BRAZILIAN STRATEGIES TO OVERCOME MOLYBDENUM CRISIS: PRESENT AND FUTURE PERSPECTIVES OF THE MULTIPURPOSE RESEARCH REACTOR

J. A. OSSO JR., R. TEODORO, C. R. B. R. DIAS, R. R. L. BEZERRA, L. A. VILLELA, J. L. CORREIA, J. A. PERROTTA, G. A. PEREIRA, C. L. ZAPPAROLI JR., J. MENGATTI

Diretoria de Radiofarmácia, Instituto de Pesquisas Energéticas e Nucleares (DIRF-IPEN)
Avenida Prof. Lineu Prestes 2242, 05508-000 – São Paulo, SP – Brazil

ABSTRACT

Nuclear Medicine applications in Brazil have been widely growing in the past few decades, following the world trends. Procedures in oncology and cardiology can be highlighted among its major contributions. Nowadays more than 80% of diagnosis procedures are performed with ^{99m}Tc, readily available from the elution of ^{99}Mo-^{99m}Tc generators. The Brazilian demand, attended solely by IPEN-CNEN/SP, reaches out more than 320 generators per week with a total activity of about 16.7 TBq (450 Ci), which corresponds to 4% of the overall ^{99}Mo global demand at an importation cost of US$20 million/year, most of it from Canada. The recent ^{99}Mo supply crisis deeply affected the distribution of generators in Brazil. A short term solution was achieved with the purchase of ^{99}Mo from Argentine and more recently from South Africa and also the distribution of generators produced by IBA and Israel. Mid term and long term projects are under way aiming the nationalization of the production of ^{99}Mo. Both solutions will use the recently approved new Brazilian Multipurpose Reactor (BMR) that will be built near Sao Paulo city and will have a 30 MW power. The mid term project consists on the production of (n,) ^{99}Mo and distribution of ^{99m}Tc and monodoses of radiopharmaceuticals labelled with ^{99m}Tc to hospitals near Sao Paulo. The long term project deals with the production of ^{99}Mo through the fission of ^{235}U using LEU targets. This work describes the efforts taken by IPEN-CNEN/SP to overcome the recent ^{99}Mo supply crisis and an up-to-date on the projects aiming the nationalization of the ^{99}Mo production.

1. Introduction

Technetium-99m (^{99m}Tc) is the workhorse of diagnostic nuclear medicine and used for approximately 20–25 million procedures annually, comprising nearly 80% of all diagnostic nuclear medicine procedures[1]. Its excellent nuclear and chemical characteristics enable high quality images with low radiation doses to patients and make it very versatile for attaching to different chemical substances. Nuclear Medicine applications in Brazil have been widely growing in the past few decades, following the world trends.

^{99m}Tc (half life: 6 h) is produced by the decay of molybdenum-99 (^{99}Mo) (half life: 66 h) and supplied via a ^{99}Mo-^{99m}Tc generator.

The Brazilian demand, attended solely by IPEN-CNEN/SP, reaches out more than 320 generators per week with a total activity of about 16.7 TBq (450 Ci), which corresponds to 4% of the overall ^{99}Mo global demand at an importation cost of US$20 million/year, most of it from Nordion, Canada. These figures are representative of the situation up to 2009.

The main route to produce ^{99}Mo is by fissioning highly enriched uranium (HEU in ^{235}U) and today, the world's supply of ^{99}Mo is centered on five large research reactor operations. The reactors are aging over 40 years old and, recently, have been unreliable due to closures for repairs of leaks, leading to an unstable supply of this important radionuclide.

In particular, the shutdown of the NRU reactor has triggered a global shortage in nuclear medical isotopes, which has made the situation particularly problematic from a medical standpoint(2). This recent ^{99}Mo 'crisis' deeply affected the distribution of generators in Brazil.
This work describes the efforts taken by IPEN-CNEN/SP to overcome the recent ^{99}Mo supply shortage and an up-to-date on the projects aiming the nationalization of the ^{99}Mo production.

2. Methods

The Radiopharmacy Center of IPEN-CNEN/SP has an established radioisotope production program to supply radiopharmaceuticals to the Nuclear Medicine community in Brazil. These radiopharmaceuticals are prepared with radioisotopes produced in both a Nuclear Reactor and a Cyclotron accelerator. IPEN has a Research Reactor, so called IEA-R1m, that nowadays operates at 4.0 MW for 64 hours continuously.
The strategies for overcoming the ^{99}Mo shortage are splitted in 3 categories: short, mid and long term projects.
Mid term and long term projects are under way aiming the nationalization of the production of ^{99}Mo. Both solutions will use the recently approved new Brazilian Multipurpose Reactor (BMR) that will be built near São Paulo city and will have a 30 MW power.

2.1. Short term project

A short term solution was achieved with the purchase of ^{99}Mo from Argentina and more recently from South Africa and also the distribution of generators produced by Belgium (IBA) and Israel.

2.2. Mid term project

The mid term project consists on the production of (n,) ^{99}Mo and distribution of ^{99m}Tc and monodoses of radiopharmaceuticals labelled with ^{99m}Tc to hospitals near Sao Paulo. The idea is to separate ^{99m}Tc from ^{99}Mo through the solvent extraction technique with metilethylketone (MEK) or the combined technique, so-called extraction chromatography using basic alumina with absorbed MEK. The ^{99m}Tc will then be distributed to the clinics near IPEN, in Sao Paulo city, and later monodoses will be prepared by labeling the lyophilized kits with ^{99m}Tc.
Figure 1 represents the mid term strategies for the production of ^{99}Mo via neutronic activation based on early experiences. Future perspectives on the development of mid term actions would be mainly dependent on the new configuration of IEA-R1m Nuclear Reactor (i.e, if the reactor power is upgraded from 4.0 MW to 5 MW) and also the use of the new Reactor.

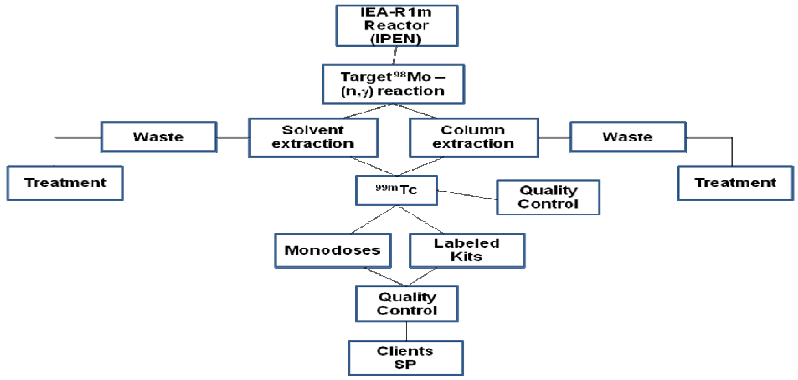

Fig 1. Mid term strategies for the production of ^{99}Mo and distribution of ^{99m}Tc.

2.3. Long term project: new Brazilian Multipurpose Reactor (BMR)

The long term project deals with the production of ^{99}Mo through the fission of ^{235}U using LEU targets. Due to the international concerns about the proliferation of weapons-usable uranium and eventually eliminating the use of HEU (>20%) the International Atomic Energy Agency (IAEA) initiated a program of developing techniques for production of ^{99}Mo using low enriched uranium (LEU)[3]. The substitution of HEU to LEU requires a modified technology. The approach to be adopted by IPEN would be largely dependent on the reactor features and the economic viability of the process employed. Figure 2 shows the strategies for the production of ^{99}Mo through the fission of ^{235}U. Two different approaches are being studied, the more conventional basic dissolution of UAlx targets and the modified Cintichem method that employs the acid dissolution of metallic U targets. This last method is being promoted by IAEA through the CRP: T1 2018 - Developing Techniques for Small Scale Indigenous Molybdenum-99 Production Using Low Enriched Uranium (LEU) Fission or Neutron Activation.

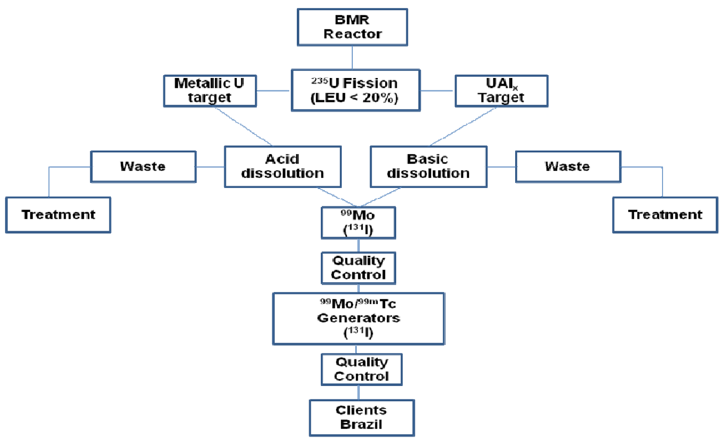

Fig 2. Long term alternatives for the production of ^{99}Mo and distribution of ^{99m}Tc via $LE^{235}U$ in the BMR.

3. Results

3.1. Short term project

Figure 3 shows the demand of ^{99}Mo in Brazil for the past few years. It is clear the effects of the crisis in 2010.

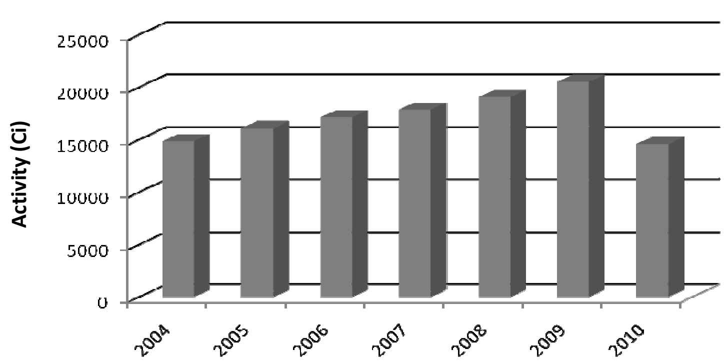

Fig 3. Demand of ^{99}Mo in Brazil (2004-2010)

In 2009, actions have been taken to overcome the shortage of ^{99}Mo supply by the main Brazilian supplier (MDS Nordion). The straight forward short term action included the purchase of ^{99}Mo from Argentina and South Africa and also the distribution of ^{99}Mo/^{99m}Tc generators from Israel and Belgium (IBA). Besides, an adequacy of the Brazilian market (i.e., from 450 Ci ^{99}Mo/week to nearly 360 Ci/week) took place. A change of trend happened; there was a higher demand for low activity generators compared to the pre-crisis higher demand for high activity generators. Another interesting point was that the nuclear medicine physicians started to employ less ^{99m}Tc activity in the exams, leading to a better use of the generators. Figure 4 shows the current scenario of ^{99}Mo-^{99m}Tc generators distribution in Brazil.

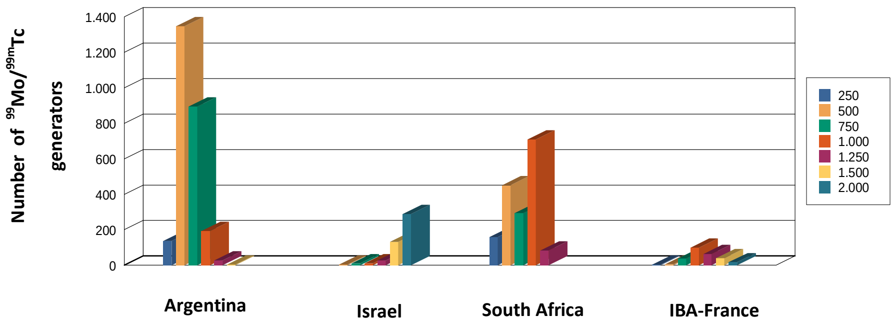

Fig 4. Distribution of ^{99m}Tc generators (jan-apr 2010).

3.2. Mid term project

In the past, IPEN has developed the route for producing ^{99}Mo by neutron activation of Mo targets in the IEA-R1m Research Reactor through the ^{98}Mo(n,)^{99}Mo reaction and developed the MoZr gel generator technology. This technology is limited so the mid term project will employ the solvent extraction principle. Experiments are under way and both the solvent extraction of ^{99m}Tc with MEK and the extraction chromatography were studied and the preliminary results showed a better behavior for the chromatography technique with a yield of more than 85% for ^{99m}Tc with adequate purity for posterior labeling.

3.3. Long term project: new Brazilian Multipurpose Reactor (BMR)

Due to the increasing needs of the nuclear medicine in Brazil and the world shortage of ^{99}Mo observed since 2008, IPEN decided to develop its skills for producing ^{99}Mo through the route of ^{235}U fission. This decision was based on: (i) the well established laboratory for producing ^{99m}Tc generators already in operation in IPEN and responsible for the Brazilian market supply; (ii) the availability of LEU (20 wt%) by the Brazilian Enrichment Laboratory; (iii) the established capacity to prepare targets of UAlx; (iv) the availability of some human resources in uranium chemistry; (v) the possibility of operating the IEA-R1 for at least ten years more; and (vi) the recent intention of the CNEN to construct a new research reactor (BMR).
Studies are under way on both routes, i.e., the basic dissolution of UAlx targets and acid dissolution of metallic U targets, always using LEU targets.

4. Conclusions

Several actions have been taken to overcome the ^{99}Mo supply crisis and also to underline the efforts towards the nationalization of ^{99}Mo production. The long term project is only possible with the construction and operation of the new Reactor, the BMR.

Acknowledgments

The authors wish to thank IAEA for the Brazilian participation in the CRP: T1 2018 - Developing Techniques for Small Scale Indigenous Molybdenum-99 Production Using Low Enriched Uranium (LEU) Fission or Neutron Activation. The authors also want to thank CNPq for granting the fellowships for this project.

5. References

1. CHAKRAVARTY, R.; DASH, A.; VENKATESH, M. A novel eletrochemical technique for the production of clinical grade ^{99m}Tc using (n,)^{99}Mo. ***Nucl. Med. Biol.***, v. 37, p. 21-28, 2010.

2. ZAKZOUK, M. The medical Isotope shortage: cause, effects and options. In: Library of Parliament Bibliothéque du Parlement. ***PRB 09-04E***, Canadá, 2009.

3. ABOIMOV, M. A.; CAPUS, G.; MAX, A.; HADFIELD, A. C. F.; KUDRIAVTSEV, E. G.; MAcMURRAY, F.; NAWADA, H. P.; MULLER, H; TOUSLEY, D. Management of high enriched uranium for peaceful purposes : Status and Trends. ***IAEA – TECDOC-1452***, v. 1, p. 1-58, 2005.