Improvements in the production of a low cost targetry for direct cyclotron production of ^{99m}Tc

G. Lucconi[a,d], E. Galloni[a], G. Cicoria[a] , A. Infantino[b,d], F. Zagni[a], L. Tositti[c], S. Fanti[e], M. Marengo[a,1]

[a] *Department of Medical Physics, University Hospital "S.Orsola – Malpighi", Bologna, ITALY*
[b] *Department of Industrial Engineering, University of Bologna, ITALY*
[c] *Department of Chemistry, University of Bologna, Bologna, ITALY*
[d] *Istituto Nazionale di Fisica Nucleare INFN, Bologna, ITALY*
[e] *Department of Nuclear Medicine, University Hospital "S.Orsola – Malpighi", Bologna, ITALY*

Introduction

The established methods for the production of ^{99}Mo, based on fission in nuclear reactors, continue to present problems as a result of the plants aging and the significant investments needed for maintenance or renewal.

Much research work is thus in progress on the study of alternative methods for the direct production of ^{99m}Tc in quantities and with the degree of purity required for clinical use. Between them, the cyclotron production of ^{99m}Tc via the ^{100}Mo(p,2n)^{99m}Tc reaction has turned out as the most attractive alternative and could be feasible in several PET centers equipped with a cyclotron.

One critical aspect regarding the production of ^{99m}Tc with cyclotron is the need for a robust and reliable target production process. Several techniques have been indicated as extremely promising such has plasma spray and laser cladding; however these methods require specialized instrumentation and complex operations to be performed handling activated materials in order to recover irradiated ^{100}Mo.

In this work we report the development of the work done at the University of Bologna, as a part of a wider INFN project, as regards the methods of preparation of solid targets of ^{100}Mo suitable for the production of ^{99m}Tc in a biomedical cyclotron normally operated for the production of PET radionuclides.

Material and Methods

Irradiations were performed with a GE PETtrace cyclotron equipped with a solid target station previously developed by our group and fully operational at our institution (1).

In the irradiation line a 16.5 MeV elliptically shaped proton beam, having the FWHM of the major and minor axis of 8 and 6 mm respectively, is degraded by a 25 µm thick Havar foil before entering the target, placed in the central cavity (Ø = 13 mm) of a backing disk (Ø = 32 mm). According to the design of the solid target station, different combinations of target and backing materials and thicknesses can be used, provided a total thickness (target + backing) not exceeding 2 mm.

In initial tests, a stack of 1 – 3 100 µm thick metallic foils of ^{nat}Mo placed in a Copper backing, were irradiated with protons in the (15.9 ÷ 9.8) MeV energy range.

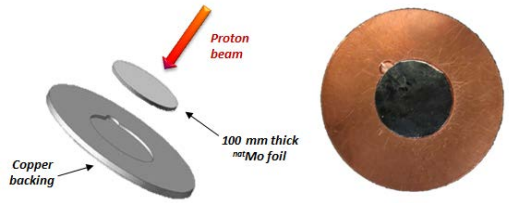

FIG. 1 Target assembly in preliminary tests: 100 µm thick foil of ^{nat}Mo

Foils were dissolved in a HNO_3-HCl solution and samples were subjected to high resolution gamma-ray spectrometry (Canberra). The HPGe detector has a 30% relative efficiency and a resolution of 1.8 keV at 1332 keV; the spectrometry system has been calibrated in the range 59–1836 keV using a multi-radionuclide certified reference solution, obtained from an accredited Standardization Laboratory (LEA CERCA, France). The calibration process has been performed according to the IEC 61452 standard (2), using Canberra Genie2000 software; a dual logarithmic polynomial efficiency curve has been used. The total calibration uncertainty amounts to about 4–5% at 1 sigma level. The measurement campaign lasted several weeks to take into account the different half-lives of the produced radionuclides. Results were extrapolated to a highly enriched ^{100}Mo target and compared to Monte Carlo simulations previously performed (3); FLUKA differential proton fluence distribution in energy within the target material was convolved with cross sections obtained with TALYS nuclear code as to calculate the saturation yield.

In order to investigate a method of preparation of the target that would make easier the recovery of the enriched material and recycling for the preparation of a new target, we subsequently studied the production of pellets of

[1]Corresponding author, E-mail: mario.marengo@aosp.bo.it

Molybdenum trioxide. $^{nat}MoO_3$ powder (Sigma Aldrich, 99.9% trace metals basis, particle size <150 µm) and 99.01% enriched $^{100}MoO_3$ powder (Isoflex) were mixed with organic binders (Sigma Aldrich, impurities ≤ 0.7%) and placed in a 13 mm die set (Chromatographie-Handel GmbH, Berlin, Germany) to prepare pellets using a 10 ton press.

Pellets obtained in this way were then sintered on a Platinum support using a CARBOLITE furnace (type: GHA 12/300; maximum temperature: 1200°C) under a controlled atmosphere in order to remove the organic binder and improve the strength of the target; the temperature was ramped according to a controlled and reproducible temperature cycle (4). Sintered pellets were weighted to assess the effective removal of the organic binder and subjected to visual inspection and mechanical tests of resistance to loading and downloading at the cyclotron target station.

$^{nat}MoO_3$ pellets were subjected to thermal tests through irradiations at increasing current up to 35 µA. A 25 µm thick Havar annulus was added in the target assembly to keep the target in place during irradiation. This geometry allowed an almost complete direct cooling on the front, while the back of the target was indirectly cooled through the Copper backing and the rear part of the solid target station.

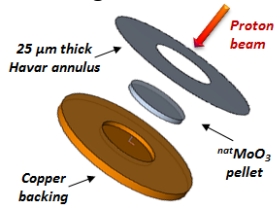

FIG. 2 Target assembly for irradiation of MoO_3 pellets

The irradiated targets were again visually inspected to check the integrity of the pellets and then weighted to assess eventual mass losses. An irradiation of 1 min at 10 µA was performed both on $^{nat}MoO_3$ and 99.01% enriched $^{100}MoO_3$ pellets to assess the saturation yield of ^{99m}Tc and the amount of impurities.

The targets were downloaded immediately after the end of bombardment (EOB) and the pellets were dissolved in 1 ml of NaOH 6M. Samples of the solutions were subjected to gamma-ray spectrometry analysis. All activities were corrected for decay during counting time, decay to EOB, detector efficiency and γ-ray intensity. The activity of ^{99m}Tc was calculated considering the interference of the 140.5 keV peak due to the decay of ^{99}Mo and subtracting out the indirect production of ^{99m}Tc as a result of ^{99}Mo decay after irradiation.

The measurement campaign lasted several weeks to take into account the different half-lives of the produced radionuclides and the results were compared with Monte Carlo simulations.

Results and Conclusion

The experimental saturation yield for ^{99m}Tc, calculated on the basis of the gamma-ray analysis of irradiated metal foils, gave an extrapolated yield of (1.132 ± 0.015) GBq/µA for a 100 µm thick 99% enriched ^{100}Mo target. On these bases, an irradiation of 3 h at 50 µA is expected to produce (16.56 ± 0.02) GBq of ^{99m}Tc. Experimental values are in agreement with the results of Monte Carlo simulations on average within a factor of 2. Considering the use of an efficient purification system, a radionuclidic purity >99.9% 2h after the EOB and a specific activity comparable with the actual standards are expected as achievable.

As for the production of pellets, the amount of MoO_3 was chosen as to have a content of Molybdenum equivalent to a 150 µm thick metal foil. The thus produced pellet was 1 mm thick and had a diameter of 13 mm; it could therefore be placed in the central groove of the target backing fitting the solid target station installed on GE PETtrace cyclotron. Negligible mass losses of MoO_3 were observed when the pellets were sintered. The sintering process allowed to obtain pellets having an improved mechanical strength capable of withstanding loading and downloading operations.

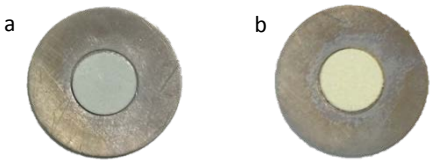

FIG. 3 Pellet of MoO_3 on a Platinum backing before (A) and after (B) sintering

Irradiation tests at beam current up to 30 µA were performed successfully with no changes in mass and mechanical properties of the pellet. At 35 µA partial fusion was observed. An improvement in the target assembly or cooling system could allow to achieve a higher maximum current with no damage of the target.

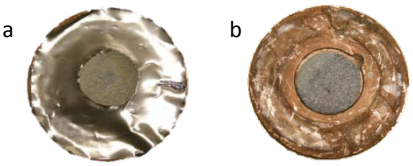

FIG. 4 Pellet of MoO_3 after irradiation at 30 µA. (a) Front and (b) rear part of the pellet

[1]Corresponding author, E-mail: mario.marengo@aosp.bo.it

The experimental saturation yield for ^{99m}Tc, calculated on the basis of the gamma-ray analysis of irradiated pellet of $^{nat}MoO_3$ and 99.01% enriched $^{100}MoO_3$, is displayed in TABLE 1 along with the results of Monte Carlo simulations; the agreement with the results of irradiations can be considered satisfactory.

	Y_{sat} (GBq/μA)
$^{nat}MoO_3$ pellet experimental values	(0.14 ± 0.07)
$^{nat}MoO_3$ pellet Monte Carlo simulation	(0.115761 ± 0.000002)
$^{100}MoO_3$ pellet experimental values	(1.32 ± 0.08)

TABLE 1. Saturation yield of ^{99m}Tc using MoO_3 pellets.

On these bases, an irradiation of 6 h at 30 μA is expected to produce (19.8 ± 1.1) GBq of ^{99m}Tc. Spectra acquired soon after EOB showed the presence of the short-lived ^{96m}Tc and ^{101}Tc, along with other isotopic impurities. The principal non isotopic impurities detected were ^{99}Mo and ^{97}Nb. Considering the use of an efficient purification system, a radionuclidic purity >99% 2h after the EOB and a specific activity comparable with the actual standards are expected as achievable.

These encouraging results suggest that sintered pellets may be a relatively inexpensive and easy solution to prepare ^{100}Mo targets for the cyclotron production of ^{99m}Tc. Their ease of production allows to prepare targets in the same Nuclear Medicine department with no need of complex and bulky equipment.

The amount of ^{99m}Tc thus produced is relatively relevant; it can contribute significantly to the workload of a nuclear medicine department, especially in case of ^{99}Mo shortage, and even fulfill the demand of a small center. Moreover the achievable radionuclidic purity is not far from actual standards relative to generator produced ^{99m}Tc.

These results have however been obtained from a limited number of experiments and need further confirmation.

At the same time, a prototype automated module based on standard industrial components is in testing phase as regards performance in the separation and purification processes as a part of a wider INFN project.

References

1. Cicoria G., Pancaldi D., Piancastelli L., Giovaniello G., Bianconi D., Bollini D., Menapace E., Civollani S., Pettinato C., Spinelli A., Boschi S., Bergamini C., Marengo, M.: *Q J Nucl Med*. **50 (suppl. 1),** pp. 3-4, 2006
2. IEC 61452, Nuclear instrumentation - Measurement of gamma-ray emission rates of radionuclides - Calibration and use of germanium spectrometers, 1995
3. Lucconi G., Cicoria G., Pancaldi D., Marengo M.: *Clin Transl Imaging* **1 (Suppl 1)**, pp. S29, 2013
4. Kimura A., Sato Y., Tanase M., Tsuchiya K.: *IOP Conf. Series: Materials Science and Engineering* **18**, 2011

Acknowledgements

The Authors would like to warmly thank Prof. (Emeritus) D. Bollini for his continuous encouragement; Prof. G. Fiorentini, Head of the INFN National Laboratories, Legnaro, Italy and Dr. G. Bruni, Head of the INFN Section of Bologna for their open minded support.

[1]Corresponding author, E-mail: mario.marengo@aosp.bo.it