Abstract 038

Cyclotron Production of ^{99m}Tc

A. Zyuzin[1], B. Guérin[2], E. van Lier[1], S. Tremblay[2], S. Rodrigue[2], J.A. Rousseau[2], V. Dumulon-Perreault[2], R. Lecomte[2], J.E. van Lier[2]

[1]Advanced Cyclotron Systems Inc., Richmond, BC, Canada

[2]Sherbrooke Molecular Imaging Center, Université de Sherbrooke, QC, Canada

Introduction. Current global interruptions of ^{99}Mo supply, aging reactors, and the staggering costs of their maintenance have accelerated the search for alternative sources of ^{99m}Tc. Direct production of ^{99m}Tc via ^{100}Mo(p,2n)^{99m}Tc nuclear reaction can be considered as one of such alternatives. The feasibility of ^{99m}Tc production with a cyclotron was first demonstrated in 1971 by Beaver and Hupf[1] and confirmed by a number of researchers.[2,3,4,5] Measured yields indicate that up to 2.1 TBq (56 Ci) of ^{99m}Tc can be produced in 12 h using a 500 μA 24 MeV cyclotron. This amount will be sufficient to cover population base of 5-7 million assuming: 15 % ^{99m}Tc losses, an average injected dose of 25 mCi and a 10 hrs decay. Initial results of the target development and thick target yields are presented in the "Mo-100 development for direct Tc-99m Production" abstract. In this work we compared the chemical and radiochemical properties and *in vivo* behavior of cyclotron- and generator-produced ^{99m}Tc.[6]

Experiment. Targets, 6-mm diameter discs, were prepared by melting ^{100}Mo pellets (99.54% enrichment) onto tantalum backing supports. Targets were bombarded for 1.5–3 h with 15.5–17.0 MeV protons (14–52 μA), using a TR-19 cyclotron (ACSI). After bombardment, ^{100}Mo targets were partially dissolved and purified by the method of Chattopadhyay *et al.*[7] The radionuclide purity of the ^{99m}Tc was >99.99%, as assessed by γ-spectroscopy, exceeding USP requirements for generator-based ^{99m}Tc. Although small peaks corresponding to ^{99}Mo were observed in the initial solute, these were not detectable in the purified ^{99m}Tc-pertechnetate solution. Minute amounts of ^{97}Nb were also quantitatively separated from during target processing. The content of other technetium isotopes was measured after allowing sufficient time (4 days) for ^{99m}Tc decay. The presence of 0.0014% ^{96}Tc and 0.0010% ^{95}Tc at the end of bombardment, was below USP requirements of 0.01% for generator-produced ^{99m}Tc. No other radionuclidic impurities were found. The radiochemical purity of cyclotron-produced [^{99m}Tc]TcO_4^-, as determined by instant thin-layer chromatography was >99.5%, well above the USP requirement of 95%. The content of ground state ^{99g}Tc ($T_{½}$ = 2.1 × 10^5 years) was not determined in these experiments and is one of the tasks for future work. For imaging studies, both cyclotron- and generator-produced ^{99m}Tc were formulated as 3 different radiopharmaceuticals: ^{99m}Tc-pertechnetate for thyroid imaging, ^{99m}Tc-methylene diphosphate (^{99m}Tc-MDP) for bone scanning, and ^{99m}Tc-hexakis-2-methoxy*iso*butyl isonitrile (^{99m}Tc-MIBI) for heart imaging. These radiopharmaceuticals account for more than 75% of all routine ^{99m}Tc scans currently used in diagnostic nuclear medicine. The latter two radiopharmaceuticals were prepared using commercially available kits. Labeling efficiency for the bone imaging agent ^{99m}Tc-MDP and heart imaging agent ^{99m}Tc-MIBI were 98.4% and 98.0%, respectively, well above USP requirements of >90%.

Animal Scans. The bio-distributions of ^{99m}Tc-pertechnetate, ^{99m}Tc-MDP, and ^{99m}Tc-MIBI, prepared with either cyclotron- or generator-produced ^{99m}Tc, were assessed in a healthy rat model. For each experiment 2 animals were simultaneously injected with a 0.3-mL physiologic saline solution containing 34–90 MBq of the selected ^{99m}Tc-radiopharmaceutical, prepared either with cyclotron- or generator-produced ^{99m}Tc. Dynamic acquisitions were continued over a 2 h period. At the end of scanning, the rats were killed and dissected to

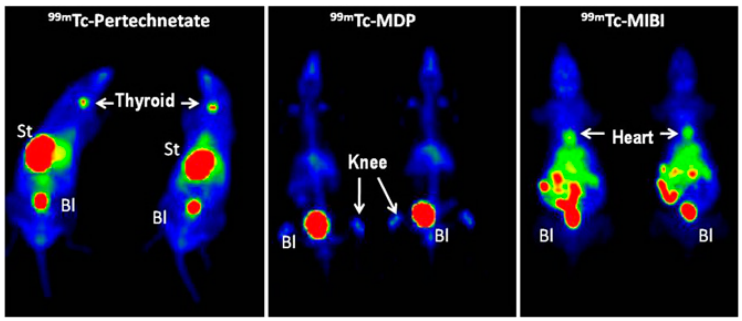

Figure 1. Whole-body scintigrams of two rats 2 h after administration of: 90 MBq of ^{99m}Tc-pertechnetate; 34 MBq of ^{99m}Tc-MDP; 15 MBq of ^{99m}Tc-MIBI, prepared from cyclotron- (right image) and generator-produced ^{99m}Tc (left image).

measure activities of target tissues. Static images obtained 2 h after administration of each of these ^{99m}Tc-radiopharmaceuticals show matching ^{99m}Tc distribution patterns, clearly delineating the thyroid with ^{99m}Tc-pertechnetate, skeleton with ^{99m}Tc-MDP, and heart with ^{99m}Tc-MIBI (Fig. 1). Uptake kinetics calculated over the target organs (thyroid, bones, and heart), show identical uptake patterns for the cyclotron- and generator-produced ^{99m}Tc-radiopharma-ceuticals (Fig. 2). Tissue activities from dissected samples collected 30 min after the end of imaging with ^{99m}Tc-MDP and ^{99m}Tc-MIBI also show matching patterns between cyclotron- and generator-derived ^{99m}Tc preparations (Fig. 3).

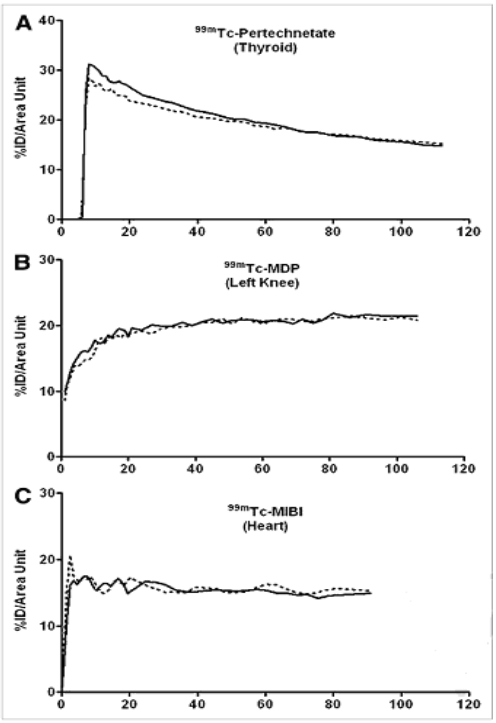

Figure 2. Time/radioactivity curves derived from regions of interest drawn around target organs (Fig.1) Dotted line: cyclotron-produced ^{99m}Tc, Solid line: generator produced ^{99m}Tc. Radioactivity is expressed as percentage of injected dose per unit area, corrected for radioactive decay.

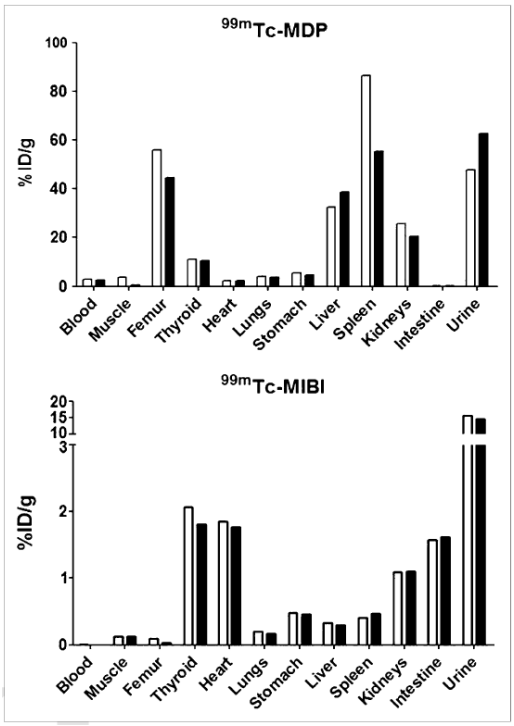

Figure 3. Tissue uptake in healthy rats, expressed as percentage of injected dose per gram of tissue, 2.5 h after intravenous injection of 34 MBq of ^{99m}Tc-MDP or 15 MBq of ^{99m}Tc-MIBI, prepared from cyclotron-produced ^{99m}Tc (open bars) or generator-produced ^{99m}Tc (solid bars).

Conclusion. The results of these *in vivo* experiments and quality control tests support the concept that cyclotron-produced ^{99m}Tc is suitable for preparation of USP-compliant ^{99m}Tc radiopharmaceuticals. Establishing decentralized networks of medium energy cyclotrons capable of producing large quantities of ^{99m}Tc may effectively complement the supply of ^{99m}Tc traditionally provided by nuclear reactors, at a fraction of the cost of a single nuclear reactor production facility, while sustaining the expanding need for other medical isotopes, including short-lived positron emitters for PET imaging.

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