A SHORT TERM SOLUTION TO THE MEDICAL ISOTOPE CRISIS VIA DIRECT PRODUCTION OF TC-99M AT LOW ENERGY: A PIECE OF THE PUZZLE

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The recent unexpected shutdown of the Chalk River, Canada reactor has caused a major disruption in the supply of the most important radionuclide used in medicine today, Mo-99. Mo-99 is the source of Tc-99m used in more than 80% of all nuclear medicine imaging procedures. There are only 5 reactors that are presently used in the production of Mo-99 and all of these reactors are over forty years old, the one in Chalk River, the NRU, is 52 years old. The NRU and the HFR reactor in the Netherlands account for more than 60% of the world's supply. The NRU is closed because of a heavy water leak in the containment vessel releasing tritiated water into the holding tank. The HFR reactor had a leak in a coolant pipe earlier in 2009 and is due for an extended shutdown in 2010 to repair this leak.

With these shutdowns the supply of Mo-99 has caused major shortages around the world causing major challenges in diagnosing patients with heart disease and cancer.

With most solutions for obtaining a reliable supply of Mo-99 taking 5 or more years, short term solutions need to be examined. Some of the long term solutions involve the use of accelerators including using electron linacs to generate photon beams for photo induced fission of natural uranium or photo induced neutron emission on Mo-100 yielding low specific activity Mo-99. Other proposals include the use of proton spallation sources to generate secondary neutrons for neutron induced fission of uranium-235. However these large projects require several years of planning and construction before the conceptual ideas can become a reality and would not be able to supply commercial quantities of Mo-99 before 2016-2020.

SUMMARY

The shutdown of the NRU reactor in Chalk River, Ontario, and the planned shutdown of the HFR reactor in the Netherlands in 2010, has caused major shortages in the supply of Mo-99 around the world, causing major challenges in diagnosing patients with heart disease and cancer.

In the recent National Academy of Sciences report *Medical Isotope Production without Highly Enriched Uranium* [1], it was suggested that direct production of Tc-99m could be used to alleviate shortages in regions close to a low energy cyclotron. It turns out that the ^{100}Mo(p,2n)^{99m}Tc reaction peaks at around 16 MeV and the entire useful excitation function is covered from about 15 MeV to 24 MeV. (see Figure 1) From the literature it appears that the production rate for this reaction is 17 mCi/μAh. [2-7] At this rate it is possible for existing low energy cyclotrons to produce tens of curies of Tc-99m per day at somewhat modest beam currents (100 μA protons). Thus existing cyclotrons such as those with proton energies of 17-19 MeV could produce significant amounts of Tc-99m for local use on a daily basis. The chemistry for isolating Tc-99m from the Mo-100 target is fairly straightforward and less complex than what is used to extract Mo-99 from the fission products and allows for the recycling of the Mo-100 for subsequent irradiations [.8]

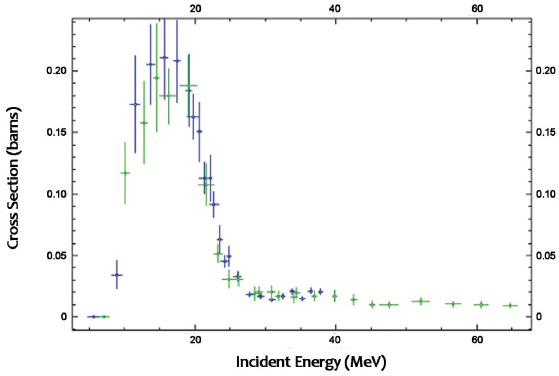

Fig.1 Production cross section for the ^{100}Mo(p,2n)^{99m}Tc reaction. Exfor, Nuclear Data Center, BNL.

While this approach is not a *fix* it does provide for an alternative that could be implemented in the short term to alleviate demands for Tc-99m from generator produced Mo-99. Such a relief would allow for the scarce Mo-99 generators to be used in locations more distant from the cyclotrons. Another layer of sophistication that should be

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explored is to form a network of existing cyclotron facilities that could coordinate production and supply. A distributed supply provides for redundancy. Such a network was funded by NSERC and CIHR in response to their special call for proposals in August 2009 seeking alternative to the existing Tc-99m based radiopharmaceuticals. This network is being explored in Canada among 5 centers in 4 cities across the country; in Vancouver (TRIUMF and the BC Cancer Agency), Edmonton (Cross Cancer Institute), London (Lawson Health Science Centre) and Sherbrooke (CHUS).

The proposal was to develop the targetry for the low energy cyclotrons (three TR19 cyclotrons, one GE PETrace and a CP42 variable energy cyclotron. The TR cyclotrons and the PETrace can operate at 50 to 100 μA while the CP42 can reach 200 μA at 24 MeV. In addition to producing Tc-99m the investigators will produce Tc-94m as a PET alternative to the SPECT based Tc-99m with the aim of determining if the existing Tc-based radiopharmceuticals can be used in PET with the direct substitution of Tc-94m (72% β+, 52 min $t_{1/2}$) for Tc-99m (140 keV γ-ray, 6 h $t_{1/2}$). Because of the shorter half life there may be radiopharmaceuticals not amenable to this approach. The project mandate is to bring the cyclotron based Tc-99m radiopharmaceuticals into human use within 2 years (Fall 2011).

While this paper does not address the directions of accelerator usage in medicine for the future it is aimed at demonstrating the utility of existing cyclotrons and of their potential for benefit to society through coordinated efforts, concepts that should be kept in mind as plans for the future are examined.

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