PhD Thesis title: 'Cyclotron Production of Technetium-99m'

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ABSTRACT:
Technetium-99m (^{99m}Tc) has emerged as the most widely used radionuclide in medicine and is currently obtained from a ^{99}Mo/^{99m}Tc generator system. At present, there are only a handful of ageing reactors worldwide capable of producing large quantities of the parent isotope, ^{99}Mo, and owing to the ever growing shutdown periods for maintenance and repair of these ageing reactors, the reliable supply ^{99m}Tc has been compromised in recent years. With an interest in alternative strategies for producing this key medical isotope, this thesis focuses on several technical challenges related to the direct cyclotron production of ^{99m}Tc via the ^{100}Mo(p,2n)^{99m}Tc reaction.

In addition to evaluating the ^{100}Mo(p,2n)^{99m}Tc and ^{100}Mo(p,x)^{99}Mo reactions, this work presented the first experimental evaluation of the ^{100}Mo(p,2n)^{99g}Tc excitation function in the range of 8–18 MeV. Thick target calculations suggested that large quantities of cyclotron-produced ^{99m}Tc may be possible. For example, a 6 hr irradiation at 500 µA with an energy window of 18→10 MeV is expected to yield 1.15 TBq of ^{99m}Tc. The level of coproduced ^{99g}Tc contaminant was found to be on par with the current ^{99}Mo/^{99m}Tc generator standard eluted with a 24 hr frequency.

Highly enriched ^{100}Mo was required as the target material for ^{99m}Tc production and a process for recycling of this expensive material is presented. An 87% recovery yield is reported, including metallic target preparation, irradiation, ^{99m}Tc extraction, molybdate isolation, and finally hydrogen reduction to the metal. Further improvements are expected with additional optimization experiments. A method for forming structurally stable metallic molybdenum targets has also been developed. These targets are capable of withstanding more than a kilowatt of beam power and the reliable production and extraction of Curie quantities of ^{99m}Tc has been demonstrated.

With the end-goal of using the cyclotron-produced ^{99m}Tc clinically, the quality of the cyclotron-produced ^{99m}Tc has been extensively compared with relevant United States Pharmacopeia (USP) specifications for the existing ^{99}Mo/^{99m}Tc production strategy. Additional quality testing, including biodistribution studies of [^{99m}Tc]pertechnetate and [^{99m}Tc]disofenin in both mice and rabbits was also evaluated. Using the strategies and results presented throughout this dissertation, this thesis concludes with the

world's first cyclotron-based ^{99m}Tc patient images obtained as part of a Phase I Clinical Trial at the University of Alberta using [^{99m}Tc]pertechnetate.

References to author publications that relate specifically to the dissertation:

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2. K. Gagnon, F. Bénard, M. Kovacs, T.J. Ruth, P. Schaffer, J.S. Wilson and S.A. McQuarrie, Cyclotron production of ^{99m}Tc: Experimental measurement of the ^{100}Mo(p,x)^{99}Mo, ^{99m}Tc, and ^{99g}Tc excitation functions from 8 to 18 MeV, Nucl. Med. Biol. 38 (2011) 907–916.

3. K. Gagnon, M. Jensen, H. Thisgaard, J. Publicover, S. Lapi, S.A. McQuarrie, and T.J. Ruth, A new and simple calibration-independent method for measuring the beam energy of a cyclotron, Appl. Radiat. Isot. 69 (2011) 247–253.