Abstract

Targeted alpha therapies using actinium-225 (^{225}Ac, $t_{1/2}$ = 9.9 d) have shown an ability to treat advanced metastatic disease, despite the insufficient availability of this radionuclide that limits their development. Radiation dosimetry for ^{225}Ac-radiopharmaceuticals is also complicated by multiple nuclides in the ^{225}Ac decay chain. This work describes efforts to produce ^{225}Ac and use multi-nuclide SPECT imaging to individually measure the biodistribution of ^{225}Ac progeny, ^{221}Fr and ^{213}Bi. Initial ^{225}Ac production used $^{\mathrm{Nat}}$U-spallation-produced and mass-separated ion beams to produce up to 8.6 MBq of ^{225}Ra, an ^{225}Ac parent, and up to 18 MBq of ^{225}Ac. This material was used to characterize performance of ^{225}Ac decay chain imaging on a microSPECT/PET/CT scanner in terms of contrast recovery, spatial resolution, and noise. Efforts to produce larger ^{225}Ac quantities used the proton spallation of thorium with focus on using ^{225}Ra/^{225}Ac generators to provide an Ac product with reduced ^{227}Ac ($t_{1/2}$ = 21.8 y) content, a nuclide with economically prohibitive and low limits on waste disposal. Targets containing Th metal foils were irradiated for approximately 36 hours with a 72 μA proton beam, producing (521 ± 18) MBq of ^{225}Ac and (91 ± 14) MBq of ^{225}Ra. These irradiations enabled ^{232}Th(p,x) cross sections measurements at 438 MeV for ^{225}Ac, ^{225}Ra, and ^{227}Ac: (13.3 ± 1.2) mb, (4.2 ± 0.4) mb, and (17.7 ± 1.7) mb, respectively. 35 other cross sections have been measured and compared to FLUKA simulations; measured and calculated values generally agree within a factor of 2. Ac was separated from irradiated thorium and co-produced radioactive spallation and fission products using a thorium peroxide precipitation followed by cation exchange and extraction chromatography. Tracer studies demonstrated this method's ability to separate Ac from most other elements, providing a directly produced Ac product (^{227,225}Ac†) with measured ^{227}Ac content of (0.15 ± 0.04)%. The second, indirectly produced Ac product (^{225}Ac*) with ^{227}Ac content of $<7.5\times10^{-5}$% is obtained by repeating the final extraction chromatography step with the ^{225}Ra-containing fraction. The ^{225}Ra-derived ^{225}Ac* showed similar or improved quality compared to the initial, directly produced ^{227,225}Ac† product in terms of chemical purity and radiolabeling capability.