separate medical radionuclides of high purity, which

* panteleev_vn@pnpi.nrcki.ru

will be implanted into 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 protective containers so that they can be transported safely to storage, or to hot cells for the post-treatment and corresponding preparations for pharmaceuticals. As it was pointed out previously, the C-80 gives a possibility of obtaining sources of high activity practically for the whole list of radionuclides produced at accelerators.



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

3. ^{82}Sr PRODUCTION AND EXTRACTION FROM RbCl TARGET MATERIAL

In the experimental tests for the production of ^{82}Sr , the powder of RbCl was used as a target material. Radionuclide ^{82}Sr with a half-life of $T_{1/2} = 25.55$ days is a generator for its daughter isotope ^{82}Rb ($T_{1/2} = 1.25$ min) which is widely used in PET diagnostics. For the separation of the target material and the produced strontium isotopes, a newly developed, high temperature method was utilized [4]. All investigations were performed with the target materials irradiated at the proton beam of 1 GeV PNPI synchrocyclotron, as the target station at RIC-80 was not constructed when the measurements were carried out. After irradiation by the 1 GeV proton beam at the PNPI synchrocyclotron, RbCl powder was placed into a vessel manufactured from stainless steel which was put into Ta-W oven heated by the direct current. In a high vacuum, the powder was heated slowly to the temperature up to 900 °C to be evaporated into an

isolated volume specially constructed to minimize losses of irradiated material in the process of its evaporation. At that temperature, evaporating of one gram of material took about one hour. For the evaporation-process control, the γ -spectrum of the vessel with irradiated RbCl was measured before and after each stage of the heating process. Additionally, after each heating, the vessel was weighted for the evaporated material mass control. In Figures 2 and 3, a portion of gamma-spectra of the irradiated sample of rubidium chloride is presented. The spectra were obtained with a high-purity germanium detector. 552 keV gamma-line corresponds to ^{83}Rb decay (half-life is 86.2 days). All the spectra have been corrected for the decay according the measurement time moment. The intensity drop indicates the efficiency of the target material evaporation. The gamma-line of the energy of 776 keV represents ^{82}Rb decay with a half-life of 1.27 min, which is the daughter isotope of ^{82}Sr and its decrease indicates the strontium radionuclide evaporation. In Fig. 2, the spectrum of the vessel with the irradiated RbCl before the heating is shown by squares. The spectrum after one hour vessel heating at a temperature 500 °C is shown by circles. In Fig. 3, the comparison of the spectra after heating at a temperature of 500°C (circles) and at a temperature of 900°C (triangles) is shown.

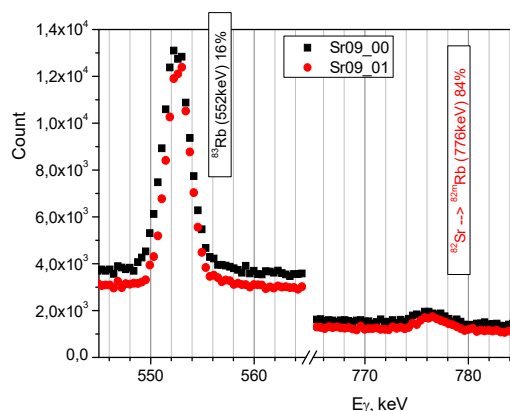


Figure 2. The spectrum of the vessel with the irradiated RbCl before the heating is shown by squares. The spectrum after one-hour vessel heating at the temperature of 500 °C is shown by circles. Also, the vessel is shown with irradiated RbCl powder after one-hour vessel heating at the temperature of 500 °C.

As it can be seen from Fig. 2, the heating of the irradiated sample at a temperature of 500°C during

one hour does not have any effect on the target material evaporation. The same result was obtained by the sample weighting before and after heating up to 500°C. At the same time, Fig. 3 shows that if the vessel with the RbCl is heated up to 900°C, the target material evaporates completely with almost a hundred percent conservation of strontium. The fact of complete evaporation of the irradiated target material has been confirmed by the sample weighting before and after heating at 900°C. Concerning the efficiency of the RbCl target material evaporation, the weighting procedure gives the value better 99.9% and gamma-spectrometry analysis (integral counts of the peak before/after heating) with the background subtraction gives of about 99% concerning the measurement errors). Finally remaining radioactive Sr atoms can be evaporated from the vessel at higher temperature [6], or washed by a small amount of an acid solution.

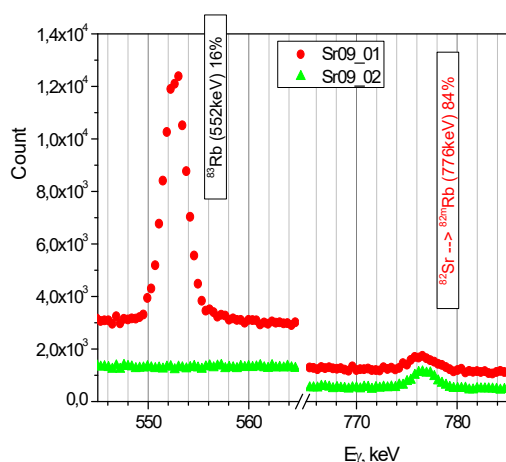


Figure 3. The spectrum of the vessel with the irradiated RbCl after heating at the temperature up to 500 °C is shown with red circles. The spectrum at the collector after one-hour vessel heating at the temperature of 1900-1950 °C [6] is shown with green triangles. The vessel is shown after one hour-heating at the temperature of 900 °C.

Therefore, as it can be seen from Figures 2 and 3, for the separation of strontium isotopes, some stages of the evaporation of the target material and produced species in the process of the target heating in a high vacuum at different temperatures should exist. In

order 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 has a considerably lower boiling point than strontium. After that, strontium was selectively extracted by washing the internal vessel volume with HCl solution. Another way of strontium extraction was the niobium or tantalum vessel use, heating it up to 1900°C [6] after the target material evaporation at 900 °C. The evaporated strontium atoms were directed to the collector cooled by the floating water. The experiments gave the efficiency of the target material separation better 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 of the production of ^{67}Cu , natural metallic Zn was used as target material. Radionuclide ^{67}Cu with a half-life of 2.57 days is considered a very promising radioisotope for the therapy of some kinds of malignant tumors. For the separation of the target material and ^{67}Cu radionuclide, a 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 Ta-W oven heated by the direct current. In a high vacuum, the irradiated zinc was heated slowly up to the temperature 700°C to be evaporated into an isolated volume specially constructed to minimize losses of irradiated material in the process of its evaporation. At that temperature, the process of complete evaporation of the target material of one gram mass took about one hour. For the evaporation process, the γ -spectrum of the vessel with irradiated zinc was measured before and after the heating process. Additionally, after the heating, the vessel was weighted for the evaporated material mass control. In Figures 4 and 5 a part of gamma-spectra of the irradiated sample of zinc is presented. The gamma line of the energy of 1115 keV belongs to the decay of ^{65}Zn with the half-life of 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 has been confirmed by the sample weighting before and after heating it at 700°C. The gamma line of the energy of 185 keV belongs to the decay of ^{67}Cu ($T_{1/2}=2.57$ days), which is the radioisotope of interest. In our experiment zinc was irradiated by 1 GeV protons. According the FLUKA code calculation the yield of ^{67}Cu is 25 higher than of ^{67}Ga . It is the reason that gamma-line 185 keV mainly belongs to ^{67}Cu . This is confirmed by the fact that the second line 300 keV, which should be the same intensity as 185 keV, if it is from ^{67}Ga decay, is about 5% from the its intensity. It confirms that 300 keV line is also from the decay of ^{67}Cu . In Fig. 4, the spectrum of the vessel with the irradiated Zn before the heating is shown by squares. The spectrum after one-hour vessel heating at the temperature of 700 °C is shown by circles.

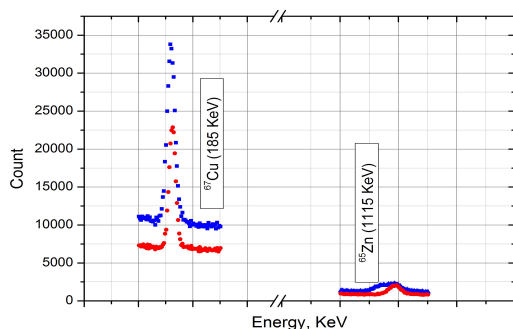


Figure 4. The spectrum of the vessel with the irradiated Zn before the heating is shown by squares. The spectrum after one-hour vessel heating at the temperature of 700 °C is shown by circles.

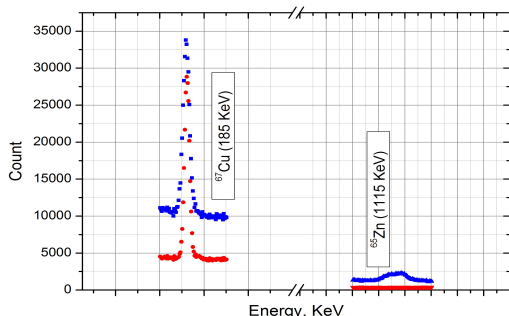


Figure 5. The evaporated copper atoms collected at the finger cooled by floating water after the vessel heating at the temperature of 1460 °C in two hours (red circles) are presented. For comparison, the spectrum of the vessel with the irradiated Zn before the heating is shown with blue squares.

As it can be seen, after the heating, the target material completely evaporated. It was confirmed by the weighting of the vessel before and after heating as well. At the same time, radioactive atoms of copper, having considerably higher boiling point (2562 °C), remained in the vessel. The method for separation Sr and Cu radionuclides from the target material uses different partial vapor pressure (which is in a good correlation with boiling points) of produced radionuclides and irradiated target material. 1 GeV proton irradiation produces wide spectrum of radionuclides via many different reaction. The production cross-section of ^{46}Sc is high enough, as all strong gamma-lines of this isotope are seen in the measured spectra. The presence of the gamma line of the energy of 1120 keV of ^{46}Sc ($T_{1/2}=83.8$ days) at the spectrum measured after the target material evaporation (Fig. 4) demonstrates that atoms of scandium, which are a rather hard volatile element (boiling point 2830 °C), do not evaporate from the target vessel at the temperature of 700 °C. The process of the target material evaporation was carried out in vacuum about 10^{-5} mbar at the temperature, when the target material should be completely evaporated during a rather short period comparing with life time of the produced radionuclide. At the same time the radionuclide of interest having much lower partial pressure (much higher boiling point) remains in the heated capsule. The evaporation process was in

vacuum without any gas admixture. The collector (copper finger with a niobium or tantalum foil at the end point), cooled by floating water, was placed at the distance about two mm from the hole of the heated capsule. The water temperature at the finger entrance was about 20 °C and at the exit about 25 °C. In the Fig. 5 the spectrum of evaporated copper atoms collected at the cold finger cooled by floating water after the vessel heating at the temperature 1460 °C in two hours (red circles) is presented. For comparison, the spectrum of the vessel with the irradiated Zn before the heating (blue squares) is shown. Therefore, as it can be seen from Figures 4 and 5, for the separation of copper radionuclides and zinc target material, two stages should exist: the first one is a slow evaporation of the target material at the temperature of approximately 700 °C; the second one is the evaporation of the produced copper species in the target heating process at the temperature of 1460 °C.

The first experiments gave the efficiency of the target material separation better than 99%. The efficiency of the copper radionuclide extraction and collection was about $(90 \pm 15) \%$. The efficiency was calculated by the gamma-spectrometry analysis, comparing the gamma line intensities from the cavity and from the collector.

In Fig. 6, a slightly different part of gamma-spectra of the irradiated sample of zinc is presented. The gamma lines of the energy of 1115 keV and 1120 keV belong to the decay of ^{65}Zn and ^{46}Sc and gamma lines of the energy of 1039 keV and 1099 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 the heating (squares) and after two hours of heating at a temperature of 700 °C (diamonds). As it can be seen from Fig.6, the target material (zinc) fully evaporated from the heated vessel. The fact of complete evaporation of the irradiated zinc-target material was confirmed by the sample weighting before and after the heating. At the same time, radioactive atoms of Ni, Fe and Sc, having considerably higher boiling point than the target material (Ni - 2562 °C, Fe - 2861 °C, Sc - 2830 °C), remained in the vessel. The boiling point of the target material Zn is 907 °C.

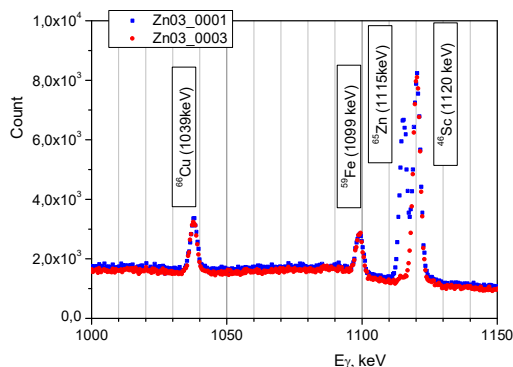


Figure 6. The irradiated Zn spectrum before the heating (squares) and after two hours of heating at the temperature of 700 °C (diamonds)

These measurements demonstrate that the target material and the produced radioisotope separation may be very efficient if the target material and the

produced species have considerably different boiling points. This method of target material separation, when the required nuclides do not escape from the target vessel, can be used only for the production of respectively long-lived radionuclides, as the process of the target material evaporation may take some hours.

Similar experiments were carried out with copper as the irradiated target material. Metallic copper sample of natural abundance was heated slowly in the tantalum capsule up to the temperature of 1500 °C. The evaporated target-material mass was controlled by the sample weighting after each step of heating. The evaporated amount of radioactive species was controlled by the measurements of their gamma-lines integral counts after each step of heating at a defined temperature. Fig. 7 shows the fraction of different radionuclides produced by nuclear reactions in the copper target material and evaporated from it at different temperatures. The evaporated fraction is given by the following equation:

$$n = [(A_1 - A_2) / A_1] \times 100\%,$$

where A_1 is appropriate γ -line integral count before the heating, A_2 is the same γ -line integral count after the heating at a defined temperature.

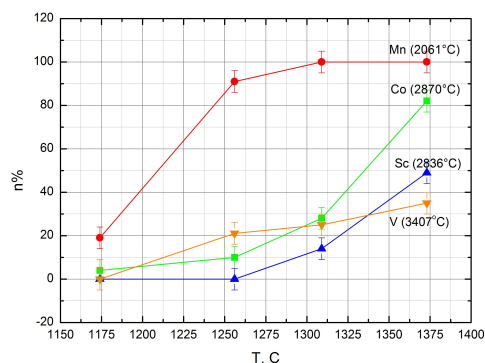


Figure 7. The evaporated fraction of different radionuclides produced by nuclear reactions in the copper target material and evaporated from it at different temperatures. The boiling points of evaporated species are presented on the right side in brackets.

As it can be seen from Fig. 7 in the measured temperature interval, the evaporated fraction of produced radionuclides is in a good correlation with their boiling points. This can give a possibility of rather effective separation of radionuclides, having considerably different boiling points as, for example, the separation of radionuclide Mn from Sc or from V. The difference in evaporation of Co and Sc, which have very close boiling points, can be explained by the fact that these metals are from different groups and the desorption energy from tantalum surface of the capsule can be different for these elements. In that case more precise measurements are needed.

5. CONCLUSIONS

At PNPI NRC KI, a high-current cyclotron C-80 with the energy of extracted proton beam of 40-80 MeV and the current up to 200 μ A has been put into operation lately. One of the main goals of C-80 is

production of a large number of medical radionuclides for diagnostics and therapy. At present time, the construction of radioisotope complex RIC-80 at the beam of C-80 is in progress. The use of the mass-separator with the target-ion source device as the target station will give a possibility of on-line, or semi on-line production of high-purity separated radionuclides. An important part of the work is devoted to the investigation of new target materials and the target developments for the new project RIC-80. R&D of new high-temperature methods of separation of produced radionuclides ^{82}Sr and ^{67}Cu from rubidium and zinc targets has been carried out. As it was demonstrated, the newly developed high-temperature method can be expanded for production of other medical radionuclides. The clear advantage of the suggested method is an absence of liquid radioactive waste which is a big problem when a radiochemical separation method of produced radionuclides is used. As to efficiencies, they are comparable for both methods ($\geq 95\%$). The comparison of radionuclide and chemical purity obtained by both methods is not possible at the moment, as further investigations of a high temperature method using the beam of 80 MeV with a big amount of the target material (about 50 g) are required.

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