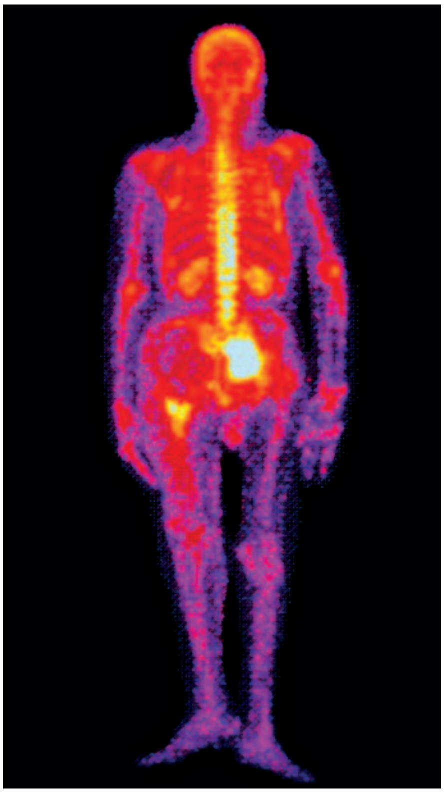
New moly-99 sources wanted

Molybdenum-99 is a vital radioactive isotope used to diagnose and detect a range of diseases, including cardiovascular problems and cancer. Millions of patients benefit from nuclear medical imaging technology every year. However, only a few, mostly very old nuclear research reactors worldwide can produce the isotope, so the reliability of its availability causes some concerns. Therefore, a number of new projects are underway to secure safe and stable long-term supply.

The moly-99 atomic nucleus contains the 42 protons common to all molybdenum atoms along with 57 neutrons. It is unstable with a "half-life" of 66 hours, decaying to the metastable technetium-99m isotope. This means that half of the moly-99 atoms will decay to technetium-99m in that time. Technetium-99m then decays with a half-life of six hours emitting a gamma ray, similar to a high-energy x-ray, that a standard medical "gamma camera" can detect. Thus, it is important for many medical diagnostic procedures. Because of its short half-life, the imaging agent cannot be stockpiled and starts to disappear as soon as it is produced. Therefore, "just-in-time" is a way of life for the isotope's tenuous supply chain. Any flight delays or traffic jams on the race from the reactor where it is produced to the clinic where it is used can become existential threats, rendering moly-99 and technetium-99m shipments useless and endangering patients who are waiting for a diagnosis.

Importance of technetium-99m in modern medicine

Technetium atoms bind to pharmacological agents that concentrate in various parts of the human body, including the bones, heart, brain, and kidneys. Gamma cameras collect the technetium's gamma radiation, a technique analogous to an x-ray CAT scan. The result is a picture of the organ that has two significant advantages over a CAT scan: the patient receives a greatly reduced radiation dose and the image contains much more detail since the signal comes directly from the organ itself. Technetium-99m is used in over 30 million tests each year throughout the world in more than 30 different medical procedures, making it by far the most important medical radioisotope.



The technetium-99m tracer reveals metastatic thyroid cancer in a colored gamma scan.
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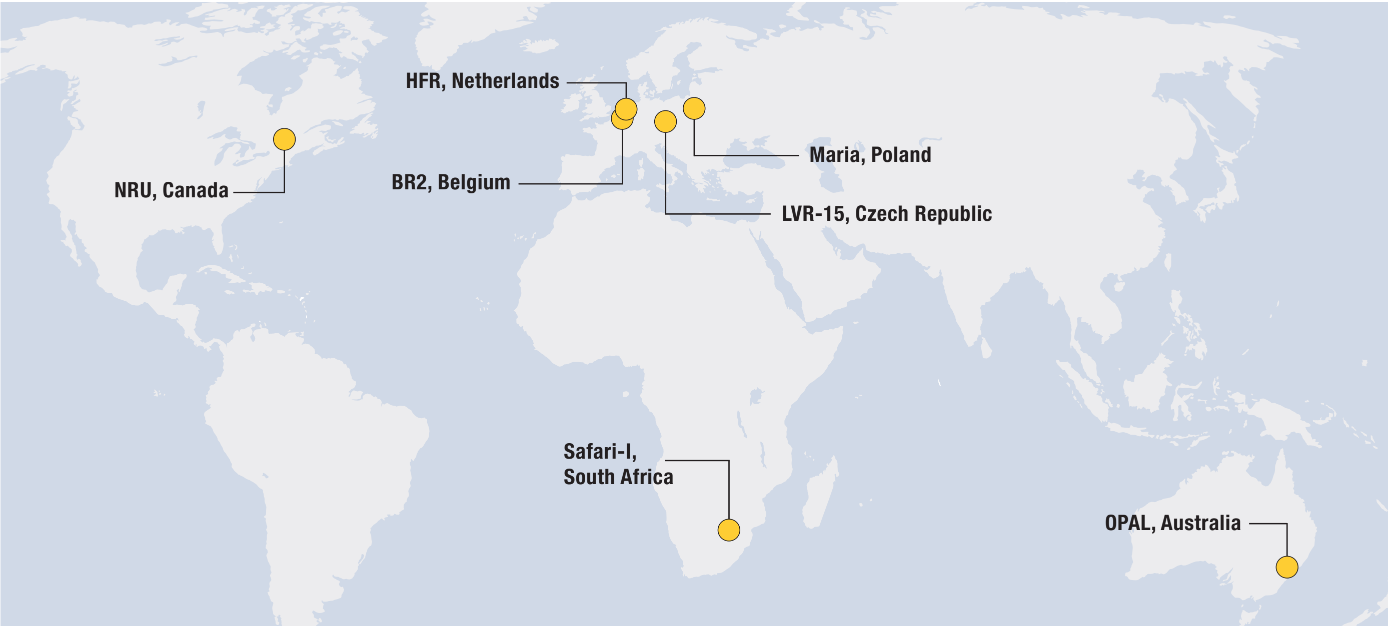
The supply problem

The problem is that the moly-99 supply chain needs to be bolstered. Nearly all the moly-99 in the Western world is produced in seven nuclear research reactors located in the Netherlands, Poland, Belgium, the Czech Republic, South Africa, Canada, and Australia. A few more produce small amounts for local distribution, and four in Russia serve primarily domestic consumption. Until recently, all but one of the reactors produced moly-99 from highly enriched uranium (HEU), a material that can be used to make a simple nuclear weapon. The international community has been trying to eliminate the use of such uranium in reactors for safety reasons.

To add to the concerns, five of the reactors are now more than 50 years old and are susceptible to lost production time due to greater maintenance needs and unexpected shutdowns. Such unplanned shutdowns of two reactors in 2009–2010 caused a critical shortage of moly-99. Canada's Chalk River reactor, which provides 20% of the world's moly-99 supply and about 40% of U.S. requirements, was shut down in 2016 after expiration of its operating license. It was reopened only in March 2018 after receiving an extension to operate until March 2028. This has provided a sense of stability for the moly-99 and technetium-99m world, but the long-term viability of the supply chain is still in question.

Path to solving the problem

In 2013 President Obama signed legislation offering federal grants to encourage American companies to develop alternative technologies to produce the crucial moly-99. SHINE (Subcritical Hybrid Intense Neutron Emitter) Medical Technologies proposed a completely new technique using a particle accelerator to produce moly-99 from low-level enriched uranium targets. In 2016, it became the first project since 1985 to receive Nuclear Regulatory Commission (NRC) approval. The company estimates that ❯



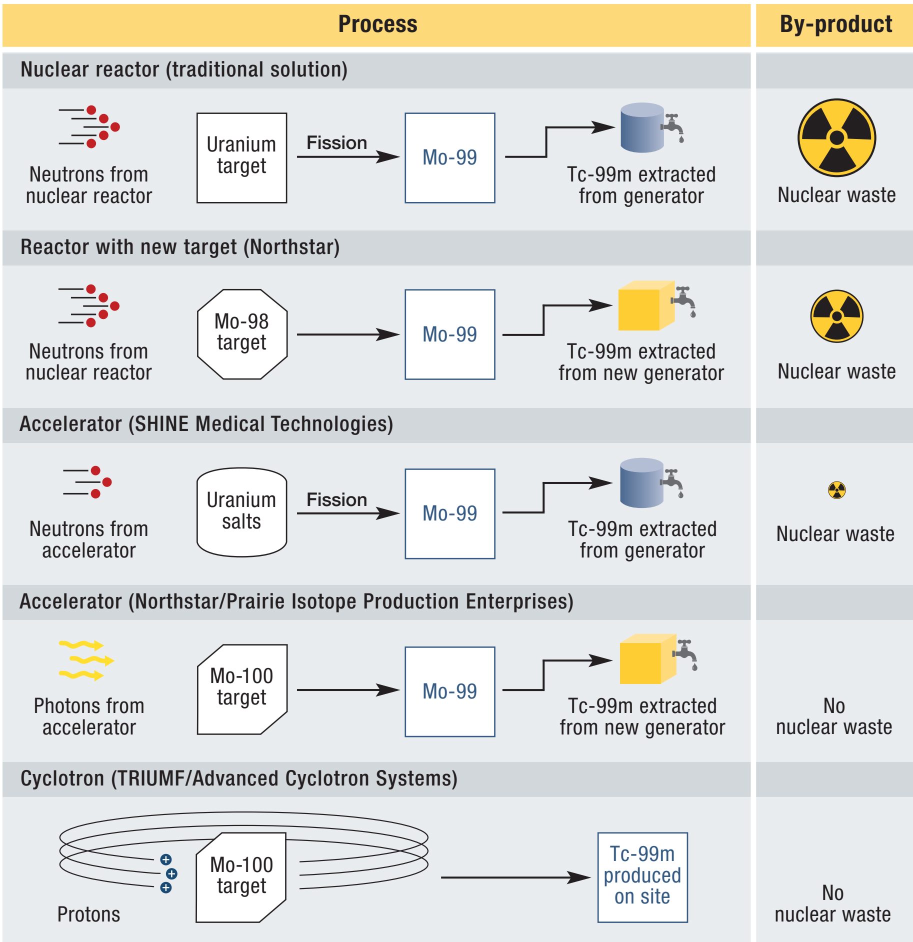
Locations of the seven research reactors which supply 95% of the world's Mo-99. Source: Molybdenum-99 for Medical Imaging, National Academy of Sciences, 2016

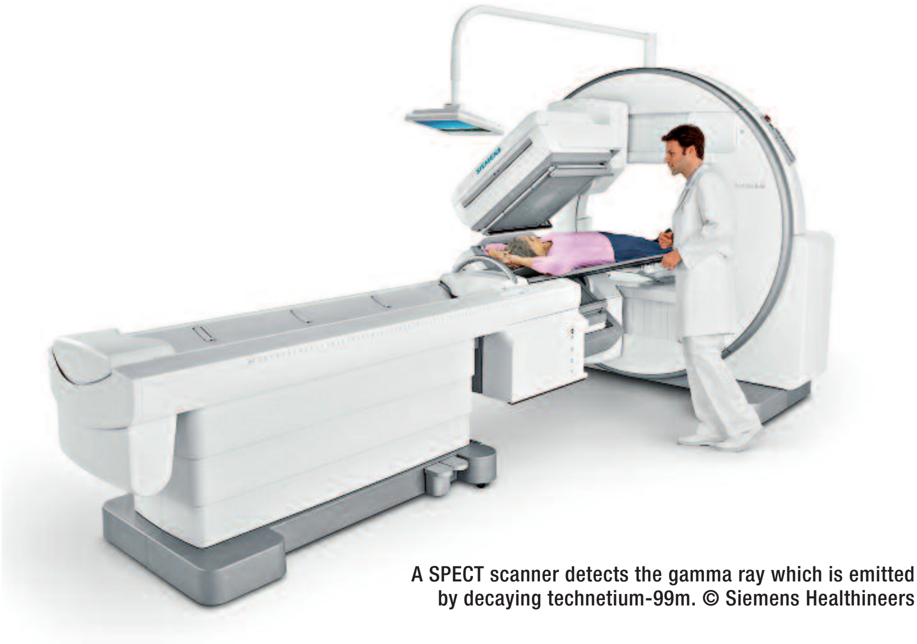
the facility will be able to produce 50,000 doses of moly-99 each week. The $25 million in federal funds covered part of the project's estimated $100 million cost, but the company has had difficulty raising the remaining funds. As a result, the project's start date has slipped to 2020 and some experts feel its startup could take longer.

NorthStar Medical Radioisotopes, located near the SHINE facility, is pursuing two technologies to produce moly-99 and has received $50 million in federal grants for their projects. One is a neutron-capture technology which irradiates molybdenum targets in an existing research reactor. The process then harvests the moly-99 created from the Mo-98 isotope which is 24% of naturally occurring molybdenum. The company is optimistic about this approach, since the U.S. Food and Drug Administration has already approved the process to extract moly-99 from the irradiated material.

NorthStar's second project uses an electron accelerator to produce Mo-99 from a target that uses the Mo-100 isotope, but it has not yet received its ❯

Traditional process and the proposed new technologies to generate Mo-99 and extract technetium-99m (Tc-99m). Adapted from Nature [10.1038/504202a], source: NEA/OECD





A SPECT scanner detects the gamma ray which is emitted by decaying technetium-99m. © Siemens Healthineers

initial NRC approval. Prairie Isotope Production Enterprises (PIPE), a Canadian non-profit consortium, is pursuing a similar methodology. This approach creates no nuclear waste, an advantage in comparison with the technologies using a uranium target.

Two other Canadian organizations CycloMed99, a consortium led by Canada's particle accelerator center TRIUMF, and Advanced Cyclotron Systems, a manufacturer of cyclotrons used to create other medical isotopes, are working on yet another technology which uses proton beams produced by hospital cyclotrons to create technetium-99m directly from a molybdenum target enriched in the Mo-100 isotope. Neither organization appears yet to have a commercially viable project, but since the technology is designed around existing equipment, their path may be less obstacle-strewn. Like the electron-accelerator approach, the proposed technology produces no nuclear waste.

In addition to all of these players, BWX Technologies recently announced a method to produce Mo-99 from a patent-pending neutron capture process. The former Babcock-Wilcox Company has years of experience in building commercial and naval nuclear reactors, but they have not released much detail about their process to make moly-99. They have acquired the Canadian firm Nordion, who have process technology that extracts technetium-99m from moly-99, so they are serious contenders.

Uncertain future

Because of the importance of moly-99 for modern medicine, many ideas and plans are in the works to solve the supply problem. While none of the projects seem to promise a quick solution, the fact that so many companies are working on new approaches increases the likelihood of developing additional capacity in the medium term. In the meantime, the world remains dependent on the reliability of seven nuclear reactors scattered about the globe, and the ultimate solution to the molybdenum-99 problem remains in the future. (Tom Ferguson, John Shields)