ACCELERATOR PRODUCTION OPTIONS FOR ^{99}MO*

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Abstract

Shortages of ^{99}Mo, the most commonly used diagnostic medical isotope, have caused great concern and have prompted numerous suggestions for alternate production methods. A wide variety of accelerator-based approaches have been suggested. In this paper we survey and compare the various accelerator-based approaches.

INTRODUCTION

The most widely used medical isotope today is ^{99m}Tc, widely used for bone scans, cardiac perfusion studies, and other diagnostic procedures. It decays with a 6-hour half-life by emission of a high-energy electron. Various chemical compounds can be tagged with ^{99m}Tc and imaged with SPECT (single photon emission computed tomography) scanners for these diagnostic studies.

Its short half-life makes this isotope difficult to transport long distances. It must be produced very close to its point of use. This can be done by use of ^{99}Mo as a ^{99m}Tc "generator;" ^{99}Mo decays to ^{99m}Tc with a 66-hour half-life. The ^{99}Mo can be transported for longer distances, adsorbed onto an alumina column. The ^{99m}Tc decay product can be rinsed out of the column to provide daily doses. This ^{99}Mo/^{99m}Tc generator concept was invented at BNL in 1958.

The current ^{99}Mo production process utilizes the ^{235}U(n,fission)^{99}Mo reaction and requires a nuclear reactor and HEU (highly enriched uranium). New reactors are very expensive and are difficult if not impossible to build due to regulatory and political concerns. HEU is highly controlled and subject to increasing governmental regulations and security concerns. The existing process does not have a promising long-term outlook. Alternative processes are needed. [1, 2]

SUPPLY

The only North American reactor to produce ^{99}Mo is the NRU reactor in Chalk River, Canada. When operational, it normally provides about 40% of world demand and 50% of US demand. Other reactors for worldwide ^{99}Mo production include HFR in Petten, the Netherlands, normally providing about 30% of world demand, BR2 in Mol, Belgium, providing about 10% of world demand, Safari in S. Africa, providing about 10% of world demand, and OSIRIS in Saclay, France, providing about 5% of world demand. The MARIA reactor in Poland has recently been approved to produce ^{99}Mo, and should be able to provide 5-10% of worldwide demand. A few other reactors provide small amounts of ^{99}Mo for regional usage, such as OPAL in Australia.

Reactor fission products are purified near the reactors, by Covidien (Netherlands), IRE (Belgium), NTP (S. Africa), or Nordion (Canada). The purified ^{99}Mo then goes to generator producers. North America has only two generator producers; Covidien and Lantheus.

The worldwide ^{99}Mo supply is quite fragile, relying on only a few aging, increasingly unreliable reactors. The NRU reactor in Canada has been shut down since May 2009 to repair heavy water circuit leaks, and is now hoped resume production in mid-2010. The HFR reactor in Petten has been down since March 2010 for scheduled maintenance. The loss of these two reactors is creating a worldwide ^{99}Mo shortage, which is being partially addressed by increased production from the other worldwide reactors. The supply chain to regions outside of northern Europe (e.g. North America, Asia) is especially fragile and unreliable, and has been impacted by recent Icelandic volcano eruptions.

DEMAND

The present worldwide need for ^{99}Mo/^{99m}Tc generators totals approximately 70k Ci of ^{99}Mo production per week. There is roughly 10% loss due to incomplete chemical separation and roughly 10-15% additional loss due to decay during the processing time. The product is measured and sold in "6-day Curies," which is the activity remaining 6 days after receipt of the isotope, or roughly 0.22x the original activity at time of receipt. Worldwide delivery is about 12k 6-day Ci of ^{99}Mo per week. The US accounts for about 50% of worldwide usage, Europe about 20%, Asia/Pacific about 20%, and Canada about 3.5%. This allows about 500k diagnostic procedures to be performed per week, worldwide.

Demand is expected to grow at 5-10% per year, worldwide. This demand is somewhat elastic. At least 25% of the current demand could be shifted to PET isotopes, if necessary. This is presently more expensive and less available than ^{99}Mo, but provides higher resolution images. Cardiac perfusion studies (perhaps 20% of current demand) can use ^{201}Tl instead of ^{99}Mo, but with a loss of resolution. If necessary, a significant fraction of current studies can be performed with lower doses of ^{99}Mo compensated by longer scanning times.

As of early 2009, the value of purified ^{99}Mo (before being made into a generator) was about \$250 per 6-day Ci, and the cost of a generator was \$500-\$1000 per 6-day Ci. Current costs are higher and unstable due to the present shortage; they may currently be a factor of 2-4 higher than the 2009 costs.

REACTOR PRODUCTION

HEU Fission

The predominant method of ^{99}Mo production, and the only method used for North American ^{99}Mo, is the

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$^{235}U(n,fission)^{99}Mo$ reaction; fission of HEU by thermal neutrons in a reactor. The HEU is generally weapons-grade, about 95% ^{235}U, in the form of a U-Al alloy. Roughly 6% of the total fission yield is ^{99}Mo. Few other Mo isotopes are produced, resulting in a "carrier-free," high specific activity product after chemical purification. The specific activity is about 5000 Ci/g.

LEU Fission

It is possible to use LEU (low enriched uranium, less than 20% ^{235}U) in a reactor rather than HEU targets. This is better from a political and regulatory standpoint, but requires about 5x the neutron flux to produce the same amount of product, due to the 5x lower abundance of ^{235}U. This method is in limited use in Australia and Argentina. It is being actively investigated in a number of other countries for small scale, regional use, with the encouragement and assistance of the IAEA. The US is now pursuing this approach as a near-term solution to continued shortages; this is the subject of the Markey legislation currently in the US Senate.

Conversion to LEU causes a number of difficulties due to the lower abundance of ^{235}U. A 5x greater neutron flux is required, but it is hoped that this can be partially offset by development of denser U-foil targets. The proportion of undesirable fission products will increase; this may require modifications to the present chemical purification process and will require new FDA regulatory approvals.

Conversion to LEU could be a good near-term solution to the ^{99}Mo supply problems. There is a possibility that the University of Missouri Research Reactor (MURR) could be added to the worldwide supply chain using LEU targets. Babcock & Wilcox (B&W) and others are investigating novel reactor concepts, such as liquid LEU solutions for both fuel and target. But LEU may not be a good long term solution to the ^{99}Mo shortage due to the expense and political difficulty of building new reactors.

Neutron Capture

The $^{98}Mo(n,\gamma)^{99}Mo$ reaction can be used to produce ^{99}Mo, eliminating the need for uranium targets. This process is in limited use in Kazakhstan and Romania. The cross section for ^{99}Mo production by neutron capture is about 300x lower than by fission. The product has much lower specific activity than the fission processes, on the order of 1 Ci/g. Thus ^{99m}Tc generators must be much larger, and purity of the eluted ^{99m}Tc is more difficult to maintain. The commercial value of these low specific activity products is estimated to be about 4x less than the high specific activity fission products. This is not a promising method for large scale production.

ACCELERATOR PRODUCTION

Hadrons

An accelerator-driven neutron source could be used for these same $^{235}U(n,fission)^{99}Mo$ or $^{98}Mo(n,\gamma)^{99}Mo$ reactions. The most energy-efficient neutron accelerator is an ADSR (accelerator driven subcritical reactor). ADSRs have been proposed for ^{99}Mo production by a number of groups, including CERN [3], ANL [4], Ion Beam Applications (IBA), and Advanced Medical Isotope Corporation (AMIC).

Another possible neutron reaction is $^{100}Mo(n,2n)^{99}Mo$ with 14MeV neutrons on an enriched ^{100}Mo target. This reaction has an order of magnitude larger cross-section than the $^{98}Mo(n,\gamma)^{99}Mo$ thermal neutron capture reaction, but yields a similar low specific activity product [5].

The $^{100}Mo(p,pn)^{99}Mo$ proton-driven reaction has been investigated by a number of researchers [e.g. 6], but it has a relatively low cross section (subject to some disagreement in the literature) and would produce a low activity product. The deuteron reaction $^{100}Mo(d,p2n)^{99}Mo$ has twice the cross-section of $^{100}Mo(p,pn)^{99}Mo$, but also requires higher energy beams [7].

Direct production of ^{99m}Tc has also been investigated via the reaction $^{100}Mo(p,2n)^{99m}Tc$, which has a relatively large cross section in the region of 20 MeV [6, 8]. This approach could possibly use regional cyclotrons to provide a local source of ^{99m}Tc for large metropolitan areas.

Electrons/Photons

Bremstrahlung photons from electron accelerators can be used for ^{99}Mo production. These possibilities have been studied in depth by TRIUMF. [9]

The photofission process can be used with either of two reactions: $^{235}U(\gamma,fission)^{99}Mo$ or $^{238}U(\gamma,fission)^{99}Mo$. About 50% higher yield is obtained with ^{235}U, but this probably does not justify the additional target cost and the difficulties of using HEU. For either reaction, roughly 6% of the total photofission yield is ^{99}Mo. The cross section is relatively low; a high electron beam power is required to make significant amounts of ^{99}Mo. Multiple accelerators with a total of hundreds of MW of electron beam power would be needed to source the entire world demand.

A photoneutron $^{100}Mo(\gamma,n)^{99}Mo$ reaction has been proposed by Kharkiv Institute of Physics and Technology (KIPT) [10], Yerevan Physics Institute, and others. This reaction with purified ^{100}Mo yields about 17x more ^{99}Mo than the $^{238}U(\gamma,fission)^{99}Mo$ reaction. The yield drops by an order of magnitude for natural Mo targets, since ^{100}Mo is about 10% of natural abundance. The ^{99}Mo product is low specific activity, in the range of 10-100 Ci/g for a 100kW electron beam. This is lower than the product from photofission, but higher than the product from $^{98}Mo(n,\gamma)^{99}Mo$. The radiation length in Mo is about 1 cm; 10-100g of ^{100}Mo would be needed per week to make good use of the photons. The cost of separated ^{100}Mo for targets is about $300/g in large quantities.

COMPARISONS

A comparison of accelerator production options is presented in Table 1. Operating costs can be estimated by assuming 30-50% wall plug to beam power efficiency and $0.10 per kWh electricity costs. Construction of a multi-MW electron linac is estimated at $50-100M [9]. Large research reactors are estimated to cost roughly 4x this amount, and MW-scale proton linacs and ADSRs would be intermediate.

An ADSR with an LEU target is an attractive solution for large-scale ^{99}Mo production. Electrical power costs plus amortized construction costs should result in less expensive ^{99}Mo than the amortized cost of a new reactor. An ADSR solution may even be marginally cost-effective at current market prices. An electron linac with an enriched ^{100}Mo target would use a more mature accelerator technology and would be less expensive to construct, but would likely result in more expensive ^{99}Mo than a new reactor. Due to economies of scale and cost of separated targets, an ADSR or electron linac would be most cost-effective for high-power systems, in the 100 kW to 3 MW power range.

Particle	Accelerator	Reaction	Energy	Beam Power	Target	6-day-Ci/wk	kWh/6-day-Ci
Proton [3]	ADSR	^{235}U(n,fission)^{99}Mo	1 GeV	1 MW	LEU	~6000	~25
Proton [3]	ADSR	^{98}Mo(n,γ)^{99}Mo	1 GeV	1 MW	^{98}Mo	~3000	~50
Proton [4]	ADSR	^{235}U(n,fission)^{99}Mo	200 MeV	100 kW	LEU	~7000	~2.5
Electron[9]	RF Linac	^{238}U(γ,fission)^{99}Mo	50 MeV	1 MW	Natural U	~180	~900
Electron[9]	RF Linac	^{100}Mo(γ,n)^{99}Mo	>30 MeV	500 kW	^{100}Mo	~500	~170
Electron[10]	RF Linac	^{100}Mo(γ,n)^{99}Mo	25 MeV	20 kW	Natural Mo	~5	~800
Proton [6]	cyclotron	^{100}Mo(p,pn)^{99}Mo	45 MeV	4.5 kW	^{100}Mo	~2.5	~270
Proton [6]	cyclotron	^{100}Mo(p,pn)^{99}Mo	45 MeV	4.5 kW	Natural Mo	~0.25	~2700

Table 1: Comparison of various accelerator options for ^{99}Mo production.

For low-power distributed systems in the 10 kW power range, a proton accelerator (linac or cyclotron) with a ^{100}Mo target could be considered, but this is not very power-efficient. Low power proton accelerators are probably better suited to direct production of "instant" ^{99m}Tc than to production of ^{99}Mo. A proton accelerator of 5 kW beam power should be able to produce about 10 Ci/hr of "instant" ^{99m}Tc [6, 8]. Small electron linacs do not seem to be competitive; they could only produce ^{99m}Tc at about half this power efficiency, and to be cost effective would require development of recirculating liquid Mo solution thick targets with continuous elution of ^{99m}Tc.

SUMMARY AND CONCLUSIONS

The current production process for ^{99}Mo does not have a long-term future due to its reliance on HEU and nuclear reactors. In the long term, new production sources will be needed.

Existing reactors were built with large government subsidies. New solutions will likely require large subsidies or increased ^{99}Mo market prices to be economically viable. Assuming one of these occurs, a number of accelerator production options could be considered. For high-power systems, ADSRs are attractive and electron accelerators with ^{100}Mo targets somewhat less so. Low-power proton accelerators for local production of "instant" ^{99m}Tc are also interesting.

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