Influence of GA Siwabessy Reactor Irradiation Period on The Molybdenum-99 (99Mo) Production by Neutron Activation of Natural Molybdenum to Produce Technetium-99m (99mTc)

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Abstract. Production of 99Mo by neutron activation of natural Mo in multipurpose reactor GA Siwabessy is an alternative solution to overcome the 99Mo shortage, particularly in Indonesia. The aim of this study is to evaluate the influence of the irradiation period of the reactor on the quality of the produced 99Mo and 99mTc. A natural molybdenum was packed in quartz ampule and aluminium capsule, irradiated in the research reactor for around 100 hours. The 99Mo - 99mTc separation was conducted in Center for Radioisotope and Radiopharmaceutical Technology using zirconium-based material (ZBM). The observed parameters are 99Mo activity, 99mTc yield percentage, adsorption capacity ZBM and 99mTc quality. Both the obtained 99Mo activity and 99mTc yield percentage were influenced by the irradiation period. On the other hand, neither the adsorption capacity of ZBM nor quality parameters of 99mTc were influenced by the irradiation period.

1. Introduction
The role of Technetium-99m (99mTc) in a medical field is very important due to its ideal characteristics as a radiodiagnostic agent [1–4]. Annually, more than 45 million diagnostic nuclear medicine procedures are carried out using 99mTc. More than eighteen 99mTc radiopharmaceutical kits are commercially available and the new ones are still developed in a laboratory [5]. The characteristics which make 99mTc become an ideal radiodiagnostic are short half-life (6.02 h), low but sufficient energy (141 keV), and availability of its generator. A 99mTc is a daughter radionuclide from Molybdenum-99 (99Mo) which usually produced from High Enriched Uranium (HEU) or Low Enriched Uranium (LEU)[6, 7].

A shortage of 99Mo produced from Uranium, i.e. fission 99Mo, is predicted to be happening in the future because of several problems regarding the production of fission 99Mo. The shutdown of couple of research reactors, NRU of Canada and HFR of Netherlands, among the seven research reactors which supply more than 95% world demand of 99Mo (NRU of Canada, HFR of Netherlands, BR2 of Belgium, Safari-1 of South Africa, Osiris of France, Maria of Poland and OPAL of Australia), become a serious issue beside the aging of the others[8]. The other problem is about 20 long-lived radionuclide produced during production of fission-99Mo with a half-life of 0.1 to 60 days and total activity hundred times higher than the obtained 99Mo. This problem and the separation of the remaining 235U lead to a waste management and disposal issues [9]. The last problem is the use of 235U which can cause nuclear security issues [9].
There are several alternative solutions to overcome these problems including a production of non-fission $^{99}$Mo from a natural molybdenum using research reactor[10]. The non-fission $^{99}$Mo production route can use natural molybdenum ($\text{MoO}_3$) which produces less radioactive waste than the fission one. This production also needs less complicated procedures and facilities for post-irradiation processing, however, it produces low specific activity $^{99}$Mo. Therefore a conventional generator technology is not suitable for non-fission $^{99}$Mo[11].

The production of non-fission $^{99}$Mo from natural molybdenum using research reactor follows $^{98}\text{Mo}(n, \gamma)^{99}\text{Mo}$ reaction. To estimate the activity of the obtained $^{99}$Mo, the following equation is used[12]:

$$A^{(99}\text{Mo}) = N^{(98}\text{Mo})\Phi \sigma (1 - e^{-\lambda t})$$

$A^{(99}\text{Mo})$ represents a $^{99}$Mo activity at end of irradiation (EOI); $N^{(98}\text{Mo})$ is the number of $^{98}$Mo element (atom); $\Phi$ is a neutron flux (neutron s$^{-1}$ cm$^{-2}$); $\sigma$ is a $^{98}$Mo cross section ($^{98}$Mo = 0,13 barn = $1.3 \times 10^{-25}$ cm$^2$)[12]. The equation shows the factors that influence a $^{99}$Mo activity. The number of $^{98}$Mo atom depends on the amount of starting material ($\text{MoO}_3$), whereas the neutron flux is varied in each research reactor and the irradiation position.

A Multipurpose reactor GA Siwabessy is the one of a research reactor in the world which produces radioisotopes including $^{99}$Mo. [13]. This reactor has neutron flux up to $1,12 \times 10^{14}$ n cm$^{-2}$ s$^{-1}$ in the Center Irradiation Position (CIP)[12]. The terrace configuration of this reactor can be seen in figure 1.

**Figure 1.** The terrace configuration of GA Siwabessy Research Reactor[12]

The multipurpose reactor GA Siwabessy has a long experience in producing both fission $^{99}$Mo and non-fission $^{99}$Mo which is supported by post-irradiation processing facilities of PT INUKI and National Nuclear Energy Agency (BATAN). A $^{99}$Mo is produced in this reactor to supply the national demand for both medical practice and research purpose.
The location of post-irradiation processing facilities for non-fission $^{99}$Mo is located in the Center for Radioisotope and Radiopharmaceutical Technology, BATAN, which has developed a zirconium-based material (ZBM) for $^{99}$Mo/$^{99m}$Tc separation. This material is a poly-zirconium compound which has an adsorption capacity to molybdenum up to 180 mg Mo/gram ZBM. This material has been examined for $^{99}$Mo/$^{99m}$Tc separation for more than three years. The objective of this study is evaluating the influence of GA Siwabessy reactor irradiation period on the production of non-fission $^{99}$Mo and its application to produce $^{99m}$Tc. This study is important to ensure the quality assurance of radioisotope production.

2. Materials and Methods

The following chemical substances were used as received from E Merck: natural molybdenum oxide (MoO$_3$), sodium hydroxide (NaOH), hydrochloric acid (HCl). Aquabidest and saline solution (NaCl 0,9%) were purchased from IPHA Laboratories. Sodium hypochlorite (NaOCl) was purchased from Sigma Aldrich and A ZBM was obtained from Center for Radioisotope and Radiopharmaceutical Technology, BATAN.

The main facilities for the study were the multipurpose reactor GA Siwabessy and hotcells laboratory for irradiation and post-irradiation processing. The pre-irradiation facilities were: welding installation, forklift for transportation and transfer cask, whereas the other post-irradiation facilities were: multi-channel amplitude pulse analyzer (MCA) Ortec GEM-30, High Purity Germanium (HPGe) detector, dose calibrator and fume hood.

2.1. Pre-Irradiation

The MoO$_3$ was weighed for 4 grams and heated at 500°C for 60 minutes to prevent a clumping of the powder after irradiation, packaged in quartz ampule and aluminium irradiation capsule. To avoid the leakage, both quartz ampule and irradiation capsule were examined for the leak test using the bubble test method. The irradiation target was irradiated in the reactor for 100 hours.

2.2. Post-Irradiation

The transportation between multipurpose reactor GA Siwabessy and Center for Radioisotope and Radiopharmaceutical Technology was conducted using a forklift and transfer cask to ensure the personal safety. After irradiation, both quartz ampule and irradiation capsule were dismantled in the hotcell.

The MoO$_3$ powder was placed and diluted using 15 mL 4N NaOH in a beaker glass. The MoO$_3$ solution was measured using dose calibrator and HPGe detector for its activity and radionuclide purity. For the $^{99}$Mo and $^{99m}$Tc separation, the ZBM was soaked into MoO$_3$ solution at 90°C for 3 hours, then packed into a glass column. The glass column was drained off with saline solution and NaOCl 0,05% to release the remained $^{99m}$Tc and enhance yield. The column which to be in tandem with alumina column was eluted using saline solution after a day to release $^{99m}$Tc.
Figure 2. Illustration of the pre-irradiation and post-irradiation process: (a) MoO$_3$ weighing; (b) heating; (c) outer capsule (top), inner capsule (middle), MoO$_3$ bulk (bottom left), and ampule (bottom right); (d) bubble testing for inner capsule; (e) bubble testing for inner ampule; (f) transportation of irradiation sample; (g) Post-irradiation process

3. Results and Discussion

The irradiation cycle of multipurpose reactor GA Siwabessy is 100 hours at power capacity of 15 Megawatt. There are two irradiation periods of the reactor, Friday – Tuesday and Monday - Friday, which depend on the agreement of the stakeholders. The results of $^{99}$Mo activities in different irradiation period are presented in Table 1.
Table 1. The comparison of $^{99}$Mo results between two irradiation periods

| Irradiation period | Friday – Tuesday | Tuesday - Saturday |
|--------------------|------------------|-------------------|
|                    | 1    | 2    | 3    | 1    | 2    | 3    |
| Amount of MoO$_3$ (gram) | 4    | 4    | 4    | 4    | 4    | 4    |
| Irradiation time (hour) | 96.75 | 95.5 | 97   | 104.5 | 103.25 | 100  |
| CIP position        | E-7  | D-6  | E-7  | E-7  | E-7  | E-7  |
| $^{99}$Mo activity (GBq) | 56.88 | 73.12 | 43.15 | 36.13 | 25.11 | 38.36 |
| Specific activity (GBq/gram) | 18.28 | 10.79 | 9.03  | 6.28  | 9.59  | 18.28 |

Table 1 showed different $^{99}$Mo activity results in two irradiation periods. Friday – Tuesday irradiation period has a higher $^{99}$Mo activity result. This phenomenon was caused by different post-irradiation processing. In Friday – Tuesday irradiation period, the irradiation target was processed a day after the end of irradiation (EOI), the decay time after EOI was less than a day. On the other hand, in Monday - Friday irradiation period, the irradiation target was processed on Monday, i.e. two days after the EOI, where the decay time after EOI was more than a day. The calculation of irradiation target decays after EOI is presented in table 2.

Table 2. The calculation of irradiation target decays after EOI

| Irradiation period | Friday - Tuesday | Monday - Friday |
|--------------------|------------------|-----------------|
|                    | 1    | 2    | 3    | 1    | 2    | 3    |
| Decay time (hour)  | 25.73 | 23.38 | 22.6  | 68.85 | 69.60 | 63.25 |
| $^{99}$Mo activity at measurement (GBq) | 56.88 | 73.12 | 43.15 | 36.13 | 25.11 | 38.36 |

A significant difference between two irradiation periods is seen in table 2. This difference leads to different parameter values in the next post-irradiation processing.

The amount of $^{99}$Mo adsorbed into ZBM is calculated by the assumption that ZBM has an adsorption capacity of 200 mg Mo/gram ZBM concluded from previous studies. The adsorption of $^{99}$Mo into ZBM is based on an ion exchange mechanism between $^{99}$MoO$_4^{2-}$ and Cl$^-$ in the surface of the material [14, 15]. The attachment of oxygen in $^{99}$MoO$_4^{2-}$ to a metal, such as Zr, is common which is usually happened in Fe or Al Oxide [16]. The mechanism can be seen in Figure 3.

Figure 3. Adsorption mechanism of $^{99}$MoO$_4^{2-}$ into ZBM[17]
Awaludin et al proposed the adsorption mechanism based on the SEM-EDX analysis[15]. The decrease of Cl and the increase of Mo after adsorption experiment indicate the ion exchange between the couple atoms. The mole ratio of Mo and Zr (1: 2) also indicates the bond pattern of the couple atoms which has described in Figure 3 [18]. The $^{99m}$TcO$_4^-$ elution mechanism is also described in Figure 3 which exhibits an ion exchange mechanism like adsorption mechanism in a reverse direction [17]. The Cl atoms in the saline solution will replace the $^{99m}$TcO$_4^-$ during the elution. The calculation of $^{99}$Mo adsorption and $^{99m}$Tc elution in this study is presented in figure 4 and figure 5, respectively.

**Figure 4.** The adsorption capacity of ZBM to molybdenum in two irradiation periods which presented by triplication data and its average.

In figure 4, the adsorption capacity of ZBM to molybdenum both on Friday – Tuesday and Monday - Friday periods are alike. Hence, the irradiation period has no influence on the adsorption capacity of the material. The adsorption capacity of the material is not influenced by a $^{99}$Mo activity which depends on the irradiation period, however, it is influenced by the MoO$_4^{2-}$ and ZBM bond. The factors which determine the bond are the acidity of MoO$_4^{2-}$ and the surface area/porosity of the material[16].

**Figure 5.** $^{99m}$Tc yield percentage in two irradiation periods which presented by triplication data and its average.

On the other hand, figure 5 shows that there is a difference between $^{99m}$Tc yield percentage in two irradiation periods. A $^{99m}$Tc yield percentage in Friday – Tuesday period is higher than the one in Tuesday-Saturday period. The higher the activity of $^{99}$Mo loaded in ZBM, the lower the $^{99m}$Tc yield percentage. This phenomenon is suspected caused by the solvated electron derived from beta irradiation of $^{99}$Mo. The electron then reduces $^{99m}$TeO$_4^-$ become the lower oxidation state, e.g. $^{99m}$TeO$_2$, which is more difficult to be eluted from ZBM[15].
The low $^{99m}$Tc yield percentage is a classical problem for $^{99}$Mo/$^{99m}$Tc generator system. To increase the $^{99m}$Tc yield percentage, an oxidizing agent, e.g. NaOCl, is usually added. The oxidizing agent oxidizes $^{99m}$Tc to the highest oxidation state which is eluted easily\cite{18}. The addition of oxidizing agent is limited by its toxic concentration level and its inhibition to radiolabeling of radiopharmaceutical kits.

To ensure the quality of $^{99m}$Tc eluate, the investigation of $^{99m}$Tc radiochemical purity, $^{99m}$Tc radionuclide purity and alumina breakthrough were conducted using Thin Layer Chromatography (TLC), HPGe detector and alumina breakthrough kit, respectively. The investigation result of the radiochemical purity and alumina breakthrough is presented in Table 3.

| Irradiation period | Radiochemical purity (%) | Alumina breakthrough ($\mu$g/mL) |
|--------------------|--------------------------|---------------------------------|
| Friday - Tuesday   | 98.9                     | < 5                             |
| Monday - Friday    | 99.9                     | < 5                             |

Radiochemical purity is a parameter which ensures that $^{99m}$Tc exists in the desired chemical form, i.e. $^{99m}$TcO$_4^-$ . Whereas, alumina breakthrough is a parameter which ensures that an alumina from the column does not exist in the $^{99m}$Tc solution. Table 3 shows that both parameters in two irradiation periods were meet the requirement\cite{19}. Hence, the irradiation period has no influence on the radiochemical purity and the alumina breakthrough. The radionuclide purities from two irradiation periods were identical. The identical spectra are presented in figure 6.

![Figure 6. The spectra of radionuclide purity of $^{99m}$TcO$_4^-$ solution.](image)

Figure 6 shows the spectra of $^{99m}$TcO$_4^-$ solution containing only Pb and $^{99m}$Tc spectrums. It means the $^{99m}$Tc was separated from $^{99}$Mo by ZBM column system. The spectrum of Pb was existed due to the interaction of the $\beta$ particle of $^{99m}$Tc with the chamber made from lead (Pb) \cite{17}.

The irradiation periods also influenced the elution days after $^{99}$Mo adsorption process. In the Monday - Friday period, the $^{99m}$Tc elution was conducted four times continuously after the adsorption process without any interruption. On the other hand, in the Friday – Tuesday period, the $^{99m}$Tc elution was conducted only two times continuously, after two holidays a $^{99m}$Tc activity became too low to be eluted.
4. Conclusion
The obtained $^{99}$Mo activity and $^{99m}$Tc yield percentage were influenced by the irradiation period. The $^{99}$Mo activity was higher in the Friday – Tuesday period due to the short decay time before post-irradiation processing, while the $^{99m}$Tc yield percentage was higher in the Monday – Friday period. On the other hand, neither the adsorption capacity of ZBM nor quality parameters of $^{99m}$Tc were influenced by the irradiation period.

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