Vol.48, Special : pp. 215-220, October 2005
ISSN 1516-8913 Printed in Brazil

BRAZILIAN ARCHIVES OF
BIOLOGY AND TECHNOLOGY

A N I N T E R N A T I O N A L J O U R N A L

# Determination of $^{99}$Mo Contamination in a Nuclear Medicine Patient Submitted to a Diagnostic Procedure with $^{99m}$Tc

**Bernardo Maranhão Dantas[1*], Ana Letícia Almeida Dantas[1], Fábio Luiz Navarro Marques[2], Luiz Bertelli[3] and Michael G. Stabin[4]**

*[1]Instituto de Radioproteção e Dosimetria; IRD/CNEN; Av. Salvador Allende, s/n; 22780-160; Rio de Janeiro - RJ - Brasil. [2]Centro de Medicina Nuclear HCFM-USP; Av. Dr. Enéas Carvalho Aguiar, 255, 3º andar; 05403-001; São Paulo - SP - Brasil. [3]Los Alamos National Laboratory; Los Alamos - NM - 87545 - USA. [4]Vanderbilt University Medical Center; Vanderbilt University; 2201 West End Avenue; Nashville - Tennessee 37235 - USA*

## ABSTRACT

*$^{99m}$Tc is a radionuclide widely used for imaging diagnosis in nuclear medicine. In Brazil it is obtained by elution from $^{99}$Mo-$^{99m}$Tc generators supplied by the Nuclear Energy Research Institute (IPEN). The elution is carried out in radiopharmacy laboratories located in hospitals and clinics. Depending of the quality of the generator and conditions of use during the elution process, $^{99}$Mo can be extracted from the column of the generator, becoming a radionuclidic impurity of the eluate used for the obtention of the radiopharmaceutical to be administered to the patient. $^{99}$Mo emits high-energy photons and beta particles and its presence degrades the quality of the image and unnecessarily increases the radiation dose delivered to the patient. An in-vivo measurement technique was developed to verify the occurrence of internal contamination by $^{99}$Mo in nuclear medicine patients. Direct measurements were made in a volunteer who underwent myocardial scintigraphy with $^{99m}$Tc-sestamibi. The results indicated the presence of internal contamination of the patien by $^{99}$Mot. The activity was tracked for several days, and an assessment of the radiation dose from the contaminant $^{99}$Mo was made.*

**Key words**: Molybdenum 99 - technetium 99m - nuclear medicine - internal dosimetry – in vivo measurements – whole body counter

## INTRODUCTION

In Brazil there are approximately 300 nuclear medicine services in routine operation, located in public and private clinics and hospitals. $^{99m}$Tc is still the most widely used radionuclide in nuclear medicine, being used in about 80% of the examinations for a variety of diagnostic procedures performed in this field. When injected intravenously, the radiopharmaceutical containing $^{99m}$Tc diffuses through the blood stream being taken up in specific sites of the body, depending on its biokinetics.

$^{99m}$Tc is obtained in the nuclear medicine services by the elution of a $^{99}$Mo-$^{99m}$Tc generator. Molybdenum-99 ($t_{1/2}$ = 66 h) decays by beta emission to $^{99m}$Tc (87%) and $^{99}$Tc (13%), emitting photons of 740 and 778 keV (LBLL, 2005). Ideally, $^{99m}$Tc eluates contain no radionuclidic impurity. However, as a consequence of generator aging or possible occurrence of a mechanical defect, $^{99}$Mo may also be extracted from the

* Author for correspondence

column during this elution process, becoming a contaminant in the eluate to be administered to the patient. The presence of $^{99}$Mo in the radiopharmaceutical solution injected in the patient represents an unnecessary radiation dose to the patients; the dose coefficient for $^{99}$Mo is about 50 times higher than that of $^{99m}$Tc. This difference is associated with the beta particle and the higher energies of the photons emitted by $^{99}$Mo. Moreover, depending on the activity of the radionuclidic impurity, the quality of the image can also be degraded.

The maximum $^{99}$Mo concentration established in the technical specifications of the Tc-generators supplied by the IPEN is 0.1% (IPEN, 2005). It is the same value suggested by both the British and European Pharmacopoeia. On the other hand, the International Atomic Energy Agency suggests a radionuclidic impurity activity limit of 0.015% in the radiopharmaceutical solution at the time of administration to the patient (IAEA, 1999).

The US requirement on radionuclidic purity of radiopharmaceuticals is equivalent to the IAEA recommendation and was established in 1986 in the 51FR36967. At that time, 10CFR 30.34 was revised to change the generator elution standard to a requirement such that licensees preparing $^{99m}$Tc radiopharmaceuticals could only use $^{99m}$Tc that contains less than 15 kBq $^{99}$Mo per MBq of $^{99m}$Tc (also 0.15 μCi of $^{99}$Mo per mCi of $^{99m}$Tc). In the USA, a licensee is also required to perform the test and retain records in accordance with 10CFR35.204. Molybdenum break through (MBT) must also be determined at least for the first elution of a particular generator (Essig, 2004)

The US National Regulatory Commission (NRC, 2005) states that "(a) A licensee may not administer to humans a radiopharmaceutical that contains more than 0.15 kilobecquerel of molybdenum-99 per megabecquerel of technetium-99m (0.15 microcurie of molybdenum-99 per millicurie of technetium-99m); (b) A licensee that uses molybdenum-99/technetium-99m generators for preparing a technetium-99m radiopharmaceutical shall measure the molybdenum-99 concentration of the first eluate after receipt of a generator to demonstrate compliance with paragraph (a) of this section."

The US standard was based on a consideration of the detection capability of dose calibrators, the need to ensure consistency of elutions from the resin column, and the desire to establish and maintain an upper limit on the MBT. These considerations help avoid unnecessary radiation exposure to the patient.

Brazilian regulations established by the National Nuclear Energy Commission (CNEN) do not mention any limit of radionuclidic impurity in radiopharmaceuticals nor do they oblige the licensees to perform quality control tests in the eluates. Currently, it requires the self-initiative of the radiopharmacist to perform quality controls on the technetium eluates.

It is believed that $^{99}$Mo impurities as high as 0.1% are unlikely to occur. However, a recent article presented in a conference on medical physics in Brazil reported levels of molybdenum higher than 0.15 kBq per 1 MBq in 7.4 % of the samples tested in a survey carried out among nuclear medicine centers located in the northeast of Brazil (Khoury et al, 2003)

According to the International Commission of Radiological Protection (ICRP, 1993), 25% of molybdenum which enters the blood deposits in the liver. Bone and kidney are also deposition sites, with fractions of 10 and 5%, respectively. The other 60% is distributed through the remaining tissues of the body. Activity deposited in the skeleton is assumed to be retained with a biological half-time of 10,000 days. In all other tissues, 10% of the activity is assumed to be retained with a biological half-time of one day and the other 90% with a half-time of 50 days (ICRP, 1979). However, experimental data gathered by recent investigations of molybdenum biokinetics and humans have shown that the current model for ingestion of molybdenum isotopes recommended by the ICRP requires some modifications (Giussani et al., 1998). Those results show that an improved description of the excretion processes and a better evaluation of the transfer coefficients enable a successful reproduction of the experimental measurements, while maintaining the general features of the ICRP models. The improved realism of the model means a more reliable application in the field of radiation protection for the evaluation of accidental incorporations and for the estimation of internal doses to patients of nuclear medicine as a consequence of the administration of $^{99m}$Tc eluates containing significant amounts of $^{99}$Mo as a radionuclidic impurity.

Based on the activity present in the body, it is possible to calculate the $^{99}$Mo intake and estimate the internal dose delivered to the patient as a consequence of the presence of radionuclidic

impurity. In this work, a standardized methodology for the determination of $^{99}$Mo internal contamination in humans by direct in vivo measurement in the whole body counter is described. Such information can be used as an input to estimate the internal dose associated with the presence of $^{99}$Mo in $^{99m}$Tc eluates administered to nuclear medicine patients. Thus, the final goal of this work was to provide basic information to improve the quality of the radiopharmaceuticals used in nuclear medicine and avoid an unnecessary radiation dose to the patients

## MATERIALS AND METHODS

*In vivo* measurements were performed in the IRD whole body counter using a NaI (Tl) 8"x 4" scintillation detector The detector is located inside a shielded room with internal dimensions of 2,5 x 2,5 x 2,5 meters. The shielding is made of 15 cm steel walls internally covered with a graded-z lining of lead, cadmium and zinc. The detection system is able to detect and quantify photon emitters in the energy range from 100 to 3000 keV (Oliveira et al, 1989).

The measurements consisted of a 30-minute counting period, during which the patient reclined in a dental chair inside the whole body counter shielding. The detector was positioned at a distance of 70 cm above the patient, as shown in Fig. 1. The subject (a 39 year-old Caucasian male) was measured seven times (one measurement per day) following two administrations of 740 MBq (20 mCi) of $^{99}$Tc-sestamibi for cardiac scans. The first administration was given under stress on Day 1 and the second on Day 2 under rest conditions. Spectra from in vivo measurements performed on Days 2 and 3 could not be analyzed because of the high activity of $^{99m}$Tc present in the body, which led to the occurrence of a high dead time. Useful data were obtained on Days 6 to 10. A typical spectrum obtained in the in vivo measurement is showed in Fig. 2.

In vivo measurements were performed in the IRD whole body counter using a NaI (Tl) 8"x 4" scintillation detector The detector is located inside a shielded room with internal dimensions of 2,5 x 2,5 x 2,5 meters. The shielding is made of 15 cm steel walls internally covered with a graded-z lining of lead, cadmium and zinc. The detection system is able to detect and quantify photon emitters in the energy range from 100 to 3000 keV (Oliveira et al, 1989).

The measurements consisted of 30-minute countings, during which the patient reclined in a dental chair inside the whole body counter shielding. The detector is positioned at a distance of 70 cm above the patient, as shown in Fig. 1. The subject (a 39 year-old Caucasian male) was measured seven times (one measurement per day) following two administrations of 740 MBq (20 mCi) of $^{99}$Tc-sestamibi for cardiac scans.

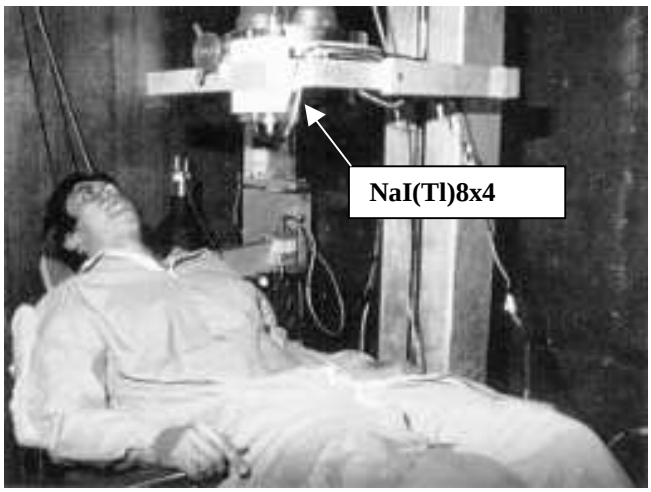


**Figure 1 -** *In Vivo* measurement of the patient in the whole body counter

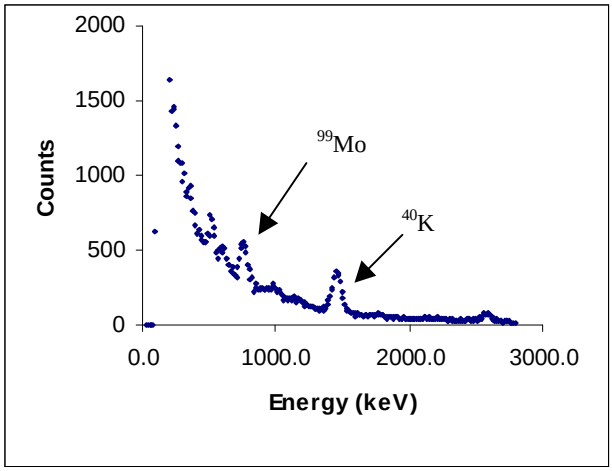


**Figure 2 -** Energy spectrum of *in vivo* measurement of nuclear medicine patient in whom 20 mCi of $^{99}$Tc-sestamibi for cardiac scan was previously administered.

The first administration was given under stress on Day 1 and the second on Day 2 under rest conditions. Spectra from *in vivo* measurements performed on Days 2 and 3 could not be analyzed because of the high activity of $^{99m}$Tc present in the body, which led to the occurrence of a high dead time. Useful data were obtained on Days 6 to 10. A typical spectrum obtained in the in vivo measurement is showed in Fig. 2.

## RESULTS AND DISCUSSION

Table 1 shows the results of the series of *in vivo* measurements performed in the patient following administration of two doses of 20 mCi of $^{99m}$Tc. The activity in the first measurement was about four times higher than the minimum detection activity of the system for 30 minutes of counting, which is about 450 Bq. The series of *in vivo* measurements was interrupted when the whole body activity was equivalent to the MDA.

**Table 1 -** Results of *in vivo* measurements of $^{99}$Mo in a nuclear medicine patient

| Day | $^{99}$Mo Activity (Bq) in whole body |
|---|---|
| 6 | 1816 |
| 7 | 1444 |
| 8 | 996 |
| 9 | 527 |

The results obtained in this work show that the detection system has sufficient sensitivity to identify and quantify $^{99}$Mo contamination in humans at the minimum detection limit of 450 Bq (12 nCi). In the case of the patient measured in this work, such activity was reached seven days after administration of two diagnostic doses of 20 mCi of $^{99m}$Tc for cardiac scan. However this activity will depend on the original MBT of the eluate. The measurement geometry allows determination of the total activity distributed in the whole body. These measurements, taken over a four-day period, suggest an effective half-time of 1.7 days, or a biological half-time of 4.4 days. The data are not sufficient to confirm or refute either the ICRP model or the suggested revisions to that model suggested by Giussani et al. For general purposes, the dose coefficients given in ICRP Publication 67 (ICRP 1993) are reasonable for use for assessing the radiation dose received by adult (or pediatric) subjects who may inadvertently receive low levels of $^{99}$Mo in administrations of $^{99m}$Tc. The dose

coefficients for oral intakes of $^{99}$Mo assume a systemic uptake fraction ($f_1$) of 1.0, equivalent to an intravenous administration. Dose estimates for important organs and effective doses given by the ICRP are given in Table 2.

**Table 2 -** Dose Coefficients (Sv/Bq) for $^{99}$Mo given by the ICRP (1993)

| | Age | | | | | |
|---|---|---|---|---|---|---|
| **Organ** | **3 months** | **1 year** | **5 years** | **10 years** | **15 years** | **Adult** |
| **Kidney** | 2.4E-8 | 1.5E-8 | 8.2E-9 | 5.5E-9 | 3.9E-9 | 3.1E-9 |
| **Liver** | 2.4E-8 | 1.6E-8 | 8.4E-9 | 5.5E-9 | 3.6E-9 | 2.8E-9 |
| **Bone Surfaces** | 6.9E-9 | 5.2E-9 | 3.3E-9 | 1.9E-9 | 1.1E-9 | 1.0E-9 |
| **Red Marrow** | 8.2E-9 | 5.0E-9 | 2.4E-9 | 1.4E-9 | 8.1E-10 | 6.1E-10 |
| **Effective Dose** | 5.5E-9 | 3.5E-9 | 1.8E-9 | 1.1E-9 | 7.6E-10 | 6.1E-10 |

The detection of internal contamination by $^{99}$Mo in patients indicates the need for the implementation of quality control procedures of the Tc-generators in the nuclear medicine clinics. The presence of internal contamination in patients also highlights the need for a more comprehensive survey on MBT in technetium eluates in order to verify compliance with standard limits.

Possible further developments could be a detailed study of the metabolic behavior of molybdenum in humans based on *in vivo* and *in vitro* measurements and the quantification of molybdenum in blood samples of the patients. This information would help to establish more reliably the biokinetics of the radionuclide in the human body, pushing towards an optimization of dosages to patients of nuclear medicine.

## RESUMO

O $^{99m}$Tc é um radionuclídeo largamente utilizado em diagnósticos por imagem em medicina nuclear. No Brasil, ele é obtido por eluição de um gerador de $^{99}$Mo-$^{99m}$Tc fornecido pelo IPEN. A eluição do gerador é feita nas clínicas onde se realizam os exames. Durante a eluição o $^{99}$Mo pode ser carreado da coluna, tornando-se uma impureza radionuclídica do eluato a ser utilizado para a obtenção do radiofármaco administrado ao paciente. O $^{99}$Mo emite fótons de alta energia e partículas beta, e sua presença, além de provocar degradação na qualidade da imagem do exame, aumenta desnecessariamente a dose de radiação no paciente. Assim, com o objetivo de verificar a possível ocorrência de contaminação interna por $^{99}$Mo em pacientes de medicina nuclear, foi desenvolvida uma técnica de medida in vivo e monitorado um paciente voluntário submetido a cintilografia do miocárdio com $^{99m}$Tc-sestamibi. Os resultados revelaram a presença de $^{99}$Mo no corpo do paciente monitorado.

## REFERENCES

Essig, T. (2004), Disponível em: http://hps.org/publicinformation /ate/q3745.html.

Giussani, A.; Cantone, M. C.; Bartolo, D.; Roth, P. and Werner, E. (1998), A revised model of molybdenum biokinetics in humans for application in radiation protection. *Health Physics*, **75** : (5), 479-486.

Instituto de Pesquisas Energéticas e Nucleares (2005), *Gerador de Tecnécio-$^{99m}$* (*Prospecto do produto*). IPEN.

International Atomic Energy Agency (1999), *Manual de protocolos de calidad de radiofármacos*. Projeto ARCAL XV - Producción y control de radiofármacos. IAEA.

International Commission on Radiological Protection (1979), *Limits for intakes of radionuclides by workers*. Oxford : Pergamon Press; ICRP.

International Commission on Radiological Protection (1993), *Age-dependent doses to members of the public from intake of radionuclides: Part 2 - Ingestion dose coefficients*. Oxford : Pergamon Press. (ICRP Publication; 67).

Khoury, H. J. ; Nogueira, F. and Lopes Filho, F. J. (2003), Evaluation of the Quality Control of radiopharmaceuticals used at the nuclear medicine clinics of Recife- PE. *Radioproteccão*, Lisboa, **2** : (2-3), 79-86.

Lawrence Berqueley National Laboratory (2005), LBNL Isotopes Project - LUNDS Universitet. WWW Table of Radioactive Isotopes. Disponível em: http://ie.lbl.gov/toi/index.asp.

National Regulatory Commission (2005), Disponível em: http://www.nrc.gov/reading-rm/doc-collections/cfr/part035/part035-0204.html. (NRC).

Oliveira, C. A. N.; Lourenço, M. C.; Dantas, B. M.; Lucena, E. A. and Laurer, G. R. (1989), The IRD/CNEN whole body counter: Background and calibration results. *Radiat. Prot. Dosm.*, **29** : (3), 203-208.

Received: July 05, 2005;
Revised: July 14, 2005;
Accepted: August 01, 2005.