Medical Isotope (Nuclear Medicine) Shortages

A Discussion of the Issue and Implications for the Health Care Industry

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Background

The use of radioactive materials to obtain X-ray images of tissues and organs (most often referred to as "Nuclear Medicine") dates back to 1937 when the first clinical use of "artificial radioactivity" was carried out in the treatment of a patient with leukemia at the University of California at Berkeley. A landmark event for nuclear medicine occurred in 1946 when a thyroid cancer patient's treatment with radioactive iodine caused complete disappearance of the spread of the patient's cancer. Clinical use of nuclear medicine became more widespread in the early 1950s.[1]

Understanding Nuclear Medicine

The use of injectable radioactive materials called "radionuclides" differs from conventional X-ray in one fundamental way: emission vs. transmission.

- In a conventional X-ray, an electronic X-ray tube produces radiation *outside* the body, and the X-ray film records the amount of radiation "transmitted" through various parts of the body.
- In a radionuclide "emission" scan (nuclear medicine), the source of the radiation is *within* the body and the image is created by using arrays of very sophisticated Geiger-counter-like sensors to identify the location and characteristics of the organ, which captures the radioactive substance.

Importantly, the radioactive substances do not last long in the body and are rendered safe by a process known as "decay." Physicists measure this by calculating "half-lives" of the material, which is the time it takes for one-half of the material to become non-radioactive. Half-lives for different radioactive materials range from millionths of a second to thousands of years; the ones used in medical imaging are typically in the range of six hours. Today, there are more than 100 different nuclear medicine procedures that uniquely provide information about nearly every major organ system within the body.

Currently, more than 80 percent of all procedures within nuclear medicine are based upon technetium-99m (Nuclear Energy Agency 2000), a radionuclide produced by individual generators (Molybdenum-99 (Mo-99)/Technetium-99m (Tc-99) Generator) that use molybdenum produced in reactors alongside those that generate nuclear energy. The most prominent suppliers have been Canada's NRU Chalk River plant (40 percent) and the Netherlands' High Flux Reactor in Petten (35 percent). At the very heart of all nuclear medicine procedures is the need for year-round, reliable availability of radionuclides. The consistent availability of these radionuclides has been compromised by repeated interruptions since 2007.[2]

The Supply of Radionuclides

In November 2007, Atomic Energy of Canada Limited (AECL) announced that it would close down operations at its NRU Chalk River plant for routine maintenance. This was a medically important issue because the plant is the primary (though not only) producer of medical isotopes used in North America. Immediately following this closure, several hospitals reported a 20-30 percent shortage in the most commonly used isotope, Tc-99m.[3]

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Then in May 2009, Chalk River halted operations again after experiencing similar problems, and announced that the production of medical radioisotopes would be suspended until the summer of 2010. Following the halt in operations at Chalk River, the Netherlands' High Flux Reactor in Petten went offline for maintenance in February 2010, and is not expected to resume production of medical radioisotopes until the summer of 2010.[4] These closures left the world's supply of Mo-99 to the BR2 reactor in Belgium, the Osiris reactor in France, the Safari reactor in South Africa and the Maria Research Reactor in Poland. The Maria reactor was reintroduced into the global supply chain for medical isotopes in February 2010, and received U. S. Food and Drug Administration (FDA) approval in March 2010. The addition of the Maria reactor was expected to provide medical isotopes for more than one million patients during its first six months.[5]

Exploring Alternate Solutions

As outlined above, current world supply is dependent upon multiple international laboratories, including one in Canada and five in Europe. Many of the disruptions have been caused by lack of cross-plant coordination of routine maintenance among the producers, with as many as five plants offline at the same time. International attention has forced better coordination and a significant interest in expanding production capacity. Along with the 2010 addition of Poland's Maria reactor, there have been discussions about harnessing the research reactor at the University of Missouri (MURR).

This U.S.-based National Radionuclide Production Enhancement (NRPE) Program has been established to address the problem and identify solutions. Program officials have noted that MURR currently provides reactor-produced radionuclides for therapeutic applications. However, it has a low-power (10MW) reactor that allows it to produce only relatively small quantities of radionuclides at a low specific activity (a few radioactive atoms and a much greater number of non-radioactive atoms), effectively limiting their use.

How U.S. Suppliers Are Coping

Covidien, a major U.S. supplier, has historically obtained most of its isotopes from the High Flux Reactor in Petten, the Netherlands. While this source has provided some insulation from the effects of the Canadian shutdown for Covidien's clients, the Dutch reactor went offline in February 2010 for maintenance until the summer of 2010. These plant shut-downs left many providers to consider how best to manage ongoing demand for these radionuclides in the absence of their routine availability. While the addition of Poland's Maria reactor to the global Mo-99 supply chain has allowed Covidien to supply Tc-99m to patients who might otherwise not have received it as scheduled, the medical isotope shortage remains. Covidien has asked providers to continue careful scheduling of patients in most critical need of the isotopes, along with planning for the most efficient use of Tc-99m.

Privately held Lantheus Medical Imaging of Massachusetts, which processes isotopes for medical use, has relied upon the Chalk River plant for the bulk of its supply. Lantheus has actively worked with other radionuclide suppliers to maximize the supply of Mo-99 to help their customers cope with the impact of the medical isotope shortage.

What Physicians Can Do

Nuclear physicians are adopting a number of different strategies to ensure that patients are not harmed by the ongoing Mo-99/Tc-99m supply shortage. These strategies have included:

1. Lowering the dose of Tc-99m-based radiopharmaceuticals
2. Eluting (or flushing) the generator more often to maximize the activity of Tc-99m extracted, thereby improving yield
3. Opening imaging departments on Saturdays to shorten the length of nuclear decay in between use of the radionuclide
4. Rescheduling examinations and providing greater access to patients in most critical need
5. Utilizing alternative isotopes (such as thallium) or alternative procedures, when appropriate

In some cases, standard bone scan procedures using Tc-99m have been replaced by fluorine-18 FDG PET scans, and thallium has been substituted for the current Technetium-based nuclides for cardiac evaluation.

NIA's Perspective

By far, the most commonly used isotope containing Tc-99m is commercially known as Cardiolite and is used in conjunction with a variety of nuclear cardiology procedures. It is important to note that when NIA issues pre-procedure authorization for a nuclear cardiology study, the authorization is not specific to a certain radioisotope. This allows the service provider flexibility in selecting the isotope that is available and/or most appropriate for the given study. This is particularly important as a significant number of nuclear cardiology studies are alternatively performed using thallium rather than Cardiolite. Many industry leaders believe these isotopes to be of essentially equal value.

Recent shortages prompted National Imaging Associates (NIA) to notify our service providers and health plans of this flexibility within our authorization process (as outlined above), and, as predicted, many examinations were simply performed using an alternative isotope (such as thallium). Some procedures were cancelled as providers identified alternate diagnostic examinations. It is to be expected that some were rescheduled.

It is worth noting that the NIA Call Center, along with our online verification system at www.RadMD.com, processes more than 3 million pre-procedure reviews annually. We did not record a statistically significant drop in utilization during the prior period of radionuclide shortage. Additionally, NIA did not observe any noticeable pent-up demand at the conclusion of the 2007 shortage. Similar patterns of use have been noted in the first quarter of 2010.

During the current medical isotope shortage, NIA is reviewing each request for a nuclear medicine procedure on an individual basis. Should the need arise for approval of a study involving an alternative isotope, the decision would be made after peer-to-peer discussion with the ordering provider.

Summary Observations

- It is reasonable for the health care industry to expect periodic shortages for the next several years, especially until there is greater coordination across all existing plants and/or until additional consistent supply becomes available.
- The communication and coordination of scheduled reactor maintenance by producers will help to ensure a continued, uninterrupted supply.
- Most technetium-based studies (cardiac) can be performed with alternate radionuclides (e.g. thallium), which are not in short supply.
- Nuclear physicians are adopting a number of different strategies to ensure that patients are not harmed by the ongoing Mo-99/Tc-99m supply shortage.

For more information or to learn more about NIA, contact your NIA representative or call 1-877-NIA-9762.

1. *Kahn J. From Radioisotopes to Medical Imaging, History of Nuclear Medicine, http://www.lbl.gov/Science-Articles/Archive/nuclear-med-history.html, accessed June 2009.*
2. *Dehn T, Nuclear Medicine (Radioisotope) Availability 2007 – 2008 A Discussion Paper prepared for NIA Client Health Plans, Magellan Health, January 2008.*
3. *Since January 2007, there have been multiple periods of serious disruption to supplies, including a month outage at Chalk River to fix safety back-up systems and a six-month shutdown of the Petten reactor from August 2008 after corroded pipes were discovered in its primary cooling circuit.*
4. *"Addition of Polish Research Reactor Helps With Worldwide Supply Shortage," Covidien News Release, Feb. 17, 2010.*
5. *Covidien Letter to Customers, March 26, 2010.*

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