MEDICAL ISOTOPES - SIDEBAR

Diagnostic imaging using radioisotopes is well-established and widely used around the world. It relies on some basic chemistry that is keyed to simple biological processes, and some relatively straightforward radiation detection, however its impact on healthcare has been profound. ^{131}I (produced either as a fission product of ^{235}U or through neutron capture by ^{130}Te) is probably the simplest isotope to understand. Iodine is selectively taken up by the thyroid, so small (few mCi) doses injected or ingested by the patient can be used to determine thyroid function by simply measuring the absorbed activity and, by using a gamma-imaging camera, the size of the thyroid gland can be determined. The uniformity of the uptake can be used to identify abnormalities. A few tens of mCi can be used to correct an overactive thyroid, and hundred-plus mCi doses are used to kill thyroid tumours.

However, the most widely used and versatile medical isotope by far, is ^{99m}Tc derived from ^{99}Mo. It is used in 60%–70% of all diagnostic medical procedures in the US [1]. This popularity is the result of several accidents of fate:

- efficient production by fission of uranium makes it widely available;
- the relatively convenient 67-hour half-life makes it possible to extract and distribute the ^{99}Mo with acceptable decay losses;
- the 6-hour half-life of ^{99m}Tc (the daughter isotope that is actually used) means that high specific activity, but short-lived radiopharmaceuticals can be delivered to a patient;
- the very different chemistries of Mo and Tc mean that the ^{99m}Tc daughter can be recovered from the ^{99}Mo as it forms using simple chemistry.
- the 140 keV decay gamma from ^{99m}Tc is well suited for efficient detection by scintillation instruments such as gamma cameras.

Medical use of cyclotron-produced isotopes generally requires a dedicated on-site (or close by) cyclotron facility and a specialised radiopharmaceutical laboratory, whereas hospitals using ^{99}Mo simply take delivery of a new Tc-generator (that is about the size of a jug of milk) every week or so. The generator is flushed with a small amount of saline solution to extract the ^{99m}Tc as needed, and chemical kits are used to convert the extract into a targeted dose for the patient. The wide availability and ease of use of Tc-generators have led to a rich variety of delivery forms being developed. Some target liver and bone marrow function and can be used to detect cancers; others bind to calcium deposits that form following a heart attack and enable doctors to confirm the occurrence (or not) of a heart attack with greater speed and reliability than electrocardiograms (ECG); still others concentrate in areas of high metabolic activity and can be used to measure heart function to investigate the need for, or effectiveness of, by-pass surgery.

The extreme popularity of these nuclear medicine techniques arises from several key features:

- they can be carried out with essentially no lead time or patient preparation;
- they are totally non-invasive making them an ideal first-choice test;
- they can target specific organs or processes in the body;
- they yield highly specific key diagnostic data quickly;
- they carry no significant risk to the patient.

Easy, quick, effective, safe.

Unfortunately for the tens of thousands of patients who need these tests every month, ^{99}Mo is now in extremely short supply. In some cases, alternative radioisotopes produced in cyclotrons can be substituted, but they are not the first choice, and their use diverts resources that were already in heavy demand for other tests.

Current commercial production relies almost entirely on highly enriched uranium (HEU) targets which raises proliferation concerns as 40–50 kg of "weapons grade" uranium is needed annually to supply world demand [1]. This comes primarily from US stockpiles, and it would be hard to imagine a better use for it. However, Argentina, South Africa and Australia have all switched to low-enrichment uranium (LEU) targets so the proliferation problem has effectively been solved.

In a typical production process used at the new Australian reactor facility (OPAL), an aluminium-clad plate of uranium aluminide about the size and shape of a 12" steel ruler is loaded into the reactor for about six days. The target is

Dominic Ryan, (P.Phys.) is a Professor of Physics at McGill University. He is also the current President of the Canadian Institute for Neutron Scattering.

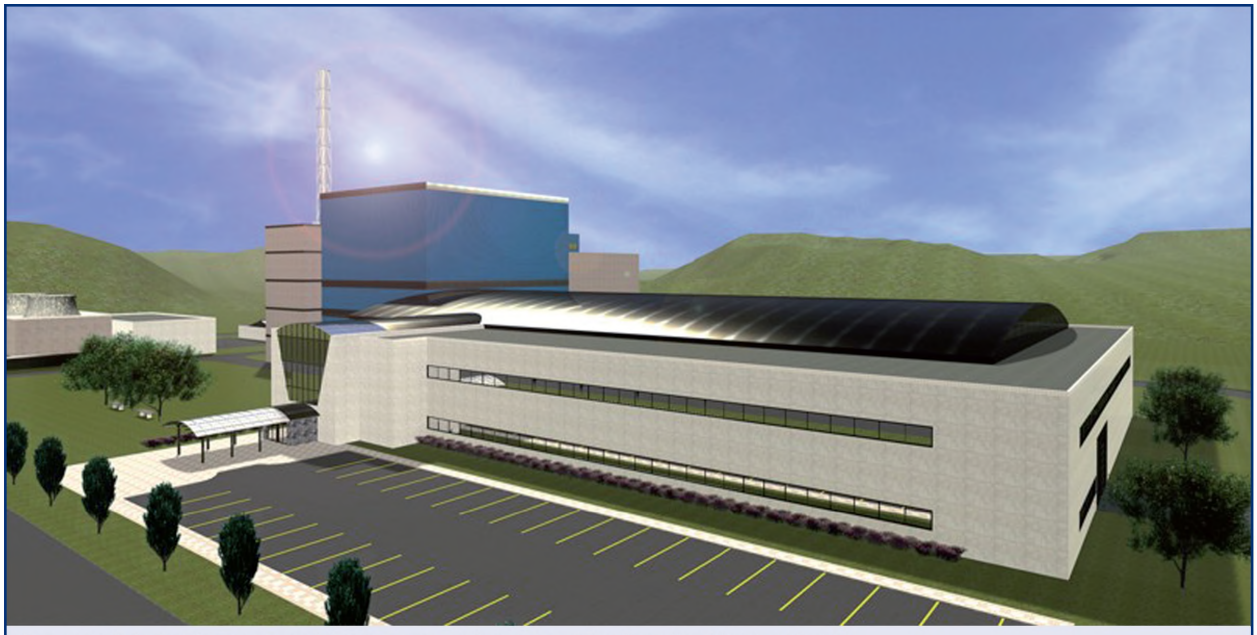
then removed, transferred to a hot cell (the activity at this stage is many thousands of Curies, so some care is required) where it is dissolved in sodium hydroxide, filtered to eliminate the solid waste and the solution is purified by ion exchange and then passed through an alumina column that selectively adsorbs the molybdate (MoO_4^{2-}) ion. The ^{99}Mo is then washed from the column and recovered as a highly pure product. ^{99}Mo recovery yields at OPAL are currently about 60%, with 80–90% expected as the process is further refined. Production levels are about 500 6-day Curies/week [2] – enough to satisfy their domestic market and allow export to South Africa, Japan and South-East Asia. For comparison, US demand in 2006 was about 6,000 6-day Curies/week [1], so a much larger facility would be needed to supply North American needs.

A few Curies of the extracted ^{99}Mo are re-adsorbed onto a pencil-sized alumina column, loaded into a shielded case and shipped to a hospital as a "technetium generator". The shortlived ^{99m}Tc builds up in the generator as the ^{99}Mo decays, and is washed out as needed using a saline solution. The extract is processed using a pre-constituted kit to create the specific radiopharmaceutical required for the test to be run. The product is delivered to the patient and the organ(s) of interest are imaged [1]. The lifetime of the generator is limited not only by the decay of the ^{99}Mo, but also by "breakthrough": increasing amounts of molybdenum appear in the extract as the generator ages and eventually (after about a week), it can no longer be used for work involving human subjects. The initial isotopic purity of the ^{99}Mo therefore plays a major role in extending the working life of technetium generators. Clearly, stockpiling ^{99}Mo is not an option, so a secure stable source is essential.

The capital costs of a reactor to produce ^{99}Mo would run to many hundreds of millions of dollars, so a single-purpose facility is not an economic option [3]. An equivalent capacity accelerator-based production facility would be at least as expensive to build, and would cost far more to run. Neither approach makes economic sense. We at the Canadian Institute for Neutron Scattering (CINS) have therefore proposed the construction of a multi-purpose research reactor that will both serve all of the stakeholders currently using NRU and also provide a stable source of ^{99}Mo for the next fifty years [4].

REFERENCES

1. "Medical isotope production without highly enriched uranium", National Academies Press, (2009), (www.nap.edu/catalog/12569.html)
2. The rather odd units are the result of the inherently perishable nature of the product. The activity is specified as that which will be present six days after it leaves the production facility.
3. "Capturing the full potential of the uranium value chain in Saskatchewan", Uranium Development Partnership, (2009), (www.saskuranium.ca)
4. "Planning to 2050 for materials research with neutron beams in Canada". CINS (2008) (www.cins.ca/CINSplan.html)



Conceptual design for a new multipurpose research reactor - The Canadian Neutron Centre.