# MINIMIZING MOLYBDENUM-99 CONTAMINATION IN TECHNETIUM-99m PERTECHNETATE FROM THE ELUTION OF $^{99}Mo/^{99m}$ Tc GENERATOR.

Ibrahim I., Zulkifli H., Bohari Y., Zakaria I. and Wan Hamirul B.W. K.

Medical Technology Division, Agency Nuclear Malaysia, 43000 Kajang, Selangor, Malaysia.

Abstract

Radioisotope Tc-99m is widely used for variety of nuclear medicine diagnostic procedures. For many commercial applications, it is prepared in a portable type generator. Nuclear Malaysia has been producing a dry type alumina chromatographic column generator utilizing fission Mo-99. This injectable Tc-99m must meet the British Pharmacopeia [1] product specification prior to be apply on patient. This paper provides a method to minimize the up to acceptable levelMo-99 in the final product. Purposely made pertechnetate contaminated with Mo-99 and re-eluate by using old generator. Excellent removal of Mo-99 impurity was achieved and more than 80% of Tc-99m total activity was recovered.

Keywords: Tc-99m, fission Mo-99, alumina chromatographic column, pertechnetate and re-eluate.

## 1.0 INTRODUCTION

A $^{99}Mo/^{99m}Tc$ generator, or colloquially a technetium cow or moly cow, is a device used to extract the metastable technetium isotope ($^{99m}Tc$) from a source of decaying $^{99}Mo$. $^{99}Mo$ has a half-life of 66 hours [2,3] and can easily be transported over long distances to hospitals. Its decay product $^{99m}Tc$ (with a half-life of only 6 hours, which is inconvenient for transportation) is extracted and used for a variety of nuclear medicine diagnostic procedures due to its short half-life.

$^{99}Mo$ can be obtained by neutron activation (n,γ reaction) of $^{98}Mo$ in a high neutron flux reactor. However, the most frequently used method requires a uranium target with high enriched uranium-235 (up to 90% $^{235}U$) or low enriched uranium (less than 20% $^{235}U$). The target is irradiated with neutrons to form $^{99}Mo$ as a fission product [2,3]. $^{99}Mo$ is then separated from other fission products in a hot cell.

The half-life of the mother nuclide ($^{99}Mo$) is much longer than that of the daughter nuclide ($^{99m}Tc$), where 50% and 75% of equilibrium activity were reached within one daughter half-life, and two daughter half-life respectively. Hence, removing the daughter nuclide (elution process) from the generator ("milking" the cow) is reasonably done as often as every 6 hours in a $^{99}Mo/^{99m}Tc$ generator.

Most commercial $^{99}Mo/^{99m}Tc$ generators use column chromatography, in which $^{99}Mo$ in the form of molybdate, $MoO_4^{2-}$ is adsorbed onto acid alumina ($Al_2O_3$). When the Mo-99 decays, it will form pertechnetate $TcO_4^-$, since single charge is less tightly bound to the alumina. Pulling normal saline solution through the column of immobilized $^{99}Mo$ will elutes the soluble $^{99m}Tc$, resulting in a saline solution containing the $^{99m}Tc$ as the pertechnetate, with sodium as the counterbalancing cation.

The decay process of $^{99}Mo$ that produces $^{99m}Tc$ was device in equation 1;

$$^{99}Mo \rightarrow {}^{99m}Tc + e^- + \nu_e \quad \text{------- equation 1}$$

It can also be express as in equation 2;

$^{99}Mo \rightarrow {}^{99m}Tc + \beta^{-} + \nu_e$ ------- equation 2

Where, $e^{-}$ (or $\beta^{-}$) denotes the electron (beta particle) emitted from the nucleus, and $\nu_e$ denotes the emitted antineutrino (or more specifically, an electron antineutrino).

$^{99m}Tc$ will then undergo an isomeric transition to yield $^{99}Tc$ and a monoenergetic gamma emission (γ) as express in equation 3:

$^{99m}Tc \rightarrow {}^{99}Tc + \gamma$----------equation 3

The solution of sodium pertechnetate with appropriate concentration was added to organ-specific pharmaceutical to be used, or sodium pertechnetate can be used. It can also be used directly without pharmaceutical tagging for specific procedures requiring only the $^{99m}TcO_4^{-}$ as the primary radiopharmaceutical. A large percentage of the $^{99m}Tc$ generated by a $^{99}Mo/^{99m}Tc$ generator is produced in the first 3 parent half lives, or approximately one week. Hence, clinical nuclear medicine unit will purchase at least one such generator per week or order several in a staggered fashion [3].

Recently, we encountered a molybdenum 99 breakthrough problem, where the content of the elution from the generator were over limit (more than 0.15μCi/mCi $^{99m}Tc$ or 0.015 %). In November 2009 more than 5 generators were contaminated by Mo-99. The International Atomic Energy Agency (IAEA) safety standard recommends that any elution containing more than 0.15 μCi of Mo-99/ mCi of Tc-99m or more than 0.015 % of MBT [3,4] should not be injected to human.

The purpose of this study is to reduce the Mo-99 breakthrough (MBT) by passing the content of the elution from the high MBT- technetium generator through the old molybdenum-technetium generator which acted as a resin column.

## 2.0 MATERIAL AND METHOD

### 2.1 MATERIAL

Fission Mo-99, normal saline and sterile evacuated vials (SEV) were purchased from PT Batan Teknologi, Indonesia. Generator with high Mo-99 content (Generator A) and previous week used generator (Generator B) were produced by Nuclear Malaysia and dose calibrator (Capintec, USA).

## 2.2 METHOD

Generators loaded with more than 0.15 µCi Mo-99/mCi Tc-99m and have different level of impurities, were prepared and labeled as A1, A2, A3, A4 and A5. One week old used generator labeled as B1, B2, B3, B4 and B5 were used as second eluted.

The level activity of Mo-99 in A series generator was analyzed from elute of Sodium Pertechnetate. The elutes is then passed through B series generator using method adopted from Isaac et al., 1968 [3] and Nosheen et al., 2008 [5]. The second eluate from B series generator are then being analyzed for chemical, radiochemicals, physicochemical, sterility and pyrogen testings [1] by Chemical Quality Control and Microbiology Quality Control units.

## 3.0 RESULTS AND DISCUSSION

Easy and effective way to minimize the Mo-99 content is by passing high MBT elution from $^{99}Mo/^{99m}Tc$ generator through an old $^{99}Mo/^{99m}Tc$ generator (as resin column). Table 1 showed the level of M0-99 impurities from eluted of A series generator. The percentage of Mo-99 breakthrough (MBT) from generator A1 to A5 showed more than limit 0.015%, the limit MBT recommended by BP 2007. These generators should not be injected to human.

Table 2 showed MBT content were reduced when elution from generator A series passed through an old generator (B series). Percentages MBT content from elution B series generators were less than 0.015% and re-eluting the B5 generator with saline 1 hour after first elution, Tc-99m was able to be recovered with a bonus of few millicuries (mCi) (B5a). Finally, approximately more than 80 % of Tc-99m was recovered from the total activity of $^{99}Mo/^{99m}Tc$ generator (A series generator).

Table 1: Level of Molybdenum-99 impurities from elute of Generator Series A

| Gen No | B/ground µCi (B) | Mo-99 µCi (M) | (M-B) µCi x 3.5 (C) | Tc-99m mCi (D) | % MBT (C/D) (<0.015 %) |
|---|---|---|---|---|---|
| *A1 | 3.28 | 27.8 | 85.82 | 255 | 0.03365 |
| *A2 | 3.28 | 30.5 | 95.27 | 283 | 0.0336 |
| *A3 | 3.28 | 32 | 100.52 | 292 | 0.03442 |
| *A4 | 3.28 | 30 | 93.52 | 268 | 0.03489 |
| *A5 | 3.67 | 64.70 | 213.60 | 668 | 0.03197 |

*A- High MBT

Table 2: Level of Molybdenum-99 impurities from elute of Generator Series B

| Gen No | B/ground µCi (B) | Mo-99 µCi (M) | (M-B) µCi x 3.5 (C) | Tc-99m mCi (D) | MBT (C/D) (<0.015 %) |
|---|---|---|---|---|---|
| *B1 | 3.28 | 5.86 | 9.03 | 142 | 0.0063 |
| *B2 | 3.28 | 8.20 | 17.22 | 160 | 0.0107 |
| *B3 | 3.28 | 4.92 | 5.74 | 150 | 0.0038 |
| *B4 | 3.28 | 6.24 | 10.36 | 143 | 0.0072 |
| *B5 | 3.67 | 7.83 | 14.56 | 493 | 0.0029 |
| *B5a | 3.67 | 5.85 | 7.63 | 60.4 | 0.0126 |

*B- Old generator (from different generator)

a- Second elution from B5 (1 hr after first elution)

Figures 1, showed series of activities Mo-99 breakthroughs content of elution from generator A`s with a very high activities. When the activities of MBT were passed through generator B series, activities less than <0.15 µCi of Mo-99/ mCi of Tc-99m or <0.15% were produced and does not exceeding the standard limit [3; 4].

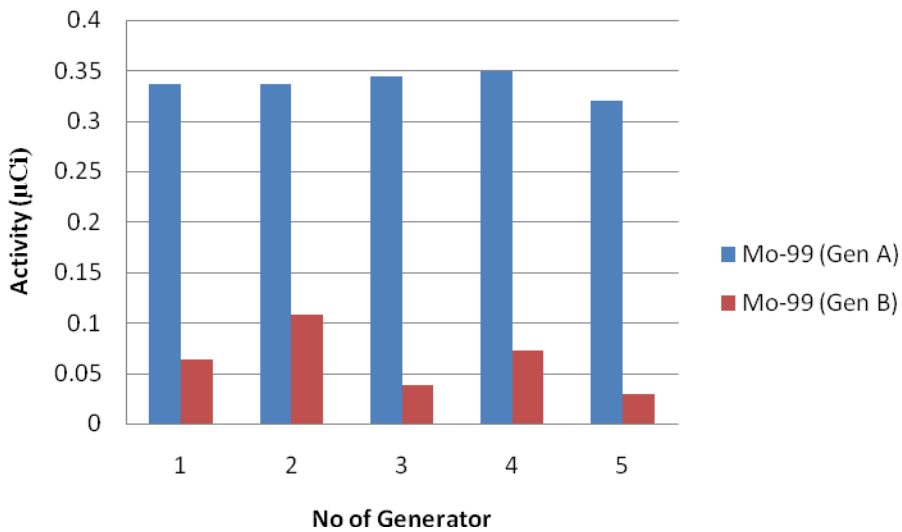


Figure 1: Activity of Mo-99 in each generator A and B

3.1 CHEMICAL QUALITY CONTROL

Tablet 3 showed, the chemical, physicochemical and radiochemical analysis of finished products of $^{99}$Mo/$^{99m}$Tc generator. The Chemical Quality Control (CQC) tests on $^{99}$Mo/$^{99m}$Tc generator was evaluated based on appearance of the products, pH range must be between pH 4.0 to pH 8.0, content of alumina breakthrough must be less than 5 ppm, more than 95 % of Tc-99 radiochemical purity, Tc-99m spectra and radionuclide purity of Mo-99 breakthrough must be less than 0.15 µCi of Mo-99 of each 1 mCi of Tc-99m eluate. The results showed, all the generators passed the CQC tests and follow the [1] specification requirements.

Table 3: Chemical, physicochemical and radiochemical analysis of finished products of $^{99}Mo/^{99m}Tc$ generator.

| Tests | Spec. (BP 2007) | Generator Number 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|
| Appearance | Clear, colorless | Clear, colorless | Clear, colorless | Clear, colorless | Clear, colorless | Clear, colorless |
| pH | 4.0 – 8.0 | 6.5 | 6.5 | 6.5 | 6.5 | 6.5 |
| Chemical testing – content of Alumina | <5 ppm | <5 ppm | <5 ppm | <5 ppm | <5 ppm | <5 ppm |
| Radiochemical purity, % | >95.00% | 99.5 | 99.7 | 99.6 | 99.6 | 99.69 |
| Identification testing $^{99m}Tc$- spectra | 140.5 keV | 140.5 | 140.5 | 140.5 | 140.5 | 140.5 |
| Radionuclide purity, MBT < 0.15 µCi $^{99}Mo$- of each 1 mCi of $^{99m}$ Tc-eluate | <0.15 µCi | 0.0635 | 0.1076 | 0.038 | 0.0724 | 0.0295 |

## 3.2 MICROBIOLOGY QUALITY CONTROL

Microbiological Tests is done to ensure that the Tc-99m generator is free from microorganism and its product will not cause infection to the patient. There are two tests on Tc-99m generator, Sterility Test and Pyrogen Test (Bacterial Endotoxin Test)

Sterility test is to reveal or ascertain the absence of any viable form of microbial population (bacteria, yeast and fungi). Two types of media (Thioglycollate medium and Trytone Soy Broth medium) were used; 2.5ml of Tc-99m eluate shall be inoculated into each media. Incubate both media in respective temperature for 14 days. Observe for any growth daily. The sterility test were PASS for generator B1, B2, B3, B4 and B5 elutes because no microbial growth in any tubes after 14 days incubation.

The pyrogen test was carried out by gel clot method using *Limulus Amebocyte Lysate* (LAL) is for determined the endotoxin concentration of Tc-99m generators. All the generators elution no exceeds 17.5 IU endotoxin limit concentration recommended by BP 2007.

## 4. CONCLUSION

MALTec Sterile Tc-99m dry types chromatographic generator produces high quality injectable sodium pertechnetate, $NaTcO^{4-}$. Although 'carrier-free' fission Mo-99 is used as 'mother' solution, contamination from Mo-99 and alumina, Al+ occasionally occur. Both contaminants can result in low image quality during diagnosis as well as less efficiency of Tc-99m binded to any radiopharmaceutical ligands.

Results obtained from this work suggested that Mo-99 contaminated can be effectively removed from final product by passing of through the one week old MALTec Sterile Tc-99m generator. This newly added preparation step can be safely used to make the failed QC test Tc-99m into a ready injectable into patient. A few millicurie Tc-99m can be reproduce by re-elution process carried out on series Generator B using saline after an hour of the previous elution. Therefore the study shows that MBT is able to be minimized and also produced Tc-99m with specific activity requirement.

## ACKNOWLEDGEMENTS

I would like to thank you to all my friends and staff Medical Technology Division, who has helped me directly or indirectly throughout my research.

## REFERENCE

1. British Pharmacopoeia, 2007. CD-ROM Version 11.0
2. Nave R. "Technetium-99m". *HyperPhysics* (Georgia State University). http://hyperphysics.phy-astr.gsu.edu/hbase/nuclear/technetium.html
3. Wikipedia, 2010 (28/05/10, 04.58 pm), *Technetium-99m*, The free encyclopedia
4. Isaac CR. Fred and Fred A., 1968. A simple method of reducing the molybdenum content of the eluate from a Mo99- Tc99m generator. AM. J. Roentgenol 1968; 103: 896
5. Nosheen F., Maseeh UZ., Kashif N., Hassan R., Javed I., Abid H., Hina H. and Salman H., 2008. Effective method to minimize molybdenum content of $^{99}$Molybdenum- $^{99m}$ Technetium generator eluate. Pakistan Journal of Radiology; 18(1); 20-21.