HOMOGENEOUS SLOWPOKE REACTORS FOR Mo-99/Tc-99m PRODUCTION IN NORTH AMERICA

J.W. Hilborn and H.W. Bonin*

Atomic Energy of Canada Ltd.(Retired), Deep River, Ontario
hilbovanw@sympatico.ca
*Royal Military College of Canada

Abstract

The 15 month shutdown of NRU in 2009 - 2010 caused an overall isotope shortage of approximately 30%; and in North America, the annual Tc-99m demand decreased from an estimated 20 million unit doses to about 15 million unit doses. Mo-99/Tc-99m is produced from HEU targets, irradiated in NRU for 11 days, and after chemical removal of uranium it is shipped to Nordion in Kanata, Ontario. Nordion further purifies the material and sends it to Lantheus Medical Imaging in the USA for manufacture of Mo-99 generators, which are then distributed to hundreds of hospital radiopharmacies throughout North America. One other American company, Covidien, manufactures and distributes Mo-99 generators like Lantheus, but they import bulk Mo-99 from Europe or South Africa.

At the hospitals, Tc-99m is chemically extracted daily from the Mo-99 generators and loaded into syringes for immediate clinical use. Fortuitously, the 66 hour half-life of Mo-99 allows the replenishment of Tc-99m in the generator over a growth period of about 20 hours; and a generator can be "milked" daily for up to two weeks.

A more efficient model is the direct production and distribution of Tc-99m unit doses to regional hospitals from 10 "industrial" radiopharmacies located at existing licensed reactor sites in North America. A 20 kW homogeneous SLOWPOKE reactor at each site would deliver 15 litres of irradiated uranyl sulphate fuel solution daily to industrial-scale hot cells for extraction of Mo-99, which would be incorporated in large Mo-99/Tc-99m generators for extraction of Tc-99m five days a week; and the Low Enriched Uranium (LEU) would be recycled. Each automated hot-cell facility would be designed to load up to 7,000 Tc-99m syringes daily, for courier delivery to all of the Nuclear Medicine hospitals within a 3 hour average range by road transport. Typically, the delivered doses would be in the range 10 to 30 mCi. Assuming an average unit dose of 25 mCi at the hospital and 5 x 52 irradiation days per year, 10 SLOWPOKE sites could deliver up to 18 million unit doses per year to approximately 500 hospitals. At $20 per unit dose, the total annual income from 10 sites would be approximately $360 million.

1. Global Medical Isotope Shortage

An estimate of the combined demand for Mo-99 in Canada and the USA for the year 2008 was 6,000 six-day Curies (Ci) per week, of which 72% came from the NRU reactor. [1] The Mo-99 is produced from HEU targets, and after removal of uranium, it is shipped to Nordion in Kanata, Ontario. Nordion further purifies the material and sends it to Lantheus in the USA for manufacture and distribution of Mo-99/Tc-99m generators.

The prefix "six-day" refers to a six-day radioactive decay factor (0.2205) used in commercial contracts for bulk purchases and sales of Mo-99, to account for the time required to extract Mo-99 from reactor target material, purify it and ship to Mo-99/Tc-99m generator manufacturers. The generators are then calibrated in "real" Curies of Mo-99 before being distributed to hundreds of regional hospitals throughout North America.

The 15 month shutdown of NRU in 2009 – 2010 caused an overall global isotope shortage of approximately 30%, with North America experiencing higher shortages than Europe. [1] A recent reference estimates current North American demand to be 5,000 six-day Curies of Mo-99 per week, produced by 8 reactors; and all of the reactors except one irradiate HEU targets. The same reference estimates the corresponding Tc-99m demand to be approximately 15 million unit doses per year. [2]

2. Production & Direct Delivery of Tc-99m Unit Doses from SLOWPOKE Reactor Sites

An alternative to the complex system of manufacturing and distributing small Mo-99/Tc-99m generators to hundreds of radiopharmacies in regional hospitals, is the manufacture and direct distribution of Tc-99m unit doses to regional hospitals from 10 "industrial" radiopharmacies, located at existing licensed sites in North America.

A 20 kW homogeneous SLOWPOKE reactor at each of the 10 radiopharmacy sites would deliver 15 litres of irradiated uranyl sulphate fuel solution daily to industrial-scale hot cells for extraction of Mo-99, which would be incorporated in large Mo-99/Tc-99m generators for elution of Tc-99m five days a week; and the Low-Enriched-Uraniun (LEU) in solution would be recycled. Fortuitously, the 66 hour half-life of Mo-99 allows the replinshment of Tc-99m in the generators over a growth period of approximately 20 hours.[3]

It is conceivable that any SLOWPOKE 2 research reactor could be converted to homogeneous operation, by replacing the fuel-rod core unit with a cylindrical tank of the same diameter.[4] The homogeneous SLOWPOKE would be designed to operate unattended, but remotely monitored at the security office within the SLOWPOKE site.

Each automated hot-cell facility would be designed to load up to 7,000 Tc-99m syringes for daily delivery to all of the Nuclear Medicine hospitals within a 3 hour average range by road transport. Typically, the delivered doses would be in the range 10 to 30 mCi, at each hospital, ready for immediate use. Assuming an average delivered dose of 25 mCi at the hospital and 5 x 52 irradiation days per year, it is estimated that 10 SLOWPOKE sites could deliver up to 350,000 unit doses per week, or 18 million unit doses per year, to approximately 500 hospitals in North America.

The two day shutdown period with reduced staff would be used for plant maintenance and radioactive waste management, but it could also be used to supply Mo-99/Tc-99m generators to any of the other radiopharmacies experiencing shortages or unplanned shutdowns. An additional two day irradiation would add 37 % to normal weekly production at a single site. [Appendix 1] With backup supply available from neighbouring sites, one SLOWPOKE reactor at each site would be adequate.

3. Location of SLOWPOKE Production Sites at Existing Nuclear Power Plant Sites

One option would be to locate the radiopharmacies at existing nuclear power plant sites close to large metropolitan centres. In North America the largest are: Mexico City, New York, Los Angeles, Chicago, Dallas-Fort Worth, Houston, Toronto, Washington, Seattle and Miami.

If small, low-temperature, unpressurized reactors producing medical isotopes were located at Nuclear Power Plant sites, they could be an important component of the utilities' public information and outreach programs. It has taken decades to overcome the negative image of commercial nuclear reactors following Chernobyl and Three Mile Island. The public will always need credible assurance that the benefits of nuclear power and medical isotopes far outweigh the risks, both real and perceived.

References

[1] Mohamed Zakzouk, "The 2009-2010 Medical Isotope Shortage: Cause, Effects and Future Considerations", Library of Parliament Publication No. 2009-04-E, Ottawa (revised Nov. 2010)
[2] Anton Khlopkov and Miles Pomper with Valeriya Chekina, "Ending HEU Use in Medical Isotope Production: Options for Russian-U.S. Cooperation", Center for Energy and Security Studies, February 24, 2014, Moscow.
[3] Ernest Rutherford, James Chadwick, and C.D. Ellis, "Radiations from Radioactive Substances", Cambridge University Press, Cambridge, 1951, pp.10-13
[4] H.W Bonin, J.W.Hilborn, G.E.Carlin, R.Gagnon & P.Busatta, "Homogeneous SLOWPOKE Reactors for Replacing SLOWPOKE -2 Research Reactors and the Production of RadioIsotopes", Proceedings of the 3rd International Technical Meeting on Small Reactors, Ottawa, Ontario, Canada, 2014, November 5 -7.

Appendix 1

Direct Distribution of Tc-99m Unit Doses from a 20 kW Homogeneous SLOWPOKE Reactor Site

Assumptions:

- Industrial radiopharmacy for production and distribution of isotopes operates 7 days /week
- SLOWPOKE reactor for Mo-99/Tc-99m production normally operates 5 days /week
- Unit doses of Tc-99m delivered Monday to Friday to hospitals within 3 hours by road
- Mo-99 production from a fission reactor: 51 Ci/kW at equilibrium (12 days, 95% equilibrium)
- Reactor irradiation time: 22 hr/day, 20.6% equilibrium, 5 days/week, 52 weeks/year

Process and Delivery:

- Cool for 1 hr after shutdown, then drain reactor tank to hot-cell: 10 min
- Refill reactor from second tank and restart SLOWPOKE: 50 min
- After draining the tank extract Mo-99: 1 hr; loss of Mo-99 in chemical extraction: 15%
- Mo-99 decay factor for reactor cooling, draining and chemical extraction; 2 hr: 0.98
- Waiting time for Tc-99m growth: approximately 20 hr
- Unit dose production and packaging at the SLOWPOKE reactor site; 4 hr decay factor: 0.630
- Average delivery time 3 hr; Tc-99m decay factor: 0.71
- Unit syringe doses delivered to the hospital radiopharmacies contain: 25 mCi = 0.925 GBq
- Price per unit syringe dose of Tc-99m not including delivery: $20

Daily and Weekly Tc-99m Unit Dose Production:

- Lantheus table shows daily elutions of generators in units of mCi Tc-99m/initial Ci of Mo-99
- Total Tc-99m production during the third week and following weeks: 11,206 mCi [Appdx. 2]
- Average daily elution during third week:11,206 mCi/ 5 = 2,241 mCi /initial Ci of Mo-99
- Number of unit doses: 20 kW x 51 Ci Mo-99/kW x 0.206 equilibrium Mo-99 x 0.85 Mo -99 extraction loss x 0.98 Mo-99 decay x 0.63 Tc-99m decay x 0.71 Tc-99m decay x 2,241 mCi Tc-99m/ initial Ci Mo-99 x 1 unit dose/25 mCi Tc-99m = 7,018/day x 5 = 35,090/week

Gross Annual Income from Tc-99m Unit Doses Five Days per Week

35,090 x $20 = $702,000 per week

x 52 = $36.5 million per year from each reactor

Additional Weekly Income from Two-Day Weekend Irradiation

(46 hour irradiation, 38.3% Mo-99 equilibrium)

(0.383/0.206) x 7,018 x $20 = $261,000 per week
= 37% increase in weekly income

Appendix 2

Daily Tc-99m Elutions from Mo-99/Tc-99m Generators

Lantheus Table: mCi Tc-99m per initial Ci Mo-99

(Assuming 85% elution efficiency)

Gen	Mon	Tue	Wed	Thur	Fri	Sat Sun	Mon	Tues	Wed	Thur	Fri	Sat Sun	Mon	Tues	Wed	Thur	Fri
1	662	541	422	328	255		120	93.0	72.2	56.1	43.6						
2		662	541	422	328		154	120	93.0	72.2	56.1						
3			662	541	422		198	154	120	93.0	72.2						
4				662	541		255	198	154	120	93.0		43.6				
5					662		328	255	198	154	120		56.1	43.6			
6							662	541	422	328	255		120	93.0	72.2	56.1	43.6
7								662	541	422	328		154	120	93.0	72.2	56.1
8									662	541	422		198	154	120	93.0	72.2
9										662	541		255	198	154	120	93.0
10											662		328	255	198	154	120
11													662	541	422	328	255
12														662	541	422	328
13															662	541	422
14																662	541
15																	662

Notes

1. The homogeneous SLOWPOKE reactor normally operates five days a week for Mo-99 production, and shuts down two hours per day to change tanks and restart.
2. Mo-99/Tc-99m generators are added daily, and in the table above they are numbered 1 to 15 for the first 3 weeks.
3. Generators are rejected after Monday and Tuesday elutions of 43.6 mCi, and Friday elutions of 43.6, 56.1 and 72.2.
4. Daily Tc-99m elutions can continue week after week, exactly the same as in the third week after the very first elution.
5. 8 generators will be available each Monday, Tuesday and Wednesday, 9 will be available on Thursday, and 10 on Friday.
6. As shown in the table, a new generator is added each week-day; and during the week five depleted generators are removed – one on Monday and Tuesday, and three on Friday.
7. Total Tc-99m elutions per 5-day week: 11, 206 mCi per initial Ci Mo-99.
8. Average daily Tc-99m elution: 2,241 mCi per initial Ci Mo-99.
9. If additional Mo-99 is required, the reactor can be operated for one or two extra days at the end of the week. (See Appendix 1)
10. Lantheus data: Google "Lantheus Imaging Tc-99m Chart Sunday" http://www.lantheus.com/Products.html