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Automated Production of Alpha-Emitting Therapeutic Radionuclides

Alpha particle therapy is predicated on high energy emissions (MeV) with path lengths of only several cell diameters (μm). It has generated tremendous interests since the approval of the first in class alpha particle emitting radionuclide, Xofigo or 223Ra-dichloride. This agent is utilized for the treatment of castrate resistant prostate cancer, with successful outcomes with patient end-of-life quality improvements and overall survival extension of 4 months. Consequently, attempts to further expand 223Ra-dichloride applications are ongoing. Many trials for expanded alpha particle emitter work are underway, particularly in the combination therapy space, however few if any have been evaluated preclinically. There is little scientific rationale for many of these proposed trials. A central issue is the lack of access to Radium-223 for preclinical testing. To address this issue, we are developing automated production tools capable of supplying 223Ra and 227Th dedicated for preclinical research. Our solution is a permanent automated production unit of ready-to-inject 223Ra-Dichloride and ready to label 227Th with low isotopic parent breakthrough, high throughput and complete parent recovery post-production for regeneration. The long lived Actinium-227 source is immobilized on a cationic polymeric resin cartridge followed by a separation and elution of each isotope in high radiopurity. The chromatographic radionuclide separator consists of an automated fluidic device allowing for a fast, low-dose exposure and reduced loss system. To this end, a modularly concentrated solution of high radioactive content is generated formulated as a ready-made drug: 223Ra solvated in sodium citrate 0.03M and saline 0.9%; as prepared for patient dose. Similarly, 227Th-Nitrates can be isolated and utilized for further radiolabeling procedures. Live monitoring of radioactive elution is conducted utilizing a gamma-detector looped to the automated separator. Further quality control is executed using High Purity Germanium detector to define the radiochemical purity of produced 223Ra or 227Th and the recovery of isotopic parents 227Ac and/or 227Th. Finally, through acidic wash the isotopic parents are recollected off the resin for recycling into a fresh cartridge for the next production cycle. To the best of our knowledge, this is the first automated synthetic unit proposed for simultaneous production of 223Ra and 227Th for preclinical production. . This approach offers a fast, low exposure and high recovery strategy to producing alpha-emitting material for research use while recollecting the isotopic parents for repeated production. In a time when restricted access makes alpha particle therapy research cost-prohibitive, having a high quality on-site production may open commercial opportunities to supply nationwide needs for preclinical testing of Radium-223 and Thorium-227.

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