MEDICAL ISOTOPE PRODUCTION USING COMMERCIALLY-AVAILABLE ACCELERATOR AND PROCESSING TECHNOLOGIES

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SUMMARY

Natural Resources Canada invited proposals last year by the private and public sectors for alternatives to producing Molybdenum-99/Technetium-99m, the key medical isotopes currently in short supply around the world. This article will describe the proposal submitted by PIPE – the Prairie Isotope Production Enterprise, which is a non-profit organization with membership consisting of a number of groups from Manitoba and Saskatchewan.

The recent shutdown of the Chalk River nuclear reactor and the subsequent worldwide shortage of medical radioisotopes have been topics of national concern. Much of this interest is on the political and medical front, but it has also spurred significant scientific research. In order to decide how to proceed in addressing this problem, Natural Resources Canada invited proposals last year by the private and public sectors for alternatives to producing Molybdenum-99/Technetium-99m, the key medical isotopes currently in short supply around the world. An expert review panel was established to evaluate the proposals, and in early December 2009, a report was delivered containing its recommendations [1]. This article will describe the proposal submitted by PIPE – the Prairie Isotope Production Enterprise, which is a non-profit organization with membership consisting of a number of groups from Manitoba and Saskatchewan [2].

Radioisotopes are used in medicine both for diagnostic and therapeutic uses, with about 90% of the procedures performed with them being diagnostic. The reason that they are so useful is that they can be attached to a chemical compound that, when introduced into a body, preferentially accumulates in a targeted area. Once there, the isotope decays by emitting gamma radiation. By measuring the amount and the energy of this radiation, one can use an external camera to non-invasively construct detailed images of the area where the radioisotope originated in a way that is less harmful than biopsy, surgery, etc. A common radioisotope used for this purpose is technetium-99m (Tc-99m). This isotope has a half-life of about six hours and decays by emitting gamma rays of about the same energy as a conventional X-ray. The short half-life makes it useful for diagnostic purposes, but also makes it inconvenient for transport over long distances. For this reason, a Tc-99m generator is used. The generator contains molybdenum-99 (Mo-99), which has a half-life of about 66 hours and produces Tc-99m when it decays. Areas of the body that are commonly imaged using this isotope include the brain, thyroid, heart, lungs, liver, kidney, spleen and bone marrow.

The standard way to produce Mo-99 is in a nuclear reactor through neutron-induced fission, whereby an intense neutron flux bombards highly enriched Uranium-235, causing a cascade of fission products that includes Mo-99 about 6% of the time. The Mo-99 is then separated in a processing facility and the product supplied to Mo-99/Tc-99m generator fabricators. However, as recent events have shown, it is important to have alternative production processes and facilities available so that a critical shortage doesn't result when an unexpected shutdown of one of the sources occurs. Three such alternative processes that have been examined in this regard are [3]:

- A neutron-capture process, in which an intense neutron beam generated by a nuclear reactor adds one neutron to a Mo-98 target to produce Mo-99.
- A photo-neutron process, where an intense photon beam generated by an electron accelerator removes a neutron from a Mo-100 target to produce Mo-99.
- A photo-fission process, where an intense photon beam generated by an electron accelerator causes a uranium target to fission to produce Mo-99.

Based on an evaluation of the currently available Tc-99m production methods, economics, the time needed to get products to patients, environmental considerations, regulatory issues, and availability of suitable linear accelerator technologies, particularly in Canada, PIPE has selected photon irradiation of selected Mo-100 compounds and physical forms as the process platform.

A critical aspect to be addressed is that, once the Mo-based target materials are irradiated with photons, the materials must then be processed to produce the Mo-99/Tc-99m

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Fig. 1 Linear accelerator used by PIPE Research Team.

generators or Tc-99m solutions for direct delivery to hospitals. The commercially available processing technologies in this regard include:

- Production of a gel-moly (zirconium or titanium molybdate) solid containing Mo-99. The gel-moly–based generators are shipped to radiopharmaceutical facilities, Tc-99m is eluted as per the standard practice, and the generators are returned for recycling.
- A generator that extracts Tc-99m from molybdenum trioxide using a melt technology. As before, the generators are returned for recycling after the Tc-99m is consumed.
- A generator that extracts Tc-99m from molybdenum trioxide crystals (powder technology), with a dissolution and recrystalization step between milkings.

A major question arising (and which we at PIPE hope to answer) in the use of this accelerator-based approach is the scalability – will this process produce enough Tc-99m to be economically viable? A study by Nelson *et al.* estimates that a 40 MeV, 14 kW accelerator can produce over 18,000 Ci per year of Tc-99m [4], which represents about 70% of Canada's current demand for Tc-99m. This will have to be confirmed through detailed studies and realistic trials. Such investigations will also determine the effects of various parameters on the production rate, such as

- Variation of Mo-99 production with beam energy
- Effects of target design and beam position, including dependence on
    - o The radial offset of the beam.
    - o The shape of the target.
    - o The effects of a tungsten layer on the Mo target.
    - o The use of a target enriched with Mo-100 isotope.

Our R&D program to address production, purification, and generator development has already begun. We have successfully produced Mo-99 by exposing natural Mo targets to an electron beam from our accelerator at Acsion Industries (Pinawa, MB). We are now preparing to make larger quantities of Mo-99 and to proceed with generator fabrication. This work has so far been done on a 10 Mev, 4 kW accelerator and ultimately a higher power accelerator is desirable. Our plan calls for the support of a 30-40 MeV machine running above 50 kW. Such accelerators are commercially available from Mevex Corporation (Ottawa, ON). Our operations would thus be expanded to generate a significant fraction of the Canadian demand if our facility were to receive funding support.

Although research and development needs to be done to answer with certainty these and other questions on the use of this technology, there are a number of significant benefits to Canada should this prove feasible, including:

- Availability of a reliable Canadian source of Tc-99m, with the potential to have multiple such facilities to ensure a consistent supply;
- A relatively short development period, with initial production beginning within 2 years and full-scale production a year after that;
- No long-term radioactive waste streams (*e.g.* with uranium) are present and product recycling is incorporated into the production process;

Probably the most important lesson to be learned from the current crisis is that neither one technology nor facility should be relied upon for producing the bulk of medical isotopes.

REFERENCES

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