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Assessment of molybdenum concentration in $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators (PAKGEN): 6 years experience

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ABSTRACT

Background: Technetium-99m ($^{99\text{m}}\text{Tc}$) is a widely used radioisotope for the diagnostic procedures in nuclear medicine. The radioisotope is eluted from $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator. Ideally there should be no Molybdenum-99 (^{99}Mo) or any other contamination; however, sometimes traces of ^{99}Mo are co-eluted from the generator. This impurity interferes labeling of $^{99\text{m}}\text{Tc}$ with pharmaceuticals result in poor quality radiopharmaceutical and unnecessary exposure to patients. The purpose of this study is to assess the contamination level of ^{99}Mo in the eluted activity of $^{99\text{m}}\text{Tc}$ used for the diagnostic procedures at Swat Institute of Nuclear Medicine, Oncology and Radiotherapy (SINOR), Swat Pakistan. Also the purpose is to check the integrity of the generators being transported by road, and it is a part of quality audit of PAKGEN $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators.

Methods: The data were collected for 166-PAKGEN $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators used over 6 years at SINOR. The generators were procured from Isotope Production Division, Pakistan Institute of Nuclear Science and Technology (PINSTECH), Islamabad, Pakistan. The ^{99}Mo impurity concentration was measured for each elution with dose calibrator (Capintech Inc. CRC-25R) and canister.

Results: Results for most of the generators (99.4%) were within the permissible limit (0.15 μCi of $^{99}\text{Mo}/\text{mCi}$ of $^{99\text{m}}\text{Tc}$) as per Pakistan Nuclear Regulatory Authority, Nuclear Regulatory Commission, and other regulatory authorities. Only one generator (0.6%) had the values out of range.

Conclusion: ^{99}Mo breakthrough concentration for most of the generators was within permissible range which shows integrity of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ PAKGEN generators and approves the quality of locally prepared $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ PAKGEN generators. The study replicates excellent manufacturing and quality control of PAKGEN generators which offers a confirmation of safe medical practices.

Keywords: Molybdenum concentration, $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator, nuclear medicine, imaging.

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Background

Radioactive isotope-based imaging modalities play central role in diagnostic and therapeutic procedures [1]. Initially there were several challenges to produce radiopharmaceuticals that fits to clinical requirements of nuclear medicine imaging [2]. These challenges include proper polarity between radionuclide physical half-life and biological half-life, good radionuclide yield, and suitable logistic viability [2]. Keeping all these considerations, ^{99}Mo , with a physical half-life of 66 hour and decays by beta emission to $^{99\text{m}}\text{Tc}$ (87%) and ^{99}Tc (13%) makes it an ideal choice for diagnostic imaging in nuclear medicine [3]. It has low cost, easily available [4-7]. $^{99\text{m}}\text{Tc}$ is obtained either by irradiation of ^{98}Mo (usually as MoO_3) with thermal neutrons or from fission of uranium-235 in a nuclear reactor. The ^{99}Mo separated

from fission products is mounted on alumina column. The adsorption capacity of alumina column is up to 20 mg Mo/g of alumina. ^{99}Mo is adsorbed on a small alumina (2-3 g) column. For the preparation of diagnostic agent, $^{99\text{m}}\text{Tc}$ is produced from $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ alumina column generator. Physiological (0.9%) saline is the most widely used eluent for alumina of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators. Purity and quality of separated $^{99\text{m}}\text{Tc}$ is vital for clinical purposes. Therefore, effective separation of $^{99\text{m}}\text{Tc}$ from $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ is central to sustainability of nuclear medicine [3,8].

Ideally, eluate should not contain any radionuclide impurity. But due to generator aging or a mechanical defect, variety of factors contributes to contamination of $^{99\text{m}}\text{Tc}$ eluate from the stage of preparation to final

separation. Elute may be contaminated with parent radionuclide and column matrix (Al^{+3}). The parent nuclide contamination may affect image quality and add to toxicity [4,7,9] as its high concentration delivers approximately 50-times greater dose than $^{99\text{m}}\text{Tc}$ [4,9,10] due to its high energy (740 and 780 keV gamma rays) and greater half-life [11,12]. The over-exposure of both patients and radiation worker is undesirable especially pediatric population [1]. ^{99}Mo contamination is calculated by molybdenum breakthrough (MBT) assay [5,6]. Permissible limit for ^{99}Mo in the eluates is 0.15 $\mu\text{Ci}/\text{mCi}$. The greater levels of ^{99}Mo contamination in the eluted $^{99\text{m}}\text{Tc}$ can be reduced to permissible level of 0.15 μCi of $^{99}\text{Mo}/\text{mCi}$ of $^{99\text{m}}\text{Tc}$ by passing through an old generator [4,7,13]. The purpose of the study is to assess the MBT level in eluted activity used for nuclear medicine diagnostic procedures and to compare the results with permissible limit. The study focuses on the integrity of the mentioned package as the institute is situated in remote area and the package is transported by road. The study is a part of a quality audit of the locally prepared (PINSTECH Islamabad, Pakistan) $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator.

Methods

The study was conducted for 166 $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators (PAKGEN) used over a period of 06 years (December 2015-2021). The ^{99}Mo contamination was measured using Capintech Inc. dose calibrator model ($\text{CRC}^{\text{R}}\text{-25R}$) and canister [6,7,11]. The out of range values of MBT concentration were brought to acceptable limit by passing the eluted activity through old generator as prescribed by Fatima et al. [4], Shah et al. [6], Reese and Mishkin [13], Memon et al. [7], and Loveless [14]. The data of ^{99}Mo contamination in locally prepared generators was compared with other published data as this is important for

a part of quality audit of the generator. For the statistical analysis of the data, Origin software was used.

Results and Discussion

The mean value for ^{99}Mo concentration was 0.011 (0.001, 0.141) with a standard deviation of 0.019792 μCi of $^{99}\text{Mo}/\text{mCi}$ of $^{99\text{m}}\text{Tc}$. However, for only one out of 166 generators (0.6%), the ^{99}Mo concentration was high (34.000 μCi of $^{99}\text{Mo}/\text{mCi}$ of $^{99\text{m}}\text{Tc}$), which was handled and removed using the discussed procedure. The measured values were compared with the permissible limit shown in Figure 1.

It was observed that for most of the generators (99.4%), the ^{99}Mo concentration values were within the permissible range of 0.15 μCi of $^{99}\text{Mo}/\text{mCi}$ of $^{99\text{m}}\text{Tc}$ as per PNRA, NRC, IAEA, and United States Pharmacopeia regulations[15,16].

In this study, the mean value for ^{99}Mo concentration was 0.011 (0.001, 0.141) with a standard deviation of 0.019792 μCi of $^{99}\text{Mo}/\text{mCi}$ of $^{99\text{m}}\text{Tc}$, which is 2.8 times greater than that of Ahmed's [17] value of ^{99}Mo concentration (0.0039 $\mu\text{Ci} / \text{mCi}$) for GE healthcare Drytec™ generator (UK) [17]. In our study, for most of the generators (165/166), the MBT level was 7.3% of the permissible limit which is comparable to the 10% of the MBT, prescribed by Memon et al. [7] for PAKGEN generators, as Memon et al. [7] recommended that additional studies must be performed on MBT for assessment and to improve the significance of this essential procedure. The reasons for contamination of ^{99}Mo with $^{99\text{m}}\text{Tc}$ activity in elution may be due to error in production process, error in mechanical parts, careless transportation, etc. [4,7,9]. However in this study the high level of ^{99}Mo in $^{99\text{m}}\text{Tc}$ elute, in only one $^{99\text{m}}\text{Tc}$ generator (1/166) may be due to rupture/fracture in column or filter damage [6] during transportation as shown in Figure 2, as all the generators are transported by road.

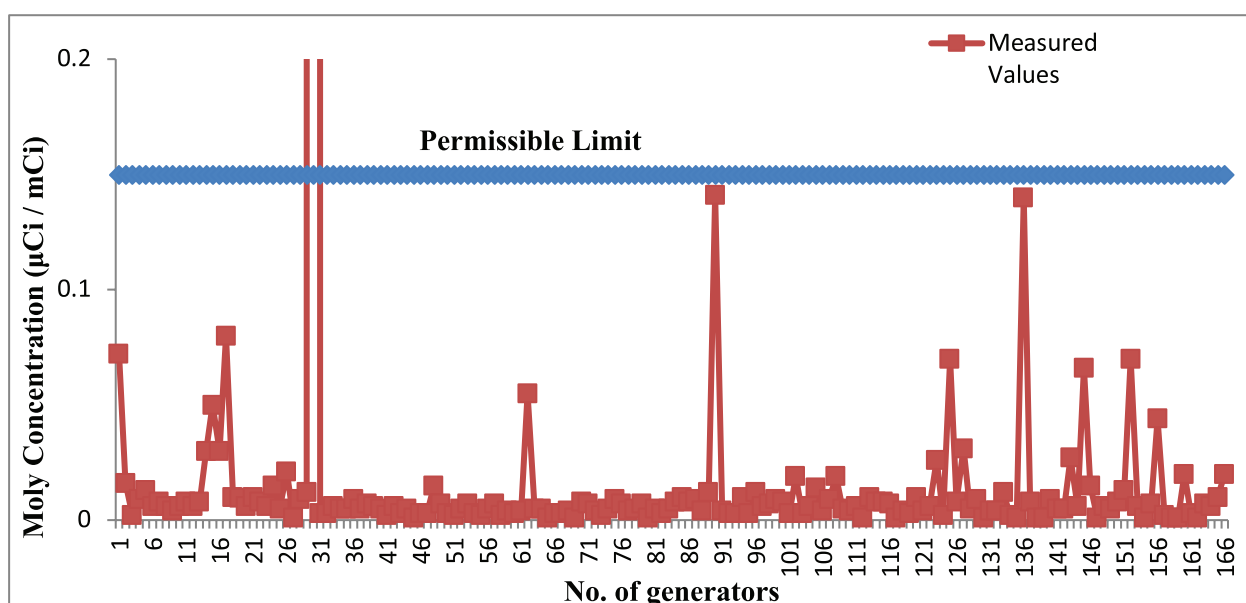


Figure 1. Comparison of Nuclear Medical hospital's MBT in $^{99\text{m}}\text{Tc}$ generators with permissible MBT level.

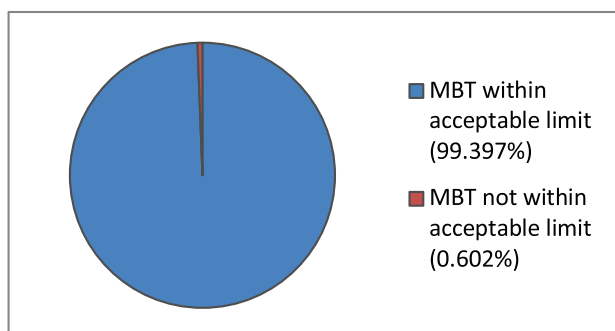


Figure 2. Percentage of MBT levels for $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators within and higher than permissible limit.

Conclusion

It was concluded that MBT concentration for most of the generators was within permissible range which shows integrity of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators being an important element keeping in view by-road transportation to the remote area. The study also shows that quality of locally of locally prepared $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ is up to the mark. The study replicates excellent manufacturing and quality control of PAKGEN generators which offers a confirmation of safe medical practices.

List of Abbreviations

NRC Nuclear Regulatory Commission
PNRA Pakistan Nuclear Regulatory Authority

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Conflict of interests

The authors declare no conflict of interest regarding the publication of this article.

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