

## Targets for Cyclotron Production of Tc-99m

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**Introduction:** The measured yields of direct  $^{99m}\text{Tc}$  production via  $^{100}\text{Mo}(\text{p},2\text{n})^{99m}\text{Tc}$  suggest that  $^{99m}\text{Tc}$  can be produced in quantities sufficient for supplying regional radiopharmacies<sup>i, ii, iii</sup>, thereby reducing our reliance on reactor-derived  $^{99}\text{Mo}$ . Cyclotron- and generator-produced  $^{99m}\text{Tc}$ -radiopharmaceuticals were shown to be radionuclidically, chemically and biologically equivalent, giving matching images and identical kinetic and biodistribution patterns in animals, indicating that a medical cyclotron can produce USP-compliant  $^{99m}\text{Tc}$ -radiopharmaceuticals for nuclear imaging procedures.<sup>iv, v</sup> In this work, several different  $^{100}\text{Mo}$  target configurations were investigated and thick target yields were measured, validating the production of clinically useful quantities of  $^{99m}\text{Tc}$  on a medical cyclotron.

**Target Holders:** Two different solid target holders were used to measure the thick target yields of the  $^{100}\text{Mo}(\text{p},2\text{n})^{99m}\text{Tc}$  nuclear reaction. The straight 90° target holder has a heat removal capacity of 1.5 kW and while the 30° tilted solid target holder has a heat removal capacity of 3.0 kW. Two different solid target holders (Advanced Cyclotron Systems Inc., Richmond, BC, Canada) were installed on three compact medical cyclotrons (TR-19, Cross Cancer Institute, Edmonton, AB, TR-19 Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke QC, Canada, GE PETrace, Lawson Health Research Institute, London ON, Canada).



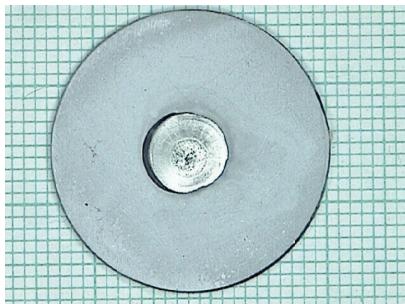
30° Solid Target Holder



Straight Solid Target Holder

**$^{100}\text{Mo}$  Targetry.** Molybdenum has been a metal of choice in accelerator targetry for several decades. With a high melting point, good thermal conductivity and chemical stability, molybdenum is nearly an ideal material for manufacturing high power targets. While a number of low and medium current cyclotron targets that use natural and enriched molybdenum isotopes have been developed and used for production of technetium isotopes:  $^{94}\text{Tc}$ ,  $^{96}\text{Tc}$  and  $^{99m}\text{Tc}$ <sup>vi</sup>, a reliable process for preparation of enriched molybdenum targets has not yet been implemented. A number of standard target manufacturing techniques are being evaluated: melting, sintering, pressing/pelletizing, rolling, plating from solutions or molten salts, formation of low melting temperature Mo alloys, brazing or soldering  $^{100}\text{Mo}$  to a target substrate, coating molybdenum with a protective layer, development of a thick target, plasma sputtering and other coating techniques.

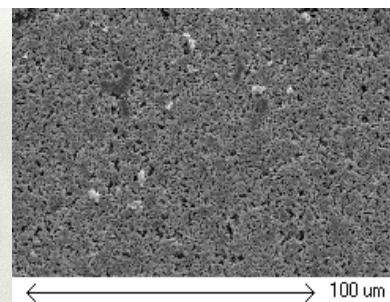
**Mo Target Preparation:** Between 100-450 mg natural and enriched  $^{100}\text{Mo}$  (99.5%) were pressed into 6 and 9.5 mm pellets at between 25,000 N and 100,000 N. The pellets were sintered in wet or dry hydrogen at 800-900°C, and subsequently mounted into a tantalum substrate, either by pressing or arc melting or electron beam melting at currents between 40-70 mA with different sweeping / focusing patterns.



1. Arc Melted Mo in tantalum



2. Pressed Mo in Ta (EOB)



3. SEM of pressed Mo

**$^{99m}\text{Tc}$  Production:**  $^{99m}\text{Tc}$  was produced via the  $^{100}\text{Mo}(p,2n)^{99m}\text{Tc}$  nuclear reaction on a 19 MeV medical cyclotron using an incident proton energy of 15-17 MeV at current between 14-52  $\mu\text{A}$ . After bombardment targets were subjected to electrochemical dissolution,  $^{99m}\text{Tc}$  was purified by ion-exchange chromatography and recovered as pertechnetate.



Electron beam melting of Mo to Tatarget substrate

**Results:** Up to 44.7 GBq (1.2 Ci) (EOB) of  $^{99m}\text{Tc}$  was produced after a 6-h bombardment at 16.4 MeV and 39  $\mu\text{A}$ . This corresponds to a thick target production yield of 0.25 GBq/ $\mu\text{A}/\text{h}$  (6.8 mCi/ $\mu\text{A}/\text{h}$ ) and 2.3 GBq/ $\mu\text{A}$  (63 mCi/ $\mu\text{A}$ ) at saturation and is in good agreement with literature data.<sup>i, ii, iii</sup> The radionuclide purity of the cyclotron-produced  $^{99m}\text{Tc}$  was >99.99%, as assessed by  $\gamma$  spectroscopy, exceeding USP requirements for generator-based  $^{99m}\text{Tc}$ . The content of other technetium isotopes was measured after allowing sufficient time (4 days) for  $^{99m}\text{Tc}$  decay and was below USP requirements of 0.01% for generator-produced  $^{99m}\text{Tc}$ . No other radionuclidic impurities were found. The radiochemical purity of cyclotron-produced  $^{99m}\text{TcO}_4^-$  was >99.5%, well above the USP requirement of 95%.

**Conclusion:** This study confirms that clinically useful quantities of  $^{99m}\text{Tc}$  can be produced on medical cyclotrons installed worldwide. Extrapolating these results to the optimal energy of 22-24 MeV indicates that over 2 TBq of  $^{99m}\text{Tc}$  can be produced daily for regional distribution on a high-current medium-energy cyclotron. Implementing networks of high-current medium energy cyclotrons would reduce reliance on nuclear reactors and attenuate the negative consequences associated with the use of fission technology.

<sup>i</sup> Scholten, B., Lambrecht, R.M., Cogneau, M., Vera Ruiz, H., Qaim, S.M., 1999. Excitation functions for the cyclotron production of  $^{99m}\text{Tc}$  and  $^{99}\text{Mo}$ . *Appl. Radiat. Isotopes* 51, 69–80

<sup>ii</sup> Takács, S.; Szűcs, Z.; Tárkányi, F.; Hermanne, A.; Sonck, M Evaluation of proton induced reactions on  $^{100}\text{Mo}$ : New cross sections for production of  $^{99m}\text{Tc}$  and  $^{99}\text{Mo}$ , *J. of Radioanalytical and Nuclear Chemistry*, 257, 1 , 2003, 195-201(7)

<sup>iii</sup> Lebeda, O.; Pruszynski, M.: New measurement of excitation functions for (p,x) reactions on natMo with special regard to the formation of  $^{95m}\text{Tc}$ ,  $^{96m+g}\text{Tc}$ ,  $^{99m}\text{Tc}$  and  $^{99}\text{Mo}$ , *Appl. Radiat. Isot.*, in press, (personal communication)

<sup>iv</sup> Guérin, B.; Tremblay, S; Rodrigue, S.; Rousseau, J.A.; Dumulon-Perreault, V.; Lecomte, R.; van Lier, J.E.; Zyuzin, A.; van Lier, E.J. Cyclotron Production of  $^{99m}\text{Tc}$ : An Approach to the Medical Isotope Crisis *J. Nuclear Med.*, 2010;51:13N-16N

<sup>v</sup> Zyuzin, A.; Guérin, B.; van Lier, E.J.; Tremblay, S; Rodrigue, S.; Rousseau, J.A.; Dumulon-Perreault, V.; Lecomte, R.; van Lier, J.E.; Cyclotron production of  $^{99m}\text{Tc}$  WTTCC 13, Abstract

<sup>vi</sup> Qaim, S.M., Production of high purity  $^{94m}\text{Tc}$  for positron emission tomography studies, *Nuclear Medicine and Biology*, 27, 4, 2000, 323-328