Canadian Association of Physicists
Association canadienne des physiciens et physiciennes

Contribution ID: **2515** Type: **Invited Speaker / Conférencier(ère) invité(e)**

Production and purification of radium-225 and actinium-225 at TRIUMF's Isotope Separation On-line (ISOL) facility and subsequent radiolabeling studies with alpha-emitter actinium-225

Tuesday, 4 June 2019 13:15 (30 minutes)

With four alpha particles in its decay chain, actinium-225 (²²⁵Ac; t_{1/2} = 9.9 d) is a promising candidate isotope for Targeted Alpha Therapy (TAT) when coupled with a disease targeting vector. The current limited global supply of ²²⁵Ac (67 GBq/year), and lack of appropriate chelating ligands able to complex this isotope has delayed the advancement of ²²⁵Ac-drugs towards the clinic [1]. Herein, we describe efforts to produce, purify, and evaluate the radiolabeling ability of ²²⁵Ac, by leveraging TRIUMF's ISAC isotope separation on-line (ISOL) facility. ²²⁵Ac alongside, parent nuclide radium-225 (²²⁵Ra; t_{1/2} = 14.8 d), were produced via spallation of uranium carbide targets with 480 MeV protons on ISOL's radioactive beam facility. Downstream from the target, a high-resolution mass separator was used to isolate ²²⁵Ra and ²²⁵Ac ions from other isotopes produced in the spallation process. The 28 keV beam was directed towards an aluminum holder in which the ions were implanted at a depth between 10 and 30 nm. Implantation yields of 1.6x10⁸ and 5.7x10⁷ ions/s resulted in isolation of 1.0 –7.5 and 1.4 –18.0 MBq of ²²⁵Ra and ²²⁵Ac, respectively. The implanted activity was etched off the sample stage with dilute acid, and ²²⁵Ac was separated in >99% yield from ²²⁵Ra using solid phase extraction (DGA resin) [2]. This method has resulted in the isolation of MBq quantities of both ²²⁵Ra and ²²⁵Ac, where the former can be stored and used as a generator for ²²⁵Ac. Subsequently, ²²⁵Ac coordination properties with a library of acyclic chelators based on picolinic acids (such as H₄(CHX)octapa [3],[4] [N₄O₄], and H₆phospa [5] [N₄O₆]) along with commercial standard DOTA (N₄O₄) were evaluated by testing radiolabeling efficiency, and complex stability. In conclusion, we have successfully established a production method for ²²⁵Ac which yields activities adequate for pre-clinical screening. Furthermore, several novel actinium-chelators showed promising ²²⁵Ac radiolabeling properties and kinetic inertness in vitro compared to DOTA, and will be tested in vivo in future studies.

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Session Classification: T3-3 Nuclear Astrophysics/Structure and Medical Isotopes in honour of Prof. John D'Auria PM-1 (DNP) | Astrophysique nucléaire / Structure et isotopes médicaux en hommage au prof. John D'Auria PM-1 (DPN)

Track Classification: Symposia Day - Nuclear Astrophysics and Medical Isotopes (in honour of Prof. John D'Auria)