2007 International Nuclear Atlantic Conference - INAC 2007
Santos, SP, Brazil, September 30 to October 5, 2007
ASSOCIAÇÃO BRASILEIRA DE ENERGIA NUCLEAR - ABEN
ISBN: 978-85-99141-02-1

STUDY OF THE ELUTION OF ^{99}Mo-^{99m}Tc GENERATORS PRODUCED AT IPEN-CNEN/SP

Paula Regina Corain Lopes[1,2] and João Alberto Osso Júnior[2]

[1, 2] Pontifícia Universidade Católica de São Paulo (PUC - SP)
Rua Marquês de Paranaguá, 111
01303-050 São Paulo, SP
corain.lopes@uol.com.br

[2] Instituto de Pesquisas Energéticas e Nucleares (IPEN/CNEN - SP)
Av. Professor Lineu Prestes 2242
05508-000 São Paulo, SP
jaosso@ipen.br

ABSTRACT

Over the last years ^{99m}Tc has become a very important asset in modern nuclear medicine, due to the emission of gamma ray of optimal energy (140 keV) and a suitable half-life (6.04 h). A further attribute of ^{99m}Tc is its formation from the decay of ^{99}Mo and the availability from ^{99}Mo-^{99m}Tc generator systems. The most common and practical generator types consist of a chromatographic column packed with aluminium oxide, onto which the highly purified fission product ^{99}Mo (imported from Canada) is adsorbed in the form of molybdate. ^{99m}Tc is further eluted with saline solution. The objective of this work is to study the performance and the elution profile of ^{99m}Tc from high activity generators in order to decrease molybdenum and aluminium concentration. The experiments involved the use of paper filters and Sep Pak columns and also the changing in the time interval between elutions. ^{99}Mo breakthrough was measured using a dose calibrator and aluminium by UV-Vis spectrophotometry. The best results were achived using a Sep Pak column containing neutral aluminium oxide.

1. INTRODUCTION

^{99m}Tc is one of the most desirable radionuclides for external imaging in diagnostic nuclear medicine, due to the emission of gamma ray of optimal energy (140 keV), a suitable half-life (6.04 h), and availability from ^{99}Mo-^{99m}Tc generators systems, in which ^{99}Mo is loaded to an alumina column, and the decay product ^{99m}Tc as TcO_4^- can be easily eluted from the column using 0.9% NaCl [1, 2].

Before the administration of a ^{99m}Tc labeled radiopharmaceutical to a patient, the activity is measured in radionuclide calibrators (activimeters) in order to obtain a reliable diagnostic result while keeping the radiation exposure of the human body as low as possible [3].

In addition, development of ^{99m}Tc radiopharmaceuticals for tumor imaging paves the way for therapeutic radiopharmaceuticals with high energy beta emitters ^{186}Re and ^{188}Re because of similar chemical properties of technetium and rhenium [1].

^{99}Mo can be produced by neutron irradiation of stable ^{98}Mo, as well as neutron fission of ^{235}U. The radioactive impurities in ^{99}Mo produced from ^{98}Mo are mainly activation products of impurities in the ^{98}Mo target. While ^{99}Mo produced from fission of uranium may contain many fission produtcs, ^{99}Mo in commercial ^{99}Mo-^{99m}Tc generators is normally produced from fission of uranium [2].

^{99}Mo of low/medium specific activity obtained by ^{98}Mo (n,γ) ^{99}Mo requires a very large alumina column to adsorb about 1-2 g of Mo for preparing chromatographic generators. The large size of the alumina column, in turn, requires large eluate volumes to recover ^{99m}Tc and the concentration of the Na^{99m}TcO$_4$ may be too low for radiopharmaceutical use [4].

The clinically useful lifetime of a fission-based ^{99}Mo-^{99m}Tc generator is generally two weeks. At the end of a working week, the radioactive concentration of the eluate is about a quarter of that at the beginning of the week [4].

The Radiopharmacy Center (CR) at Instituto de Pesquisas Energéticas e Nucleares (IPEN-CNEN/SP) commercially produces about 300 ^{99}Mo-^{99m}Tc generators per week with different activities ranging from 9.25 to 74 GBq (250 to 2000 mCi).

The quality control results of these generators has indicated that 74 GBq (2000 mCi) generators can sometimes present high amounts of aluminium and ^{99}Mo during the elution process of ^{99m}Tc.

Therefore, the aim of this work is to study the performance and the elution profile of ^{99m}Tc from high activity generators and assess the decrease molybdenum and aluminium concentrations.

2. EXPERIMENTAL PROCEDURE

2.1. ^{99}Mo-^{99m}Tc Generators

The alumina-based chromatographic ^{99}Mo-^{99m}Tc generators systems were obtained from the Radiopharmacy Center at IPEN-CNEN/SP and were prepared with fission [^{235}U(n,f)^{99}Mo]^{99}Mo. The ^{99m}Tc activity of the generators was 74 GBq (2000 mCi), and the generators were daily eluted with 6 mL of 0.9% saline solution.

Some add-ons were placed in the generators in order to reduce the amount of aluminium and ^{99}Mo eluted together with ^{99m}Tc. Some of the generators were prepared with a piece of paper filter 2S or 2M from Millipore placed before the glass frit on the generator column.

Another set of generators was prepared with chromatographic separation columns placed after the columns and before the 0.22 μm Millipore filter. The tested commercial columns were Neutral Alumina Sep Pak Plus columns.

2.2. Quality Control of ^{99m}Tc

Samples of ^{99m}Tc eluted from all the generators had the quality controls tests performed as follows:

2.2.1. Radionuclidic Purity

The amount of ^{99}Mo was measured in a dose calibrator (CRC-10BC, CAPINTEC Inc., USA) and the samples were placed inside an adequate lead canister to eliminate ^{99m}Tc counts.

2.2.2. Radiochemical Purity

The amount of ^{99m}Tc as $^{99m}TcO_4^-$ was determined by paper chromatography using 1M paper from Whatman as support and saline solution as the solvent.

2.2.3. Chemical Purity

The concentration of aluminium was measured by UV-Vis spectrophotometer model U-2010 from Hitachi. The presence of aluminium was analysed by UV-Vis spectroscopy, using the spectrophotometer Model U-2010 from Hitachi.

Aluminium was complexed with ericromocianine R in acid medium, and the wavelength of 535 nm was used in the measurements. Calibration curves were built using aluminium standards solutions.

3. RESULTS

The main impurity observed in the ^{99m}Tc elutions was aluminium that sometimes was over the permissible levels (10 µg/mL), as can be seen in Figure 1.

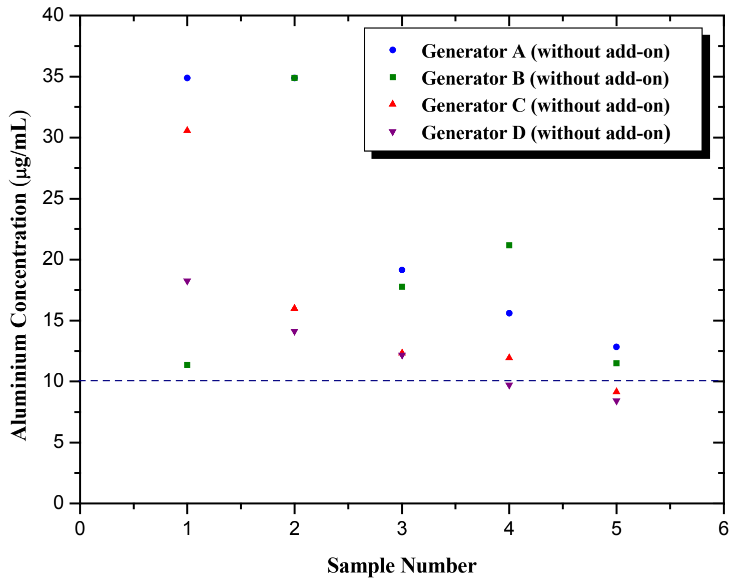

Figure 1. Aluminium impurity in the ^{99m}Tc elutions from the generators without any add-on.

The Figure 2 illustrates the use of paper filters for the reduction of the aluminium impurity.

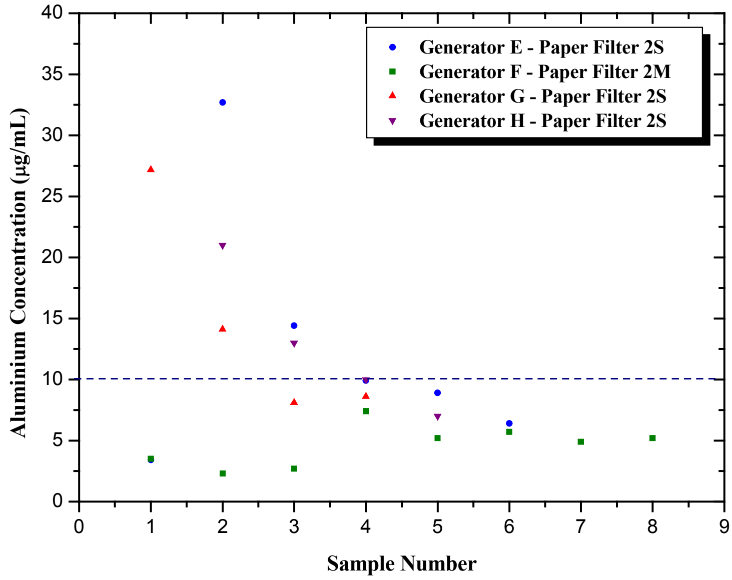

Figure 2. Aluminium impurity in the ^{99m}Tc elutions from the generators with paper filters.

The results show that in some experiments the use of paper filter is very effective in (for) reducing aluminium levels, but it is a result that could not be reproduced.
The Figure 3 shows a typical result of the use of Neutral Alumina Sep Pak columns.

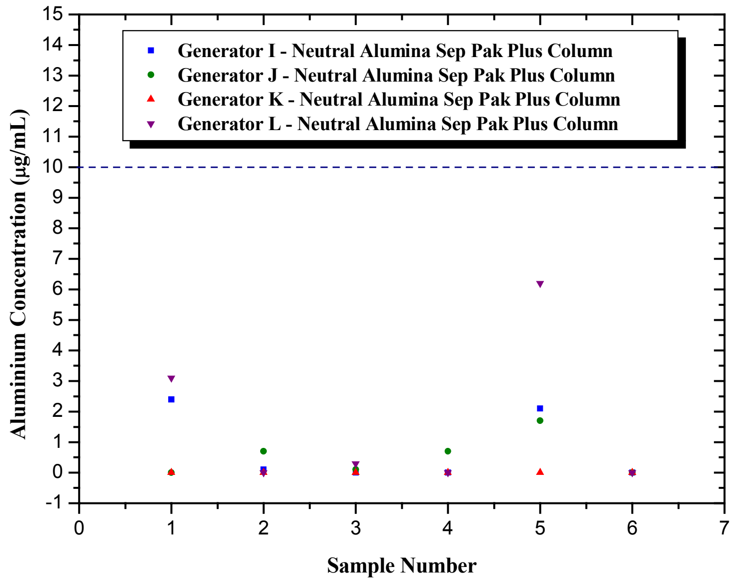

Figure 3: Aluminium impurity in the ^{99m}Tc elutions from the generators with Neutral Alumina Sep Pak columns**.**

It is very clear that the use of this kind of column reduces the amount of aluminium to the permissible levels. The results are reproducible, and although the results of ^{99}Mo breakthrough were always bellow the permissible level (< 10^{-3}%), the use of alumina columns reduces its level as well. In all the experiments the radiochemical purity was higher than 99%.

CONCLUSIONS

The results of the present work show that aluminium is the main impurity for high activity ^{99m}Tc generators, and its level can be effectively reduced by using commercial Neutral Alumina Sep Pak Plus columns. This technique is going to be applied in routine production of 74 GBq (2000 mCi) ^{99m}Tc generators at IPEN.

ACKNOWLEDGEMENTS

The authors thank Radiopharmacy Center (IPEN-CNEN/SP) for providing ^{99m}Tc-^{99}Mo generators for the present study, Pontifícia Universidade Católica de São Paulo (PUC-SP) for the support and CNEN for providing a fellowship for this project.

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