BARC–TIFR Pelletron Linac Facility Beam Time Request @2024

Title of the Experiment: Production of ^{52}Mn via ^{nat}Cr (p, n) ^{52}Mn reaction and its radiochemical separation for preparation of radiopharmaceuticals

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Motivation of the experiment: Manganese-52 ($T_{½}$ =5.6 d, $E_{\beta+max}$ = 575 keV; average $E_{\beta+}$ = 242 keV, branching ratio β^+ = 29.4 %) is an emerging radiometal that holds tremendous potential in nuclear medicine. The ^{52}Mn-based radiopharmaceuticals can be used in multimodal imaging involving positron emission tomography (PET) and manganese-enhanced magnetic resonance imaging (MEMRI), which provide accurate diagnosis of disease in various organs such as liver, pituitary glands, bone and intestine in preclinical and clinical settings. The radioisotope can be produced in a low-energy particle accelerator using natural Cr-metal target via ^{52}Cr (p, n) ^{52}Mn reaction. Production, radiochemical separation and purification are the vital steps towards obtaining no-carrier-added (NCA) grade ^{52}Mn in a form suitable for formulation of radiopharmaceuticals for cancer imaging.

Beam details: Proton beam, proton beam energy: 16 MeV, current: 200 nA, beam port: 6M.

Buncher requirement: ~~Yes/~~ No

Number of shifts (1 shifts=8 hr.) required: 12 shifts

Experiment details:

1. **Objective of Experiment:**

Manganese-52 ($T_{½}$ =5.6 d, $E_{\beta+max}$ = 575 keV; average $E_{\beta+}$ = 242 keV, branching ratio β^+ = 29.4 %) is an emerging radiometal that holds tremendous potential in nuclear medicine [1-4]. The ^{52}Mn-based radiopharmaceuticals can be used in multimodal imaging involving positron emission tomography (PET) and manganese-enhanced magnetic resonance imaging (MEMRI), which provide accurate diagnosis of disease in various organs such as liver, pituitary glands, bone and intestine in preclinical and clinical settings. The radioisotope can be produced in a low-energy particle accelerator using natural Cr-metal target via ^{52}Cr (p, n) ^{52}Mn reaction. Production, radiochemical separation and purification are the vital steps towards obtaining no-carrier-added (NCA) grade ^{52}Mn in a form suitable for formulation of radiopharmaceuticals for cancer imaging. There have been several reports on the radiochemical separation of ^{52}Mn from Cr target using precipitation, ion exchange and solvent extraction-based methods [1-4]. Most of these separation methods involves multiple steps, cumbersome and hence difficult to execute in a shielded facility for preclinical studies. In this study, an efficient and facile electrochemical method will be developed for radiochemical separation of ^{52}Mn from the irradiated target for formulation of radiopharmaceuticals.

References:

[1] Lewis CM, Graves SA, Hernandez R, Valdovinos HF, Barnhart TE, Cai W, Meyerand ME, Nickles RJ, Suzuki M. ^{52}Mn production for PET/MRI tracking of human stem cells expressing divalent metal transporter 1 (DMT1). Theranostics. 2015;5(3):227-39.

[2] Pyles JM, Massicano AVF, Appiah JP, Bartels JL, Alford A, Lapi SE. Production of ^{52}Mn using a semi-automated module. Appl Radiat Isot. 2021;174:109741.

[3] Fonslet J, Tietze S, Jensen AI, Graves SA, Severin GW. Optimized procedures for manganese-52: Production, separation and radiolabeling. Appl Radiat Isot. 2017; 121:38-43.

[4] Pyles JM, Omweri JM, Lapi SE. Natural and enriched Cr target development for production of Manganese-52. Sci Rep. 2023;13(1):1167.

2. Description of Experiment:

In this study, 250 mg of natural Cr-metallic powder will be pressed into a pellet of 5 mm diameter and 100 μm thickness using hydraulic press (20 kN cm^{-2}). The pellet will be covered with 1 mil (0.0254 mm) aluminum foil to prevent sputtering of the target material during irradiation. The target will be irradiated with 16 MeV proton at 200 nA current for 96 h. After irradiation, the radioactive target will be transferred to Radiopharmaceuticals Division, BARC with regulatory approval from the BARC Safety Council. The irradiated target will be dissolved in HNO_3 in a shielded facility. ^{52}Mn will be electrochemically separated from the radioactive solution by selective electrodeposition of the radioisotope on a platinum electrode. Subsequently, the ^{52}Mn radioactivity will be stripped in 0.1 M HCl solution. Rigorous quality control studies will be performed by determining the radionuclidic purity (by gamma spectrometry using HPGe detector coupled with multichannel analyser), radiochemical purity (by thin layer chromatography), chemical purity (by inductively coupled plasma atomic emission spectrometry) to determine the suitability for preclinical studies. The radioisotope will be used for labeling peptides and antibodies and the radiolabeled formulation will be intravenously administered in mice model for visualization of the disease by positron emission tomography (PET) imaging.

- **Whether the experiment is part of PhD /Post Doc. Work:** No
- **Details of Beam time availed of in recent past on this experiment and / or by the PI:** In the recent past, proton beam time was availed for production of ^{69}Ge and ^{44}Sc for formulation of PET radiopharmaceuticals.
- **Details of papers published / presented in journals / symposia, etc. based on recent experiments:**

[1] Intrinsically ^{69}Ge-Labeled Gum Arabic Glycoprotein Coated Gallium Oxide Nanoparticles: A New Nanoprobe for PET Imaging

Sanchita Ghosh, Sourav Patra, Apurav Guleria, Annu Balhara, Santosh Kumar Gupta, Avik Chakraborty, Sutapa Rakshit, Sanjay Vishwanath Thakare, Anil Krishna Debnath, Sudipta Chakraborty, Rubel Chakravarty*, Ind. Eng. Chem. Res. 2023, 62, 47, 20269–20279.

[2] Accelerator Production, Radiochemical Separation and Nanoradiopharmaceutical Formulation using ^{69}Ge: A Next Generation PET Probe

Sourav Patra, Sanchita Ghosh, Khajan Singh, Bijaideep Dutta, Avik Chakraborty, Naresh Gamre, S. V. Thakare, K. C. Barick, Sutapa Rakshit, P. A. Hassan, Sudipta Chakraborty, Rubel Chakravarty*

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