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Simulation of Medical Isotope Yield at an Accelerator-Driven System

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Abstract—We study a possibility of using an accelerator-driven system of the Prometheus proton therapy complex to obtain medical isotopes. The electronuclear setup is simulated using the Geant4 software package. The yield curves of the ^{99}Mo isotope are calculated, and the results of simulating a number of other isotopes are presented.

Keywords: accelerator-driven system, medical isotope

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Along with nuclear reactors, charged particle accelerators are widely used for the production of medical isotopes [1–3]. In November 2015, the domestic proton therapy complex Prometheus was launched. It is designed for highly effective treatment of oncological diseases with high throughput. The manufacturer of the Prometheus complex is the Russian company AO Protom, which was founded in 2001 for the serial production of proton accelerators based on the scientific developments of the Lebedev Physical Institute. To date, more than 800 patients have been successfully treated at two experimental complexes in Protvino (Physico-Technical Center of the Lebedev Physical Institute), and in Obninsk (country's leading oncology center, the A.F. Tsyb Medical Radiological Research Center). Proton synchrotrons in the Prometheus accelerator have been commissioned and are being put into operation for the treatment of patients in foreign centers in Europe, China, Israel, Australia, and the USA. The intensity of the therapeutic proton beam of the Prometheus accelerator is on average 10^9 particles per cycle of complete beam extraction, the energy of which can vary from 30 to 280 MeV with a possibility of increasing to 330 MeV [4–6].

The Geant4 software package is often used to model dosimetric planning [7–11]. However, medical applications of the Geant4 software package are not limited to calculating the energy release of penetrating radiation in materials of complex geometry. The package can also be used to assess changes in the isotopic composition of materials under the influence of neutrons of a wide range of energies.

In this paper, we study a possibility of expanding the scope of the Prometheus complex, in particular for the production of medical isotopes. The proton beam in the electronuclear setup allows neutrons of a wide energy spectrum to be generated. The paper presents calculations of the yield of medical isotopes formed in the neutron field from a proton beam in the framework of the Geant4 software package.

Figure 1 shows a simplified scheme of the simulated electronuclear setup. The proton beam (*1*) is incident on a water-cooled target (*2*) made of molybdenum. The target, in which neutrons are produced under the action of protons, is surrounded by a lead diffuser (*3*), which expands the spectrum of neutrons emitted from the target due to scattering. The setup is surrounded by neutron shielding (*4*) made of a combination of heavy and light materials for reflecting and cooling neutrons, respectively.

Irradiated samples (*5*), for example, a plate of natural molybdenum, are placed in the diffuser opposite the target. The plate size is selected to optimize the rate of production of the medical isotope. Figure 2 shows the dependences of the yield of the medical isotope ^{99}Mo on the plate thickness t. One can see that the yield from the entire plate increases with increasing thickness (solid line). If we divide the yield by the mass of the plate, i.e., normalize the result per gram, then the yield decreases with thickness (dashed line). Obviously, the process of neutron capture on the surface of the plate reduces the rate of isotope production

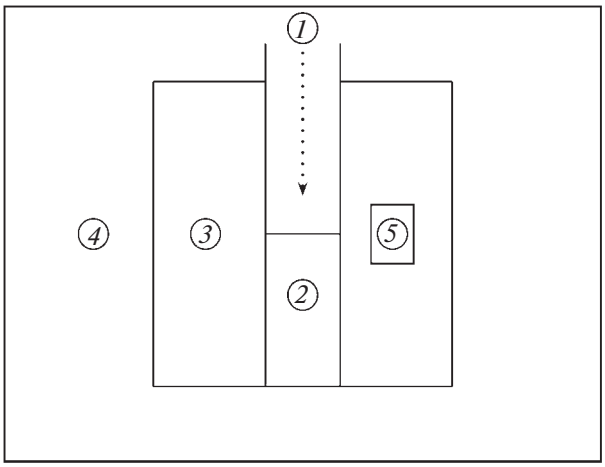

Fig. 1. Schematic of the electronuclear setup: (*1*) proton beam, (*2*) target, (*3*) diffuser, (*4*) neutron shielding, and (*5*) irradiated sample.

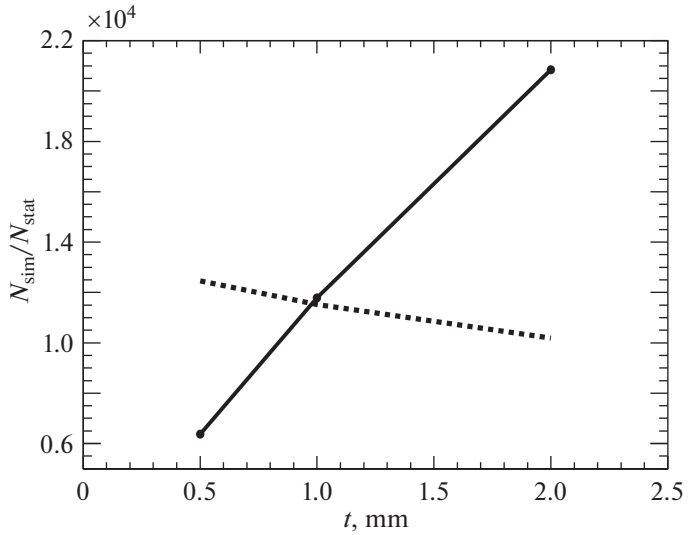

Fig. 2. Dependence of the ^{99}Mo isotope yield on the thickness of the initial molybdenum plate. The solid and dashed curves show the dependence on the thickness calculated for the entire plate and the yield per gram of plate mass, respectively.

per gram. There comes a point when not the entire thickness of the plate effectively works to increase the yield of the isotope. From the figure, at the intersection point of two lines, we can determine the optimal thickness of the plate, which in this case is $t = 1$ mm. Therefore, the specific geometric parameters of the irradiated plates are selected based on the requirements of medical procedures.

The simulation was performed using the FTF_BERT_HP set of physical models, which provides a reliable description of the passage of a wide range of neutrons through various materials.

The Geant4 package allows one to select events when the isotope in question is formed in the volume under consideration. These events were summed up, which made it possible to determine the number of formed nuclei of the medical isotope. Then this number was normalized to the number of protons incident on the target; i.e., the final ratio was calculated, which, without taking into account the decay of the isotope, determined the rate of the formation of isotope nuclei per one incident proton. The effects of the

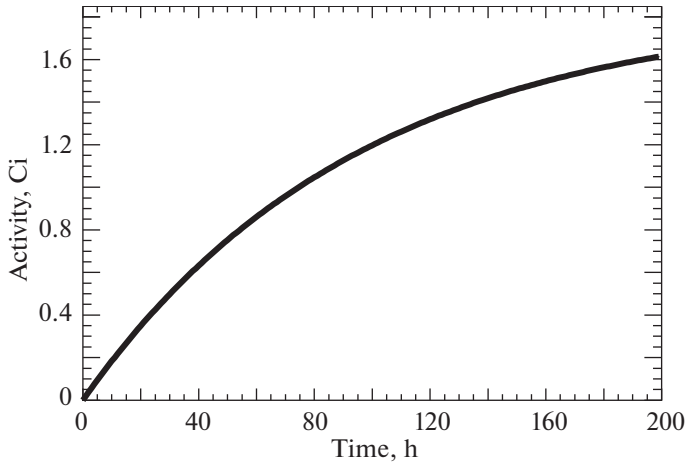

Fig. 3. Calculated dependence of the ^{99}Mo isotope activity on the exposure time in a proton beam with an energy of 300 MeV and a current of 100 μA.

decay of isotope nuclei during exposure were taken into account approximately, since they did not go beyond the statistical error of the production rate.

The calculations corresponded to a proton beam energy of 300 MeV at a current of 100 μA. Then the rate of the formation of the isotope per incident proton per second is determined by the relation:

$$R_0 = \frac{N_{\text{sim}}}{N_{\text{stat}}} \frac{10^{-4}}{1.6 \times 10^{-19}}, \tag{1}$$

where N_{sim} is the number of isotope nuclei formed as a result of irradiation with primary protons, the number of which is N_{stat}. The change in the number of isotope nuclei formed over time can be approximately determined from the equation:

$$\begin{cases} \dfrac{dN}{dt} = R_0 - \dfrac{N(t)}{\tau}, \\ N(0) = 0, \end{cases} \tag{2}$$

whence

$$N(t) = R_0 \tau [1 - \exp(-t/\tau)], \tag{3}$$

where $\tau = T_{1/2}/\ln(2)$, and $T_{1/2}$ is the half-life of the isotope. The time dependence of the accumulated activity of the isotope is $A(t) = N(t)/\tau$. The time dependence of the activity $A_{\text{sample}}(t)$ after the end of irradiation for a time t_0 (usually 10 hours) is approximately equal to:

$$A_{\text{sample}}(t) = R_0 [1 - \exp(-t_0/\tau)] \exp[-(t - t_0)/\tau], \quad (t_0 \sim 10 \text{ h}). \tag{4}$$

The activity for a proton beam with an energy of 300 MeV and a current of 100 μA in curie units is $\sim N_p 1.7 \times 10^4$. Here, $N_p = N_{\text{sim}}/N_{\text{stat}}$.

Figures 3 and 4 show the dependences of the change in the activity of the ^{99}Mo isotope during and after irradiation, respectively. In addition to the ^{99}Mo isotope, the simulation was performed for a number of other isotopes of interest for use in medicine. Table 1 contains both the parameters of the materials used in the simulation and the results of calculating the yields and activities of the isotopes.

The results of the simulation procedure show the possibility of using the Prometheus proton therapy accelerator complex for the production of medical isotopes. The advantage of this method is the faster logistics of isotope delivery from the point of production to the point of the medical procedure, since the

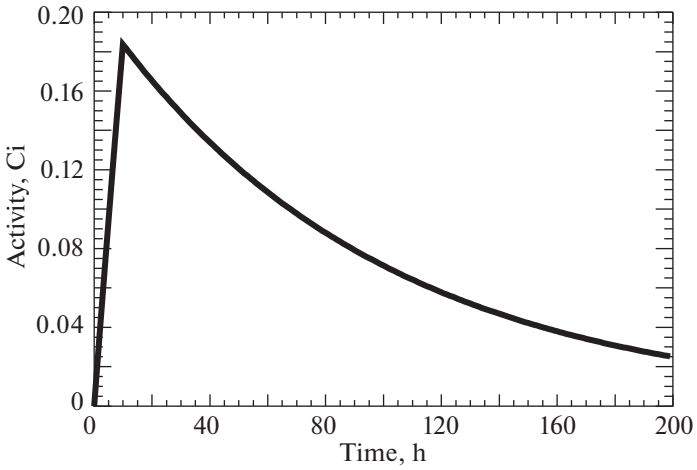

Fig. 4. Calculated dependence of the ^{99}Mo isotope activity on the exposure time in a proton beam with an energy of 300 MeV and a current of 100 μA and after its termination. The irradiation time was 10 h.

compact proton synchrotron of the Lebedev Physical Institute allows it to be placed directly in the medical institution. The efficiency of the accelerator also increases, since sessions of medical isotope production can be carried out at night, and usually 10 hours are enough.

In this paper, we do not specify the geometric parameters of the facility, since this is still a matter of adjustment, and the results presented are the first and preliminary. It should be noted that calculations of the yield of medical isotopes require significant computer power, although some progress is observed, and it can be predicted that such calculations will be more accessible in the near future.

Table 1. Parameters of the materials and results of calculating the isotope activities

Material	Mo → ^{99}Mo	Lu → ^{177}Lu	Re → ^{188}Re	Ho → ^{166}Ho
Volume (cm^3)	6.33 × 6.323 × 0.1	19.8 × 19.8 × 0.1	2.76 × 2.76 × 0.1	3.373 × 3.373 × 0.1
Density (g/cm^3)	10.22	9.84	21.02	8.795
Mass (g)	40.91	385.8	16.01	10
$T_{1/2}$ (h)	65.976	6.65 × 24	17.004	26.83
τ (h)	95.18	230.17	24.53	38.71
$N_p = N_{\text{sim}}/N_{\text{stat}}$	0.000109	0.0433876	0.0020878	0.0031826
N_p Statistical error (%)	3	0.15	0.69	0.55
A_{10h} (Ci)	0.1836	31.16	11.81	12.24

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CONFLICT OF INTEREST

The authors of this work declare that they have no conflicts of interest.

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