Radioisotopes are important tools for tracing biological, chemical, and physical processes. The National Superconducting Cyclotron Laboratory (NSCL) and the upcoming Facility for Rare Isotope Beams (FRIB) have the potential to supply unique radioisotopes that are otherwise difficult to produce. The challenge of obtaining these rare isotopes from NSCL and FRIB is in the need for rigorous chemical or physical purification of sub-nanogram quantities of individual elements from a complex mixture of spallation and fragmentation products. The purpose of my research is to parse and purify the stock of co-produced radionuclides to obtain both high radioisotopic purity and high specific activity for application in basic science, medical, chemical and biological research. Of particular interest are transition and rare earth radiometals for use in the development of new diagnostics and therapeutics against invasive disease.

**Radiometals in Medicine** – Research into the molecular identity of cancerous and other malignant cells has identified biological vectors that can seek out disease sites in vivo. In order to trace the biodistributions and pharmacokinetics of these new vectors, preclinical Positron Emission Tomography (PET) has expanded beyond the organic and pseudo-organic radionuclides (¹³C, ¹⁴N, ¹⁸O, ¹⁸F) to include a host of longer-lived and unconventional radiometals (e.g. ⁴⁷Sc, ⁴⁷Ti, ⁵²Mn, ⁶⁴Cu, ⁸⁹Zr, and ¹⁴⁰Nd). Beyond receptor- and epitope-based PET, radiometals also facilitate development of metal-based drugs, allow tracing of the native and mimetic nature of metals in the body, can be used to track nanoparticle drug delivery vehicles, and in some cases have unique exploitable decay properties (e.g. ¹⁴⁰Nd in Figure 1 below). Further, the diagnostic metals are often isotopically matched to therapeutic nuclides, motivating a rapid transition from diagnostic imaging to targeted radionuclide therapy.

A new water-cooled beamstop at NSCL will provide access to a selection of radiometals including ⁴⁷Sc, a therapeutic analog to the positron emitter ⁴⁷Sc. ⁴⁷Sc forms following ⁴⁷Ca decay (Figure 2), which is co-produced in high yield during ⁴⁷Ca irradiations at NSCL.

![Figure 1: (left) Pre- and (right) post-mortem PET/CT scan of a mouse 16h after injection with a somatostatin receptor 2 (sst2) targeting peptide, DOTA-LM3, labeled with ¹⁴⁰Nd. The white circle is drawn over the pancreas (sst2 +) where the difference in the pre- and post-mortem pancreatic signal is due to rapid diffusion of ¹⁴⁰Nd’s short-lived daughter nuclide, ¹⁴⁰Pr, from the highly perfused pancreas into the blood stream. With further development, similar techniques with ¹⁴⁰Nd may be used to determine the in vivo internalization status of labeled therapeutics.]

![Figure 2: A simplified decay scheme for ⁴⁷Ca and ⁴⁷Sc. The low energy beta particles from ⁴⁷Sc are therapeutic, and the 159 keV gamma ray has an appropriate energy for imaging with single photon computed tomography (SPECT).](image)

Isolation of ⁴⁷Ca allows production of a ⁴⁷Sc generator that extends the usable lifetime of ⁴⁷Sc in addition to providing it in high purity and with high specific activity.

**Gregory W. Severin**

**Assistant Professor**

Radiochemistry

*Assistant Professor, 2012-2015, Technical University of Denmark; Senior Researcher, 2015-2016, Technical University of Denmark.*

517-353-1087

**Selected Publications**

* Novel Preparation Methods of ⁵²Mn for ImmunoPET Imaging, Graves, SA et al., Bioconjug. Chem. 2015, 26(40), 2118-2124.
* Bringing radioracing to titanium-based antineoplastics: solid phase radiosynthesis, PET and ex-vivo evaluation of antitumor agent [⁴⁷Ti(salan)]Ti(dipic), Severin, GW et al., J. Med. Chem. 2015, 58(18), 7591-7595.