ESSAY

Accelerating production of medical isotopes

The global problem of a safe and reliable supply of radioactive isotopes for use in critical hospital procedures can be solved with accelerators, not nuclear reactors, says **Thomas Ruth**.

Physicians and patients around the world are increasingly anxious about the shortage of nuclear isotopes used in medical imaging. A single radionuclide — technetium-99m (^{99m}Tc) — is used in four-fifths of all such imaging procedures worldwide. Yet its supply is remarkably fragile. In 2007, the unanticipated closure of a single nuclear-reactor facility in Canada slashed isotope stocks in North American hospitals by about 80%, causing much panic and the cancellation of 50,000 medical procedures over five weeks. Some patients went into surgery without the scans their doctors usually rely on. The medical-isotope supply came back online, but the fragility of the system did not improve. In 2008, isotope shortages struck again.

Shockingly, there are no clear plans in place for how to tackle this problem. My colleagues and I see viable mid-term and long-term solutions. Each relies on a very different plan. But both involve accelerators, rather than reactors.

Nuclear medicine, developed following the Second World War, relies on the injection of a radioactive compound into the bloodstream, and instruments that can then detect and map, in three dimensions, the distribution of the injected radioactivity and its decay products. It is used primarily to locate tumours in the body, monitor cardiac function following heart attacks, map blood flow in the brain, and guide surgery. About 70,000 diagnostic images are taken each day, worldwide.

Some 85% of the ^{99m}Tc used in Europe and North America comes from the decay of molybdenum-99 (^{99}Mo) made at just two reactor facilities: the High Flux Reactor in Petten, the Netherlands, and the National Research Universal reactor in Chalk River, Ontario, Canada. Supplies are shipped continuously to hospitals. Stockpiling the ^{99}Mo radioisotope for more than a couple of days is impossible, as it has a half-life of just 66 hours.

In November 2007, the Chalk River facility was closed for one month owing to a regulatory dispute over its maintenance. The shutdown and subsequent isotope shortage became the subject of such a public outcry that the Canadian government ordered the reactor to restart; the president of the national Nuclear Safety Commission, who had ordered the shutdown, was removed from her position in the process. Then in August 2008, the reactor in Petten was closed because of a leak in the coolant system. There couldn't have been a worse time: the four next-largest facilities, including Chalk River, were already offline for unrelated reasons. The press latched on to a comment that this was a 'perfect storm' for isotope availability. In December 2008, the Chalk River reactor was again shut for a few days for routine maintenance, but unexpected difficulties kept it down for longer than expected. This again put a pinch on supplies. Meanwhile, the reactor in Petten is not expected to reopen until February 2009 (recent reports indicate that it may even be later in the year).

ZUMA/NEWSCOM

BSIP, RAGUET/SPL

Canada's ageing Chalk River nuclear reactor (top) is prone to unexpected closures; supplies of medical isotopes for diagnoses (bottom) remain critical.

Both reactors are relatively old, and it's not clear how long they might last. There are plans to replace the Petten reactor in 2015. The Chalk River facility's licence to operate ends in 2011, with an expected renewal to 2016; anything beyond that date is uncertain. The problem is critical. Earlier this month, the Union of Concerned Scientists issued a call for more medical-isotope production capacity in the United States to help secure supplies.

Unfortunately, there are no near-term or even long-term solutions being implemented that could provide a reliable and adequate supply for Europe and North America. The operator of the Chalk River facility was helping to build two dedicated radionuclide-producing replacement reactors, called the MAPLE reactors, which would have had the capacity to meet the entire world's supply needs. But in June 2008, the project was cancelled following extended technical difficulties that had delayed full operation for more than eight years. A new project in Australia might be able to make up 10–20% of North America's requirement within a few years of its anticipated opening this year. And there are plans to retrofit the Missouri University Research Reactor to produce ^{99}Mo, but a fully successful upgrade within the next five years will probably result in the reactor having the capacity to meet only half of North America's needs. This is not enough.

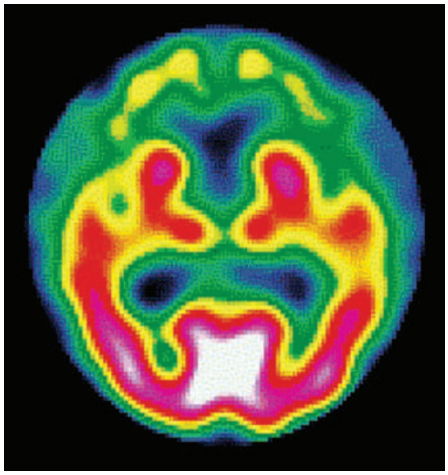
Complicating the scene further is the issue of using highly enriched uranium, containing about 93% of the nuclear isotope uranium-235 (^{235}U), in these reactors. Such reactors may use highly enriched uranium, as a fuel source and as a source material from which to create ^{99}Mo. The International Atomic Energy Agency and the US National Nuclear Security Administration have for years been involved in converting reactors to operate with low-enriched uranium fuel, so as to lower the risks associated with terrorists getting access to highly enriched material. But a problem remains with the target material. All major reactors currently in use bombard ^{235}U with neutrons to initiate fission and produce ^{99}Mo.

Future fission

There is, however, an alternative. Instead of using a reactor to fire neutrons at ^{235}U, an accelerator can fire photons at the relatively stable uranium isotope, uranium-238. This also spurs the needed fission process. The production rate of ^{99}Mo is several orders of magnitude lower, but this is outweighed by the advantage of using safer materials.

The challenge, then, is to generate a high-intensity beam of photons to produce commercially practical yields equivalent to those that can be generated by existing reactors. The science and engineering of high-intensity electron machines has advanced significantly over the past few years (led by DESY, the German electron synchrotron physics lab in Hamburg). Accelerator physicists believe that it is now possible to build a machine that fits the bill by converting accelerated electrons into light.

The Canadian government is interested enough in alternatives to reactor-produced ^{99}Mo that the Department of Natural Resources sponsored a workshop in October 2008, co-hosted by TRIUMF — Canada's national laboratory for particle and nuclear physics — where I work, to explore the possibility of designing and building such an electron linear accelerator. This workshop concluded that these accelerators could in principle be built and routinely operated, and that several research projects should be initiated to verify that. If an accelerator were given the green light to proceed by the Canadian government, perhaps within the next five years, it would take about three years and between US$50 million and $125 million to build. If our calculations are borne out, it would be capable of producing enough ^{99}Mo to meet Canada's needs (about 10% of North America's needs or 5% of world demand). So several machines would be required to replace the existing reactors. But these accelerators would be cheaper than reactors, which on average cost between US$500 million and $1 billion, as one does not need to worry about the same level of nuclear containment. Also, decommissioning of an accelerator facility is less complicated than for a reactor. Once feasibility is proven, they could be easily cranked out in high numbers.



A SPECT scan shows blood flow in the brain.

INSTITUT PAOLI-CALMETTES, ISM/SPL

Shifting picture

In the long term, accelerators of a different type will surely play a growing role in medical imaging. Although ^{99m}Tc is the dominant medical isotope, that picture is changing.

The type of scan that ^{99m}Tc is used for is called single photon emission computed tomography (SPECT). But an alternative type of scan, called positron emission tomography (PET), is coming to the fore. Both techniques make use of biologically active molecules tagged with radionuclides, but the radionuclides decay differently.

PET allows users to see fine details more clearly, largely thanks to the fact that it relies on a radionuclide that emits two decay products in opposing directions at the same time. Tracing these decay products allows a PET system to define more precisely where the radiation has come from within the body, and how strong the radiation is at that point. The tracer used in SPECT, by contrast, emits only one decay product. Thus a SPECT system has a harder time tracing where that radiation came from, and cannot tell if a smaller signal is the result of less-intense radiation, or because that radiation travelled out from deeper within the body. The result is a blurrier picture.

"The problem is critical."

In addition, the tracers used for PET are easier to attach to small molecules that bind to specific factors within the body, such as a certain hormone. This can be very useful in making diagnoses.

PET uses isotopes that are made in an accelerator, not a reactor. But the half-lives of these radioisotopes are even shorter than those used for SPECT, so hospitals must be equipped with their own cyclotrons, or have access to a regional facility. The most versatile radionuclide for PET imaging, carbon-11, has a half-life of just 20 minutes, and the most commonly used PET tracer for oncology, fluorine-18, has a half-life of 110 minutes. This makes PET, for now, a more expensive proposition than SPECT.

Today, only 2,000 of the 12,500 nuclear medicine installations in the United States have PET scanners, and access to the needed radioisotopes is still limited. During the shortage at the end of 2007, a number of centres with access to PET successfully used this as an alternative to SPECT for cancer diagnoses. Ideally, every hospital would be equipped in this way. For this to become a reality, cyclotrons and PET scanners will have to become more affordable, and governments will have to provide incentives. In China, the government has almost leapfrogged SPECT and is investing directly in PET. Prices for PET scanners are dropping rapidly, and cyclotrons are becoming more affordable with time; but it will be a decade before PET can outcompete SPECT.

Time for action

Meanwhile, the major markets in the United States and Europe will continue to need ^{99}Mo/^{99m}Tc. Decisions must be made quickly to determine whether the accelerator approach is viable and preferable to reactors while the replacement facilities can still be completed in a timely fashion.

At the time of writing, the Chalk River reactor has developed a leak that will require a significant shutdown for its repair. Both the Petten and Chalk River reactors are ageing, and such leaks are not unexpected. How much longer can these devices be kept in safe and efficient operation?

The Canadian government has an opportunity to continue its legacy of being the leader in the nuclear field. Although the production and delivery of radioisotopes for medicine has been in the private sector, the well-being of the citizens of the world requires significant involvement of both the private sector and governments at all levels. Action is required before it is too late. ■

Thomas Ruth is a research scientist at TRIUMF and a senior scientist at the British Columbia Cancer Agency, both in Vancouver, Canada.
e-mail: truth@triumf.ca