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Original research paper

NEW METHOD DEVELOPMENT FOR MEDICAL RADIONUCLIDE ^{223,224}Ra, ^{225}Ac PRODUCTION*

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Abstract. *The cyclotron C-80 capable of producing 40–80 MeV proton beams with a current of 100–200 μA has been constructed and put into operation at PNPI NRC KI (Petersburg Nuclear Physics Institute of National Research Center "Kurchatov Institute") [1]. Presently, the system for the simultaneous beam transportation to the target stations for radioisotope production and to the medical box for the treatment of ophthalmologic diseases is being developed. One of the main goals of the C-80 cyclotron is the production of a wide spectrum of medical radionuclides for diagnostics and therapy. For this purpose, the project of the radioisotope complex RIC-80 (Radio Isotopes at the cyclotron C-80) has been developed. A high vacuum, high resolution mass-separator application at one of the three target stations of RIC-80 will allow on-line or semi on-line production of high-purity radioisotopes. Among them are ^{223,224}Ra and ^{225}Ac, which decay by alpha particle emission and are used for the therapy of malignant tumors at the early stage of their appearance. Results of the target and ion source tests for the production of ^{223,224}Ra and ^{225}Ac radioisotopes by different methods, including the one with the mass-separator use, are presented.*

Key words: *Medical radionuclides of high purity, radioisotope complex, production targets, mass-separator, alpha- and gamma-spectroscopy*

1. INTRODUCTION

The use of high current cyclotrons provides very good opportunities for nuclear medicine. Nuclear medicine technologies are based on the application of artificially produced radioactive isotopes with specific properties. In this paper, the mass-separator method for production of the alpha-particle emitters ^{223,224}Ra, ^{225}Ac at the new installation RIC-80 (Radioactive Isotopes at cyclotron C-80) [2], [3] is discussed. RIC-80 is planned to produce widely used medical radioisotopes including ^{64,67}Cu, ^{68}Ge, ^{82}Sr, ^{111}In, ^{123,124}I, ^{223,224}Ra, and ^{225}Ac, utilized 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 of the experiments, making use of a new method [4] of a high temperature release and mass-separation of ^{223,224}Ra and ^{225}Ac from ^{238}UC (uranium mono-carbide of a high density) as a target material, are presented. Pharmaceuticals produced on the base of these alpha-emitting radionuclides are of great importance for malignant tumors treatment at a very early stage of their appearance.

2. PRODUCTION AND EXTRACTION OF RADIUM ISOTOPES FROM A URANIUM CARBIDE TARGET OF A HIGH DENSITY

2.1. Separation of ^{223,224}Ra from a target material by a high-temperature extraction method

Radionuclides decaying by alpha-particle emission are very effective tools for the therapy of different malignant tumors at a very early stage of their formation [5], [6]. One of the general advantages of an alpha particle is its very short range (60-80 μm) in biological tissue. The action of a radionuclide, decaying by alpha particles, is very effective, as it is very local and does not destroy the surrounding healthy tissues. Alpha-decaying radionuclides used for therapy are the ^{223}Ra ($T_{1/2}$=11.4 days), ^{224}Ra ($T_{1/2}$=3.66 days), and ^{225}Ac ($T_{1/2}$=10.0 days). They can be produced by proton irradiation of uranium or thorium targets. The measured cross-sections of ^{227}Th and ^{225}Ac production from a thorium target by the 80 MeV protons are 30 and 5 mb, respectively [7]. A high-temperature method of extraction of ^{223,224}Ra produced by protons in ^{238}UC was described in detail in [8]. In Fig. 1, the alpha spectrum of species evaporated at 2400°C from a UC target on a cooled tantalum collector is shown. ^{223}Ra is produced in the subsequent alpha decay of ^{227}Th:

^{227}Th(18.7d) → ^{223}Ra(11.4d) → ^{219}Rn(3.96s) → ^{215}Po(1.8ms) → ^{211}Pb(36.1min) → ^{211}Bi(2.14min) → ^{207}Tl(4.77)min → ^{207}Pb(stable).

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^{224}Ra is produced in a similar way from the alpha decay of ^{228}Th. As seen from the decay chain presented above, the decay of ^{223}Ra gives four alpha particles; this leads to a considerable increase of the method efficiency. These experiments on ^{223,224}Ra production demonstrated a principal possibility to obtain these radionuclides from a high-density UC target. However, as one can see from Fig.1, samples extracted at high temperature are a strong mixture of ^{223}Ra and ^{224}Ra. Separation of these radionuclides is not very efficient, as they have rather close half-lives.

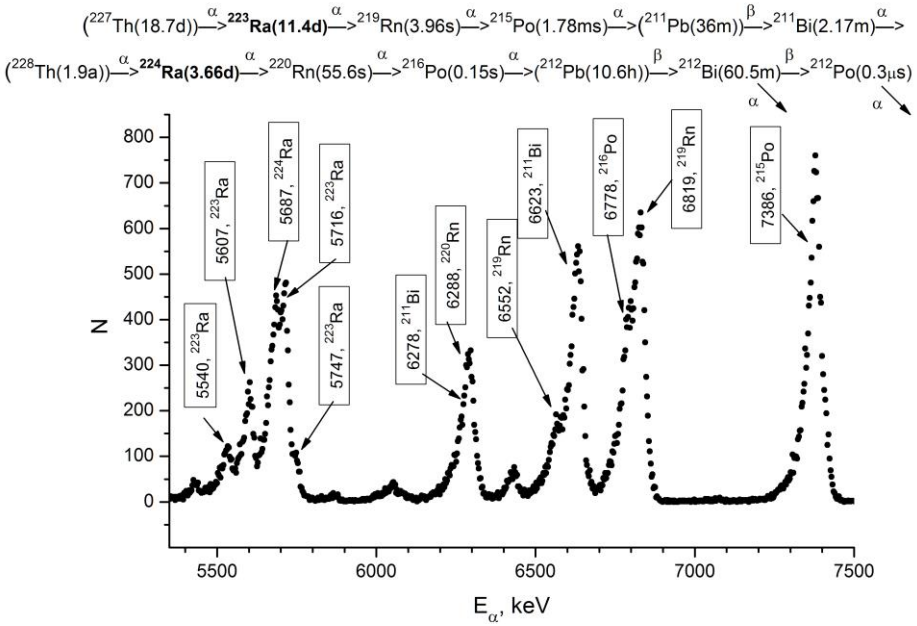

Figure 1. Alpha spectrum of species evaporated at 2400°C from a UC target on the cooled tantalum collector [8]

2.2. On-line production of mass-separated isotopes ^{223,224}Ra and ^{225}Ac at the IRIS mass-separator

The mass-separated isotopes ^{223,224} Ra and ^{225}Ac were produced at the ISOL facility IRIS (Investigation of Radioactive Isotopes at Synchrocyclotron) [9] working on-line with a 1-GeV proton beam of the synchrocyclotron of Petersburg Nuclear Physics Institute (Gatchina, Russia). ^{223,224}Ra and ^{225}Ac were produced in a UC target, ionized in a high-temperature surface ionization source, were extracted and accelerated by a 30 kV potential difference. After passing the mass-separator magnet, separated radioactive ion beams were produced. For on-line measurements of the alpha and gamma spectra of the produced radionuclides, the selected ion beams were directed through a vacuum ion guide to a tape-station collector. According to the chosen mass-separator magnetic field, the ion beams with mass numbers 223, 224, 225 were in turn implanted into the tape-collector and after accumulation during a certain time, the radioactive sources were moved to the alpha or gamma detector station for appropriate spectra measurements. For further manipulations, the separated radioisotopes were implanted into collector foils placed in the focal plane of the mass-separator magnet. Several isotope beams were implanted simultaneously during 5-10 hours. After 10 days of radiation cooling, the foils with implanted radionuclides were taken out from the collector chamber of the mass-separator and cut into strips of 5 mm width. To get the experimental value of the magnet dispersion, the strips with implanted separated radionuclides in the mass region 223 – 225 were measured with alpha and gamma detectors. In Fig. 2, the relative amount of the separated radionuclides ^{223}Ra and ^{225}Ac implanted into the aluminum foil collector disposed in the focal plane of the mass-separator magnet measured by their gamma-lines are presented as a function of the strip position. As one can see from Fig. 2, the mass lines 223, 225 are resolved rather well, although there is some cross-contamination due to their long “tails”. The mass line resolution can be considerably improved by a more precise alignment of the tube of the surface ionization ion source and optimization of its geometry. Also, special slits in the front of the focal plane of the mass-separator magnet should be installed to cut the mass-line “tails”.

In Fig. 3, the alpha spectra of mass-separated ^{223}Ra and ^{225}Ac are presented. Ions of ^{223}Ra and ^{225}Ac were implanted into the aluminum foil-collector installed in the collector chamber in the focal plane of the mass-separator magnet. As pointed above, the process of implantation was carried out simultaneously in the atomic mass region of 223-225 for 5-10 hours. There are no alpha lines of ^{224}Ra with half-life $T_{1/2}$ = 3.66 days in the presented alpha spectra, as the measurements of foils-collectors were carried out after 10 days of radiation cooling. However, mass-separated ^{224}Ra could be obtained as well, if the time of radiation cooling would be much shorter.

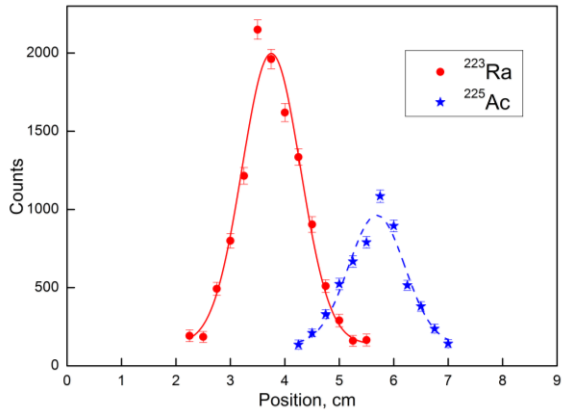

Figure 2. The relative amount of the separated radionuclides ^{223}Ra and ^{225}Ac as a function of the distance from the edge of the collector alpha spectrum

As one can see from Fig. 3, there is a rather good separation of ^{223}Ra and ^{225}Ac accumulated in the mass-separator collector. However, in every measured alpha spectrum there is an admixture (5-10%) of alpha lines of the neighbor radionuclide: there are weak alpha lines of ^{223}Ra in the spectrum of ^{225}Ac and vice versa. This fact is a result of a poor mass-separator resolution. Ways to improve the separator mass resolution were discussed above.

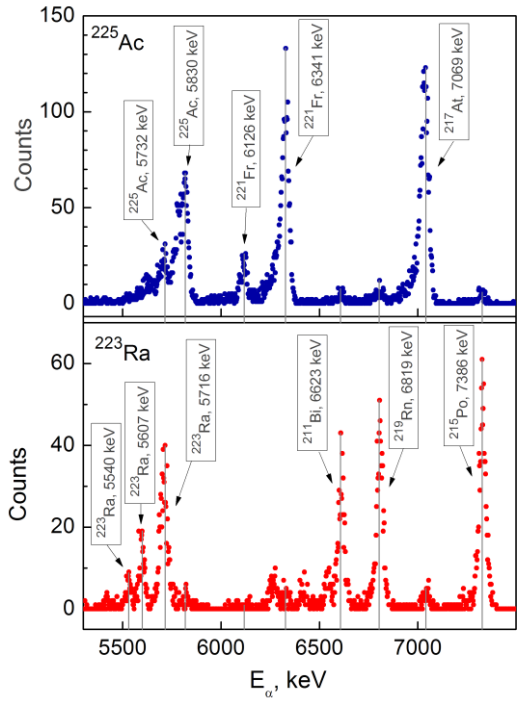

Figure 3. Alpha spectra of mass-separated ^{225}Ac and ^{223}Ra (^{225}Ac($T_{1/2}$=10d) → ^{221}Fr($T_{1/2}$=4.9min) → ^{217}At($T_{1/2}$=32.3ms) → ^{217}Bi($T_{1/2}$=98.5s) → ^{213}Po($T_{1/2}$=3.72 μs) → ^{209}Pb($T_{1/2}$=3.23h)) and (^{223}Ra($T_{1/2}$=11.4d) → ^{219}Rn($T_{1/2}$=3.96s) → ^{215}Po($T_{1/2}$=1.8ms) → ^{211}Pb($T_{1/2}$=36.1min) → ^{211}Bi($T_{1/2}$=2.14min) → ^{207}Tl($T_{1/2}$=4.77min))

3. On-line production efficiency

The production efficiency of some long-lived radionuclides was estimated. This value was determined as the ratio of the amount of the isotope accumulated in the mass-separator collector to its amount produced in the target at the same period of time. The values of the efficiency of a similar surface ionization source with the use of the off-line mass-separator were determined for Sr and Rb in our previous experiments [3]. The values obtained in off-line and on-line experiments were in a good agreement within the limits of experimental errors. It is necessary to point out here that, as a high-temperature surface ionization ion source, a specially manufactured tungsten tube with a high work function, 5 eV of the internal tube surface, was utilized. In Table 1, the values of the production efficiency for some radionuclides determined in on-line measurements are presented.

Table 1. Values of the production efficiency for some radionuclides determined in on-line measurements

Element	Ionization potential (eV)	Efficiency (%)
Cs	3.9	51(15)
Rb	4.2	47(10)
Ra	5.3	38(10)
In	5.8	33(8)
Tl	6.1	21(8)

4. Efficiency of extraction of implanted radium isotopes from the collector foil

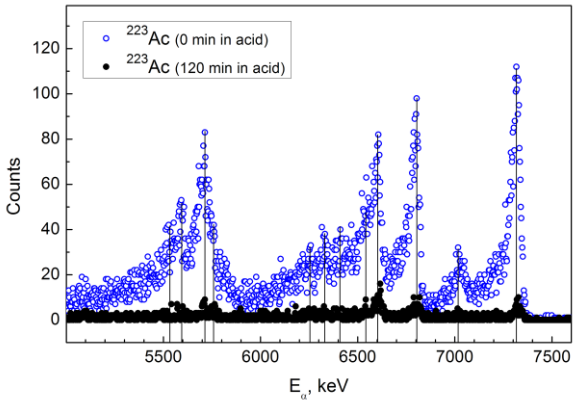

Figure 4. Alpha spectrum of the sample of ^{223}Ra from a foil-collector before (blue circles) and after (black squares) keeping it for 2 hours in 3 ml of 10% of HCl solution

For the first experiments of testing the extraction efficiency of implanted radium isotopes, a 100-μm-thick aluminum foil was utilized as the collector material. The implantation area was a 3-4 mm diameter spot separated from its neighbor implantation spot by about 10 mm in this mass region. 10% of HCl solution (3 mg) was used for the extraction and washout of ^{223}Ra atoms from the spot which has the implantation depth of about 50 Å. In Fig.4, the result of the washout of ^{223}Ra from a foil-collector after

keeping it for 2 hours in 3 ml of 10% of HCl solution is presented. As one can see, the washout process was rather efficient, as 90% of radium atoms have been washed away from the collector. The dissolving process of collector material in chlorine acid was controlled as well by weighing the collector before and after the washout process. With accuracy at the level of 0.1%, the dissolving of the 40 mg collector was not observed.

5. Conclusion

The presented work reports the development of new methods for the production of the medical radionuclides ^{223,224}Ra and ^{225}Ac, decaying by alpha-particle emission used for the therapy of malignant tumors. For the extraction of the produced radionuclide, two methods were used: high-temperature separation of the produced species from the target material in high vacuum and on-line production of mass-separated radionuclides with the IRIS facility. As it was demonstrated, both methods give a high efficiency of production of the required radionuclides at a temperature of the target material in the region of 2300–2400 C. It was also shown that the surface ionization source, prepared in a special way from a tungsten mono-crystal with a work function of the inner surface of 5 eV, allows obtaining production efficiency for the required radioisotopes of about 40%. This efficiency can be increased up to 80-100% [10]. It is necessary to stress that the mass-separator method provides simultaneous implantation of several isotope-separated beams of required radionuclides, which can be easily extracted from the collector by a washout in a small amount of an acid solution. As it was demonstrated by the first experiments, the efficiency of radium extraction from an aluminum collector reaches 90%. Additionally, it is necessary to point out that high density thorium carbide planned to be utilized as a target material for the production of ^{223,224} Ra and ^{225}Ac at RIC-80, possesses very similar physical and chemical properties to uranium carbide used in our experiments. At the same time, the production cross-sections are expected to be much higher. The next step will be R&D of targets prepared from ThC for ^{223,224} Ra and ^{225}Ac radionuclide production.

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