University of Basel

Swiss Nanoscience Institute

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Center of Excellence supported by the University of Basel and the Canton of Aargau

Molecular containers: Enabling the challenging separation of radionuclides via the entrapment inside

PI: Konrad Tiefenbacher, Department of Chemistry, University of Basel, konrad.tiefenbacher@unibas.ch
CoPI: Patrick Steinegger, Laboratory of Radiochemistry, Paul Scherrer Institute, patrick.steinegger@psi.ch

This Ph.D. project aims to introduce **a novel concept** for the separation of radionuclides, exemplified by the exploration of a novel ^{44}Ti/^{44}Sc generator principle. In contrast to adsorption to a solid support, we propose a **molecular encapsulation/destruction approach** to readily separate radionuclides. The introduction of this novel separation concept may have tremendous application potential.

Nuclear medicine plays an integral part in clinical practice worldwide. Positron emission tomography (PET) and radionuclide therapy (RNT) have contributed immensely in this regard. An accelerator-independent provision of radionuclides can be established via so-called radionuclide generators. Hereto, a long-lived mother radionuclide ensures the provision of the usually much shorter-lived daughter radionuclide at regular intervals.[1] ^{44}Sc is a highly attractive isotope as it features a comparably long half-life ($t_{1/2}$ = 4 h), thus enabling late timepoint imaging and a better spatial resolution due to the lower positron energy.[1] Moreover, the coordination properties of the trivalent ^{44}Sc are very favorable, enabling the formation of stable radioconjugates. However, the development of a suitable ^{44}Ti/^{44}Sc generator, featuring an effective separation of the ^{44}Ti mother radionuclide from the daughter radionuclide ^{44}Sc, has been elusive. Previous approaches were exclusively relying on adsorption-based separation techniques and have been limited by a significant ^{44}Ti breakthrough, low yields of ^{44}Sc, and/or the requirement of further processing of the obtained ^{44}Sc solution.[1]

The main objective of this proposal is to explore an alternative separation technique for radionuclides, using ^{44}Ti/^{44}Sc as a first example. It is based on the entrapment of the mother radionuclide inside a closed supramolecular container ("carcerand"). As the carcerand is insoluble in aqueous solutions, the breakthrough of ^{44}Ti should be suppressed. Only due to the decay of ^{44}Ti to ^{44}Sc, and the concomitant emission of nuclear radiation, the molecular container will likely break (due to radiolysis) and will release the formed ^{44}Sc. The thus liberated ^{44}Sc can be directly extracted with a physiological NaCl solution. This will be a significant advantage over current adsorption- based separation techniques, which require acid additives in the eluent to enable the release of the radionuclide. The project, thus, has the potential to overcome currently faced limitations. The project is structured in three work packages (WPs).

WP1, Establishing molecular containers ("carcerands") for metal cation binding. First, we will develop a synthesis of suitable molecular containers, and fully characterize them.

WP2, Radiation hardness and ^{44}Ti/^{44}Sc separation. In the next step, the radiation hardness of the titanium- carcerand will be tested with external gamma-irradiation using available strong sources of ^{60}Co (EPFL) or ^{137}Cs (PSI).

WP3, Exploration of the application scope. The new carcerand-based separation will be tested with increasing amounts of ^{44}Ti toward clinically relevant activities

Your profile

We are looking for a highly self-motivated researcher. Ideally, you are a well-trained organic chemist with a strong background in synthetic organic chemistry. You have performed multi-step synthetic sequences yourself before, and can independently separate compounds via column chromatography. Experience in radiochemistry is of advantage but not a prerequisite. You will be jointly supervised by KT and PS. Initially, you will mainly work in the KT group and focus on WP1. As soon as titanium entrapment has been achieved, the application potential will be explored within WP2&3 in the LRC/CRS at the PSI.

(1) Schmidt, C. E.; Gajecki, L.; Deri, M. A.; Sanders, V. A. Current State of 44Ti/44Sc Radionuclide Generator Systems and Separation Chemistry. *Curr. Radiopharm.* **2023**, *16* (2), 95–106.