Comprehensive Theoretical Studies on 11-MeV Proton Based Tc-99m Production

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Comprehensive Theoretical Studies on 11-MeV Proton Based Tc-99m Production

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Abstract

The shortage of nuclear-reactor-based Tc-99m supply has led to increased research on cyclotron-based Tc-99m production. In this paper, Tc-99m radionuclides produced by a 11-MeV proton cyclotron is theoretically discussed in terms of the optimum thickness of natMo, natMoO₃, and enriched 100Mo targets; expected impurities; and radioactivity yields of several (p,2n), (p,n), and (p,γ) based nuclear reactions. The SRIM 2013 codes and TALYS 2014 codes are employed to calculate the range of 11-MeV proton beams in the Mo-based targets and the excitation functions of the selected nuclear reactions, respectively. The calculated results indicate that 94m,95m,96m Tc radionuclides would give rise to radionuclide impurities at the end of irradiation for natMo targets, whereas no significant impurities were theoretically detected for the enriched 100Mo target. At the end of bombardment, nearly 42.18 GBq/µA.hr of Tc-99m radionuclide is predicted to result in the 11-MeV proton-irradiated 100Mo target.

Keywords: Tc-99m, cyclotron, proton, molybdenum, nuclear medicine, SPECT

Introduction

Over the past few years, reports on technetium-99m (Tc-99m) shortages have raised important concerns [1-3], since gamma emitting radioisotopes are the most important medical radioisotope used in nuclear medicine for Single Photon Emission Computed Tomography (SPECT) [4-5]. One of the reasons for Tc-99m shortages is that such radioisotopes have been largely produced using nuclear reactors while the rate of new nuclear reactor establishments is slowing down and the number of aging reactors is increasing.

An alternative method of producing Tc-99m using cyclotrons has been proposed [6-7] to tackle the abovementioned issues, whereas another means of generating Tc-99m using laser-driven proton beams has also been studied [8]. Medium-energy protons in the range of 8–18 MeV have been proposed for irradiation of molybdenum (Mo) targets [9], either natural or enriched Mo, in order to obtain high specific activity of Tc-99m, although enriched Mo-100 is preferred for better yields [10]. While high-energy protons theoretically result in higher end-of-bombardment (EOB) yield, they could potentially lead to significant amount of radioactive
impurities, as reported by Qaim et al. [11], which could complicate the Tc-99m preparation. To the best of the author’s knowledge, there has been no theoretical or experimental research in Indonesia on cyclotron-based Tc-99m production; thus, this theoretical approach aims at elucidating medical radionuclide generation. In this paper, comprehensive studies on ⁹⁹mTc production using the Stopping and Range of Ion in Matter (SRIM) 2013 and TALYS 2014 codes are discussed; in particular, the optimum target thickness, predicted nuclear reactions, possible impurities, and the end-of-bombardment (EOB) yields for ¹⁰⁰Mo and enriched ¹⁰⁰Mo targets irradiated by 11-MeV protons are studied.

Methods

**SRIM calculations.** The energy loss and range of proton beams in several targets, including natural molybdenum (⁹⁹Mo), natural molybdenum oxide (⁹⁹MoO₃), and enriched molybdenum (solid ¹⁰⁰Mo) targets, were calculated by using the SRIM Codes version 2013 [12]. The SRIM calculations have been used for calculating the range of protons in nickel targets [13]. In these calculations, over 90,000 particles of 11-MeV protons were simulated in the proton–Mo target collisions. Natural molybdenum (⁹⁹Mo) consists of ⁹⁵Mo (14.84%), ⁹⁶Mo (9.25%), ⁹⁷Mo (15.92%), ⁹⁸Mo (16.68%), ⁹⁹Mo (9.55%), ⁹⁸Mo (24.13%), and ¹⁰⁰Mo (9.63%), whereas enriched Mo targets simulated in these calculations consist of 99.9% ¹⁰⁰Mo. In the SRIM codes, the generally agreed formula for the stopping power S(E) and range R(E) of protons in a compound target are given in equations (1) and (2), respectively:

\[
S(E) = -\frac{dx}{de} = \frac{4\pi k_z^2 z^2 e^4 n}{mc^2 \beta^5} \left[ \ln \frac{2mc^2 \beta^2}{I(1-\beta^2)} - \beta^2 \right] \tag{1}
\]

\[
R(E) = \int_0^E \frac{1}{S(\varepsilon)} d\varepsilon \tag{2}
\]

where \(k_z = 8.99 \times 10^9 \text{ Nm}^2\text{C}^{-2}\), \(z = \text{atomic number}, e = \text{charge of electron (in Coulomb), \(n = \text{number of electron per unit volume of the target (in electrons/m}^3\), m = \text{mass of electron at rest (\(m = 9.1 \times 10^{-31} \text{ kg}\)), c = \text{speed of light in vacuum (c = 3 \times 10^8 \text{ m/s}), \beta = \text{ratio of the speed of the incident particle to the speed of light, I = \text{average excitation energy of the target (in MeV), E = \text{proton energy (MeV), and \(x = \text{distance over which the protons travel through a target (in m)}\right)\]

**TALYS calculations.** TALYS Codes version 2014 was employed to calculate the nuclear cross-sections of ⁹⁹Mo(p,2n), ⁹⁹Mo(p,n), ⁹⁹Mo(p,γ), ¹⁰⁰Mo(p,2n), and ¹⁰⁰Mo(p,n), as a result of secondary neutron bombardment was not considered since the 11-MeV proton beams performed in this study would result in insignificant numbers of secondary neutrons. The TALYS calculated data have been widely used for nuclear cross-section studies in the literature [13-14]. In TALYS codes, nuclear cross-section for an incident particle \(a\) and target \(b\), \(\sigma_{ab}\), was calculated by the compound nucleus formula for a binary cross-section, which can be simplified as:

\[
\sigma_{ab} = \frac{2\pi T_b E}{N_A \bar{W}_{ab}} \tag{3}
\]

where \(\pi\) is the parity, \(k\) is the wave number of relative motion, \(T\) is the transmission coefficient, \(W\) is the width fluctuation correction factor, and \(T_b\) is the outgoing transmission coefficient. Details on the numerical calculation have been widely discussed elsewhere [15].

**EOB yield calculations.** In the theoretical yield calculations, 11-MeV proton beams were employed in order to compute the EOB yields \(Y\) of Tc-99m radionuclide, and other technetium radionuclides were possibly found as impurities during the medical radionuclide production. The 11-MeV proton energy was chosen in conjunction with the available medical cyclotron at Dharmais Cancer Hospital in Indonesia [16], which will be used for future Tc-99m production. The yield calculations were based on the following well-known equation, as discussed elsewhere [13]:

\[
Y = \Phi \left(1 - e^{-\lambda t}\right) N_A \rho M \int_{E_i} E_{\text{th}} \left[ \frac{\sigma(E)}{dE} \right] dE \tag{4}
\]

where \(\Phi\) is the number of charged particles per unit of time, \(\lambda\) is the decay constant of the resulting radioisotope, \(t\) is the duration of irradiation (in this calculation, it is set to be 1 h), \(N_A\) is the Avogadro number, \(\rho\) and \(M\) are the mass density and atomic mass of the target, respectively, \(E_i\) is the initial energy of the incident particle, \(E_{\text{th}}\) is the threshold energy, \(\sigma(E)\) is the nuclear cross-section at a particular energy, and \(d(E)/dx\) the stopping power or energy loss of the incident beam. In the EOB yield calculation, the TALYS-calculated cross-section data and SRIM-calculated stopping powers and ranges were used as data inputs for equation (4).

**Results and Discussion**

**Proton energy loss and range in natural and enriched molybdenum.** Energy loss and range of 11-MeV proton beams in natural and enriched Mo are shown in Table 1, from which it can be seen that the protons suffer greater energy loss when they travel through pure Mo than the ones travelling through Mo oxide. As a result, the range of the proton beams in pure Mo atoms is shorter than that in Mo oxide. In pure Mo atoms, the range of an 11-MeV proton beam is between 0.272 and 0.295 mm, whereas in ⁹⁹MoO₃ at ¹⁰⁰MoO₃, the range is between 0.645 and 0.663 mm.

It is well understood that when the targets are too thin (thinner than the range of proton in the targets), then the proton beam could pass through the targets, which
eventually could lead to the production of residual radionuclides, as discussed earlier [16]. Furthermore, this could also lead to radiation safety concerns in the target chamber and cyclotron vault, if the proton beam activates materials around the target chamber. Conversely, when the targets are too thick, some fraction of the target cannot be reached by the proton beam, which results in inactivated targets and complex handling of the post-irradiated targets. Based on the range calculations above, one can recommend the optimum thickness for Mo target irradiation to effectively produce Tc-99m radionuclide. For example, when an 11-MeV proton beam is employed for Tc-99m production, the prepared targets should be around 0.65 mm for the $^{99m}$MoO$_3$ target or nearly 0.3 mm for the enriched $^{100}$Mo target.

Table 1. Energy Loss and Range of 11-MeV Protons in Several Mo Targets

| Target   | Proton energy loss (MeV/mm) | Proton range (mm) |
|----------|-----------------------------|-------------------|
| $^{92}$Mo | 23.92                       | 0.272             |
| $^{94}$Mo | 23.41                       | 0.278             |
| $^{95}$Mo | 23.17                       | 0.281             |
| $^{96}$Mo | 22.94                       | 0.283             |
| $^{97}$Mo | 22.69                       | 0.286             |
| $^{98}$Mo | 22.46                       | 0.289             |
| $^{100}$Mo| 22.01                       | 0.295             |
| $^{99m}$MoO$_3$ | 9.85                   | 0.645             |
| $^{100m}$MoO$_3$ | 9.58                  | 0.663             |

Predicted nuclear reactions. For 11-MeV proton beams, nuclear reactions expected to occur during the proton irradiation of $^{95m}$Mo and enriched $^{100m}$Mo are listed in Table 2, which indicates that technetium radionuclides coming from (p,2n), (p,n), and (p,γ) nuclear reactions are the most important radioactive products, ranging from $^{91m}$Tc to $^{105m}$Tc. It should be noted that there are several technetium radionuclides potentially contributing to the amount of impurities during Tc-99m production, namely $^{93m}$Tc, $^{94m}$Tc, $^{95m}$Tc, $^{96m}$Tc, and $^{97m}$Tc, owing to their relatively long half lives (greater than 40 min). The other possible impurities maybe insignificant since their half lives are less than 5 min. In order to evaluate their significance, TALYS codes have been used to calculate their nuclear cross-sections, and their presence in the targets several hours after irradiation are also evaluated based on their decay.

In addition, the decay modes of the resulted impurities are either by γ, β, or isomeric transition (IT), as shown in Table 2. In the isomeric decay, there are two possible isomeric transitions, namely γ emission and internal conversion, in which the γ energy is used to excite the atom’s electrons.

Based on the TALYS calculated results for the three types of nuclear reactions discussed here, in general, the higher the atomic mass of the target, the lower the threshold energy for (p,2n) and (p,n) nuclear reactions.

| Nuclear reactions | Gamma energy (MeV) | Half life | Decay mode |
|-------------------|--------------------|-----------|------------|
| $^{95m}$Mo(p,2n)$^{94}$Tc | 0.139              | 3.3 min   | β$^-$ (99%), IT (1%) |
| $^{95m}$Mo(p,n)$^{95}$Tc | 0.270              | 1.03 µs   | β$^-$ |
| $^{95m}$Mo(p,γ)$^{95}$Tc | 0.392              | 43.5 min  | IT (76.6%), β$^-$ (23.4%) |
| $^{95m}$Mo(p,2n)$^{94}$Tc | 0.392              | 43.5 min  | IT (76.6%), β$^-$ (23.4%) |
| $^{95m}$Mo(p,n)$^{95}$Tc | 0.076              | 52 min    | β$^-$ (99.9%), IT (1%) |
| $^{95m}$Mo(p,γ)$^{95}$Tc | 0.039              | 61 day    | β$^-$ (96.1%), IT (3.9%) |
| $^{95m}$Mo(p,2n)$^{94}$Tc | 0.076              | 52 min    | β$^-$ (99.9%), IT (1%) |
| $^{95m}$Mo(p,n)$^{95}$Tc | 0.039              | 61 day    | β$^-$ (96.1%), IT (3.9%) |
| $^{95m}$Mo(p,γ)$^{95}$Tc | 0.034              | 51.5 min  | IT (98%), β$^-$ (2%) |
| $^{95m}$Mo(p,2n)$^{94}$Tc | 0.039              | 61 day    | β$^-$ (96.1%), IT (3.9%) |
| $^{95m}$Mo(p,n)$^{95}$Tc | 0.034              | 51.5 min  | IT (98%), β$^-$ (2%) |
| $^{95m}$Mo(p,γ)$^{95}$Tc | 0.097              | 91.4 day  | IT (99.7%), EC (0.3%) |
| $^{95m}$Mo(p,2n)$^{94}$Tc | 0.034              | 51.5 min  | IT (98%), β$^-$ (2%) |
| $^{95m}$Mo(p,n)$^{95}$Tc | 0.097              | 91.4 day  | IT (99.7%), EC (0.3%) |
| $^{95m}$Mo(p,γ)$^{95}$Tc | 0.091              | 14.7 µs   | γ |
| $^{95m}$Mo(p,2n)$^{94}$Tc | 0.034              | 91.4 day  | IT (98%), β$^-$ (2%) |
| $^{95m}$Mo(p,n)$^{95}$Tc | 0.091              | 14.7 µs   | γ |
| $^{95m}$Mo(p,γ)$^{95}$Tc | 0.143              | 6.02 h    | IT (99.99%), β$^-$ (.0037%) |
| $^{100m}$Mo(p,2n)$^{99}$Tc | 0.143              | 6.02 h    | IT (99.99%), β$^-$ (.0037%) |
| $^{100m}$Mo(p,n)$^{100}$Tc | 0.200              | 8.32 µs   | IT (99.99%), β$^-$ (.0037%) |
| $^{100m}$Mo(p,γ)$^{101}$Tc | 0.208              | 636 µs   | γ |
The most possible nuclear reactions occurring during \(^{92,94,95,96,98,100}\)Mo or \(^{102}\)Mo target bombardment with an 11-MeV proton beam are \((p,n)\) reaction for \(^{92,94,95,96,98,100}\)Mo and \((p,2n)\) reaction for \(^{97,98,100}\)Mo target since their threshold energy is below 11 MeV. However, \(^{97,98,100}\)Mo(\(p,2n\)) nuclear reaction may result in insignificant amount of radioactivity owing to its low nuclear cross-section (less than 2 mbarn), as can be seen in Figure 1(a,b,c) and Table 3. Radionuclide \(^{95m}\)Tc can be produced via \(^{95m}\)Mo(\(p,n\))\(^{95m}\)Tc and \(^{95m}\)Mo(\(p,2n\))\(^{95m}\)Tc nuclear reactions. However, the threshold energy for \(^{95m}\)Mo(\(p,2n\))\(^{95m}\)Tc reaction to occur is 11.75 MeV, and thus, it cannot be produced when the target is irradiated with an 11-MeV proton beam. Nevertheless, \(^{95m}\)Tc generated through \(^{95m}\)Mo(\(p,n\))\(^{95m}\)Tc nuclear reaction could dominate the presence of impurities in \(^{95m}\)Tc production once the target of interest is \(^{92}\)MoO\(_3\).

The high nuclear cross-sections for \(^{92}\)Mo(\(p,n\)) and \(^{92}\)Mo(\(p,2n\)) reactions, as shown in Table 3, also confirm possible impurities present during Tc-99m production using 11-MeV proton beams. While \(^{92}\)Mo(\(p,n\))\(^{95m}\)Tc radio-nucleides quickly decay into their stable nuclides 10 h after the end of irradiation, other radionuclides such as \(^{95m}\)Tc remain significant, as can be seen in Figure 2.

**Figure 1.** TALYS Calculated \((p,2n)\), \((p,n)\) and \((p,\gamma)\) Nuclear Cross-sections of (a) \(^{92,94,95}\)Mo, (b) \(^{96,97}\)Mo, and (c) \(^{98,100}\)Mo Targets

**Table 3.** TALYS Calculated Threshold Energy and Nuclear Cross-sections of Several Mo Targets (\(p,2n\), \(p,n\), and \(p,\gamma\)) Nuclear Reactions

| Target  | Threshold energy (MeV) | Nuclear cross-section at 11-MeV proton beam (mbarn) |
|---------|------------------------|---------------------------------------------------|
|         | \((p,2n)\) | \((p,n)\) | \((p,\gamma)\) | \((p,2n)\) | \((p,n)\) | \((p,\gamma)\) |
| \(^{92}\)Mo | 19.89 | 8.98 | 0 | 0 | 154 | 1.84 |
| \(^{94}\)Mo | 13.81 | 5.17 | 0 | 0 | 682 | 1.11 |
| \(^{95}\)Mo | 12.54 | 2.54 | 0 | 0 | 692 | 0.78 |
| \(^{96}\)Mo | 11.75 | 3.83 | 0 | 0 | 763 | 0.87 |
| \(^{97}\)Mo | 10.69 | 1.22 | 0 | 89.78 | 660 | 0.59 |
| \(^{98}\)Mo | 9.85 | 2.51 | 0 | 362 | 416 | 0.73 |
| \(^{100}\)Mo | 7.79 | 1.14 | 0 | 672 | 103 | 0.73 |
At this time, the radioactivity of $^{99m}$Tc radionuclide remains at 32% of its initial value. However, as discussed earlier, the high threshold energy (>11 MeV) for $^{96}$Mo(p,2n)$^{96m}$Tc reaction rules out any possibility of finding the $^{95m}$Tc impurity, although it can presumably be observed via the $^{95}$Mo(p,n)$^{95o}$Tc reaction. For such irradiation conditions (proton energy 11 MeV, cooling time 10 h), the impurity mostly found in the target is $^{95m}$Tc radionuclide when $^{94m}$MoO$_3$ is employed as the target to produce $^{99m}$Tc, whereas no impurity is expected to be observed when enriched $^{100}$Mo is used as the target. In contrast, several radionuclide impurities such as $^{94m}$Tc could possibly be present for such irradiation conditions when no time is given for cooling of the $^{94m}$MoO$_3$ target after the end of bombardment. Note that oxygen atoms in the oxide compounds will not significantly contribute to the radioactivity levels.

**EOB yields of proton produced Tc-$^{99m}$**. In this section, the EOB yields of $^{94m,95m,96m,98m}$Tc radionuclides are discussed, particularly from $^{94m}$Mo(p,n)$^{94o}$Tc, $^{95m}$Mo(p,n) $^{95m}$Tc, $^{96m}$Mo(p,n) $^{96o}$Tc, and $^{98m}$Mo(p,2n) $^{98m}$Tc nuclear reactions, which represent radionuclide impurities, as well as from $^{100}$Mo(p,2n)$^{100m}$Tc, $^{100m}$Mo(p,n)$^{100y}$Tc, and $^{100}$Mo(p,$\gamma$)$^{101m}$Tc nuclear reactions, which correspond to the desired medical radionuclide product, as indicated in Table 4. Note that in the calculations, all individual Mo atoms are considered in their natural abundances.

It can be seen from Table 4 that at the end of the 11-MeV proton beam bombardment, relatively high yield of $^{94m}$Tc (up to 23.55 GBq/uA.hr) is expected to be generated from $^{94m}$Mo(p,n)$^{94o}$Tc, while even higher yields of $^{96m}$Tc (up to 48.22 GBq/uA.hr) from $^{96}$Mo(p,2n)$^{96o}$Tc reaction, and 10.01 GBq/uA.hr from $^{96}$Mo(p,n)$^{96o}$Tc reaction) are predicted to occur. However, the $^{95m}$Mo(p,n)$^{95o}$Tc reaction results in a small amount of $^{95o}$Tc (nearly 0.04 GBq/uA.hr). Overall, for the $^{94m}$Mo target, $^{96m}$Tc radionuclide dominates the radionuclide products during the 11-MeV proton beam bombardment. While only a total yield of 4.06 GBq/uA.hr $^{99m}$Tc resulted from 11-MeV proton irradiation of the $^{94m}$Mo target, a greater amount of 42.18 GBq/uA.hr $^{99m}$Tc yielded from the enriched $^{100}$Mo target.

**Conclusions**

Comprehensive theoretical calculations have been carried out to study the feasibility of Tc-$^{99m}$ production using 11-MeV proton beams. In this study, the SRIM 2013 codes have been employed to calculate the range of 11-MeV protons in $^{94m}$Mo, $^{94m}$MoO$_3$ and enriched $^{100}$Mo targets, while TALYS codes have been used to compute the excitation functions of (p,n), (p,2n), and (p,$\gamma$) nuclear reactions. The SRIM calculated results indicate that when an 11-MeV proton beam is employed for Tc-$^{99m}$ production, the thickness of the prepared targets should be around 0.65 mm for the $^{94m}$MoO$_3$ target or nearly 0.3 mm for the enriched $^{100}$Mo target. Several radionuclide impurities such as $^{94m,95m,96o}$Tc are expected to be observed at the end of the 11-MeV proton bombardment of the $^{94m}$Mo target, whereas no
significant impurity is theoretically present in the enriched $^{100}$Mo target. Extremely high yield of 42.18 GBq/uA.hr of Tc-99m radionuclide is predicted to be produced at the end of the bombardment.

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