



Published in final edited form as:

JACC Cardiovasc Imaging. 2009 March ; 2(3): 369–371. doi:10.1016/j.jcmg.2008.10.008.

Breaking America's Dependence on Foreign...Molybdenum

Andrew J. Einstein, MD, PhD, FACC

Department of Medicine, Cardiology Division, and Department of Radiology, Columbia University College of Physicians and Surgeons, New York, New York

Brief Unstructured Abstract

Approximately 9 million nuclear cardiology studies performed each year in the United States employ technetium-99m, which is produced from the decay of molybdenum-99. The fragility of the worldwide technetium-99m supply chain has been underscored by current shortages caused by an unplanned shutdown of Europe's largest reactor. The majority of the United States' supply derives from a reactor in Canada nearing the end of its lifespan, whose planned replacements have been recently cancelled. In this article, the clinical importance of technetium-99m and our tenuous dependence on foreign supply of Molybdenum is addressed.

With gasoline prices reaching record highs last year, Americans have become keenly aware of our reliance on foreign oil. In hindsight, earlier attention to developing alternative energy sources may have averted the consequences of this dependence.

Lost amidst the news about oil prices is another type of energy crisis in the making. The recent announcement by an obscure state-controlled Canadian company that it had discontinued plans to develop two nuclear reactors has garnered virtually no attention, but it should be of great concern to all, and to cardiologists in particular. This announcement sets the stage for an impending crisis in our nation's radioisotope supply, leading to difficult triage decisions, delayed procedures, and worse outcomes in some patients for whom clinically indicated imaging will be denied, deferred, or performed sub-optimally. Thankfully, unlike for oil, this is a situation in which we still have time to act before paying the serious consequences of foreign dependence.

Roughly 40 million nuclear medicine procedures are performed worldwide each year, half of these in the United States. The most commonly performed nuclear medicine test, accounting for half of all nuclear medicine procedures, is a myocardial perfusion imaging study. In the U.S., approximately 9 million such nuclear stress tests are performed each year.(1)

Although there are many radioisotopes used in nuclear medicine, the field's workhorse is technetium-99m, which is incorporated into over 30 different radiopharmaceuticals. Approximately four out of five patients undergoing nuclear medicine studies receive a

Address for Correspondence: Andrew J. Einstein, MD, PhD, Columbia University Medical Center, 622 West 168th Street, PH 10-408, New York, NY 10032, phone 212-305-6812, fax 212-305-4648, email E-mail: andrew.einstein@columbia.edu.

Potential Conflict of Interest Statement: Dr. Einstein reports receiving an American Society of Nuclear Cardiology/Nuclear Cardiology Foundation research grant that was sponsored by Covidien (\$25,000 grant, Covidien's support was only disclosed to Dr. Einstein after receiving the grant), consulting fees from GE Healthcare (<\$10,000, unrelated to GE's SPECT, PET or radiopharmaceutical units), and travel expenses (e.g. plane tickets to meetings) covered by GE Healthcare, INVIA, Philips Medical Systems, and Toshiba America Medical Systems.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

technetium-99m-based radiopharmaceutical(2), including 97% of patients undergoing nuclear stress testing.(1) For myocardial perfusion imaging, technetium-99m labeled perfusion tracers offer several advantages over their common alternative, thallium-201, which is cyclotron produced, and utilization of thallium-201 has declined steadily over recent years.(1) Attenuation of photons as a function of soft tissue depth is a potential limitation of thallium-201 in patients with large body habitus. In addition, because of the long physical half-life of thallium-201, the amount of thallium administered to a patient is confined by its radiation burden.(3) Although there are alternative myocardial perfusion tracers, such as rubidium-82 and N-13 ammonia, imaging these perfusion tracers require positron emission tomography (PET), which is not as readily available as the single photon emission tomography (SPECT) cameras used for imaging technetium-99m and thallium-201.

Technetium-99m is produced from the decay of molybdenum-99. Since the half-life of molybdenum-99 is only 66 hours, it cannot be stockpiled and therefore the medical benefits of technetium-99m are dependent on a reliable and continuous supply chain of molybdenum-99. Over ninety percent of the world's supply of molybdenum-99 derives from the irradiation of uranium targets at five nuclear reactors, in Canada, Belgium, the Netherlands, France, and South Africa (Table 1).(2) There has not been a U.S. source capable of producing significant amounts of molybdenum-99 in two decades.(4,5)

The majority of the molybdenum-99 used in this country is imported from Canada, where it is produced at a reactor in Chalk River, Ontario prior to processing. This National Research Universal (NRU) reactor is now over 50 years old. It was slated to be replaced with two new reactors, referred to as Multipurpose Applied Physics Lattice Experiment (MAPLE) reactors. These completed construction in 2000, but were never commissioned for use. After eight years of design flaws, budget overruns, and safety concerns, Atomic Energy of Canada Limited cancelled the program in May 2008, deeming the new reactors not feasible to operate, and the Canadian government subsequently announced that the decision is final.

This leaves America's molybdenum-99 supply dependent on the old NRU reactor, which has been subject to multiple shutdowns. A planned four day maintenance shutdown in November 2007 was extended to four weeks due to safety concerns, leading to molybdenum shortages and the intervention of Prime Minister Stephen Harper to restart production prior to completion of a mandated safety upgrade. A current industry estimate is that the NRU, which was originally scheduled to close in 2005, could last until 2014.(6) This would require an extension of the current operating license, which expires in 2011, and further safety concerns could arise at reinspection.

After the NRU ceases operations, the four other high-capacity reactors could not ramp up production, in order to meet worldwide molybdenum demand, for a stretch of more than a few weeks. Moreover, each is at least 40 years old, and transport of molybdenum from these facilities across the Atlantic is associated with sizable radioactive decay, requiring more isotope at greater cost. The fragility of worldwide molybdenum supply has been further underscored by the temporary closure in August 2008 of each of the five major reactors producing molybdenum-99.(7) Four reactors, including the NRU, were down for scheduled maintenance, and the reactor in the Netherlands that produces the majority of Europe's molybdenum and is the second largest source for the U. S. was down due to a leak into its cooling system caused by corrosion of its pipework.(8) This situation, which at the time of this writing is expected to last until February 2009, has led to a decrease in the supply of technetium-99m generators available in the U. S. In Europe, which is more dependent on the Dutch reactor, more pronounced shortages and rationing have occurred, a harbinger for what we can expect here post-NRU unless a good solution is in place.

The long-term solution to the United States' molybdenum needs is a domestic source. This has been recognized by professional societies for over a decade, and has been recommended by multiple advisory committees, most recently in a National Academies report published a year ago (9) and a recent letter from the Nuclear Energy Advisory Committee offering recommendations to the Department of Energy.(10) We are now in the end-game in terms of the current molybdenum supply chain, and how we play it will determine whether Americans have a continuous supply of technetium-99m or a crisis in which patients are unable to obtain essential medical tests.

An interrelated issue is that each of the five major reactors producing molybdenum-99 uses highly enriched uranium targets, which contain at minimum 36% and in most cases 93% uranium-235. Highly enriched uranium is considered by many experts to be a global non-proliferation concern.(11) The Energy Policy Act of 2005 mandated a National Academy of Sciences study, due in December 2008, that is investigating the possibilities for—and cost-effectiveness of—providing for the nation's medical isotope needs from sources that do not use highly enriched uranium.(12)

Fortunately, there are potential solutions to America's molybdenum needs. One would be for governmental support of domestic low-enrichment uranium-based molybdenum production. A research reactor already in place could be adapted to provide at least half of U.S. molybdenum-99 demand, although this would require capital to build a processing facility, which would cost an estimated \$40 million. Most likely this would necessitate federal funding, probably through the Department of Energy. Such funding, which is advocated in the Nuclear Energy Advisory Committee's letter to the Secretary of Energy (10), would require a change in the current language in the Senate's proposed 2009 Energy and Water Development and Related Agencies Appropriations Act, which provides for a feasibility study (13) but not for development of a processing facility.

Another strong possibility for a domestic molybdenum source, although likely on a longer timetable, is an effort in the private sector to develop a novel type of reactor technology, called an aqueous homogenous reactor, in which uranium dissolved in water and acid serves as both the reactor's target and fuel. An aqueous homogenous reactor would generate significantly less radioactive waste than do current processes. Both of these potential solutions to our molybdenum needs would use low-enriched uranium targets for molybdenum production.

With the cancellation of the MAPLE reactor project, it is clear that the present U.S. molybdenum-99 supply chain is not sustainable for the long term, and thus it is imperative that we explore potential domestic sources. Our continued ability to provide the best healthcare to our patients lies in the balance.

Acknowledgments

Financial Support: Dr. Einstein is supported in part by an NIH K12 institutional career development award (5 KL2 RR024157-03).

References

1. 2005 Nuclear Medicine Census Market Summary Report. Des Plaines, IL: IMV Medical Information Division; 2006.
2. Bonet, H.; David, B.; Ponsard, B. Production of Mo-99 in Europe: status and perspectives. Paper presented at: 9th International Topical Meeting on Research Reactor Fuel Management; April 10–13, 2005; Budapest: European Nuclear Society in cooperation with the International Atomic Energy Agency; 2005 [Accessed November 4, 2008]. Available at: <http://www.euronuclear.org/pdf/RRFM2005-Session1.pdf>

3. Einstein AJ, Moser KW, Thompson RC, Cerqueira MD, Henzlova MJ. Radiation dose to patients from cardiac diagnostic imaging. *Circulation* 2007;116:1290–1305. [PubMed: 17846343]
4. Cintichem to decommission research reactor. *J Nucl Med* 1990;31:37A.
5. Hickey, JWN. Nuclear Regulatory Commission: Notice of license termination of the Cintichem, Inc. New York facility. FR Doc. 98–22190; Federal Register. 1998 [Accessed November 4, 2008]. p. 44293-4. Available at:
<http://frwebgate5.access.gpo.gov/cgi-bin/PDFgate.cgi?WAISdocID=810031471310+1+2+0&WAISSaction=retrieve>
6. Horner D. Scrapping of Maple fans speculation that US isotope production likely. *Nucleonics Week* May 29;2008 :6–8.
7. Medical community eyes reactor shutdowns. *World Nuclear News*. Aug 282008 [Accessed November 4, 2008]. Available at:
http://www.world-nuclear-news.org/RS_Medical_community_eyes_reactor_shutdowns_2808082.html
8. Reactor Petten restarts on the 16th of February 2009 [news release]. Petten, Netherlands: Nuclear Research and Consultancy Group; October 14, 2008. Available at: <http://www.nrg-nl.com/general/nieuws/2008/20081014en.html>. Accessed November 4, 2008.
9. Committee on State of the Science of Nuclear Medicine; National Research Council. *Advancing Nuclear Medicine Through Innovation*. Washington: The National Academies Press; 2007 [Accessed November 4, 2008]. Available at: http://books.nap.edu/openbook.php?record_id=11985
10. Martin W. Nuclear Energy Advisory Committee Letter to Secretary of Energy Samuel Bodman. October 1;2008
11. von Hippel FN, Kahn LH. Feasibility of eliminating the use of highly enriched uranium in the production of medical isotopes. *Science and Global Security* 2006;14:151–162.
12. Energy Policy Act of 2005. Public Law 109–58-August 8, 2005. Washington: Government Printing Office; 2005 [Accessed November 4, 2008]. Available at:
http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=109_cong_public_laws&docid=f:publ058.109.pdf
13. Energy and Water Development Appropriations Bill, 2009. Report 110–416. Washington: Government Printing Office; Jul 142008 [Accessed November 4, 2008]. Available at:
http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_reports&docid=f:sr416.110.pdf

Table 1
Major Worldwide Reactors Producing Mo-99 and Their Distributors

Reactor	Location	Owner*	Operation (Days/Year)	Mo-99 Distributor	% of Worldwide Mo-99 Supply
National Research Universal (NRU)	Chalk River, Canada	Canada	315	MDS-Nordion	40
High Flux Reactor (HFR)	Petten, Netherlands	European Union	290	Covidien IRE	20 10
South African Fundamental Atomic Reactor Installation 1 (SAFARI-1)	Pelindaba, South Africa	South Africa	315	NTP	10
Belgian Reactor 2 (BR2)	Mol, Belgium	Belgium	115	Covidien IRE	5 4
OSIRIS	Saclay, France	France	220	IRE	3

* through government's solely owned entity or public utility

IRE = Institut National des Radioéléments, Belgium

NTP = Nuclear Technology Products, owned by South Africa

Adapted from Bonet et al (2).