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ARGONNE ACTIVITIES FOR THE PRODUCTION OF MO-99 USING LINAC IRRADIATION OF MO-100

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ABSTRACT

Experiments are being performed at Argonne National Laboratory to demonstrate production of ^{99}Mo using an electron linear accelerator. ^{99}Mo is the parent of ^{99m}Tc, the most commonly used radioisotope for nuclear medicine in the U.S. We have studied the ^{100}Mo(γ,n)^{99}Mo reaction in an enriched ^{100}Mo target. The Mo target and the cooling and data acquisition system were designed by Los Alamos National Laboratory. Three scaled low-power production experiments using a 20-MeV electron linac at Argonne National Laboratory have been performed to date. Two of these experiments used natural Mo targets and produced a total of 613 μCi of ^{99}Mo. The third experiment used an enriched ^{100}Mo target and produced 10.5 mCi of ^{99}Mo. Following irradiation, the targets were dissolved using an electrochemical dissolution method, and the low specific-activity Mo solution was processed through an ARSII generator from NorthStar Medical Radioisotopes. Yields of ^{99m}Tc > 95% have been observed.

1. Introduction

^{99m}Tc ($T_{1/2}$=6h) for nuclear medicine is produced from the decay of the longer-lived ^{99}Mo ($T_{1/2}$=66h). ^{99m}Tc is the most commonly used radioisotope for nuclear medicine, used in approximately 50,000 diagnostic nuclear medicine procedures every day in the United States. Due to short half life, the isotope's availability is very sensitive to disruptions in production or distribution. The entirety of the U.S. supply of ^{99}Mo for nuclear medicine is produced in ageing foreign reactors using highly enriched uranium (HEU) targets. These targets are generally enriched to ~93% ^{235}U. Maintenance and repair shutdowns of these reactors have significantly disrupted the supply of ^{99}Mo, and hence ^{99m}Tc imaging agents, in the last year.

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The National Nuclear Security Administration's (NNSA) Global Threat Reduction Initiative (GTRI), in partnership with commercial entities and the U.S. national laboratories, is working to address the need for a reliable domestic supply of ^{99}Mo for nuclear medicine, while also minimizing the civilian use of HEU. The objective of the effort is to aid the development of a reliable, domestic, commercial supply of ^{99}Mo that avoids a single point-of-failure and does not require the use HEU. There are four technology pathways currently under development as part of this effort (1) Low enriched uranium (LEU) targets in fission reactors, (2) LEU solution reactors, (3) Neutron capture and (4) Accelerator production. The goal for each technology pathway is to produce 3,000 6-day Ci per week by December 31, 2013. This work discusses engineering design support activities in support of the accelerator production technology pathway.

2. Accelerator Production Pathway

One of the possible technology pathways to achieve reliable domestic supply of ^{99}Mo for nuclear medicine while also minimizing the civilian use of HEU is the production of 99Mo using accelerators. Argonne National Laboratory (ANL) and Los Alamos National Laboratory (LANL) are performing engineering, design, and proof of concept experiments in support of this effort. This accelerator-based production uses the photonuclear reaction, ^{100}Mo(γ,n)^{99}Mo, in an enriched ^{100}Mo target. The threshold for the reaction is 9 MeV; the maximum cross section is 150 mb at 14.5 MeV (Figure 1). A high-power electron accelerator is used to produce the required flux of high-energy photons through bremsstrahlung. Enriched ^{100}Mo for the targets are commercially available from several vendors for between $400 and $600 per gram when purchased in large quantities.

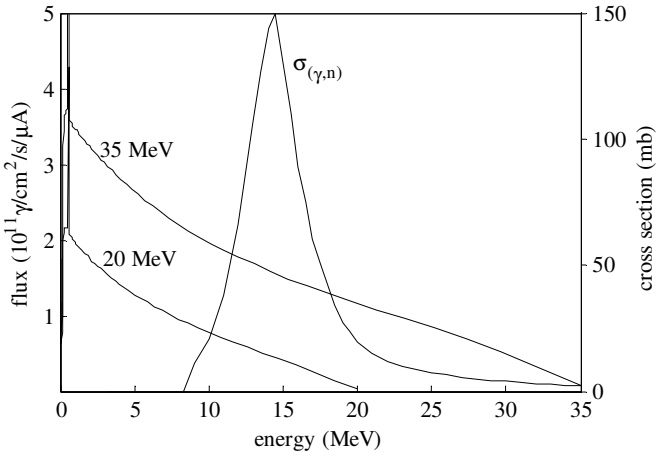

Figure 1. Photonuclear cross section of ^{100}Mo and average bremsstrahlung photon spectra produced with a 20- and 35-MeV electron beam in a Mo target

As part of this work, a series of scaled low-power demonstration experiments have been conducted to validate the process of accelerator production of ^{99}Mo through this method. These experiments were conducted using the low energy accelerator facility (LEAF) at ANL. For these tests, 6-mm-diameter and 21-mm long segmented cylindrical targets (Figure 2b) were irradiated with a 20-MeV, 6-mm FWHM electron beam from an L-band electron accelerator at the LEAF.

Beam powers incident on target were typically < 1 kW for these experiments. An isolated target cooling-water system was designed by LANL to remove the heat from the target during irradiation. A photograph of the experimental setup is shown in Figure 2. A collimator with a 6-mm aperture was used to limit beam diameter and prevent this excess beam from heating the target housing. Modeling indicated that production of ^{99}Mo in the target was highly dependent on the properties of the beam such as beam energy, current, position, and profile. In order to quantify these parameters during the experiments, several beam diagnostics were deployed. The beam energy was measured before and after the target irradiation using a magnetic energy analyzer upstream of the irradiation position. Beam current was measured upstream and downstream of the collimator with beam current transformers. The average beam profile on target is measured using activation in Mo foil placed immediately in front of the target housing. The target cooling system also contains multiple diagnostics including flow rate, temperature rise, pressure, and resistivity sensors.

After each irradiation, the target holder was extracted from the housing and placed into the lead shielded cask for transportation to the chemical laboratory where molybdenum disks were removed from the target holder for gamma counting and dissolution.

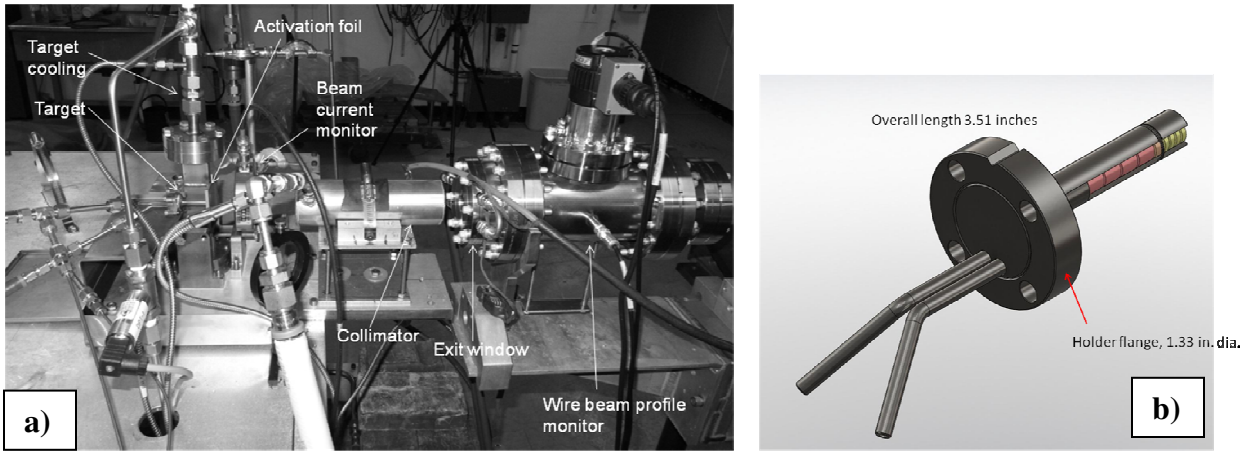

Figure 2. a) Picture of the test setup at ANL, the electron beam originates on the right and is incident on the target at left. Shown are the beam pipe on the right, downstream wire beam profile monitor, exit window, collimator, downstream beam current monitor, activation foil, target housing, and cooling connections. b) Close-up of the target holder and segmented Mo target. In each irradiation target consisted of seven 3 mm thick, 6 mm diameter disks was used.

3. Gamma Analysis

Measurements to quantify the amounts of radioisotopes produced from the irradiation of natural Mo and ^{100}Mo enriched targets were performed by gamma spectrometry using a germanium detector (ORTEC). The detector was calibrated both for energy and efficiency for the entire spectrum of interest using a multi-nuclide point source standard (Eckert & Ziegler). The two primary isotopes identified were ^{99}Mo, analyzed at 740 keV, and ^{99m}Tc, analyzed at 141 keV.

4. Description of Dissolution of Mo Targets

Since the final solution of molybdenum to be used in the ARSII is in sodium hydroxide, the focus for the dissolution studies was to develop a technique that would produce a solution of molybdate easily convertible or already prepared in sodium hydroxide with the concentration in the range of 5-6 M. Several methods for the dissolution of 6-mm diameter and 3-mm thick natural Mo metallic and sintered disks were investigated: (1) dissolution in NaOH at elevated temperature, (2) electrochemical dissolution in NaOH, and (3) dissolution in 30% H_2O_2 at elevated temperature. Based on the experiments performed, all accelerator-irradiated Mo targets were dissolved electrochemically in sodium hydroxide with additions of hydrogen peroxide using a nickel electrode as a holder (working electrode). However, the dissolution in H_2O_2 is also very promising and will be further investigated. Nickel was chosen as a material for the electrode because it has good electrical conductivity and low solubility in sodium hydroxide during electrolysis. The potential of the electrode was controlled by a Princeton Applied Research VersaSTAT 4 potentiostat with a 20-A power booster. A 10×12 cm nickel foil was used as the cathode. Potential applied was in the range of 2-5V. As the mass of Mo disks differed from experiment to experiment and during the dissolution the current was usually in the range of 10-20 A. The solution was mixed with overhead mixer (IKA RW 20 digital) at ~1000 rpm.

5. ARSII Generator

The Automated Radionuclide Separation System (ARSII) from NorthStar Medical Radioisotopes is a commercial multi-module automated chemical chromatography system capable of separating analytes during a single unattended instrument operation cycle. The chemical separation of ^{99m}Tc from ^{99,100}Mo on the ARSII relies on the highly selective resins utilized in the disposable chemistry module (Figure 3).

This module needs to be replaced before every separation. The chemistry module is a kit containing two chromatography columns: Primary Separation Column (ABEC®) and Guard Column (Alumina). The ^{99,100}Mo parent solution in 5 M NaOH, with the ^{99m}Tc at some level of in growth is initially passed through the Primary Separation Column (ABEC®), which selectively captures the Tc while passing the molybdenum into the parent recovery vessel (see Figure 3). After a rinse of the Primary Separation Column (PSC) with 5 M NaOH followed by a rinse with gluconic acid/gluconate buffer solution, the ^{99m}Tc is stripped from the PSC with normal saline solution. The ^{99m}Tc thus eluted is passed through the Guard Column (GC), which is selective (under the strip conditions) for any Mo(VI) that may be present. The use of the GC is equivalent to a second purification step of the final Tc product from the parent radioisotope. The purified Tc is captured in the daughter receiving vessel.

6. Results and discussion

6.1. Target irradiation

To date, three low-power scaled production experiments have been completed. Two experiments were performed with natural Mo targets, and one experiment was performed with an enriched ^{100}Mo target. All experiments were performed with 20-MeV electron beam energy. The two tests with natural Mo targets produced a total of 613 μCi of ^{99}Mo. The test using the enriched ^{100}Mo target produced 10.5 mCi of ^{99}Mo. A summary of these tests is contained in Table 1.

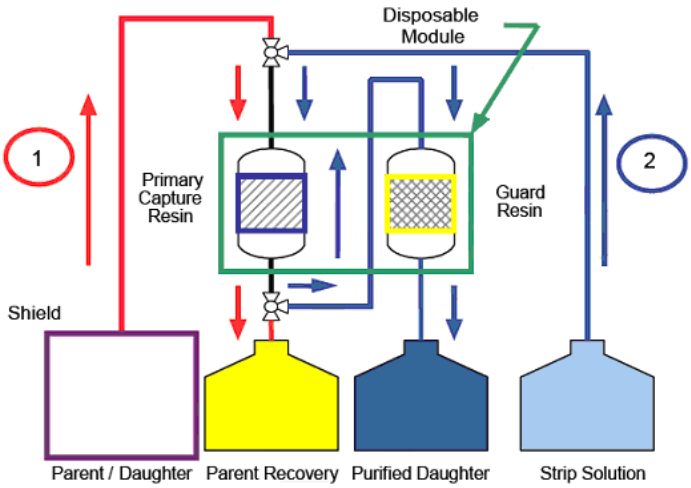

Figure 3. Scheme of $^{99m}Tc/^{99}Mo$ separation with ARSII

Table 1. Results from the scaled production experiments with a 20 MeV electron beam

Target Material	Natural Mo	Natural Mo	Enriched 100Mo
Run Time (min)	~20	23	82
Average beam power on target (W)	~600	~600	770
99Mo Activity Produced (mCi)	0.236	0.377	10.5

6.2. Target processing

After all three irradiations, the disks were black in appearance due to a thin layer of molybdenum oxide on the surface. The disks were weighed and only small differences in the weight were noticed. The difference in weight for a few samples was less than 0.7% and for most of the samples less than 0.3%, which could have been due to a partial dissolution of the target in cooling water during the irradiation. After weighing, the disks were submitted for gamma analysis and then electrochemically dissolved in 5M NaOH. Shortly after the dissolution started, the solution turned a brown color due to the formation of molybdenum species with lower oxidation state. The color disappeared after adding a few milliliters of concentrated hydrogen peroxide; therefore, ~1 mL of H_2O_2 was added every 5 minutes thereafter. The data for the dissolution of Mo disks after three irradiations are summarized in Table 2. As can be seen, the volume necessary for the dissolution of 7 irradiated disks decreased from 150 mL to 80 mL, which was due to change in the setup of dissolution apparatus. The design of the spinning electrode (Figure 4) used for dissolution of Mo targets after 2nd and 3rd irradiation allowed significant decrease in the volume required. The dissolution after 1st irradiation was performed using Ni mesh envelope.

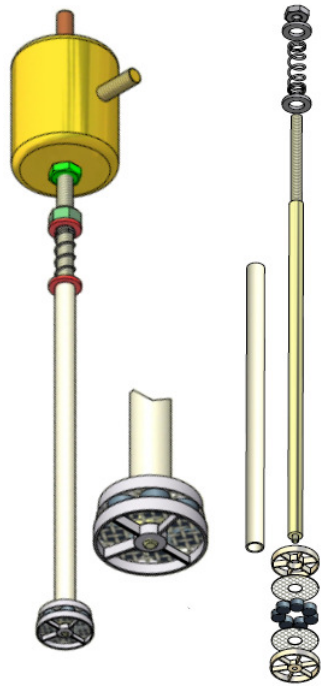

Figure 4. The spinning dissolution holder for seven Mo targets that serves as a working electrode for electrochemical dissolution of Mo

Reasons for a non-complete dissolution were probably a passivation of the disk surface insufficient electrical contact between Mo disks and electrode due to shrinking of the disks, and not optimum contact between disk and electrolyte solution containing hydrogen peroxide. To destroy any hydrogen peroxide remaining after dissolution, the solution was heated for 30-40 minutes. After cooling, twenty mL of this solution was fed into ARSII for separation of the ^{99m}Tc from ^{99}Mo.

Table 2. Dissolution data for Mo targets after 3 irradiation experiments

# irradiation	Mo disks	Mo dissolved, g	Mo dissolved, %	time, min	Volume 5M NaOH, mL	c Mo, mol·L^{-1}
1	nat. metal	5.7439	96.6	135	150	0.4
2	nat. metal	5.5676	95.0	120	100	0.58
3	sintered Mo-100	5.7145	97.8	120	80	0.71

6.3. Separation of Tc-99m and Mo-99 using ARSII

ARSII was tested for reproducible recovery of ^{99m}Tc in the product vial. Distribution of ^{99}Mo and ^{99m}Tc in the ARSII system was monitored by gamma analysis on PSC, GC, and sterility filter and in the waste solution after every run. Results from the monitoring of ^{99m}Tc and ^{99}Mo activities in the system show that about 1% of available activity of ^{99}Mo was lost after every run. After ^{99m}Tc in the product vial decayed, pH of the solution was measured and the concentration of Mo and Al were determined by ICP-MS analysis.

Results from ARSII show that the type of alumina column used can significantly affect the pH of the solution in Tc-product vial. Moreover, the breakthrough of aluminum in the Tc-product solution is strongly affected by pH as shown in Figure 5. In addition, it was experimentally confirmed that pH of the gluconic acid/gluconate buffer and its volume also play an important role in final pH value of the product solution. An average yield of available ^{99m}Tc after 3rd irradiation was 99.11% ± 4.34%. The pH of the product solution was in the range of 5.0-5.5. The product solution meets the USP requirements for pH, and Mo and Al breakthrough.

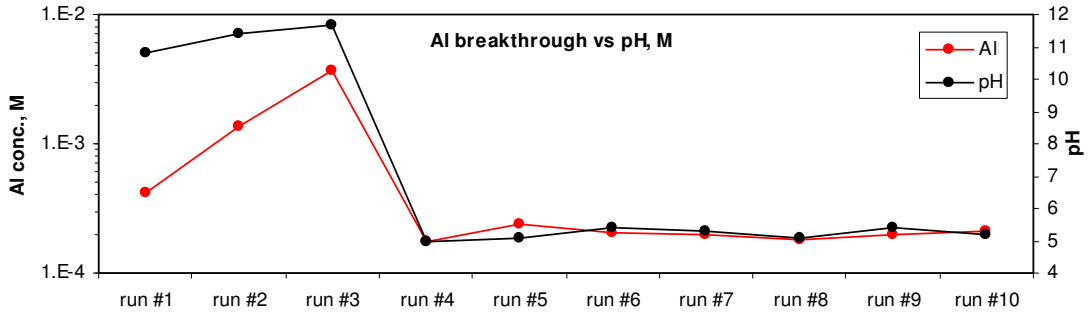

Figure 5. The breakthrough correlation of Al with the pH in the Tc product solution

5. Conclusions

Three scaled low-power production experiments using a 20-MeV electron linac at Argonne National Laboratory have been performed. In first two experiments, natural Mo targets were irradiated producing a total of 613 μCi of ^{99}Mo. The third experiment used an enriched ^{100}Mo target and produced 10.5 mCi of ^{99}Mo.

Electrochemical dissolution of molybdenum in sodium hydroxide is promising method for the processing of irradiated Mo targets. It leads to solution of sodium molybdate in NaOH that can be directly fed to the ARSII without any further purification step. The total processing time for the dissolution of ~6 g of Mo is about 2 hours.

Using ARSII chromatography system, more than 95% of available technetium was consistently recovered in the product vial, which is considerably higher than achievable by the standard ^{99m}Tc generators now being used throughout the world.

6. Acknowledgement

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