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Measurements of the Cumulative Yield of the ^{103}Ru Radioisotope through the ^{100}Mo(^{4}He, $n + p$)^{103}Ru Reaction and a Technique for Gas Thermal Separation of ^{103}Ru from a ^{100}MoO$_3$ Target

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Abstract—The cumulative yield of the ^{103}Ru radioisotope was measured using the activation method when a ^{100}MoO$_3$ target was irradiated by ^{4}He nuclei with an energy of 60.3 MeV at the U-150 cyclotron of the Kurchatov Institute National Research Center. The measured ^{103}Ru yield was $(4.93 \pm 0.84) \times 10^4$ Bq/(μA h). An experimental technique has been developed for prompt gas thermal separation of ^{103}Ru radioisotope from an irradiated target. An experimental setup has been created to implement the ^{103}Ru extraction technique. The design of the setup and the principle of its operation are presented. It is shown that the technique ensures the extraction of at least 97% ^{103}Ru from the target material and the return of at least 96% ^{100}MoO$_3$ for reuse. The developed technique can find practical application in the production of the ^{103}Ru radioisotope by irradiating of ^{100}MoO$_3$ cyclotron targets with ^{4}He nuclei.

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INTRODUCTION

A new approach to cancer therapy is currently discussed in a number of publications. This approach is based on the use of modular nanotransporters (MNT) [1]. MNT are synthesized on the basis of a polypeptide platform and are capable of delivering therapeutic “short-range” radionuclides to a cancer cell nucleus. Loading MNTs with “short-range” radionuclides can effectively destroy both individual cancer cells and micrometastases that are not detected by modern diagnostic methods. At the same time, they hardly have a negative cytotoxic effect on healthy cells and tissues. This technique can be used both after surgery and after chemotherapy as a finishing therapeutic procedure aimed at eliminating the cancer recurrence.

It is proposed to use Auger electron emitters in tandem with MNT as therapeutic “short-range” radionuclides [2]. Auger electrons have a short range and a high specific linear energy loss. They are capable of damaging cells within a few tens of nanometers without having a cytotoxic effect at long distances. ^{103m}Rh isotope is considered to be one of the most promising Auger electron emitters for immunotherapy [3]. It has the smallest ratio of the number of emitted γ rays to the number of electrons and can be produced using the generator method. The ^{103}Ru radionuclide ($T_{1/2}$ = 39.274 days) is the ^{103m}Rh ($T_{1/2}$ = 56.1 min) precursor in the generator. One of the ways to obtain ^{103}Ru at the U-150 cyclotron of the Kurchatov Institute National Research Center can be the ^{100}Mo(^{4}He, $n + p$)^{103}Ru reaction. Experimental data on the ^{103}Ru cumulative yield in the ^{100}Mo(^{4}He, $n + p$)^{103}Ru reaction are not available in the literature. In order to clarify the efficiency of ^{103}Ru production in this reaction, the cumulative yield of ^{103}Ru was measured upon irradiating a ^{100}MoO$_3$ target by ^{4}He nuclei with an energy of 60.3 MeV.

The developed gas-thermal technique was used to extract ^{103}Ru from the irradiated ^{100}MoO$_3$ target. An experimental setup was manufactured to implement the technique. The structural elements used in the setup and the temperature conditions were selected to ensure the target gasification and almost complete ^{103}Ru separation from the ^{100}MoO$_3$ matrix.

MEASUREMENT OF THE ^{103}Ru CUMULATIVE YIELD IN THE ^{100}Mo(^{4}He, $n + p$)^{103}Ru REACTION

The yield of the ^{103}Ru radioisotope was determined using an activation technique. A target in the form of a disk with a diameter of 8 mm and a thickness of 3 mm

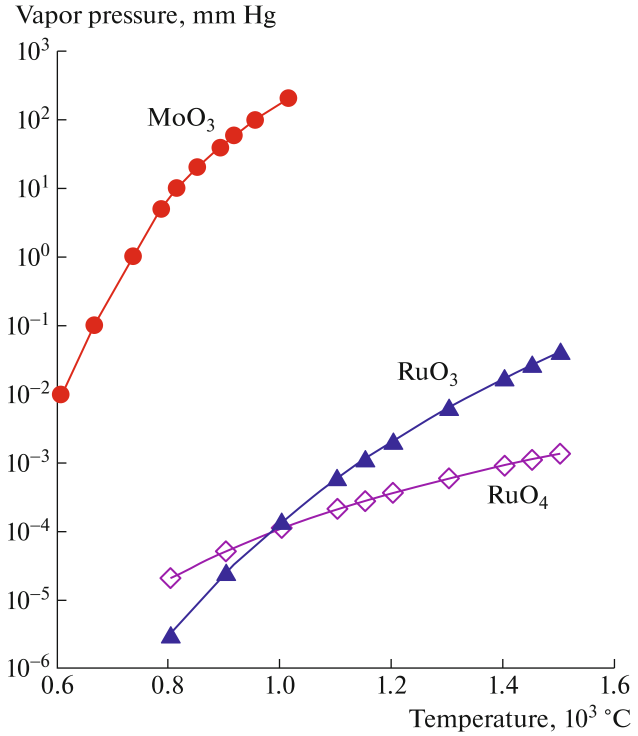

Fig. 1. Temperature dependences of the MoO_3 vapor pressure and the partial RuO_3 and RuO_4 pressures over the RuO_2 in the atmosphere O_2.

was made of MoO_3 powder with molybdenum enriched to 99.7% in the ^{100}Mo isotope. It was packed into a target device that had a 100-μm-thick aluminum foil window at the beam inlet. The target device was placed in the chamber of the U-150 cyclotron of the Kurchatov Institute National Research Center and was irradiated with ^4He nuclei at a current of ≈0.15 μA until a total charge of ≈0.3 μA h was attained. The target had a bulk density of 2.0 g/cm^3, which was determined by weighing. The energy of the ^4He nuclei at the entrance to the $^{100}MoO_3$ target was 60.3 MeV. The range of ^4He nuclei, calculated using the SRIM program [4], fit into the target thickness. The total charge of nuclei incident on the target during irradiation was measured using a special integrating device. The energy of the accelerated nuclei was determined by the cyclotron parameters.

After the target was irradiated and then held for 3 days, the ^{103}Ru activity was determined by the full-energy peak of γ rays with energy E_γ = 497.085 keV (K_γ = 91%) [5]. The measurements were made using an ORTEC GEM 35P4 γ spectrometer (United States) with a high-purity germanium detector with a volume of ~100 cm^3. The targets were placed at a distance of 40 cm from the end surface of the detector during the measurements. The dead time of the spectrometer did not exceed 5% in the activity measurements. The energy dependence of the γ-ray detection efficiency was determined experimentally using reference spectrometric γ-ray sources from an OSGI kit. The acquisition time of γ spectra was 1 h. The target activity was measured several times during the ^{103}Ru half-life.

The ^{103}Ru yield was determined using the formula

$$V = AZ_1[1 - \exp(-\lambda T_1)]/\{Z_2[1 - \exp(-\lambda T_2)]\}, \quad (1)$$

where V [Bq/(μA h)] is the ^{103}Ru yield; A [Bq] is the ^{103}Ru activity in the target, referred to the end of irradiation; Z_1 [rel. units] is the current-integrator reading that corresponds to a charge of 1 μA h; λ [s^{-1}] is the decay constant of ^{103}Ru; T_1 [s] is the irradiation time equal to 1 h; Z_2 [rel. units] is the current-integrator reading over the irradiation time; and T_2 [s] is the the actual time of the target irradiation.

The ^{103}Ru cumulative yield obtained in the experiment was (4.93 ± 0.84) × 10^4 Bq/(μA h). The measurement error of the yield was 17% with a confidence probability of 68%. The following error components were taken into account: the error in determining the detector efficiency, the error in determining the full-energy peak area in the measured γ-ray spectrum, and the error of the branching fraction.

TECHNIQUE FOR GAS THERMAL SEPARATION OF ^{103}Ru FROM A $^{100}MoO_3$ TARGET

The developed technique for gas thermal separation of ^{103}Ru from a $^{100}MoO_3$ target irradiated at the cyclotron is based on a significant difference in the volatility of MoO_3 and Ru oxides. Figure 1 presents comparative data on the temperature dependence of the MoO_3 vapor pressure [6] and the partial pressures of RuO_3 and RuO_4 [7, 8] over RuO_2 in an oxygen atmosphere. According to Fig. 1, the partial pressures of MoO_3 vapors and Ru oxides in comparable temperature ranges differ by several orders of magnitude.

A setup has been created to implement the technique for separating $^{100}MoO_3$ and Ru oxides; its diagram is shown in Fig. 2. The setup was evacuated by forevacuum pump *10* and was filled with oxygen from cylinder *1* using reducer *16*. The central elements of the setup were two coaxial fused-silica ampoules *4* and *5*, which were connected to a gas stand, and crucible *7* with irradiated $^{100}MoO_3$ powder. The external fused-silica ampoule *4* was connected to the gas stand using a vacuum seal through a fitting made of D16 aluminum alloy. One end of the fitting was glued to the ampoule by ED-6 epoxy resin, and the other was connected to the flanges of the stand using gaskets. Such a device simplifies the sealing process, since it allows less stringent requirements for the quality of the fused-silica ampoule (the degree of its ellipsis and the surface roughness) and reduces the risk of ampoule splitting during the sealing. The vacuum or the required O_2

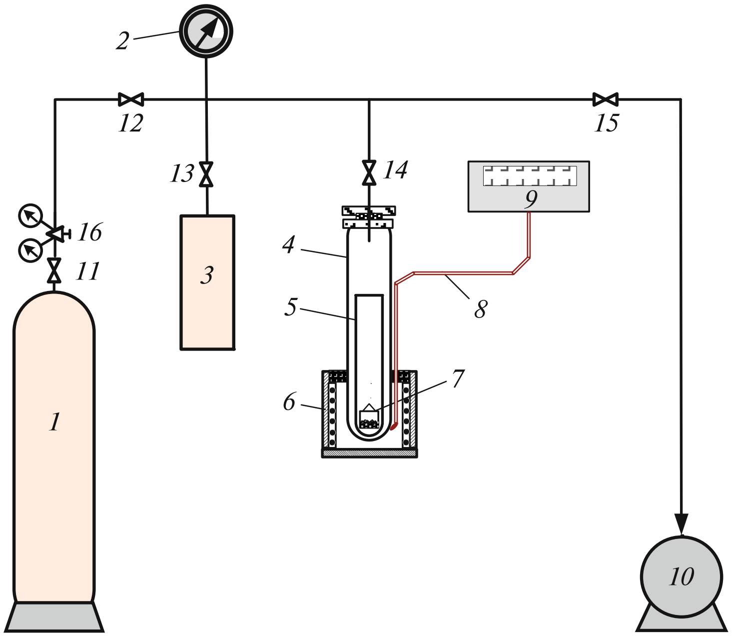

Fig. 2. Block diagram of the experimental setup for separating ^{103}Ru from the cyclotron $^{100}MoO_3$ target: (*1*) oxygen cylinder, (*2*) AIR-20-M2-DA pressure gauge, (*3*) 1.9-L measuring flask, (*4*) external fused-silica ampoule (D_{out} = 35.5 mm, d_{in} = 31 mm, l = 400 mm), (*5*) two replaceable internal fused-silica ampoules (D_{out} = 27 mm, d_{in} = 22.5 mm, l = 250 mm), (*6*) thermostat–heater, (*7*) fused-silica crucible (D_{out} = 15 mm, d_{in} = 12 mm, l = 17 mm) with irradiated $^{100}MoO_3$ powder containing ^{103}Ru, (*8*) chromel–alumel thermocouple, (*9*) IRT/M2 temperature meter, (*10*) NVR-5D forevacuum pump, (*11–15*) valves, and (*16*) GSE gas reducer.

pressure in ampoule *4* was maintained at various temperature conditions provided by thermostat–heater *6*.

While testing the technique, we noticed that a black deposit of $^{100}MoO_2$ appeared on the walls of the crucible after vacuum sublimation of $^{100}MoO_3$ at 700°C, and its weight was ≈1% of the initial $^{100}MoO_3$ weight.

According to [9, 10], the appearance of MoO_2 was caused by the content of a certain proportion of lower oxides (Mo_2O_5, Mo_4O_{11}, Mo_5O_{14}) in MoO_3. When MoO_3 sublimates in vacuum, they disproportionate according to the schemes Mo_2O_5(solid) ↔ MoO_3(gas) + MoO_2(solid) and Mo_4O_{11}(solid) ↔ $(MoO_3)_3$(gas) + MoO_2(solid), thus leaving MoO_2 in a solid state under these conditions.

Therefore, after removing the bulk of $^{100}MoO_3$, we needed an additional technological operation to gasify the residual $^{100}MoO_2$.

In view of the above, the developed ^{103}Ru separation technique consisted of a sequence of three technological operations implemented in three stages. Figure 3 illustrates the results obtained at each of the three stages.

At the first stage, $^{100}MoO_3$ was distilled in vacuum at a temperature of 700°C. To do this, irradiated $^{100}MoO_3$ powder with a mass of 113 mg was loaded into crucible *7*. After that, the crucible was inserted into inner ampoule *5*, which in turn was placed in outer ampoule *4*. Ampoule *4* was sealed and then connected to the vacuum stand upon immersing in thermostat–heater *6* to a depth of 10 cm. Evacuation to a pressure of ≈2×10^{-2} mm Hg was carried out using forevacuum pump *10*. A voltage was then applied to the thermostat–heater, the temperature was raised to 700°C for 45 min, and this temperature was maintained for 20 min. the $^{100}MoO_3$ sample was sublimated and deposited on the walls of ampoule *5*. At the end of the sublimation process, the thermostat-heater was removed, the system was cooled, and the inner ampoule and crucible were withdrawn. The crucible and ampoule *5* were weighed to balance the masses. Monitoring of the ^{103}Ru activity in the crucible before and after the technological operation was carried out by the relative intensity of the 497.08-keV γ-ray peak of ^{103}Ru. It was stated that at least 99% of the $^{100}MoO_3$ mass were removed from the crucible at the first stage, but the ^{103}Ru activity in the crucible did not change. However, a smoky black coating of $^{100}MoO_2$ remained on the crucible walls (see Fig. 3, stage 1).

The $^{100}MoO_2$ remaining in the crucible was oxidized to $^{100}MoO_3$ at the second stage. To do this, the crucible was placed in a clean internal ampoule, and the preparatory operations described above were performed. The entire system (with open valves *12–15*)

0	Stage 1	Stage 2	Stage 3
			
Irradiated $^{100}MoO_3$ sample in the crucible before treatment	After $^{100}MoO_3$ sublimation in vacuum at 700°C	After treatment in O_2 atmosphere at 75 kPa and 475°C, $^{100}MoO_2$ oxidized to $^{100}MoO_3$	After $^{100}MoO_3$ sublimation in vacuum at 700°C
Residue in the crucible			
100% ^{103}Ru, 100% $^{100}MoO_3$	100% ^{103}Ru, $\leqslant$1% $^{100}MoO_3$	$\geqslant$97% ^{103}Ru, $\leqslant$1% $^{100}MoO_3$	$\geqslant$97% ^{103}Ru, $\leqslant$0.01% $^{100}MoO_3$

Fig. 3. Illustration for the results of the phased ^{103}Ru separation from $^{100}MoO_3$.

was pumped down to a pressure of ≈2 × 10^{-2} mm Hg. Valve *15* was then closed, and the entire system was filled with oxygen from cylinder *1* using reducer *16* to a pressure of 75 kPa, which was monitored by pressure gauge *2*. Next, valve *12* was closed, a voltage was applied to the thermostat—heater, the temperature was raised to 475°C, and this value was maintained for 20 min. After ampoule *4* was cooled, the crucible was removed, the intensity of the 497.08-keV γ-ray peak of ^{103}Ru was measured by the area of the full-energy peak, the crucible was weighed, and the mass of molybdenum oxides contained in it was determined. As a result of oxidation (see Fig. 3, stage 2), the smoky black coating of $^{100}MoO_2$ on the walls of the crucible acquired a light gray color that is characteristic of $^{100}MoO_3$. (The mass change during this operation was within the measurement error.) It was found that the relative decrease in the activity of ^{103}Ru in the crucible after the oxidation procedure, which was determined by the intensity of the 497.08-keV γ-ray peak of ^{103}Ru, did not exceed 3%.

At the third stage that was similar to stage 1, $^{100}MoO_3$ residues (i.e., the oxidized $^{100}MoO_2$) were sublimated from the crucible in a vacuum at a temperature of 700°C. The ^{103}Ru activity in the crucible did not change, and the walls of the fused-silica crucible became transparent (see Fig. 3, stage 3).

To close the circulation cycle of the ^{100}Mo raw isotope, the $^{100}MoO_3$ deposit on the walls of ampoule *5* was washed off with a 10% solution of ammonium hydroxide (NH_4OH). As a result of the $^{100}MoO_3$ interaction with ammonium hydroxide, ammonium paramolybdate $(NH_4)_6{}^{100}Mo_7O_{24}$ was formed in the solution. By evaporating the solution and calcining the ammonium paramolybdate deposit, $^{100}MoO_3$ was obtained from the reaction $(NH_4)_6{}^{100}Mo_7O_{24} = 6NH_3\uparrow + 7{}^{100}MoO_3 + {}^3H_2O\uparrow$ according to the technique [11, 12]. The $^{100}MoO_3$ loss during ammonium paramolybdate calcination did not exceed 4%.

CONCLUSIONS

The cumulative yield of the ^{103}Ru radioisotope was measured for the first time using the activation method. The $^{100}MoO_3$ target was irradiated by ^{4}He nuclei with an energy of 60.3 MeV. The value of the measured ^{103}Ru yield was $(4.93 \pm 0.84) \times 10^4$ Bq/(μA h). The experimental technique was developed for express gas thermal separation of ^{103}Ru radioisotope from the irradiated $^{100}MoO_3$ cyclotron target. The technique ensured the extraction of at least 97% of ^{103}Ru from the target material and the return of at least 96% $^{100}MoO_3$ for reuse.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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