UDC 621.039.8.002
DOI: 10.20535/1810-0546.2017.6.103692

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THE STUDY OF ^{99m}Tc PRODUCTION USING MEDICAL CYCLOTRONS IN UKRAINE

Background. Tracer production for nuclear medicine.
Objective. The aim of the paper is to consider the possibility of ^{99m}Tc tracer production using low-energy medical cyclotrons installed in Ukraine applying enriched ^{100}Mo targets.
Methods. The cross sections of ^{100}Mo(p,2n)^{99m}Tc nuclear reactions and reactions, leading to formation of impurities were calculated. The technical aspects of irradiation process were considered. Necessary target thickness and ^{99m}Tc tracer yield for the Eclipse RD (Siemens) and PETtrace (GE) cyclotrons were estimated.
Results. Within the framework of proposed concept, ^{99m}Tc tracer yield equals 3.7 and 35.5 GBq after 2h of bombardment for Eclipse RD and PETtrace cyclotrons, respectively.
Conclusions. The obtained results showed satisfied ^{99m}Tc tracer yields and feasibility of further development of this method, which will significantly improve the efficiency of cyclotron installations.

Keywords: tracer production; cyclotrons; nuclear medicine.

Introduction

Radioactive isotopes have found widespread applications in medicine, including not only therapy and diagnostics procedures but also calibration and quality control of medical equipment. For diagnostics performance, the commonly used tracers have a short life-time, and therefore production of radiopharmaceuticals plays a crucial role in nuclear medicine. The most frequently used isotope for SPECT diagnostics in Ukraine is ^{99m}Tc ($T_{1/2}$ = 6.0 h), however, there is no any production center of this tracer in the country and hospitals have to buy it abroad.

Nowadays the main way to produce ^{99m}Tc is the parent nuclide ^{99}Mo ($T_{1/2}$ = 66 h) extraction from the fission products of ^{235}U(n, f)^{99}Mo reactions in nuclear reactors. Because of the closure of the 2 main production centers (NRU reactor, Canada, and HFR reactor, Netherlands), that cover more than 70 % of the world demand [1], the massive shortage of isotope supply is expected with subsequent price escalation. Thus, today one of the relevant questions in this field is the searching for new suppliers and the development of alternative ways of tracer production, where the cyclotron's technology is considered as a priority method [2–8]. Despite relatively low isotope yield in comparison with reactors, cyclotron production has its own advantages that are absence of contamination, low cost, and decentralization.

Problem statement

This work considers the possibility of ^{99m}Tc production using medical cyclotrons in Ukraine, in particular using 11-MeV Eclipse RD (Siemens) and 16-MeV PETtrace (GE) cyclotrons, installed in Clinical Hospital "Feofaniya" and Kyiv City Clinical Oncological Center, respectively. Nowadays these cyclotrons are successfully exploited for ^{18}F production and the technical basis of which is described in Ref. [9, 10].

The cross-section calculations

The ^{99m}Tc isotope can be produced through the (p,x) reactions via protons irradiation of molybdenum target, enriched with ^{100}Mo isotope. Table 1 shows the available reaction channels resulting to ^{99m}Tc with corresponding Q-values and Fig. 1 shows the cross sections of these reactions, taken from TENDL-2014 database [11]. From Fig. 1 it is clear, that cross section of (p,2n) reaction in the 7-16 MeV energy range is higher than for (p,pn) and (p,2p) by several orders, thus ^{100}Mo(p,2n)^{99m,g}Tc is considered as the basic reaction during bombardment. The contribution in this reaction from each possible channel (with creation of ground and metastable states) and formation of impurities, such as from ^{100}Mo(p,3n)^{98}Tc and ^{100}Mo(p,n)^{100}Tc reactions were estimated with the help of theoretical calculations in Empire 3.2 code [12] with default set of input parameters. The results of the calculations are presented in Fig. 2.

Making an analysis of cross section values from Fig. 1, *b* it can be seen, that the sum cross section for ^{99m,g}Tc production for the initial energy of 16 MeV is about 4 times greater than for 11 MeV protons. The cross-section of ^{99}Tc production in the metast-

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able state starting from 11 MeV and higher is nearly constant, while for ground state this value increases with the protons energy (see Fig. 2, *a*). So, on the one hand for 16 MeV the tracer yield will be higher than for 11 MeV, but on the other hand, the relative tracer yield in the metastable state is better for 11 MeV, namely $(\sigma_m/\sigma_g)_{16\to7.7\text{ MeV}} = 36.4\ \%$ for 16 MeV and $(\sigma_m/\sigma_g)_{11\to7.7\text{ MeV}} = 51.7\ \%$ for 11 MeV protons.

***Table* 1.** Proton induced reactions resulting to ^{99}Tc production

Nuclear reaction	Q-value, MeV
^{100}Mo(p,2n)$^{99\text{m,g}}$Tc	–7.7
^{100}Mo(p,pn)^{99}Mo→$^{99\text{m}}$Tc	–8.3
^{100}Mo(p,2p)^{99}Nb→^{99}Mo→$^{99\text{m}}$Tc	–11.25

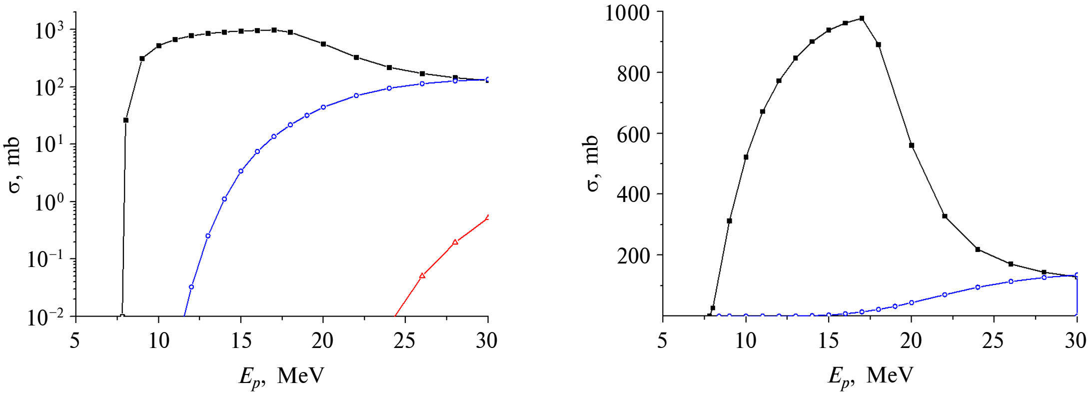
Concerning impurity formations (see Fig. 2, *b*), the obtained results show the intensive yield of ^{98}Tc starting from 17 MeV and higher and the maximum cross section for ^{100}Tc creation corresponds to the energy of 8 MeV (i.e. near the threshold of ^{99}Tc production). In this connection, the optimal energy of protons should be in the range of

$$7.7\text{ MeV} < E_p < 16.7\text{ MeV} \tag{1}$$

(where 16.7 MeV is the threshold of ^{100}Mo(p,3n)^{98}Tc reaction).

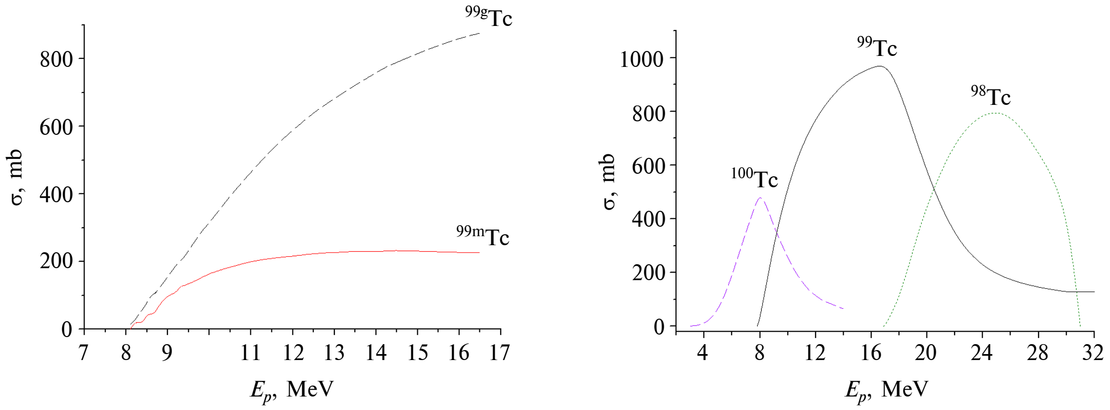
Irradiation conditions and yield calculations

The maximum energy of protons in cyclotrons Eclipse RD (11-MeV) and PETtrace (16-MeV) is the energy at the end of the particles trajectory and where they enter the vacuum window (25 μm, Al), separating target module from the cyclotron tank. The incident protons on a target have slightly lower



a *b*

Fig. 1. The cross sections of ^{99}Tc production via (p,2n) (—■—), (p,pn) (—○—) and (p,2p) (—△—) reactions from ^{100}Mo, versus protons energy E_p expressed in logarithmic (*a*) and linear (*b*) scales (TENDL-2014)



a *b*

Fig. 2. The cross sections of $^{99\text{g}}$Tc, $^{99\text{m}}$Tc (*a*) and ^{100}Tc, ^{99}Tc, ^{98}Tc (*b*) production depending on an energy of protons E_p calculated using Empire 3.2 code: ------ – ^{100}Mo(p,2n)$^{99\text{g}}$Tc; ——— – ^{100}Mo(p,2n)$^{99\text{m}}$Tc; ······· – ^{100}Mo(p,3n)^{98}Tc; ——— – ^{100}Mo(p,2n)^{99}Tc; – – – – – ^{100}Mo(p,n)^{100}Tc

energies due to the energy losses in a vacuum window and helium cooling system that withdraws heat from vacuum and target windows.

Considering the geometry of irradiation in 11-MeV Eclipse RD cyclotron, the ^{99m}Tc production can be realized by installation of molybdenum foil instead of the target window. Fig. 3 represents the technical aspects of irradiation in this case and corresponding energy distribution of the penetrating proton beam (the energy loss in a helium cooling system is less than 0.001 MeV).

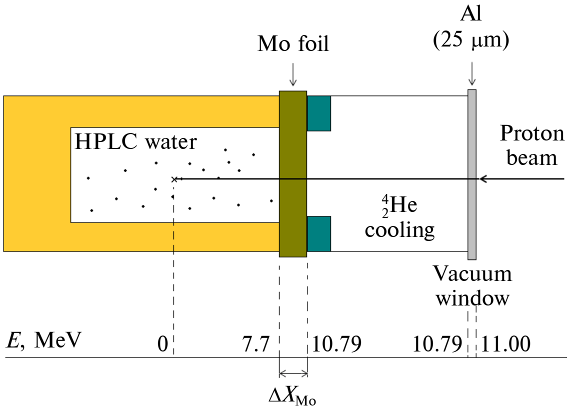


Fig. 3. The irradiation conditions in the Eclipse RD (Siemens) cyclotron

In order to meet the requirement (1), the thickness of molybdenum foil was estimated with the help of Bethe–Bloch formula for the energy losses dE/dx of protons in molybdenum:

$$\Delta X_{\text{Mo}} = \int_{E_{p_{\text{in}}}}^{E_{p_{\text{out}}}} dE/(dE/dx)$$

$$= \int_{10.79}^{7.7} \left[-\frac{2 \cdot \pi \cdot z \cdot z_p^2 \cdot e^4 \cdot \rho \cdot N_{\text{A}} \cdot m_p}{m_e \cdot E \cdot M} \right.$$

$$\left. \times \left(\ln\left(2 \cdot m_e \frac{2 \cdot E}{I \cdot m_p} \right) - \ln\left(1 - \frac{2 \cdot E}{c^2 \cdot m_p} \right) - \frac{2 \cdot E}{c^2 \cdot m_p} \right) \right]^{-1}$$

$$\times dE = 119.1\ \mu\text{m},$$

where $E_{p_{\text{in}}}, E_{p_{\text{out}}}$ – incident and output proton energy; z, M – atomic number and mass of ^{100}Mo isotope; z_p, m_p – the charge and mass of proton; e, m_e – elementary charge and electron mass; $\rho = 10.22$ g/cm^3 – the density of Mo foil; c – the speed of light; N_{A} – Avogadro constant; I – the mean excitation potential, calculated using formula from Ref. [13]:

$$I = (9.76 + 58.8 \cdot z^{-1.19}) \cdot z = 448.45\ \text{eV}.$$

The cross section of ^{100}Mo(p,2n)^{99m}Tc reaction in the range 10.79–7.7 MeV equals

$$\sigma_{(p,2n)} = \int_{10.79}^{7.7} \sigma(E)dE = 98\ \text{mb},$$

and taking into account the thickness of molybdenum foil $\Delta X_{\text{Mo}} = 119.1\ \mu\text{m}$ and current of protons $I_p = 40$ μA the produced tracer activity A was calculated using the following expression:

$$A = \frac{\rho \cdot \Delta X_{\text{Mo}} \cdot S_p \cdot N_{\text{A}}}{M} \varphi_p \cdot \sigma_{(p,2n)} \cdot (1 - e^{-\frac{\ln 2}{T_{1/2}} \cdot t}),$$

where $S_p \cong 0.53\ \text{cm}^2$ – the proton beam area on target, $\varphi_p = 4.72 \cdot 10^{14}\ \text{cm}^{-2} \cdot s^{-1}$ – the proton flux density, $T_{1/2} = 6.0$ h – the half-life of ^{99m}Tc, t – irradiation time. The same calculations were performed for PETtrace (GE) cyclotron, where the maximum energy of protons is 16 MeV and the current of protons can reach the value of 130 μA. The obtained results for tracer yield are shown in Fig. 4.

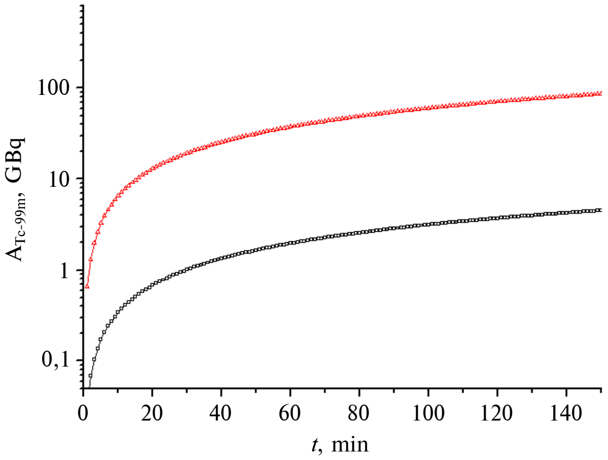


Fig. 4. The calculated ^{99m}Tc tracer yield in Eclipse RD (—□—) and PETtrace (—△—) cyclotrons

According to obtained results, the produced activity of ^{99m}T after 2 h of irradiation will be relatively equal to 3.7 GBq for the Eclipse RD cyclotron with corresponding saturation yield of 0.44 GBq/μA. For the PETtrace cyclotron, produced activity will be significantly higher and during 2 h of bombardment, it is possible to achieve almost 35.5 GBq (in this case the saturation yield appeared to be 2.64 GBq/μA).

In the assumption of 400 MBq/patient, the time between injections 30 min, elution yield 50 % and 40 min for quality control of radiopharmaceutical, the 3.7 GBq is enough only for 3 patients and can cover own hospital needs. Obviously, that 35.5 GBq is enough not only for own needs but also for other hospitals.

Conclusions

The possibility of ^{99m}Tc tracer production was studied using low-energy medical cyclotrons. For this analysis, the cross sections calculations of required reactions were performed and technical aspects of irradiation process were considered. The target thickness was estimated with subsequent calculations of tracers yield for Eclipse RD and PET-trace cyclotrons that appeared to be 3.7 GBq and 35.5 GBq respectively for 2h of irradiation. Due to the 6-hour ^{99m}Tc half-life, the time of irradiation can be extended up to 3 or even 4 times almost without loss of production efficiency, leading to higher amounts of the tracer.

Concerning economical side, it is important to note the sum expenses for Mo foil and cyclotrons work in comparison with tracer cost, that to date equals about 80–100 $/GBq. The 99 % enrichment with ^{100}Mo isotope costs 2–4 $/mg [14], so it is easy to see that Mo foil will be paid off after >115 min of irradiation for 11-MeV, while for 16-MeV even 30 min will be enough for this purpose. Taking into account that nowadays considered cyclotrons are exploited only a few hours per day (mostly for ^{18}F production for PET diagnostics), the implementation of ^{99m}Tc production in these facilities will increase not only the number of diagnostics examinations but also the efficiency of cyclotrons usage.

Further investigations in a field of accelerator-based technologies are an integral part of successful implementation of tracer productions using low-cost accelerators instead of reactors that require high safety measures and investments. Moreover, this area of research can be considered as an alternative way to HEU (High Enriched Uranium) techniques for isotope productions for medical and commercial objectives.

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КОНЦЕПЦІЯ ВИРОБНИТЦВА $^{99M}\mathrm{Tc}$ НА МЕДИЧНИХ ЦИКЛОТРОНАХ В УКРАЇНІ

Проблематика. Виробництво радіоактивних ізотопів для ядерної медицини.

Мета дослідження. У роботі досліджується можливість виробництва $^{99m}\mathrm{Tc}$ на базі низькоенергетичних медичних циклотронів, встановлених в Україні, з використанням збагаченої ізотопом $^{100}\mathrm{Mo}$ молібденової мішені.

Методика реалізації. Виконано теоретичні розрахунки перерізів $^{100}\mathrm{Mo}(p,2n)^{99m}\mathrm{Tc}$ реакцій та реакцій, що призводять до утворення домішкових ізотопів у коді Empire 3.2. Розглянуто технічні аспекти опромінення, оцінено необхідні товщини зразків і виходи радіонукліда $^{99m}\mathrm{Tc}$ на циклотронах Eclipse RD (Siemens) і PETtrace (GE).

Результати дослідження. У рамках запропонованої концепції вихід ізотопу $^{99m}\mathrm{Tc}$ був визначений рівним 3,7 та 35,5 ГБк після 2-годинного опромінення для циклотронів Eclipse RD та PETtrace відповідно.

Висновки. Отримані результати показали високий вихід радіонукліда $^{99m}\mathrm{Tc}$ і доцільність подальшого розвитку запропонованої методики, що дасть можливість суттєво підвищити ефективність використання циклотронних установок.

Ключові слова: виробництво ізотопів; циклотрон; ядерна медицина.

Б.М. Бондар, И.Б. Михницкий, Я.В. Кметюк

КОНЦЕПЦИЯ ПРОИЗВОДСТВА ^{99M}Tc НА МЕДИЦИНСКИХ ЦИКЛОТРОНАХ В УКРАИНЕ

Проблематика. Производство радиоактивных изотопов для ядерной медицины.

Цель исследования. В работе исследуется возможность производства ^{99m}Tc на базе низкоэнергетических медицинских циклотронов, установленных в Украине, с использованием обогащенной изотопом ^{100}Mo молибденовой мишени.

Методика реализации. Проведены теоретические расчеты сечений ^{100}Mo(p,2n)^{99m}Tc ядерных реакций и реакций, приводящих к образованию примесных изотопов. Рассмотрены технические аспекты облучения, оценены необходимые толщины образцов и выходы радионуклида ^{99m}Tc на циклотронах Eclipse RD (Siemens) и PETtrace (GE).

Результаты исследования. В рамках предложенной концепции, выход изотопа ^{99m}Tc равен 3,7 и 35,5 ГБк после 2-часового облучения для циклотронов Eclipse RD и PETtrace соответственно.

Выводы. Полученные результаты показали высокий выход радионуклида ^{99m}Tc и целесообразность дальнейшего развития данной методики, что позволит существенно повысить эффективность использования циклотронных установок.

Ключевые слова: производство изотопов; циклотрон; ядерная медицина.

Рекомендована Радою
фізико-математичного факультету
КПІ ім. Ігоря Сікорського

Надійшла до редакції
07 липня 2017 року