Improvement of the Automatic Extraction / Separation Module for the High Purity Accelerator-Tc-99m Production by Conventional Medical Cyclotrons

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INTRODUCTION

The Molybdenum-99 (99Mo) mass production crisis occurred in 2009 and 2010, based upon the unscheduled nuclear reactors shutdown, affected the worldwide supply of Technetium-99m (99mTc) (t1/2=6h, Eγ=140keV). The APOTEMA project, funded by CSNS INFN (2012-2014), has demonstrated the feasibility of replacing the current reactor-based method with the accelerator-based one by the 100Mo(p,2n)99mTc nuclear reaction [1]. In the framework of the APOTEMA research project we have developed an automatic extraction module, based on solvent extraction method [2-3], for the 99mTc separation and purification from pre irradiated enriched 100Mo (99.05%) metal targets.

This work is part of the new TECHN-OSP project, funded by CSNS INFN (2015-2017) and focused on the possibility of a homeland accelerator99mTc production network based on existing/operating hospital cyclotrons in Italy. In particular, the purpose of this work was the improvement of the remotely controlled automated module with a system set up able to process not only a foils configuration target but also the standard solid target (backing material like copper, gold, tantalum or other) compatible with conventional medical cyclotron.

The previous automated module prototype was basically composed by:
- a chemical reactor, housing the heater for the dissolution step process of the foils target, (A in Fig. 1);
- a separation column vial (length=10cm, $\phi$=1cm) for the solvent extraction step, (B in Fig. 1);
- silica and acidic alumina columns for the purification step.

In order to test the efficiency of the module six molybdenum metal foils ($\phi$=0.9cm, thickness=24μm, mass=20.8mg each foil) 100Mo-enriched (99.05%) were irradiated in stacked foils configuration for 70 min at 25 μA with a proton beam with energy 17 MeV and subsequently treated with the automatic procedure. In a total 70 minutes the module allowed to recover higher than 90% of the initial activity.

Experiments were performed at the Research Laboratory of the Nuclear Medicine of the Sant’Orsola Hospital in Bologna and the module was adapted to the configuration condition imposed by the 16 MeV GE PETtrace cyclotron solid target station.

Fig. 1. The previous automated Tc-99m Solvent Extraction Module Configuration set up.

EXPERIMENTAL

The modified automatic prototype was assembled by using modular units (Eckert and Ziegler).

Components of the module are (figure 2): PLC, PC with software (modular lab), helium and nitrogen lines, three modular units with two and three-way valves, homemade reactor heater with a bottom-opened vial designed to fit solid target (Fig 2-a), a silica column (Waters SEP-PAK CARTRIDGE), an acidic alumina column (Waters SEP-PAK CARTRIDGE), tubing, fittings, a longer separation column vial (length=15cm, $\phi$=1cm) (C in Fig 2-b), vials for reagent, solvent, washing and two vials for waste and final solution.

In order to test the efficiency of the module two natural molybdenum metal foils ($\phi$=0.9cm, thickness=100μm, mass=125mg each foil) were irradiated in stacked foils configuration for 5 min. at 5μA with a proton beam with 16 MeV energy and subsequently treated with the automatic procedure. The foils-target was transferred into the reactor vial and dissolved by a three step procedure that consists of the addition of fresh small amount (1.5 ml x3) H2O2 30% at 90°C. After cooling to 50°C 6 ml of NaOH 6N was added to the dissolved target, in order to form the species molybdate and pertechnetate.
The resulting mixture (aqueous + organic solutions) was slowly transferred to the separation column from the bottom of the vial and mixed by vigorous He-bubbling for 4 min in order to maximize the contact between the two phases. After the separation phase (2 min), the organic solution placed at the top of the column was transferred through silica and alumina columns in order to purify pertechnetate from MEK; on the contrary, in the bottom of the separation column vial remained the aqueous phase. This step was repeated with other 2 ml of fresh MEK in order to maximize the extraction yield of pertechnetate from the aqueous phase. The $^{99m}$TcO$_4^-$ adsorbed on the alumina column was eluted with 6 ml saline and collected in FINAL vial. A detailed Radionuclidic Purity (RNP) evaluation was performed by HPGe gamma spectrometry.

RESULTS AND DISCUSSION

The recent concluded APOTEMA project has demonstrated the feasibility for an accelerator-$^{99m}$Tc production with comparable quality as generator-$^{99m}$Tc. In this context we have developed a fully automatic extraction module, based upon the solvent extraction method, for the separation and purification of $^{99m}$Tc from irradiated $^{100}$Mo-enriched metal foils-targets. This prototype was calibrated to process small quantity of metallic Molybdenum in thin foils configuration target (thickness=20μm and mass=30 mg each foil).

The goal of the following (ongoing) TECHN-OSP project is the development of a dedicated technology for the accelerator-production of Tc-$^{99m}$ directly in hospital by the common PET cyclotron. Therefore, an improvement of the automatic module was necessary. The solid target station of the GE PETirace cyclotron (16 MeV) in Sant’Orsola Hospital in Bologna was our reference for such a research. The solid target comprises a backing made of Gold, Copper, Tantalum or other conductive materials on which the metal of interest is directly deposited with proper thickness for high activity production.

To such an extent the initial prototype has been modified by replacing the old reactor system, housing a homemade reactor heater with a bottom-opened vial designed to fit solid targets.

We used two natural molybdenum metal foils (thickness=100μm and weigh=125 mg each foil) to simulate the solid target configuration. To treat bigger masses and thickness of Molybdenum a dedicated three step dissolution process has been setup. Each step involved 1.5ml of fresh H$_2$O$_2$, after few minutes of reaction with the metal target the solution obtained was moved in the separation column to allow the introduction of new and fresh H$_2$O$_2$ in the reactor vial for the next dissolution step. In this way we are able to dissolve all the molybdenum mass in effective and fast way. The increasing of Molybdenum mass implies greater volumes of dissolution, therefore was necessary to change the previous separation column with a longer one. Moreover, the new column permits a better stirring of the organic and aqueous phases increasing the extraction yield of TcO$_4^-$. Indeed, the HPGe gamma spectrometry highlighted that the improved automatic module allowed to recover higher than 93% of the initial activity in about 60 minutes.

### Table 1. Radionuclidic Abundances (%) in different step of the separation process (MDA=minimum detectable activity)

<table>
<thead>
<tr>
<th>Isotopes</th>
<th>$\text{Al}_2\text{O}_3$</th>
<th>Residual Aqueous phase</th>
<th>Waste</th>
<th>SiO$_2$</th>
<th>Washing</th>
<th>Final Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99}$Tc</td>
<td>0.23</td>
<td>5.75</td>
<td>0.03</td>
<td>0.22</td>
<td>0.55</td>
<td>93.22</td>
</tr>
<tr>
<td>$^{100}$Mo</td>
<td>&lt;MDA</td>
<td>&lt;MDA</td>
<td>&lt;MDA</td>
<td>&lt;MDA</td>
<td>2.04</td>
<td>&lt;MDA</td>
</tr>
<tr>
<td>$^{97}$Nb</td>
<td>&lt;MDA</td>
<td>98.31</td>
<td>&lt;MDA</td>
<td>&lt;MDA</td>
<td>1.69</td>
<td>&lt;MDA</td>
</tr>
</tbody>
</table>

CONCLUSION

As expected, the separation efficiency of the water/MEK solvent system was excellent due to the well-known high affinity of [TcO$_4^-$] for this organic phase. The MEK-based automated module could be a system able to fully meet the requirements of a nuclear medicine of sodium pertechnetate for clinical use starting from a cyclotron irradiated enriched $^{100}$Mo metal targets. The completely module automation by remote control ensures an optimal operator radioprotection.

In conclusion, the accelerator-Tc-$^{99m}$m production through cyclotron irradiation of highly enriched $^{100}$Mo metal, and purified using the automated module here described here, constitutes a valuable alternative to generator-produced Tc-$^{99m}$. Moreover it could provide a convenient source of this important diagnostic radionuclide in the event of a shortage of the conventional production route based on the decay of fission $^{99}$Mo.