

Fig. 1 (abstract SP-098). Structure of $\text{Re}(\text{CO})_3\text{-Bn-NODAGA-Ser}_2\text{-RM}_2$.

ongoing. The excellent *in vitro* stability and hydrophilic character of the complex show great promise, warranting further evaluation in *in vitro* receptor affinity and *in vivo* biodistribution studies.

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SP-099

Evaluation of [^{47}Sc]Sc-HOPO toward radioscandium based radiopharmaceuticals

¹Michael Phipps, ²Shelbie Cingoranelli, ³Jannatul Ferdous, ³N. V. S. Dinesh Bhupathiraju, ²Suzanne Lapi, ⁴Jason Lewis, ³Lynn Francesconi, ⁵Melissa Deri

¹University of New York, United States, ²University of Alabama at Birmingham, United States, ³Hunter College, United States, ⁴Memorial Sloan Kettering Cancer Center, United States, ⁵Lehman College, CUNY, United States

Objectives: Scandium-44 (^{44}Sc) ($t_{1/2} = 4$ h, $E_{\beta^+ \text{max}} = 1.47$ MeV, $\text{BR}_{\beta^+} = 94.3\%$) and ^{47}Sc ($t_{1/2} = 3.3$ d, $E_{\beta^+ \text{max}} = 0.6$ MeV, $\text{BR}_{\beta^+} = 100\%$) are a potential matched pair of radionuclides for developing theranostic agents for positron emission tomography (PET) imaging and targeted radioimmunotherapy. ^{47}Sc has a gamma emission ($E_\gamma = 159$ keV) suitable for use in single photon emission computed tomography (SPECT) imaging. DOTA is a standard chelator for many radiometals and has been radiolabeled with ^{44}Sc [1]. However, DOTA may not be the optimal chelator for radioscandium, so there is interest in developing better Sc chelators [2]. 3,4,3-LI(1,2-HOPO) (referred to as HOPO) can form octadentate constructs through its oxygen donors and demonstrates high affinity and fast kinetics with hard positive ions at the macroscopic and tracer scales [3–5].

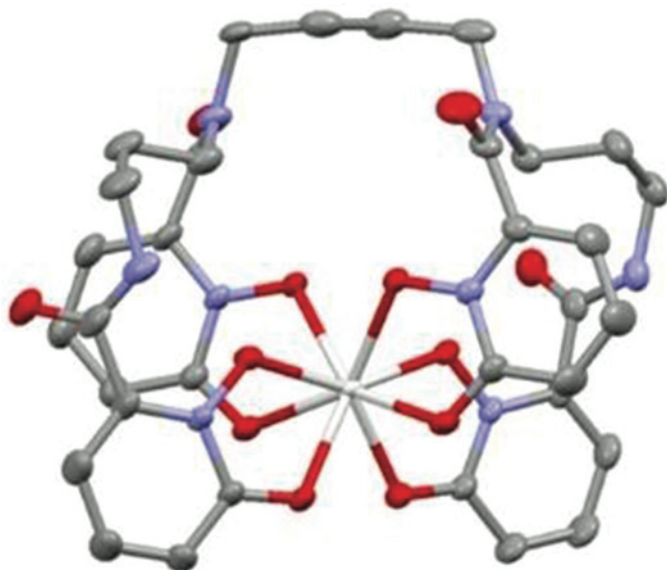


Fig. 1 (abstract SP-099). Sc-HOPO structure extracted from X-ray crystal structure. H atoms are excluded.

Methods: Before radioactive work, stable ^{45}Sc -HOPO was characterized by methods including IR, $^1\text{H-NMR}$, $^{45}\text{Sc-NMR}$, HPLC, mass spectrometry, and crystallography. ^{47}Sc was produced via cyclotron at the University of Alabama at Birmingham. Radiochemically pure ^{47}Sc was produced from an enriched $^{50}\text{TiO}_2$ target by the $^{50}\text{Ti}(p,\alpha)^{47}\text{Sc}$ reaction and separated adapting methods from Loveless et al. [6]. Targets were irradiated at 24 MeV on the UAB TR24 cyclotron. ^{47}Sc was extracted using BDGA resin, isolated in 0.1 M HCl, and shipped to Memorial Sloan Kettering Cancer Center. The radiolabeling of HOPO and DOTA with ^{47}Sc at 37°C was optimized and compared. Stability studies, including EDTA challenge at various pH values (5, 6, 7, 8), metal ion challenge (with Fe^{3+} , Mg^{2+} , Cu^{2+} , Zn^{2+}), and human serum stability were evaluated for ^{47}Sc -DOTA and ^{47}Sc -HOPO. Radiolabeling and stability studies were monitored by ITLC using 50 mM EDTA at pH 5. Biodistribution and SPECT imaging with free ^{47}Sc and ^{47}Sc constructs in healthy mice are underway.

Results: Radiolabeling optimization resulted in 90% and >99% RCY at 37°C for ^{47}Sc -DOTA and ^{47}Sc -HOPO respectively. Formation of

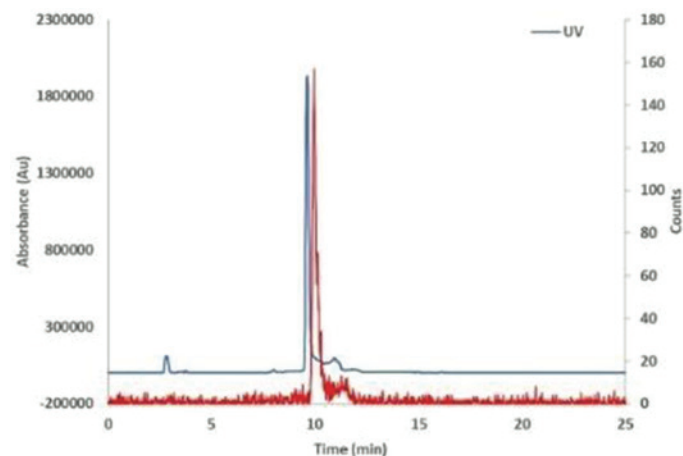


Fig. 2 (abstract SP-099). HPLC coinjection of ^{47}Sc -HOPO with a nonradioactive Sc-HOPO.

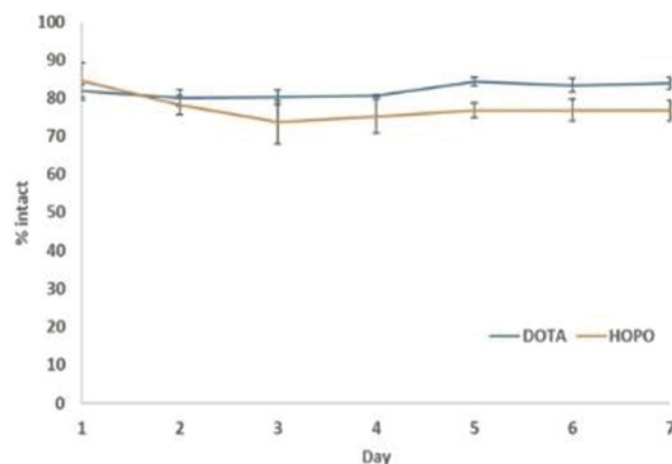


Fig. 3 (abstract SP-099). Human serum stability of ^{47}Sc -DOTA and ^{47}Sc -HOPO.

^{47}Sc -HOPO was verified by HPLC coinjection with a nonradioactive, well-characterized ^{45}Sc -HOPO standard. ^{47}Sc -DOTA and ^{47}Sc -HOPO had comparable performance in stability studies.

Conclusions: ^{47}Sc -HOPO has been synthesized and has demonstrated high stability under various conditions. Its *in vivo* behavior is being investigated as well. This work will be followed by the evaluation of the bifunctional analogue *p*-SCN-Bn-HOPO as well as HOPO-antibody conjugates formed with the bifunctional ligand. In addition, analogous HOPO chelators such as 3,3,3-Li(1,2-HOPO) will be investigated.

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SP-100

An improved separation scheme for ^{44}Sc purification from proton irradiated calcium

¹Elena Kurakina, ²Luke Wharton, ³Cornelia Hoehr, ¹Eldar Magomedbekov, ⁴Dmitry Filosofov, ³Valery Radchenko
¹Mendelev University of Chemical Technology of Russia, Russian Federation, ²University of British Columbia, Canada, ³TRIUMF, Canada, ⁴Joint Institute for Nuclear Research, Russian Federation

Objectives: ^{44}Sc is of high clinical interest for application as a positron emission tomography (PET) radionuclide due to its favourable nuclear properties ($t_{1/2} = 3.97$ h, $E_{\beta^+} = 1.47$ MeV, branching ratio 94.3%) and known chelation chemistry. ^{44}Sc in combination with ^{47}Sc ($t_{1/2} = 3.35$ d, β^-) can be used for simultaneous PET imaging and targeted radionuclide therapy [1]. In the present work ^{44}Sc was produced via $^{44}\text{Ca}(p,n)^{44}\text{Sc}$ using TR-13 cyclotron at TRIUMF and an improved separation scheme for ^{44}Sc from bulk calcium was designed.

Methods: ^{44}Sc was produced by irradiating ^{nat}Ca targets (≈ 68 mg) with 12.8 MeV protons during 1 h at beam current of 10 μA . For scandium purification, a combination of solid phase extraction and ion-exchange chromatography techniques was applied. The $\text{Ca}^{2+}/\text{Sc}^{3+}$ separation scheme consisted of two steps: separation on a column filled with DGA resin (branched, 50–100 μm) using HCl solutions and purification on a column with cation-exchanger Dowex 50Wx8 (200–400 mesh) using ammonium α -hydroxyisobutyrate (pH=4.8). Further radiolabeling was performed with 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) at 10^{-3} – 10^{-7}M and assessed via instant thin layer chromatography.

Results: At the end of bombardment 100 ± 5 MBq of ^{44}Sc was produced. Saturation yield for ^{44}Sc was estimated to be 61 ± 5 MBq/ μA . $\text{Sc}^{3+}/\text{Ca}^{2+}$ separation factor was $> 10^6$. The RCY for the proposed scheme was $95 \pm 2\%$. Purified ^{44}Sc was applied successfully for radiolabeling of DOTA at 10^{-3} – 10^{-5}M (0.5 M NH_4OAc , pH=5.0, 85°C , 40 min, RCY = 100%).

Conclusions: The proposed scheme demonstrated good potential for routine and cost-effective production of ^{44}Sc . The described method has several advantages over conventional techniques: using cation-exchanger increases the separation factor and purity of the final fraction following extraction chromatographic resin, elution with ammonium α -hydroxyisobutyrate serves as a suitable medium for further radiolabeling. Finally, radiolabeling with DOTA showed the applicability of final product for radiopharmaceutical application.

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SP-101

Extraction chromatographic separation of selenium and arsenic for accelerator target processing

¹Jakob Baumeister, ¹Dmitri Medvedev, ¹Cathy Cutler, ²Silvia Jurisson, ³Heather Hennkens, ⁴Yawen Li, ⁴D. Scott Wilbur
¹Brookhaven National Laboratory, United States, ²University of Missouri-Columbia, United States, ³University of Missouri, USA, ⁴University of Washington-Seattle, United States

Objectives: Selenium-72 ($t_{1/2} = 8.4$ d; $e = 100\%$) decays by electron capture to the daughter radionuclide ^{72}As ($t_{1/2} = 26.0$ h; $E_{\beta^+}^{\text{max}} = 3.334$ MeV), a positron-emitting radionuclide with significant potential for positron emission tomography (PET). The $^{72}\text{Se}/^{72}\text{As}$ radionuclide pair offers the ability to supply ^{72}As to clinical institutions in the form of a radionuclide generator. Accelerator production of ^{72}Se is achieved by the irradiation of As metal or GaAs targets with medium energy protons. The current methods for processing irradiated As targets are time-consuming and laborious leading to significant ^{72}Se activity losses. There is a need to develop rapid and facile $^{72}\text{Se}/\text{As}$ separation methods. The design of separation schemes for As and Se is challenging as each element can access multiple oxidation states leading to complex speciation chemistry. Several reports have described the separation of Se(IV) from As(V) by trioctylamine (TOA) [1,2]. This approach involves the extraction of Se as $[\text{SeCl}_6]^{2-}$ using 0.1 M TOA in xylenes. Based on these reports, a separation of ^{72}Se using tetravalent extraction chromatographic resins seemed achievable. The aim of this research is to design a robust extraction chromatographic separation method for the isolation of ^{72}Se from As targets.

Methods: Distribution coefficients for As (III and V) and Se (IV and VI) on several tetravalent extraction chromatographic resins (e.g., TK201, TBP) were determined from batch adsorption experiments in chloride media. Experiments were conducted with speciation standards and analyzed by ICP-OES in order to distinguish between the different oxidation states of As and Se. Column separations were performed with ^{73}As ($t_{1/2} = 80.3$ d) and ^{75}Se ($t_{1/2} = 119.8$ d) in order to develop a separation suitable for large-scale As target processing. Batch separation studies were performed to determine the optimum resin volume, loading matrix, and elution conditions.

Results: The tetravalent extraction chromatographic resins exhibited preferential uptake of Se(IV) over As(V) in concentrated HCl allowing for a facile separation of the two species. The commercially available extraction chromatography resin TK201 was found to be most suitable for As/Se separations. A model target solution consisting of ^{75}Se and ^{73}As in 10 M HCl was added to a small TK201 resin column and then eluted with 10 M HCl. Under these conditions, ^{75}Se is quantitatively retained on the column while ^{73}As is quantitatively eluted. Recovery of ^{75}Se is achieved by washing the column with H_2O , and then eluting with ethanol. Selenium breakthrough in the loading solution was negligible even when macroscopic quantities of As were present. The recovery of ^{75}Se was 75–85%. Experiments are ongoing to further optimize Se recovery.