PRODUCTION AND APPLICATIONS OF LONG-LIVED POSITRON-EMITTING RADIONUCLIDES

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Abstract

Positron emission tomography (PET) is a medical imaging modality capable of determining the in vivo spatial distribution of a biologically relevant molecule which has been labeled with a positron-emitting isotope. The use of molecules such as monoclonal antibodies and nanoparticles for therapeutic and diagnostic applications has expanded preclinically in recent years. As these larger molecules tend to have longer circulation times and slow clearance kinetics, positron-emitting isotopes with half-lives longer than conventional medical radioisotopes are required for PET applications.

This dissertation details methods for the production of ^{51}Mn ($t_{1/2}$: 45.4 min), ^{52g}Mn ($t_{1/2}$: 5.59 d), ^{64}Cu ($t_{1/2}$: 12.7 h), ^{76}Br ($t_{1/2}$: 16.2 h), ^{89}Zr ($t_{1/2}$: 3.27 d), and ^{194}Au ($t_{1/2}$: 38.0 h) on low-energy medical cyclotrons, including targetry considerations, radiochemical separation methods, and analysis of resulting purity. Pursuant to the production of these isotopes, several instrumentation developments have been made including implementation of an automatic nuclide identification library for gamma spectroscopy; development of methods for dead time correction and background estimation in auto-gamma counting; and the creation of a new linearly-filled Derenzo-type PET phantom. Measurement of the radioactive half-lives of ^{51}Mn and ^{52g}Mn are presented in addition to their use in a variety of preclinical molecular imaging applications, including immunoPET, stem cell tracking, functional β-cell mass determination, and probing the impact of isoflurane on acute pancreatic function. An analytic model of effective specific activity is formed and tested against preliminary trace metal analysis results. Measurements of excitation functions for the large-scale production of medically relevant isotopes, including ^{52g}Mn, at the Los Alamos National Laboratory Isotope Production Facility (100 MeV p^+) are presented. The results described herein have enabled and informed a variety of novel investigations in the fields of nuclear medicine and molecular imaging.