Fission-Produced ^{99}Mo Without a Nuclear Reactor

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^{99}Mo, the parent of the widely used medical isotope ^{99m}Tc, is currently produced by irradiation of enriched uranium in nuclear reactors. The supply of this isotope is encumbered by the aging of these reactors and concerns about international transportation and nuclear proliferation. **Methods:** We report results for the production of ^{99}Mo from the accelerator-driven subcritical fission of an aqueous solution containing low enriched uranium. The predominately fast neutrons generated by impinging high-energy electrons onto a tantalum convertor are moderated to thermal energies to increase fission processes. The separation, recovery, and purification of ^{99}Mo were demonstrated using a recycled uranyl sulfate solution. **Conclusion:** The ^{99}Mo yield and purity were found to be unaffected by reuse of the previously irradiated and processed uranyl sulfate solution. Results from a 51.8-GBq ^{99}Mo production run are presented.

Key Words: ^{99}Mo; fission; accelerator

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The daughter of ^{99}Mo (half-life, 66 h), ^{99m}Tc (half-life, 6 h), is used in more than 45 million diagnostic nuclear medicine procedures annually worldwide, with approximately 16.7 million procedures performed in the United States alone (*1*). Despite being the largest single user of ^{99m}Tc, the United States currently imports 100% of its supply (*2*). Current supply chains of ^{99}Mo rely on aging nuclear reactors, such as the High Flux Reactor in The Netherlands and the National Research Universal reactor in Canada (*1*). The major U.S. supplier, located in Canada, will cease normal production in late 2016 but will maintain the ability to produce ^{99}Mo for another 2 y, if a severe shortage occurs (*3*). The High Flux and National Research Universal reactors have exceeded their initial design lifetimes of 40 y, having been in operation for 55 and 59 y, respectively. In 2009–2010, both reactors were shut down for extended periods of time, causing a severe ^{99}Mo shortage (*4,5*). The ^{99}Mo shortage forced clinicians to ration imaging procedures, which delayed critical diagnostic tests or resulted in older, less effective techniques that in many cases increased the radiation dose to the patient (*6*). The U.S. ^{99}Mo market is also fragile because it relies solely on international air transportation, which has been halted in the past due to inclement weather, natural phenomena, flight delays, and terrorist threats (*6*).

The predominant global ^{99}Mo production route is irradiation of highly enriched uranium (HEU, $\geq$20% ^{235}U) solid targets in nuclear reactors fueled by uranium (*2*). Other potential ^{99}Mo production paths include $(n,\gamma)^{98}$Mo and $(\gamma,n)^{100}$Mo; however, both routes require enriched molybdenum material and produce low-specific-activity ^{99}Mo, which cannot be loaded directly on a commercial ^{99m}Tc generator. The U.S. National Nuclear Security Administration implements the long-standing U.S. policy to minimize and eliminate HEU in civilian applications by working to convert research reactors and medical isotope production facilities to low enriched uranium (LEU, $<$20% ^{235}U) worldwide (*7*). In 2009, the Global Threat Reduction Initiative program began supporting multiple potential U.S. producers and national laboratories to help establish a U.S. domestic supply of ^{99}Mo using non-HEU–based technologies. Concurrently, the U.S. Congress passed the American Medical Isotopes Production Act, which was signed into law on January 2, 2013, to ensure a reliable U.S. supply of ^{99}Mo and to eliminate the export of HEU for the production of medical isotopes.

Argonne National Laboratory is performing research and development to facilitate ^{99}Mo production within the United States to support the development of diverse technologies that will effectively and efficiently produce, recover, and purify ^{99}Mo without the use of HEU. We have facilitated development of the technology proposed by SHINE Medical Technologies, which will use a deuterium/tritium accelerator to induce subcritical fissioning of ^{235}U in an LEU uranyl sulfate solution (*8*). A key aspect of the SHINE technology is that medical isotopes such as ^{99}Mo can be produced subcritically, eliminating the need for a nuclear reactor (*8*).

^{99}Mo is traditionally produced via irradiation of solid uranium-aluminide dispersion targets in a nuclear reactor (*2*). The dissolution/digestion of these solid targets to release the ^{99}Mo is time-intensive and generates significant amounts of radioactive waste. In contrast, an aqueous uranium-salt target solution can be processed immediately after irradiation, reducing ^{99}Mo loss due to decay. Additionally, the target solution can be recycled, resulting in a significantly smaller amount of waste generated per irradiation cycle.

Several challenges currently hinder development of a solution-based commercially viable process. One challenge is that repeated irradiations will lead to buildup of long-lived fission products and transuranium elements, which could complicate purification processes and may ultimately degrade the ^{99}Mo purity required for use in medical applications. This challenge can be met by periodic cleanup of the solution to remove accumulated long-lived fission products. Argonne has developed a process that uses sulfate-to-nitrate conversion followed by the nitrate-based uranium extraction process for treating the recycled solution (*9*). Another challenge

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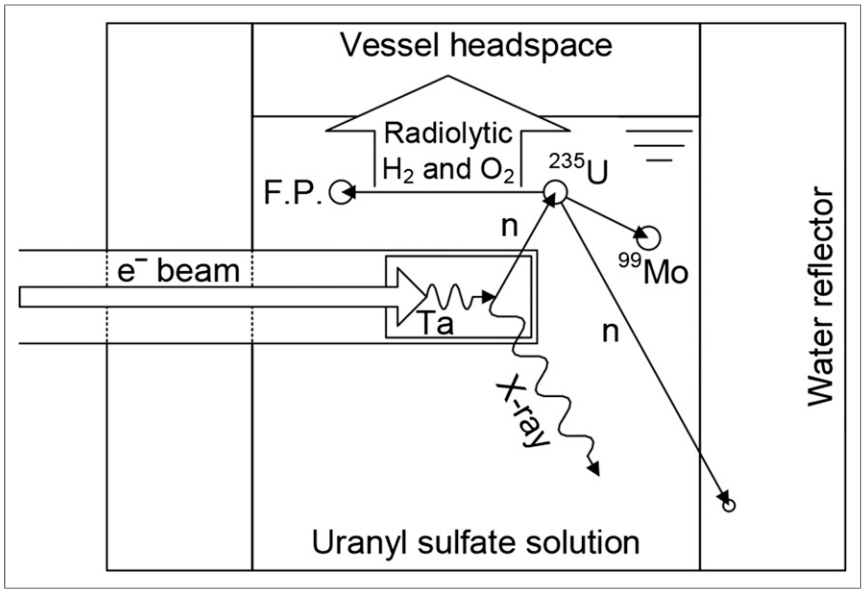

FIGURE 1. Schematic for neutron generation in a tantalum target to induce fission in ^{235}U for production of ^{99}Mo. F.P. = fission products.

is that radiolysis of aqueous sulfate solutions generates hydrogen and oxygen, which need to be carefully managed. Moreover, radioactive xenon, krypton, and gaseous iodine are produced during the fission process and must be captured. A third challenge is that the presence of chemically active radicals and intermediate products (e.g., hydrogen peroxide) pose complex solution chemistry complications, potentially affecting the oxidation or physical state of key components, including molybdenum.

MATERIALS AND METHODS

Herein, we discuss the results of our experimental program and pilot-scale demonstration for the production of greater than 37 GBq of ^{99}Mo from a recycled LEU uranyl sulfate solution, which had been used in 9 production runs. The molybdenum was produced by subcritical fission induced with an electron linear accelerator.

Figure 1 illustrates the experimental configuration. The accelerator-driven electron beam strikes a water-cooled solid tantalum convertor, generating x-rays/photons via the Bremsstrahlung process with concomitant ejection of neutrons. Tantalum was chosen for its high Z value, photoneutron production cross section, high melting point, chemical stability, and good machinability (*9*). Fast neutrons generated by this process are moderated to thermal energies by the LEU solution and surrounding water reflector, inducing fission of ^{235}U to produce ^{99}Mo (6.1% fission yield). The reflector water also serves to moderate the solution temperature to 80°C.

The acidic LEU solution is passed through an extraction column (TiO_2, 110-μm particle size; Sachtopore), where ^{99}Mo along with a fraction of impurities is retained (Fig. 2). The retained ^{99}Mo is stripped from the extraction column by an alkaline solution, acidified, and passed through a concentration column (TiO_2, 40-μm particle size; Sachtopore) to obtain a solution volume acceptable for final purification (*10,11*). The concentrated ^{99}Mo undergoes final purification by the LEU Modified Cintichem (LMC) process, which removes impurities—primarily iodine, ruthenium, and rhodium (*12–14*).

RESULTS

To demonstrate the process, we irradiated 5 L of a recycled 0.63 M uranyl sulfate (19.8% ^{235}U, pH 1) solution with neutrons produced from bombardment of a tantalum converter with a 35-MeV electron beam of 10-kW nominal beam power. A peak fission power density of 0.1 kW/L (1/10th of that expected in the SHINE system) was obtained. Monte Carlo N-Particle eXtended calculations predicted a theoretic yield of 66.6 GBq of ^{99}Mo after 18 h of irradiation at 10 kW of continuous beam power (*15,16*). Analysis of the irradiated solution showed 51.8 ± 3.7 GBq of ^{99}Mo after 20 h, including beam tune-up time. The tune-up periods and operation at 10 kW resulted in a 10-kW equivalent irradiation time of 15 h (59.2 GBq theoretic yield).

DISCUSSION

Radioactive gases—mainly xenon and iodine isotopes—produced during the irradiation were collected and stored for decay. The concentrations of H_2 and O_2 produced during irradiation were continuously monitored and recombined to form water vapor using a heated platinum and palladium–impregnated alumina and cordierite catalyst.

Molybdenum recovery—using a LabVIEW (National Instruments)-based control system—began 5 h after irradiation to allow for decay of short-lived fission products. A remotely operated system was required for processing because of the high dose rates in the room after irradiation. An LEU target solution (5 L) containing 0.0023 mM Mo (stable molybdenum was added as Na_2MoO_4 to reflect SHINE process conditions) was passed through a 2-cm-inner-diameter × 10-cm-long extraction column in 2 h, and ^{99}Mo was retained on the extraction column. The ^{99}Mo-loaded column was washed with sulfuric acid (pH 1) and water and stripped using 0.1 M NaOH. Uranium and most fission products passed through the extraction column. The crude ^{99}Mo product was co-eluted with iodine—predominately as ^{131}I, ^{133}I, and ^{135}I—along with ^{103}Ru, ^{105}Rh, ^{125}Sn, and ^{127}Sb (the supplemental materials

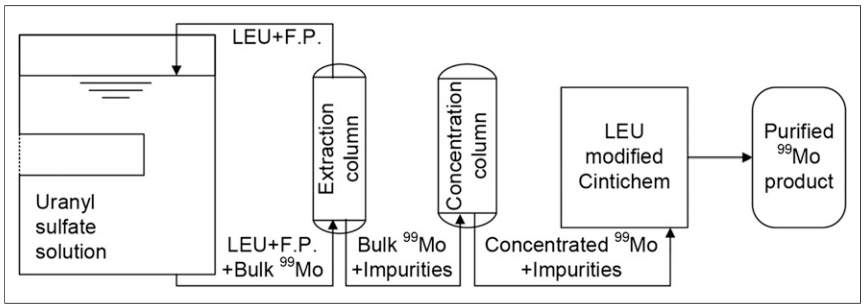

FIGURE 2. Key components of ^{99}Mo recovery and purification process. F.P. = fission products.

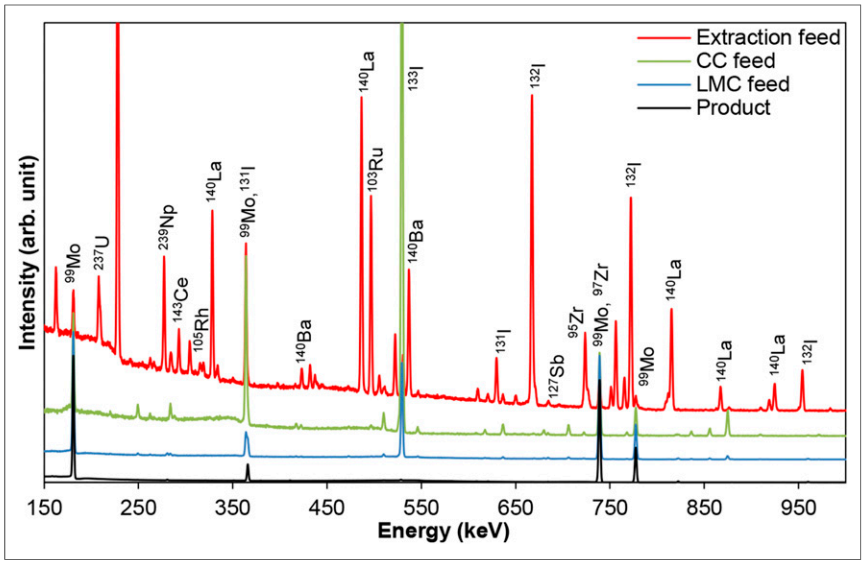

FIGURE 3. Spectra shown for irradiated target solution/extraction column feed (red), concentration column feed (green), LMC feed (blue), and final product (black).

[available at http://jnm.snmjournals.org] describe a complete partitioning of radionuclides). Subsequently, the molybdenum product (~0.9 L) was transferred directly to a shielded cell, acidified to pH 2, and passed through a ^{99}Mo concentration column (1-cm inner diameter × 1-cm length) in 1 h. The column was then washed with 0.01 M HNO_3, followed by water, and the molybdenum was quantitatively stripped with 1 M NaOH to obtain 25 mL of ^{99}Mo product—a solution volume acceptable for the LMC process (<50 mL). Most of the coeluted iodine isotopes, along with ^{103}Ru (~90%) and ^{105}Rh (~60%), were separated from the molybdenum in the concentration column loading step, with more than half of ^{125}Sn and ^{127}Sb partitioning in the alkaline molybdenum strip step (complete portioning of fission products between process streams is included in the supplemental materials).

For final purification by the LMC process, the concentration column molybdenum product was converted to 1 M HNO_3 using 10 M HNO_3. Any remaining iodine was removed from the ^{99}Mo product by precipitation of AgI. The key purification step was the selective precipitation of molybdenum with α-benzoin oxime. Precipitated molybdenum complex was washed to remove residual radioisotopes, primarily iodine, ruthenium, and rhodium (minor amounts of radioactive zirconium, niobium, europium, lanthanum, cerium, and cesium were at measurable levels). The molybdenum precipitate was then dissolved with alkaline peroxide and passed through a 3-phase column of silver-coated charcoal (removal of organics and iodine), hydrated zirconium oxide (removal of cations), and activated charcoal (removal of organics). Purified ^{99}Mo was recovered as sodium molybdate in approximately 55 mL of about 0.2 M NaOH. The product was sampled for analysis and shipped to GE Healthcare in the United Kingdom for product testing. The chemical yield of ^{99}Mo was greater than 80%.

Figure 3 shows the γ-spectra (150–950 keV) for several important samples collected during the extraction, concentration, and purification of ^{99}Mo. Most of the fission products and uranium were removed with the extraction column, whereas the concentration column removed major portions of iodine, ^{103}Ru, and ^{105}Rh. After the LMC process, only ^{99}Mo peaks were identifiable in the γ-spectrum.

The ^{99}Mo produced using recycled LEU uranyl sulfate solution met the European Pharmacopeia purity specifications and fit into the existing supply chain by GE Healthcare (*17*). The product was successfully loaded onto a commercial ^{99}Mo/^{99m}Tc generator, and then the ^{99m}Tc was eluted from the generator and successfully tested with 2 commercial radiopharmaceutical kits. The ^{99m}Tc eluate met the U.S. Pharmacopoeia standards.

CONCLUSION

To our knowledge, this is the first time greater than 37 GBq of ^{99}Mo have been produced by inducing fission in an LEU uranyl sulfate solution using an electron linear accelerator. Accelerator production of ^{99}Mo using an aqueous LEU salt solution will allow repeated use of the target solution and reduced waste generation. Under the conditions studied, the complex solution chemistry of the irradiated solution did not have a negative effect on ^{99}Mo recovery or purity, nor did it have adverse physical or chemical effects on the LEU solution. Also, long-lived radioisotopes that built up over 9 previous irradiations did not affect product purity. The recovery and purification process used here produced ^{99}Mo that met purity specifications and was demonstrated to fit in the existing supply chain. Argonne phase II experiments will produce up to 740 GBq of ^{99}Mo.

DISCLOSURE

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