NUCL 3977487

Adsorption of uranyl on alumina (012) studied by resonant anomalous X-ray reflectivity

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Understanding the mobility of uranium (U) in the vicinity of former U mines is crucial to ensure a sustainable supply for clean water. Reactive transport modeling for risk assessments of these sites can achieve higher accuracies when based on robust molecular-level information about ion adsorption structures. This information can be gained by studying ion adsorption on specific crystallographic orientations of mineral phases such as α-alumina (012), which serves as a model-system for many abundant Al-bearing minerals, e.g., aluminum (hydr)oxides.
Here, we deploy cutting-edge in-situ high-resolution X-ray reflectivity (XR) as well as resonant anomalous X-ray reflectivity (RAXR) to investigate adsorption of uranyl ions to alumina (012) over a range of U concentrations (0.01–1 mM U) and pH values (2–5) relevant to waters in tailings of former U mines. The data show a relatively low and constant amount of adsorbed U^{VI}, i.e., approximately 0.18–0.27 µmol/m^2, for all studied conditions. These results show that adsorption overcomes the repulsion between the positively-charged surface and the uranyl cation, showing uranyl's specific affinity to the alumina surface.
Structural investigations using RAXR reveal that uranyl adsorbs on alumina (012) as several distinct species that change their fractional coverages with increasing pH. At pH 2, a monodentate inner-sphere complex forms at a height of ~2.3 Å above the terminal oxygens. Based on closest approach calculations, we suggest that this complex has four water molecules remaining in the primary U hydration shell. Moreover, two outer-sphere complexes are identified, which are found to become the dominant species at pH~5.

NUCL 3977643

Vibrational sum frequency generation spectroscopy for interfaces of lanthanide and actinide solvent extractions

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The interfaces of oil and aqueous phases in solvent extractions are the gates for metals to transfer between the two phases. It would be that something special occurs at the interfaces because extractants, which are ligand reagents that facilitate metal transfer

into the oil phase by surrounding and stabilizing metals in the oil phase, are surfactants tending to form layers at the interfaces. We have investigated the interfaces of lanthanide and actinide solvent extractions using vibrational sum frequency generation spectroscopy both in homodyne and heterodyne detection methodologies. Vibrational signals of coordinating chemical groups of extractants and interfacial water OH stretch revealed molecular structures of lanthanide and actinide complexes with extractant forming at the interfaces, providing some aspects of phase transfer mechanism of lanthanide and actinide between the oil and aqueous phases.

NUCL 3977945 - Withdrawn

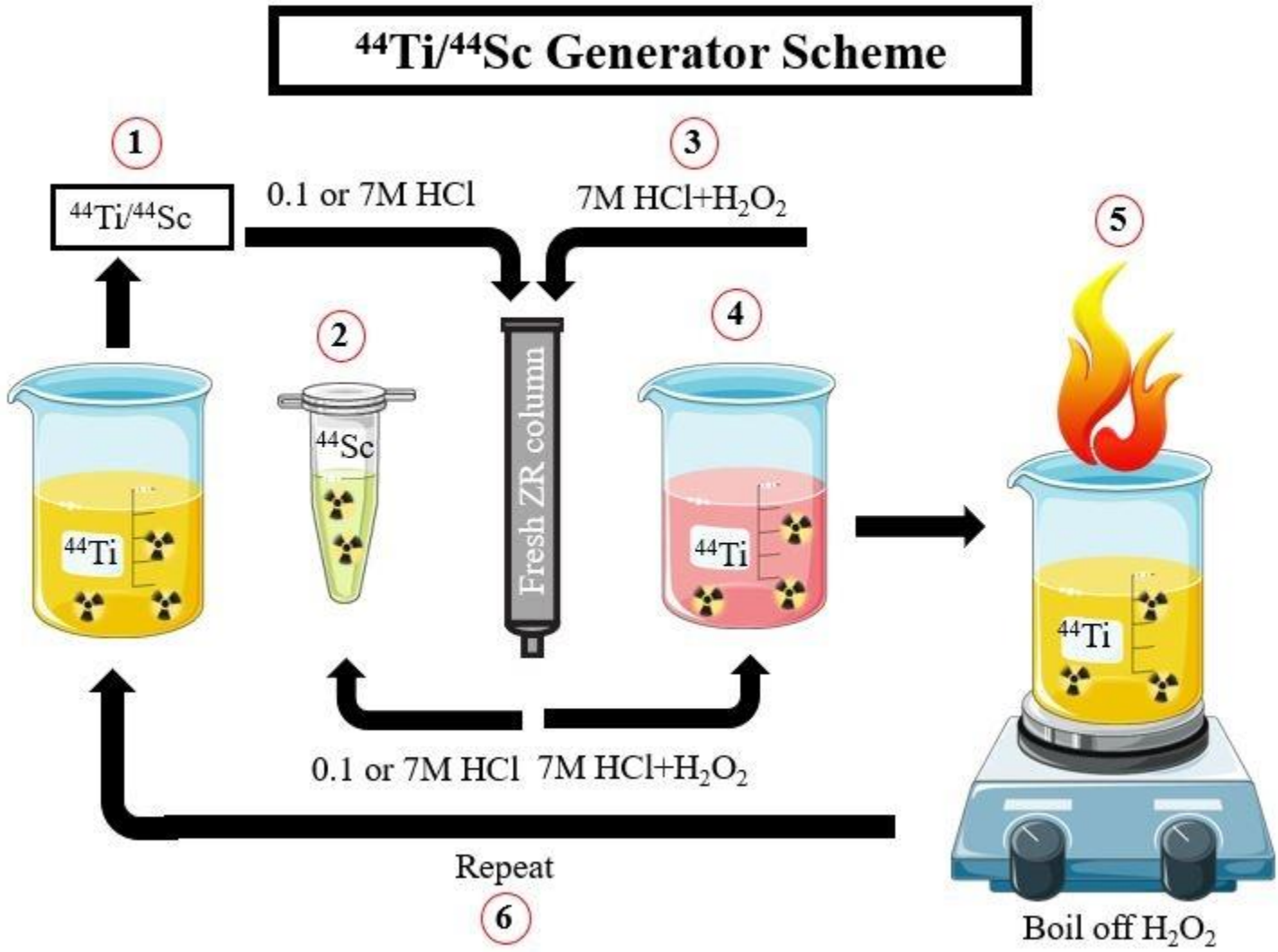
NUCL 3978205

New approach to 44Ti/44Sc generator design

Shelbie Cingoranelli[1,2]*, sjcing@uab.edu, Steffen Happel*[3]*, Fnu Shefali*[1,2]*, Mangi Lal Godara*[1,2]*, Suzanne E. Lapi*[1,2]*. (1) Radiology, University of Alabama at Birmingham, Birmingham, Alabama, United States(2) Chemistry, The University of Alabama at Birmingham College of Arts and Sciences, Birmingham, Alabama, United States(3) Triskem, Bruz, France*

Introduction: Scandium-44($t_{1/2}$=3.97 h) is a promising PET imaging agent that is a diagnostic counterpart to the therapeutic ^{47}Sc. There's a growing interest in harnessing the decay of ^{44}Ti($t_{1/2}$=59.9 y) to develop a generator system for ^{44}Sc, similar to the well-established ^{68}Ge/^{68}Ga system. Current efforts with the ^{44}Ti/^{44}Sc system rely on ZR resin with multiple elutions. However, prolonged use of these columns has resulted in ^{44}Ti breakthrough, leading to the need to optimize this generator to ensure its viability for both preclinical and clinical applications.
Objective: Building upon the existing work, we aim to develop a stripping technique to remove the ^{44}Ti after ^{44}Sc collection, then recondition it for capture on a fresh ZR column. This strategy aims to circumvent resin degradation issues.
Methods: The shorter-lived ^{45}Ti($t_{1/2}$=3.08 h) radioisotope was used to determine Ti retention on varying masses of ZR resin (ranging from 50 to 200 mg) at different HCl molarities (from 6 to 10 M). The ^{45}Ti was recollected using different H_2O_2 and H_2O_2/ HCl mixtures. Heating parameters were also investigated to effectively remove the H_2O_2 before loading the HCl solution containing the ^{45}Ti onto a fresh ZR resin.
Results: Columns were tested with 1.29±0.05 mCi of ^{45}Ti. The retention of ^{45}Ti on the ZR column increased with the ZR resin mass: where 50.8±1.1 mg columns retained 60.5±7.7%, 77.9±1.2 mg columns retained 73.6±2.3% and 170±3.1 mg columns retained 98.9±0.9 %. A comprehensive system using two columns was tested. The average of the two columns was 104.6±0.4 mg, which retained 99.8±0.1% of ^{45}Ti. The average elution of ^{45}Ti using 5 mL 28% H_2O_2 was 14.03±1.08%, followed by 10 mL of 7MHCl/7.5%H_2O_2, resulted in 85.06±0.53% of ^{45}Ti collection. Both fractions were dried down and reconstituted in 7M HCl. The average of ^{45}Ti retained on the second ZR column with respect to the starting amount before the first column was 96.9±2.9%.
Conclusions: This study demonstrates a promising alternative approach to the

^{44}Ti/^{44}Sc generator. Ongoing efforts are focused on optimizing resin mass, loading solutions, and ^{45}Ti/Sc collection methods, with the goal of creating a preclinical generator system using ^{44}Ti.



NUCL 3978205

New approach to 44Ti/44Sc generator design

Shelbie Cingoranelli[1,2]*, sjcing@uab.edu, Steffen Happel*[3]*, Fnu Shefali*[1,2]*, Mangi Lal Godara*[1,2]*, Suzanne E. Lapi*[1,2]*. (1) Radiology, University of Alabama at Birmingham, Birmingham, Alabama, United States(2) Chemistry, The University of Alabama at*

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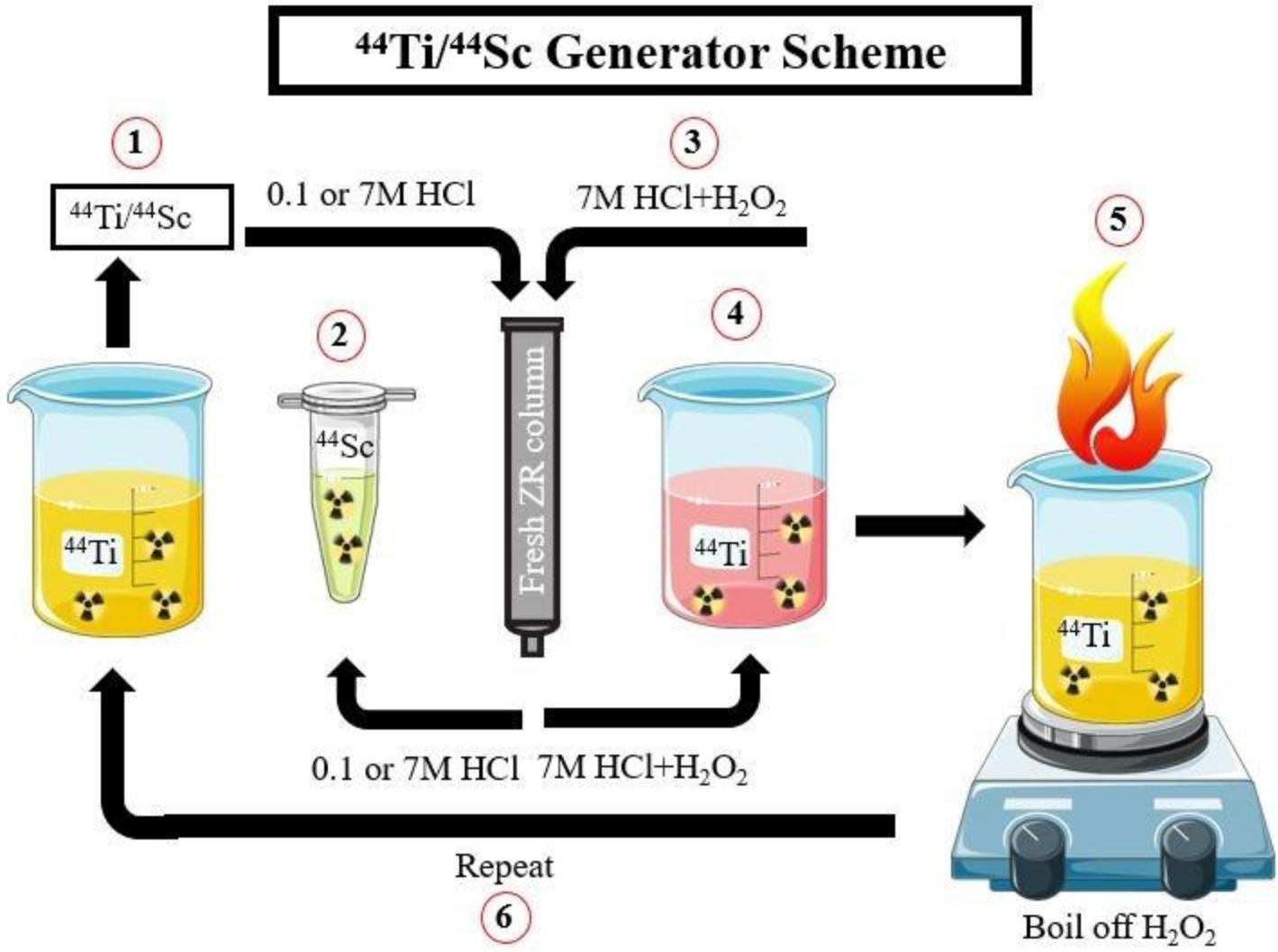
Conclusions: This study demonstrates a promising alternative approach to the ^{44}Ti/^{44}Sc generator. Ongoing efforts are focused on optimizing resin mass, loading solutions, and ^{45}Ti/Sc collection methods, with the goal of creating a preclinical generator system using ^{44}Ti.



NUCL 3979367

Comparison of ^{89}zr- radiopharmaceuticals for PET imaging of SSTR+ neuroendocrine tumors

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Neuroendocrine tumors (NETs) are a class of neoplasms originating from neuroendocrine cells that can arise anywhere in the body. Each year, ~12,000 people

are diagnosed with NETs in the U.S. The 1- and 5-year mortality rates for patients are ~27.2% and 60.4%, respectively, highlighting the need for early diagnosis. Somatostatin receptor 2 (SSTR2) is frequently overexpressed on the surface of NETs, making it an excellent target for the development of receptor specific agents. Positron Emission Tomography (PET) is underway as a leading diagnostic tool with the recent approvals of three positron emitting radiopharmaceuticals for SSTR+ NETs. This work aims to test the in vivo stability of two zirconium-89 (^{89}Zr) chelators, deferoxamine (DFO) and tetraxetan (DOTA), conjugated with the long-lived somatostatin analogue, octreotide (TOC). ^{89}Zr is a promising radionuclide for the development of PET tracers, due to its favorable nuclear characteristics ($t_{½}$ = 3.27 days, β^+ = 22.3%, β_{avg}= 395.5 keV) and chemical characteristics (+4 oxidation state, preferential coordination number of 7/8, and favorable aqueous chemistry). ^{89}Zr-DFO-TOC and ^{89}Zr-DOTA-TOC will leverage these excellent characteristics and dissect the in vivo stability of the chelators, DFO and DOTA, in hopes of developing a novel radiopharmaceutical for improved PET imaging of SSTR+ NETS at longer timepoints. Our aim is to determine the suitability in detecting and diagnosing SSTR+ NETs with ^{89}Zr probes. Using ^{89}Zr will also allow for dosimetry information pertinent for future theragnostic applications with long-lived therapeutic radionuclides, such as ^{177}Lu. If successful, this work will demonstrate the ability to utilize the excellent nuclear and chemical properties of ^{89}Zr for sensitive detection and diagnoses of SSTR+ NETs, while giving insight into the preferential coordination complex formed by ^{89}Zr during radiolabeling. This work has the potential to greatly impact patient care through the possibility of earlier detection and improved NET diagnoses.

NUCL 3979408

Synthesis and evaluation of pyridothiophene compounds for imaging α-synuclein with PET

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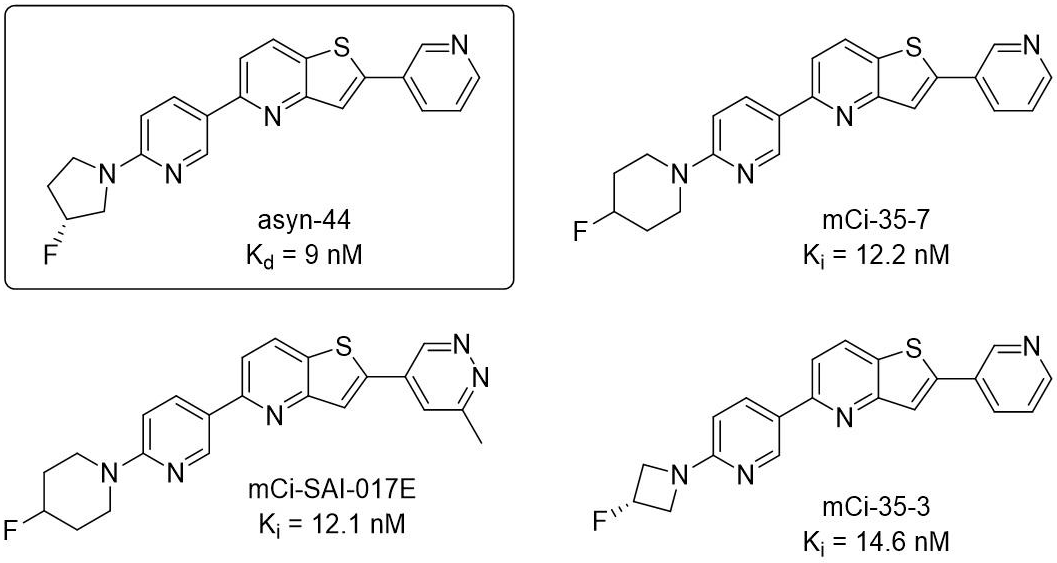
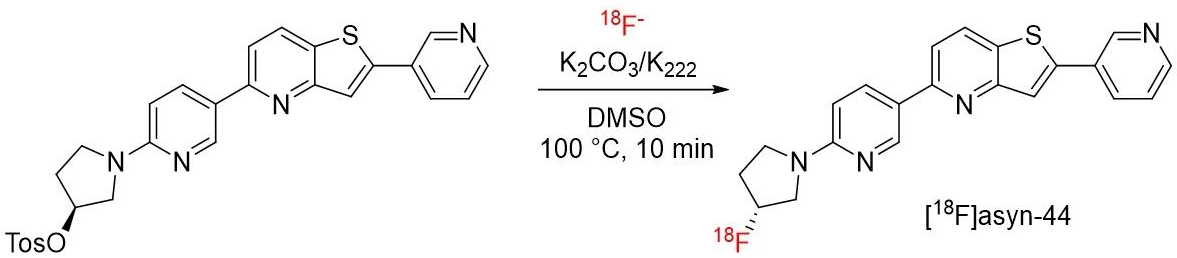
Background: Aggregated α-synuclein protein is a pathological hallmark of Parkinson's disease (PD) and dementia with Lewy bodies. Development of positron emission tomography (PET) radiotracers to image α-synuclein aggregates has been a longstanding goal. We synthesized new pyridothiophenes and determined their binding affinity to α-synuclein aggregates in human PD tissues. The most potent compounds were radiolabeled and evaluated in rodent PET imaging studies.
Methods: A potent compound, asyn-44 (K_d = 9 nM) was synthesized and radiolabeled with tritium. 64 derivatives of asyn-44 were synthesized and screened against [^{3}H]asyn-44 in competitive binding assays using post-mortem PD brain homogenates, and K_i values of the most potent compounds were determined. [^{18}F]Asyn-44 was labelled by aliphatic nucleophilic ^{18}F-fluorination of the tosyloxy precursor at 100 °C in DMSO. The log$D_{7.4}$ of [^{18}F]asyn-44 was determined via the shake-flask method. Healthy rats (M/F)

were injected intravenously with [^{18}F]asyn-44 and dynamically scanned for 2 h. Brain and plasma radiometabolites were determined at 30 and 60 min.
Results: From the 64 screened derivatives, three had K_i's in the lower nanomolar range (12-15 nM, Figure 1A). [^{18}F]Asyn-44 was synthesized with a radiochemical yield of 6±1% (decay-corrected, n=3) and a molar activity of 175±58 GBq/μmol. The logD was 4.16±0.04 (n=8). Preliminary PET imaging showed high initial brain uptake (>1.5 SUV), fast washout (~0.5 SUV at 60 min), and low variability (Figure 1C). Radiometabolite analysis showed 60-80% parent tracer in the brain after 30 and 60 mins.
Conclusion: While [^{18}F]asyn-44 displayed good *in vitro* properties and acceptable brain uptake, troublesome radiometabolites precluded further PET imaging studies. The synthesis and *in vitro* evaluation of additional derivatives with the goal of attaining improved affinity, selectivity, and metabolic stability are underway.

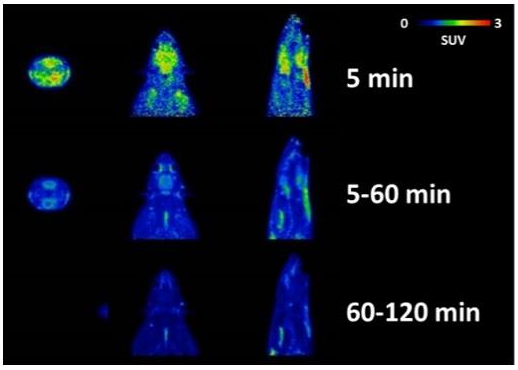
A Structure of asyn-44 and equipotent derivatives



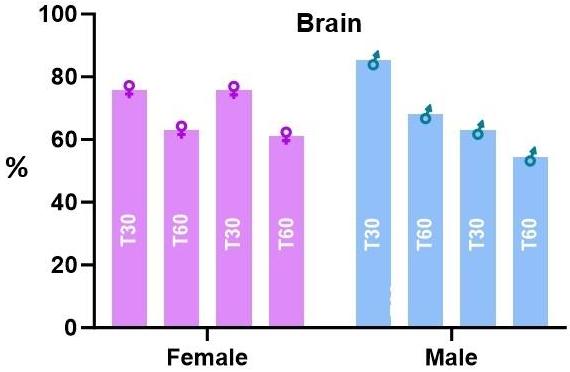
B Radiosynthesis of [^{18}F]asyn-44



C PET imaging of [^{18}F]asyn-44 in healthy rats



D Intact radiotracer at 30 and 60 min



NUCL 3980114

Rare-earth element separation with ionic liquid impregnated resin

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1. Introduction.

Rare-earth elements (REEs) have vital applications in 21st century technology and medicine, and their low concentrations in mineral deposits demands the need for recycling. Separation of adjacent lanthanides has proven to be a challenge, but the use of ionic liquids as extractants is a promising solution. Lanthanides are particularly difficult to separate due to their preferential +3 oxidation state and similar ionic radii. This work aims to develop Cyphos IL 104 impregnated resins to study extraction of rare earth elements from an acid matrix.

2. Methods.

Ionic liquid impregnation began by mixing ionic liquid into one of four solvents: Acetone, 33.4% Ethanol, n-Hexane, and Kerosene at concentrations of 0.05, 0.2, and 0.5 $mol_{IL}/L_{solution}$. 10 mL of solution was mixed with 1 gram of dry resin for 24 hours. The liquid was separated from the resin and the impregnated resin was dried before being analyzed with IR spectroscopy. Extraction equilibrium experiments were conducted by adding 1 mL of 1ppm REE mix (pH=2.2) to 50 mg of resin. The samples were shaken for 5 min before the resin was separated from the solution using a PES membrane filter. 0.5 mL of solution was diluted in Nitric Acid and analyzed with ICP-MS to determine final REE concentrations. ICP-MS data was used to calculate equilibrium constants using the following equation: $K_d = (C_{initial}-C_{final})/C_{final}*V_{sol}/m_{resin}$.

3. Results and Discussion.

K_d values were calculated from the ICP-MS data, and the log of those values was plotted. All solvents used in resin impregnation showed a similar extraction trend of rare-earth elements. At a 5 min equilibrium time, extraction using Cyphos IL 104 appeared to favor elements with lower ionic radii. This is consistent with other ionic liquids and extractants. The ionic radii dependent extraction may be exploited further by varying pH to improve near-lanthanide separation. This will manifest through column separations that will vary loading and separation environments to improve adjacent lanthanide selectivity.

4. Conclusion.

The development of more efficient methods to separate REEs is vital in ensuring continued use and improvements in advanced technology. Resin impregnated ionic liquids are an environmentally friendly alternative for separating REEs and show promise in separating near-lanthanides for various technology and medical applications.

NUCL 3980141

Demonstration of a drop-on-demand approach to precise preparation of radioactive sources from micrograms of aqueous acid solution

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Inkjet dispensing of picoliter droplets affords spatially accurate deposition of precisely controlled amounts of liquid, supporting diverse applications in microfabrication and sample preparation. Drop-on-demand (DOD) devices are ideal for quantitative applications and may provide an attractive approach for the preparation of low-activity radioactive sources including sources for decay energy spectrometry (DES) with low-temperature detectors. DOD excels where traditional approaches to gravimetric source preparation struggle: achieving the small masses (~1 mg) and spatial precision (target areas ≤ 1 mm^2) required for optimal DES sources. Improvements in inkjet metrology are required for DOD to compete in terms of gravimetric precision, where traditional methods routinely achieve combined standard uncertainties < 0.05 %.
We describe the DOD preparation of a series of sources from a well-characterized Am-241 reference material. Drops were deposited into liquid scintillation (LS) vials containing scintillator, onto nanoporous gold foils, and onto steel disks. The LS sources were counted using primary methods to provide high-precision radiometric confirmation of the gravimetric dispensing technique. The gold foils were mounted onto transition edge sensor chips for DES, demonstrating direct links of activity assays by LS and DES. The steel disks were investigated as autoradiography phantoms with traceable activity. Improvements in DOD methods and hardware and refined corrections for evaporation-in-flight result in relative combined standard uncertainties on droplet masses < 0.3 % and the observed difference between gravimetric and radiometric evaluations is 0.08(7) % (where the stated uncertainty is statistical only). The methods are further validated using a stable-isotope mass spectrometry approach. Future advances in inkjet metrology may be supported by precision radioactivity measurements. The same advances will then afford DOD preparation of low-activity reference materials for forensics and environmental monitoring, of imaging phantoms with well-defined geometry and traceable activity, and of alpha spectrometry and DES sources with homogeneous sample distribution for minimal self-absorption.

NUCL 3980187

Novel ^{18}f labeled radiotracer for Neuroimaging activin receptor like kinase 2

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Introduction. Activin receptor-like kinase 2 (ALK2) is a pharmaceutical target of interest for the rare pediatric cancer diffuse intrinsic pontine glioma (DIPG), which currently does not have any effective chemotherapies. The previous lead radiotracer targeting ALK2, [^{11}C]M4K2127, demonstrated high brain uptake and moderate washout kinetics in rodents, but was subsequently deemed unsuitable due to the significant presence of radiometabolites in the brain. The goal of the present work is to develop novel radiolabeled 3,5-diphenylpyridines with improved metabolic stability compared to the first-generation of ALK2 radiotracers. **Methods.** M4K2009 and M4K2176 were synthesized as previously described. Radiolabeling was performed in a one-pot, two-step fashion using a [^{18}F]fluoroethyl tosylate intermediate. Reactions were automated on a GE Tracerlab FXN synthesis module, with non-decay corrected radiochemical yields (RCY) calculated relative to dried [^{18}F]fluoride. Radio-HPLC was used to confirm radiotracer identity, molar activities (A_m), and radiochemical purities (RCP). Digital autoradiography (ARG) was performed in fresh-frozen rodent tissue (10 μm thick) to assess total and non-specific binding in rodent tissue. Preclinical PET imaging was carried out in healthy rodents (i.e. Sprague Dawley rats, C57BL/6 mice) and radiometabolite analysis was conducted using column-switching HPLC. **Results.** [^{18}F]M4K2176 was synthesized in average RCY of 1.7%, A_m of 284 GBq/μmol, and RCP of >95% (n = 4). [^{18}F]M4K2176 displays good specific binding in rodent tissue (~70%, n = 3). Preliminary rodent imaging shows moderate maximum brain uptake (SUV 1.6-1.8) with good washout kinetics and minimal bone uptake, signifying minimal defluorination (n = 6). Results from ongoing radiometabolite and further imaging studies will be presented. **Conclusion.** [^{18}F]M4K2176 is a promising second-generation radiotracer for neuroimaging ALK2 in DIPG.

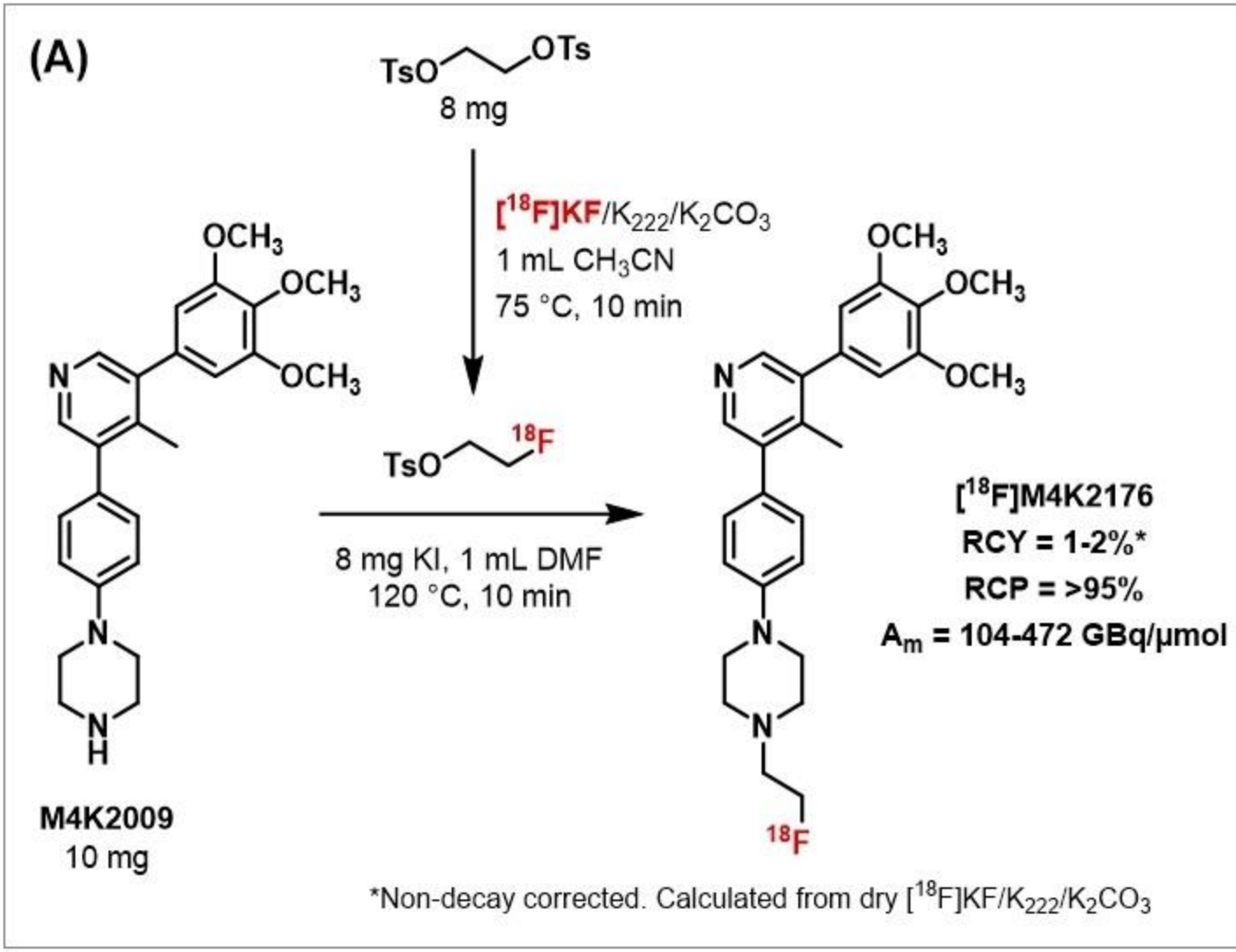

Figure 1. (A) Radiosynthetic scheme for [^{18}F]M4K2176. **(B)** Total and non-specific binding in rodent brain tissue (fresh-frozen, 10 um thick). Representative PET/CT summation images (0-120 min) in **(C)** Sprague-Dawley rat and **(D)** C57BL/6 mouse.

NUCL 3980509

Defining optimal instrument parameters for high-resolution and high-throughput Raman spectroscopic mapping for Uo_2f_2

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Raman spectroscopy is an emerging technique for rapid, nondestructive analysis of nuclear materials for forensic and nonproliferation applications as it is a powerful tool for distinguishing between multiple chemical forms of materials with similar stoichiometries. Recent developments in spectroscopic software have enabled rapid data collection with high-speed Raman spectroscopic mapping capabilities. However, some uranium-rich materials are susceptible to degradation in humid air, laser-induced phase transformations, or both. To mitigate environmental or measurement-related degradation of potential samples of interest, we have taken a systematic approach to define optimized collection parameters for UO_2F_2, an important intermediate material in the nuclear fuel cycle. We investigated the influence of optical magnification (5–100×), laser power, and exposure time on the resulting Raman signal for identical particles of UO_2F_2 and found that using 20× optical magnification consistently provides the greatest signal when normalized to noise. We also ensured sample integrity during data collection using multivariate statistical methods and collected spectroscopic maps using optimized parameters to reduce the time needed to obtain spatially resolved spectroscopic information.

NUCL 3980520

High energy resolution X-ray spectroscopy for Actinide Science

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Understanding the mechanisms of various chemical reactions involving actinides at the atomic level is a crucial step towards the safe disposal of nuclear waste and the identification of the physical and chemical processes of radionuclides in the environment. In recent years, scientists have progressively recognized the role of electronic structure in the characterization of the chemical and physical properties of actinide-based materials. High-energy resolution X-ray spectroscopy emerged as a promising direction because this method can probe material properties at the atomic level. Such experiments are performed at the synchrotron facilities, which offer a number of unique advantages. One of them is the element-selectivity using the energy of incident X-rays, which can be tuned and thus allows one to probe electronic transitions on a very small amount of sample without vacuum conditions. Moreover, synchrotron methods are non-destructive and bulk sensitive to the materials being studied.

This contribution provides an overview of recently conducted studies on materials

containing uranium, thorium, and plutonium at the Rossendorf Beamline (ROBL) of the European Synchrotron (ESRF) in Grenoble, France. This innovative and unique experimental station was utilized for studying actinide systems through various experimental methods, including X-ray absorption spectroscopy in high-energy resolution fluorescence detection (HERFD) mode, Resonant Inelastic X-ray Scattering (RIXS) at the An L_3 and $M_{4,5}$ edges, and X-ray diffraction (XRD). I will demonstrate that the experimental data, analyzed using electronic structure calculations, can: a) Provide fingerprint information on the actinide oxidation state and ground state characteristics. b) Probe 5f occupancy, non-stoichiometry, and defects. c) Investigate the local symmetry and effects of the crystal field. This research may be of interest to fundamental research in the chemistry and physics of nuclear materials, as well as in applied science.

NUCL 3981178

Source material-specific spectroscopic signatures in U_3O_8

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The most stable oxide form of uranium, U_3O_8, is commonly produced as an intermediate phase within the nuclear fuel cycle. Its stability and high relative uranium density make it optimal for transit and storage, and because of its major involvement within the fuel cycle, U_3O_8 continues to be of significant interest to nuclear forensics research. Raman spectroscopy is commonly employed for analysis of uranium oxides and, as such, is ideal for rapid, nondestructive analysis of samples with unknown origins. In this work, we report an investigation using the Raman spectra of various U_3O_8 samples produced from different source materials and synthetic routes, including carnotite, diuranates (sodium, magnesium, and NH_4), and uranyl nitrate; analysis techniques include peak fitting and spectral centroid analysis. We discuss unique indicators of the process history that we observed in the spectra, and such characterization can aid future studies into source fabrication material fingerprinting.

NUCL 3981537

Coordination radiochemistry of manganese-52 for PET imaging applications

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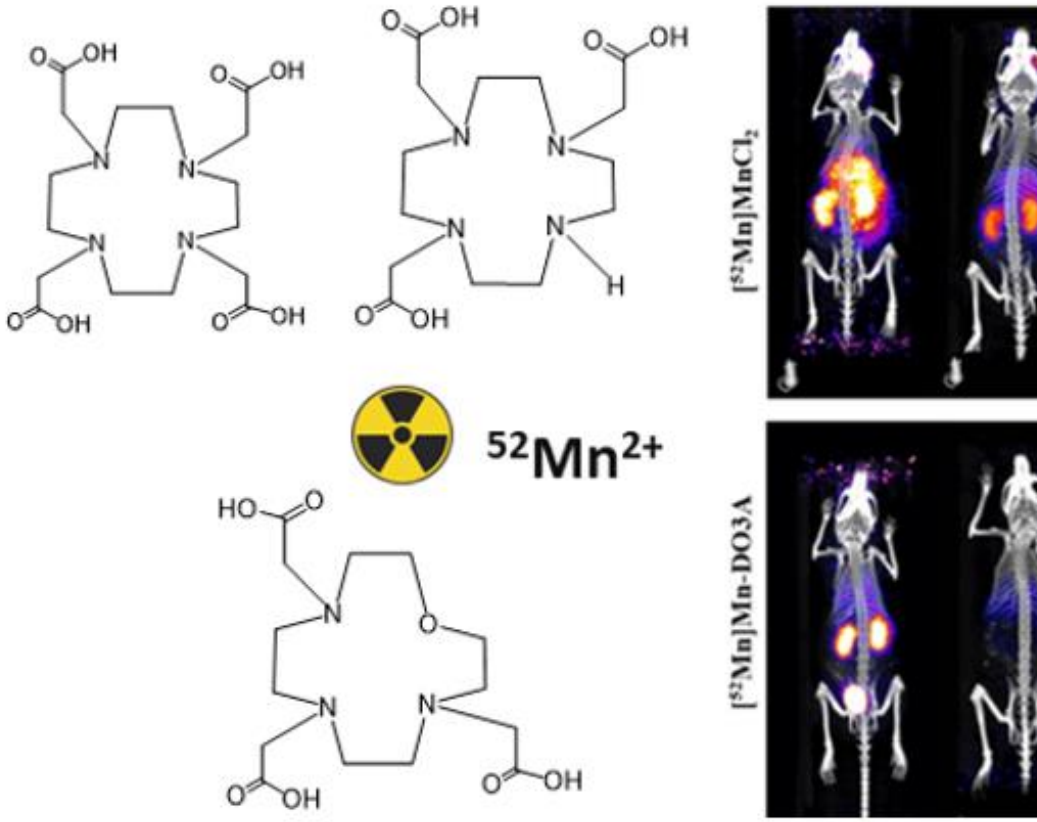
Positron Emission Tomography (PET) is a diagnostic technique that allows visualization, characterization, and quantification of biological processes and disease biomarkers through noninvasive imaging. Research interest in the use of ^{52}Mn ($t_{1/2}$ = 5.6d, β^+ = 29.6%, $E_{\beta ave}$ = 242keV) to enable the development of long-lived PET radiopharmaceuticals has gained momentum. Its long half-life of 5.6d, low average positron energy (242keV), and high positron decay branching ratio (29.6%) make this radionuclide suitable for radiolabeling of macromolecules for investigation of biological processes at longer time points post-injection. Prior work pertaining to ^{52}Mn has been mainly limited to the production and purification of the radioisotope leaving the radiochemistry largely underdeveloped and this has limited its applications in PET imaging. The goal of this work is to establish suitable chelators for ^{52}Mn that can easily be radiolabeled at mild conditions.

^{52}Mn was produced through the nuclear reaction ^{Nat}Cr(p,n)^{52}Mn by irradiation of natural chromium targets on a TR24 cyclotron followed by purification through ion exchange chromatography. The radiolabeling efficiencies of various chelators, including DOTA, DiAmsar, TETA, DO3A, NOTA, 4′-Formylbenzo-15-crown-5, OXO-DO3A, and DFO, were assessed by investigating the impact of pH, buffer type, and temperature. 5µg of each chelator was combined with 1.85MBq of [^{52}Mn]$MnCl_2$, pH 7 and the reactions were incubated at either 40°C or 80°C for 1h. Percent radiolabeling was assessed by Radio-TLC. The radiocomplexes were evaluated *in vivo* and their distribution patterns compared to that of [^{52}Mn]$MnCl_2$ in female athymic nude mice at 1h and 24h post injection.

Most of the chelators yielded greater than 70% binding at 80^{o}C. NOTA, DO3A, DOTA, and OXO-DO3A chelators were readily radiolabeled with greater than 95% radiochemical yields at mild conditions (room temperature to 37°C, pH 4-8). Manganese radiocomplexes of OXO-DO3A, DOTA, and DO3A remained stable *in vitro* and exhibited suitable *in vivo* properties. Clearance of [^{52}Mn]Mn-DOTA, [^{52}Mn]Mn-DO3A, and [^{52}Mn]Mn-OXO-DO3A from the organs was faster than [^{52}Mn]$MnCl_2$. These chelators can be used as bifunctional chelators in radiolabeling of biomolecules with ^{52}Mn for PET imaging.



NUCL 3981793

Rapid post-synthetic metal extraction with fluorous mesoporous silica nanoparticles for application as PET-MR imaging probes

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The implementation of hybrid imaging instruments, specifically dual PET-MRI, in clinical practice demands a probe with optimized functionality for both imaging types. While there is significant literature precedent for small molecule and nanoprobes for the respective imaging modalities, little work has been conducted into the development of a dual imaging probe. To address this challenge and keep up with the implementation of clinical PET-MRI instruments, I have designed a nanoprobe that alleviates the challenges associated with hybrid imaging. To do so, I have implemented the use of hollow mesoporous silica nanoparticles (MSNs) loaded with a fluorous core containing the extractant (perfluoroheptanoyl)acetone (acac-FH) in perfluoro-15-crown-5-ether

(PFCE). Preliminary work demonstrates the optimization of the MSN synthesis, and successful metal ion extraction with stable iron(III) citrate. Selection of iron(III) allowed initial experiments to be conducted without radioisotopes. This work seeks to use the information gained from iron extraction to improve upon the lengthy synthesis times associated with nuclear medicine, and the direct competition with the desirable short half-lives of medically relevant isotopes. Although the current scope of future work is focused on the implementation of imaging isotopes like 45Ti (t1/2= 3 hr), 68Ga (t1/2= 68 min), and 89Zr (t1/2= 78 hr); there is great potential for the application of this system as a theranostic probe.

NUCL 3983084

Customizable porphyrin platform enables folate receptor PET imaging using copper-64

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Introduction: Folate receptors including folate receptor alpha (FRα) have been found to be overexpressed in up to 90% of ovarian cancers, and cancers overexpressing FRα exhibit higher degrees of drug resistance and worse therapeutic outcomes. Therapies targeting FRα include antibodies, antibody-drug conjugates, and small molecules. The FRα-targeting compound O5 was based on a readily customizable porphyrin platform. O5 radiolabeling with copper-64 was optimized and binding to FRα was assessed in cells and followed by evaluation in a murine xenograft model of ovarian cancer.
Methods: O5 was obtained via standard porphyrin synthesis followed by Cu-mediated click chemistry to introduce water-solubilizing groups and γ-PEGylated folic acid. O5 was radiolabeled in several buffers in ratios of 100 – 1000 μCi/μg. Stability was assessed in human serum and PBS using HPLC. Cell uptake and subcellular fractionation studies were performed using FRα-overexpressing IGROV1 human ovarian cancer cells. PET/CT imaging and blocking studies were used to determine the tumor targeting ability of [^{64}Cu]Cu-O5 in mice bearing IGROV1 tumors.
Results: O5 was synthesized at >95% purity, was soluble in water at >1 mg/mL, and was radiolabeled at a specific activity of 1000 μCi/μg with copper-64 at 37°C in HEPES buffer. [^{64}Cu]Cu-O5 remained 100% intact in PBS and human serum for 24 h. Cell uptake of studies showed 535 ± 12% bound/mg at 0.04 nM, which was reduced to 24.9 ± 30.6% when blocked with 2000 nM of unlabeled O5 ($P < 0.0001$). Subcellular fractionation of IGROV1 cells incubated with [^{64}Cu]Cu-O5 showed most radioactivity was associated with the cytoplasmic (39.4 ± 2.7%) and chromatin bound nuclear fractions (53.0 ± 4.2 %). PET/CT imaging revealed clear tumor uptake of [^{64}Cu]Cu-O5 from 1–24 h post injection. Tumor standardized uptake value at 24 h post injection was 0.34 ± 0.16 versus 0.06 ± 0.07 in the blocking group.
Conclusion: [^{64}Cu]Cu-O5, prepared at a high specific activity, was stable in serum, and

had very high binding to FRα-overexpressing cells with uptake clearly visible in mouse tumor xenografts.

NUCL 3983465

Nanoparticles as a radionuclide generator for alpha-emitting radionuclide pairs ^{225}Ac/^{213}Bi and ^{230}U/^{226}Th

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Short-lived alpha emitters, like ^{213}Bi ($t_{1/2}$ = 45.6 m) and ^{226}Th ($t_{1/2}$ = 30.6 m), are of interest for targeted alpha-therapy and require on-site radionuclide generators. Current radionuclide generators use resin-based columns that degrade at activities required for clinical use (> 70 mCi) due to the high linear energy transfer of alpha particles. The development of novel radionuclide generators with high radiolytic stability is therefore necessary for large-scale adoption of ^{213}Bi or ^{226}Th in the clinic. Herein we report work towards developing superparamagnetic iron oxide nanoparticles (SPIONs) to encapsulate ^{225}Ac and ^{230}U while allowing the daughters, ^{213}Bi and ^{226}Th, respectively, to escape due to the recoil effect. The parent radionuclides are co-precipitated with the SPIONs (10 nm in diameter) during synthesis with > 90% radiolabeling. A Monte Carlo based program, Stopping Range of Ions in Matter (SRIM), was used to estimate the release of ^{213}Bi and ^{226}Th from the SPIONs to be > 99%. Additionally, we report initial efforts to recover the daughter radionuclides using magnetic precipitation of the SPIONs, which consistently show re-binding to the SPION surface. Further work is being done to alter the surface properties of the SPIONs to prevent the re-binding of the daughter radionuclides. Ultimately, we plan to develop SPIONs to rapidly separate parent from daughter utilizing the recoil effect with magnetic precipitation of the SPIONs.

NUCL 3983937

Development of silica-based resins for lanthanide separation

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Production of high specific activity radiolanthanides for nuclear medicine is challenging due to the chemical similarities between each of the lanthanides. Towards future separations based on Szilard Chalmers reaction, we have synthesized various diglycolamide (DGA)-based solid-phase extractants (SPEs). Current techniques for separating lanthanides and actinides rely primarily on liquid-liquid extraction, which generates large volumes of hazardous organic waste. This process can be improved by using a solid-liquid separation system that replaces the organic phase with a SPE, thereby lowering the risk of cross-contamination and decreasing the volume of waste produced. The work presented here will include the synthesis, characterization, and stability testing of a DGA-functionalized mesoporous silica materials, with varying degrees of pre-arrangement, and their sorption behavior towards a selection of trivalent cations.

NUCL 3984426

Ink-jet printing of actinide thin films for nuclear applications

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I will report on a new target production technique that utilizes ink-jet printing to accurately deposit chemical layers that can then be converted into oxides through heat treatment. Printing offers the advantage that materials are completely converted from solution to oxide material efficiently; furthermore, the precision of ink-jet printing allows for control of the thickness and size of the films. Thin films have a wide range of applications from the irradiation experiments of nuclear reaction measurements to energy research.

NUCL 3984428

Solution combustion synthesis of $(Th_{1-x}U_x)O_2$ nanomaterials and thin films for irradiation studies

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ThO_2 materials are important for long-term developments in the nuclear fuel cycle both as a fuel in future breeder reactors and as a potential additive in traditional UO_2 fuel materials. However, the primary method for studying radiation effects in ThO_2 and mixed oxide $(Th_{1-x}U_x)O_2$ materials are through long-term studies on fuel pellets. This work aims to use solution combustion synthesis (SCS), a self-propagating exothermic redox reaction between an organic fuel and a metal nitrate, which produces uniform mixed

metal oxide nanoscale materials with a high crystallinity and tailored morphology, to provide rapid validation of materials for fuel studies. Specifically, I will present work on a thorium nitrate + uranyl nitrate + acetylacetone (fuel) + 2-methoxyethanol (solvent) system. Our work has shown that varying the ratio of fuel to metal nitrate (φ) as well as the starting concentration of uranyl nitrate can impact the resulting product grain size and surface morphology. Spectroscopic, crystallographic, and TGA-DSC methods were used as diagnostic tools to investigate the intermediate species and the mechanistic processes of combustion (temperature, gas product formation, and solution decomposition). Mechanistic results are combined with powder x-ray diffraction, transmission electron microscopy, and BET analysis to develop a relationship between starting synthesis conditions and product properties. In addition to SCS mechanisms, I will present preliminary results for work on irradiating mixed oxide thin films, synthesized from electrospray deposition coupled with SCS, to investigate radiation-induced structural changes in materials.

NUCL 3984495

Uranyl and water adsorption on an epitaxial graphene electrode

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Understanding uranyl complexation and water structuring near carbon-based electrodes is imperative for advancing electrochemical separation strategies, such as capacitive deionization. In these systems, ion adsorption onto and near the electrode impacts the energy efficiency and device performance. Despite the importance of ion behavior near these charged surfaces, little direct experimental information is available due to the challenges of studying the solid-liquid interface. We deploy two complementary x-ray scattering techniques to understand uranyl adsorption onto a model graphene electrode. *In-situ* high resolution x-ray reflectivity allows direct examination of the solution-graphene surface and reveals significant changes in the local structure when a negative potential is applied. We link these changes to uranyl adsorption and subsequent rearrangement of interfacial water. Resonant anomalous x-ray reflectivity is element-specific and confirms that uranyl mainly adsorbs in a diffuse layer near the graphene electrode, consistent with previous studies of trivalent yttrium. The combination of these techniques provides critical, molecular-scale information about uranyl complexation at this electrode surface.

NUCL 3985453

Sorption data: Enhancement of geochemical modeling by chemically evident surface speciation

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Modeling geochemical scenarios for the safety analyses of disposal of hazardous radioactive and (chemo)toxic waste requires comprehensive and consistent thermodynamic data as well as sorption data for the surrounding host rocks. Whereas there are several projects running worldwide to develop at the comprehensive and consistent thermodynamic database for the aqueous phase and forming solids, the situation is much more complicated concerning the reactions on the mineral-water interface. For sorption data, there is currently no database providing quality assured thermodynamic surface complexation modeling (SCM) data. Even though spectroscopic methods to determine the actual surface species have made great progress in recent years, the SCM data still contain questionable to assuredly non-existent species. This leads to hardly comparable results in geochemical modeling.
To address this problem, publicly available SCM (protolysis and sorption) data are currently being reevaluated and new reaction data are generated building on spectroscopically evidenced surface complexes. Critical data gaps shall be closed by the use of analogies (for both radionuclides' chemistry as well as the mineral phases) or established estimation methods (e.g. linear free energy relationship). The RES^{3}T sorption database, the PSI Chemical Thermodynamic Database as well as the LLNL's sorption raw data compilation provide the solid basis for this work. In combination with surface site density data from crystallographic calculations, this approach yields realistic and robust models that significantly improve sorption in geochemical calculations e.g. through so-called smart K_d values. The results of this work will be published within the THEREDA framework including ready-to-use parameter files for common geochemical codes (e.g. GEMS, Geochemist's Workbench, PHREEQC).

NUCL 3985536

Cyclotron production and purification of Scandium-47 (^{47}Sc) from natural vanadium targets

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Introduction: Scandium-47 has been of interest for use as a β^- therapeutic isotope in counterpart with the diagnostic radioisotopes ^{43}Sc/^{44}Sc. This study aimed to produce high-purity ^{47}Sc for preclinical use in targeted radiotherapy via proton irradiation of natural vanadium (^{nat}V) targets. **Methods:** ^{nat}V foils were bombarded with 24 MeV protons. Two target designs were employed; a 90° angle target with 92 mg of ^{nat}V and a 30° slanted target design using 300 mg of ^{nat}V. The parameters varied from 5 to 80 µA of current and from 1 to 8 hours of irradiation time. A separation method was developed using AG MP-50 and carboxymethyl (CM) weak cation exchange resins. Targets were dissolved in 7 M HNO_3, dried, and reconstituted in 8 M HCl. The 8 M HCl solution was

loaded onto the column, followed by elutions of 8 M and 4 M HCl and Chelex water to remove ^{nat}V and chromium-51 (^{51}Cr) impurities. 1 M ammonium acetate pH 4.5 was used to elute the ^{47}Sc from the MP-50 column directly on to the CM column. Chelex water was passed through the CM column before eluting the ^{47}Sc in 1 M HCl. The radionuclidic purity of ^{47}Sc was determined by High Purity Germanium Spectroscopy (HPGe). The chemical purity was determined by Inductively Coupled Plasma Mass Spectroscopy (ICP-MS). The ^{47}Sc was dried and reconstituted in 0.1 M HCl. Titrations were performed to determine the apparent molar activity (AMA). **Results:** The average yields of the bombardment at 24 MeV were 125.2 ± 1.7 µCi of ^{47}Sc and 581.1 ± 63.4 µCi of ^{51}Cr, for 40 µA, 40 µA for 4 hours was 827.1 ± 82.6 µCi of ^{47}Sc and 4.77 ± 0.36 mCi of ^{51}Cr, and for 80 µA for 8 hours was 2.2 ± 0.01 mCi of ^{47}Sc and 23.1 ± 12 mCi of ^{51}Cr. The average recovery of ^{47}Sc eluted from the AG MP-50 resin was about 93.7 ± 2.9%, and the recovery with the addition of the CM resin step was 70 ± 3.6 %. The radionuclidic purity of ^{47}Sc was 99 ± 0.5 %. The vanadium target and ^{51}Cr were removed in both HCl washes, and ICP-MS validated the absence of residual target material within the purified ^{47}Sc collection with a detection limit of < 0.1 ppb. The AMA was 205.39 ± 3.5 mCi/µmol. **Conclusions:** High purity ^{47}Sc can be produced at reasonable yields from ^{nat}V foil targets with minimal impurities with a recovery of 70 ± 3.6 %.

NUCL 3985819

Increasing the availability of at-211: Investigating the chemical behavior after shipment

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Interest in α-emitting radionuclides for applications in Targeted Alpha Therapy (TAT) continues to grow. With its relatively short half-life (~7.2 h) and its rather simple decay scheme, At-211 is one of the most advantageous nuclides for this purpose. The majority of existing processes start with α-particle bombardment of bismuth metal targets via the Bi-209(α,*2n*)At-211 reaction, followed by target dissolution in nitric acid. Our group has developed a chemical system where the astatine can be separated, purified, and recovered from the excess bismuth directly from nitric acid in less than 20 min. This process is based on an extraction chromatography column, utilizing 3-octanone impregnated porous beads, which requires no additional chemical treatment of the nitric acid dissolution solution prior to the separation. Alternatively, the free-standing liquid can be removed from the column, allowing it to be shipped to various locations. Current investigations are focused on better understanding the chemical behavior and speciation of astatine after shipment, which will be discussed in detail.

NUCL 3985820

Evaluation of alpha irradiation of [^{153}Eu]Eu_2O_3 and [^{155}Gd]Gd_2O_3 targets for producing high specific activity ^{155}Tb

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Several terbium (Tb) radioisotopes hold high promise for the development of theranostic agents due to their diagnostic and therapeutic emissions. Those radioisotopes include ^{149}Tb, ^{152}Tb, ^{155}Tb, and ^{161}Tb. An example theranostic pairing is the β^- emitting therapy candidate, ^{161}Tb, and the diagnostic SPECT imaging candidate, ^{155}Tb [5.32 d half-life, ε 100%, γ 86.6 keV (32.0%) and 105 keV (25.1%). This work examines the ^{153}Eu(α,2n)^{155}Tb and the ^{155}Gd(α,4n)^{155}Dy→^{155}Tb nuclear reactions as potential routes for production of high specific activity (HSA) ^{155}Tb.
Natural abundance Eu_2O_3 and Gd_2O_3 targets and enriched [^{153}Eu]Eu_2O_3 and [^{155}Gd]Gd_2O_3 targets were prepared by hydraulically pressing their powder form between a layer of pyrolytic graphite sheet (PGS) and an aluminum disk into an aluminum backing. Cross section data obtained from TENDL-2021 was utilized to select multiple irradiation energy windows of interest to determine the experimental production rates of ^{155}Tb and other radionuclidic impurities. Each target was irradiated with an alpha beam for a total charge of 0.25 μAh, followed by gamma ray spectroscopic analysis.
Direct production of ^{155}Tb using the ^{153}Eu(α,2n)^{155}Tb nuclear reaction in a 28-22 MeV window provided the highest overall yield of 3.5 MBq/μAh at the end of bombardment (EOB). The 28-22 MeV window also generated the highest ^{155}Tb purity (96.2% at 100 hours from EOB) with ^{156}Tb (5.35 d half-life) as the major contaminant. The indirect production route utilizing the ^{155}Gd(α,4n)^{155}Dy nuclear reaction showed a decrease in the production rate of ^{155}Dy proportional to the decrease in the incident beam energy. It appears that the maximum ^{155}Tb yields achievable from the irradiated [^{155}Gd]Gd_2O_3 targets within the energy range of our cyclotron is significantly lower than that from [^{153}Eu]Eu_2O_3 targets. Results of preliminary studies on the separation of ^{155}Tb from irradiated [^{153}Eu]Eu_2O_3 targets using an LN resin packed column will also be presented.

NUCL 3985981

Synthesis of ester-functionalized symmetric bis-(1,2, 4)-triazinyl pyridine (BTP) complexants towards minor actinide separations of spent nuclear fuel (SNF)

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The efficient separation of minor actinides such as ^{241}Am and ^{244}Cm from lanthanides in spent nuclear fuel (SNF) poses a challenge in harnessing the use of nuclear energy. Addressing this challenge is important for both nuclear waste management and the development of sustainable nuclear energy. Prior work in our group has afforded asymmetric and symmetric mono-(1,2,4)-triazinyl pyridine (MTP) and bis-(1,2,4)-triazinyl pyridine (BTP) scaffolds, which have shown potential for this separation. However, there is continued interest on enhancing the performance of these complexants towards this separation. This research seeks to provide a novel solution through the synthesis of symmetric (BTP) complexants with ester functional groups to enhance solubility and selectivity for separation of minor actinides from lanthanides. The development of these novel complexants offers the potential to remediate the SNF reprocessing by providing efficient method for separating hazardous minor actinides, which poses long-term radiotoxicity concerns. Experimental work began with a two-step telescoped synthesis approach by alkylating 3,3'dihydroxybenzil and optimizing the synthetic pathway. Acyl benzils, a precursor in the BTP synthesis were successfully obtained followed by condensation with Bis-hydrazonamide to afford the ester-functionalized BTP complexants. Subsequently, a series of ester functionalized BTPS were obtained. Characterization studies using NMR spectroscopy ensured the successful synthesis of the synthesized compounds. Further, solubility tests were performed to ascertain the solubility in common extraction solvents and stability under acidic conditions (1M HNO_3 and 6M HNO_3);both vital factors in separation processes. In addition, the perfomance of these novel complexants will be evaluated through gamma-counting assays to assess their efficiency in separating minor actinides from lanthanides under various conditions and relevant-diluents. Current synthetic results, characterization data, acid contact data and solubility studies of this complexant will be presented.

NUCL 3986164

Comparative studies on As and Sb labeling with a trithiol-based ligand

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Antimony (Sb) and its homologue arsenic (As) share similar thiophilicity and affinity for the same charge states. Antimony-119 ($t_{½}$ = 38.2 h, ~24 Auger electrons per decay) is a radionuclide for therapeutic applications, whereas positron-emitting ^{71}As ($t_{½}$ = 65.3 h,

28% β^+) and ^{72}As ($t_{½}$ = 26.0 h, 87% β^+) can be used for diagnostic imaging. This work investigates whether a theranostic relationship between As and Sb radionuclides can be realized due to their chemical homology. Comparative labeling studies were conducted using a trithiol-based chelating ligand, TT (**Figure 1**), for tridentate coordination of the 3+ pnictogens. Prior studies have shown a 2-step As reaction is required, wherein As is first reacted with a monothiol ligand, SR (**Figure 1**), to make $As(SR)_3$, followed by transchelation with TT to form the desired product (^{nat}As-TT, 80% yield). Conversely, high ^{nat}Sb-TT yield (85%) was obtained via direct labeling with TT, while the 2-step reaction yield was low (10%) due to poor transchelation from $Sb(SR)_3$. Good TT radiolabeling yields (by TLC/HPLC) were obtained with reactor-produced ^{77}As (2-step method, >95%) and cyclotron-produced ^{120m,122}Sb (direct method, 63%) surrogate radiotracers. The $logD_{7.4}$ value of ^{77}As-TT was +1.4 ± 0.1. The shorter HPLC retention time for Sb-TT (24 min) vs. As-TT (31 min) with the same gradient (50%-90% acetonitrile in water, both with 0.1% trifluoroacetic acid, over 40 min) suggests a lower $logD_{7.4}$ value for Sb-TT. This measurement and additional comparative As/Sb studies are ongoing.

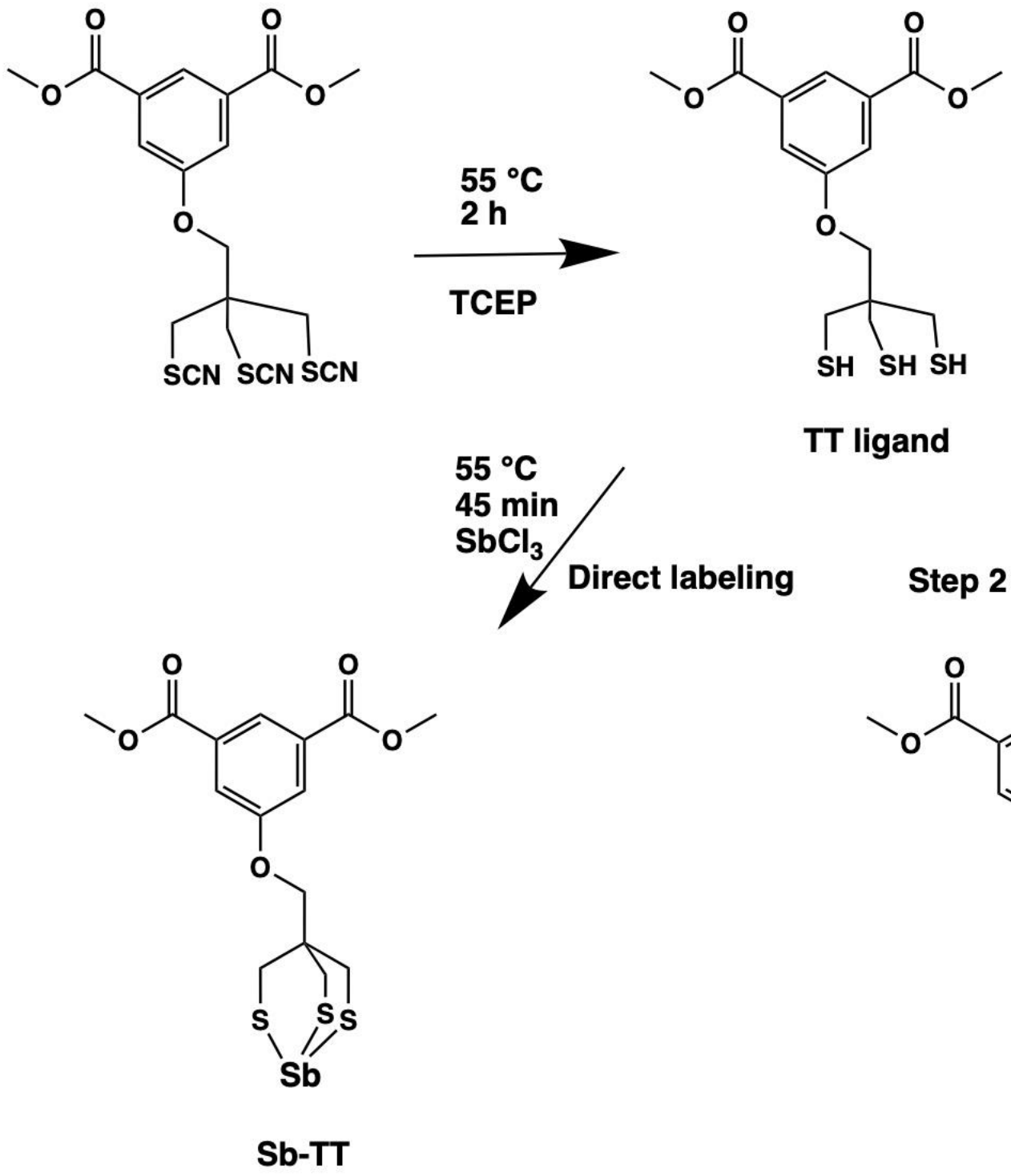

Figure 1. Labeling routes for As and S

NUCL 3986238

Progress towards the synthesis of unsymmetric tridentate complexants for application to minor actinide separations

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Minor actinides (MA) are highly radioactive and contribute to the toxicity and high heat load of spent nuclear fuel (SNF). Effective separation of MA from SNF will make SNF more environmentally safe, for geological disposal. A major research effort in this laboratory is to develop convergent methods for the synthesis of soft-Lewis basic complexant scaffolds for application in separation of MA in SNF. Taking into consideration the properties of an ideal complexant; sufficient solubility in process relevant diluents, high selectivity and affinity for the target ion, excellent kinetics, and stability, synthetic options to construct unsymmetric tridentate complexants are being explored. With soft-Lewis basic unsymmetric complexants, substituents with different electronic properties can be introduced on both sides of the complexant and can aid the efficiency in separating MA in SNF. The synthesis of 1,2,4-monotriazinylpyridyl-1,2,4-triazoles (MTP triazole), an unsymmetric tridentate complexant is in progress. Current synthetic results for this class of unsymmetric complexants, relevant substrate scope, a scale-up reaction, and future directions will be presented.

NUCL 3986566

Structural and spectroscopic properties of uranyl oxalates relating to counter-cation radii

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Uranyl oxalate compounds are of interest due to the strong and versatile coordination of the oxalate ligand to actinides, the use of oxalate as a precipitating agent in the nuclear fuel cycle, and the ubiquity of oxalate in the environment as a major degradation product of humic and fulvic acids. A series of uranyl oxalate hydroxide compounds with the same sheet topology but different monovalent counter-cations exists ($M[(UO_2)_2(C_2O_4)_2OH]\cdot xH_2O$ where M= Na, K, NH_4, Rb, or Cs and x= 1 or 2). The members of this series crystallize in different space groups with various numbers of interstitial waters, likely relating to the ionic radii of the monovalent cation. The structural variations due to counter-cation ionic radii are examined in this work. Several

unreported uranyl oxalate compounds with monovalent counter-cations were synthesized and characterized using X-ray diffraction and Raman spectroscopy to probe structural and spectroscopic feature variation with the ionic radii of the monovalent counter-cation.

NUCL 3986781

89Zr-immunoPET targeting IL13Ra2 for imaging of glioblastoma

Leah Gajecki[1]*, gajeckil@mskcc.org, Irina Lebedeva*[2]*, Daisy Ambriz*[2]*, Samantha Lovibond*[1]*, Darren R. Veach*[1]*, Lukas Carter*[1]*, Heiko Schoder*[1]*, Steve Larson*[1]*, Simone Krebs*[1]*. (1) Memorial Sloan Kettering Cancer Center, New York, New York, United States(2) Weill Cornell Medicine, New York, New York, United States*

Interleukin 13 receptor alpha 2 (IL13Ra2) has recently emerged as a promising tumor associated antigen and biomarker in glioblastoma (GBM) as there is elevated expression in 76% of GBM cases and it is corelated with poor prognosis. Additionally, IL13Ra2 has negligible expression in healthy tissue making it an ideal candidate for targeting in radioimmunotherapy. So far, no human IL13Ra2 antibody is clinically available. Five novel human monoclonal antibodies (KLG-1-5), which specifically target IL13Ra2, were developed at the Sanders Tri-TDI by standard hybridoma technology using AlivaMab Mouse (Ablexis LLC) transgenic mouse strains. Initial proof of principle studies were conducted with these antibodies that had been conjugated with DFO and radiolabeled with ^{89}Zr. These antibodies demonstrated excellent target binding to the IL13Ra2 antigen in *in vitro* immunoreactivity assays (90-98%) and cellular uptake (2.5-10.3%) in U87-MG cells as well as nanomolar binding affinity (0.27-1.63 nM). ImmunoPET imaging studies were conducted on nude mice bearing subcutaneous U87-MG xenografts, where mice were injected with 20 mg of antibody (~ 80 mCi of ^{89}Zr) and imaged 2 days post tracer injection. Remarkably, all five antibodies showed similar image contrast with tumor-to-blood, tumor-to-kidney and tumor-to-muscle ratios of 2.73-3.66, 8.25-9.84 and 18.18-28.1 (tumor [%ID/g]max/ tissue [%ID/g]mean). High tumor uptake ([%ID/g] max) was observed for all antibodies (KLG-1: 39.08 ± 5.88, KLG-2: 39.33 ± 5.76, KLG-3: 70.94 ± 16.98, KLG-4: 54.79 ± 3.11, KLG-5: 45.10 ± 4.59). This pilot data supports the hypothesis that specific targeting of IL13Ra2 in GBM is feasible by immunoPET and is an attractive target for radioimmunotherapy.

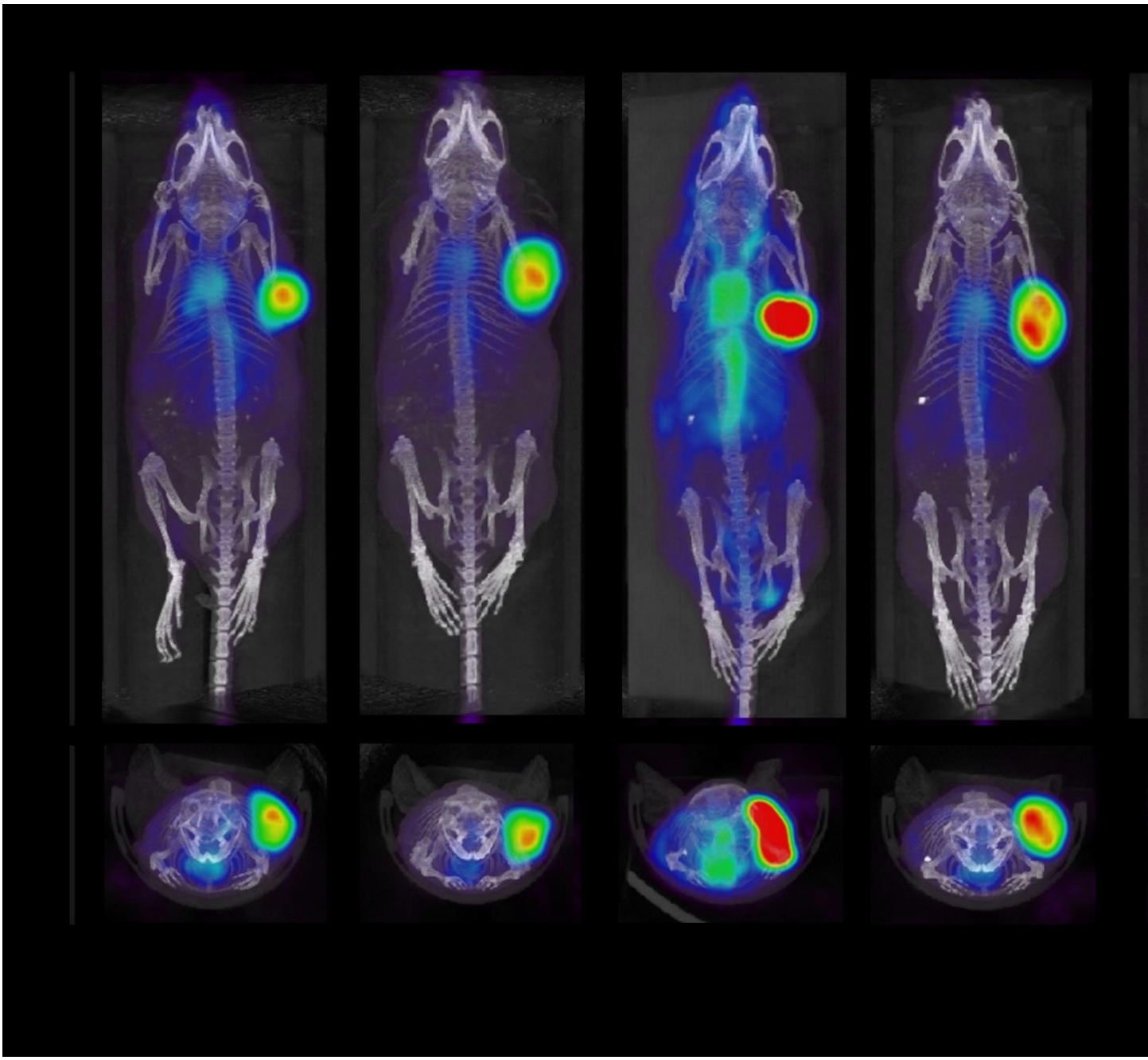

Figure 1. Representative MIP and axial PET/CT images of nude mice bearing U87-MG xenografts injected with 20 mg of ^{89}Zr labeled IL13Ra2 antibodies. Imaging conducted two days post injection.

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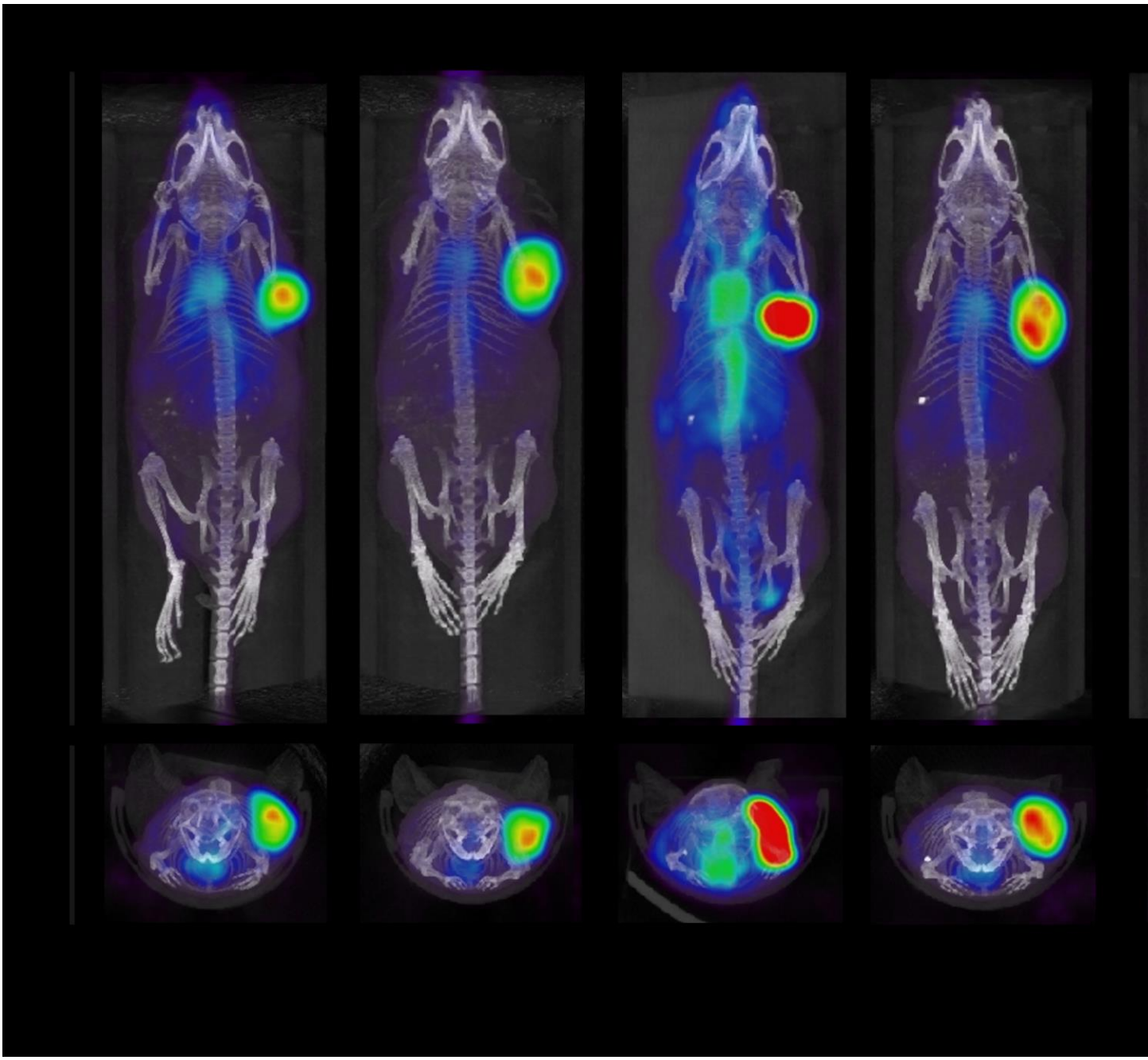

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NUCL 3986818

Radiochemical synthesis of novel demyelination PET tracer [18F]5-methyl-3-fluoro-4-aminopyridine via Csp2–18F/19F exchange

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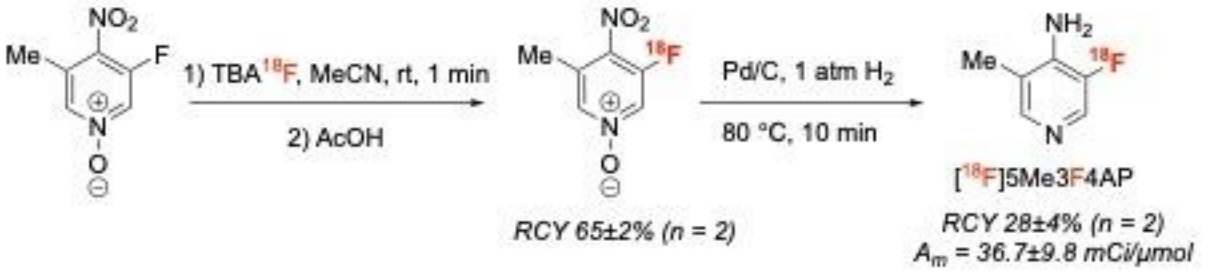
The pyridine motif is prevalent in many drugs and radiotracers. However, fluorine-18 labeling of electron-rich pyridines presents a considerable challenge due to their electron density, the lone pair electrons on the nitrogen atoms, and the potential bulkiness introduced by electron-donating groups. Yet, fluorine-18 is favored for positron emission tomography (PET) radiotracer labeling, given its optimal decay half-life. A successful example is [^{18}F]3-fluoro-4-aminopyridine ([^{18}F]3F4AP), synthesized *via* multi-step processes from precursors harboring a N-oxide group or a methyl ester group. This tracer exhibits a strong affinity for potassium (K^+) channels in demyelinated axons and shows promise for visualizing demyelinated lesions in animal models. However, recent human studies have revealed significant *in vivo* metabolism of [^{18}F]3F4AP, potentially confounding the PET signal.

To address this issue, we investigated the metabolism of [^{18}F]3F4AP and identified 5-hydroxylation as the primary metabolic pathway. In response, we designed a new radiotracer, [^{18}F]5-methyl-3-fluoro-4-aminopyridine ([^{18}F]5Me3F4AP), featuring a methyl group at the 5-position to block this metabolic route. This novel compound maintains a comparable target affinity and offers superior biophysical properties (Fig. 1).

We tried multiple synthesis methods for [^{18}F]5Me3F4AP, including copper-mediated fluorination of boronic acid precursors, without success. Alternatively, we utilized an ^{18}F/^{19}F exchange of a pyridine N-oxide precursor followed by Pd/C-mediated hydrogenation, achieving [^{18}F]5Me3F4AP with 4% decay-corrected isolated yield (Scheme 1). Notably, the ^{18}F/^{19}F-pyridine N-oxide has low stability at high temperatures and basic conditions. Therefore, to achieve optimal synthesis efficiency, we used a brief reaction time at room temperature, opted for less basic [^{18}F]tetrabutylammonium fluoride over [^{18}F]potassium fluoride, and promptly neutralized the reaction mixture with acetic acid. Furthermore, we are actively pursuing a no-carrier labeling approach to booster molar activity *via* halogen exchange of the chloride or bromide counterpart.

Figure 1. Structures of [^{18}F]3F4AP, 5-hydroxy-3F4AP and [^{18}F]5Me3F4AP.

Scheme 1. Radiochemical synthesis of [^{18}F]5Me3F4AP and radiochemical yield (RCY) based on radioHPLC.



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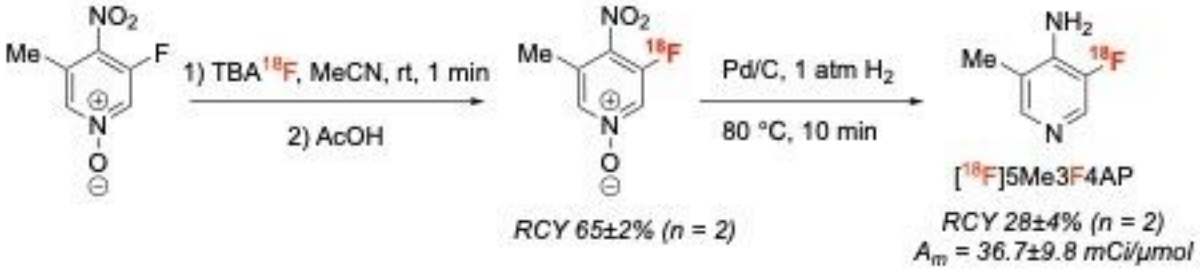

NUCL 3987083

Research scale separation of radioterbium using electro-amalgamation and extraction chromatography methods

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The elementally-matched pair of terbium-155 (^{155}Tb, diagnostic) and terbium-161 (^{161}Tb, therapeutic) radioisotopes shows promise for theranostic radiopharmaceutical applications. Terbium-155 ($t_{1/2}$ = 5.32 d, ε 100%, E_γ = 86.6 keV (32.0%), 105 keV (25.1%)) decays by electron capture accompanied by soft gamma rays, which makes it

suitable for single photon emission computed tomography (SPECT) imaging. Terbium-161 ($t_{1/2}$ = 6.89 d, β^- 100%, $E_{\beta max}$ = 594 keV) emits β^- particles and Auger/conversion electrons, which are suitable for therapy. The objective of this research is to isolate ^{155}Tb produced from the cyclotron-based ^{153}Eu(α,2n)^{155}Tb nuclear reaction and to recover and recycle the enriched ^{153}Eu target material. In this work, we developed electro-amalgamation and extraction chromatography methods for the separation of Tb(III) from Eu(III). Electro-amalgamation reactions with stable elements were initially conducted to optimize key parameters for the Eu debulking step: 7 V operating potential, pH 6.5, 0.7-0.8 A current, 0.2 M lithium citrate (electrolyte) concentration. After the debulking step, extraction chromatography was carried out using Triskem resins: TK-212 (nitric acid media), TK-221 and A8 (hydrochloric acid media). Translation of the optimized methods to the radiotracer scale utilized ^{161}Tb (as a ^{155}Tb surrogate) and 100 mg of Eu_2O_3 (production-scale mass). Inductively coupled plasma optical emission spectroscopy (ICP-OES) data from the radiotracer studies revealed that 75% of the Eu was separated into the Hg layer from the ^{161}Tb aqueous layer at the end of a 25-min electro-amalgamation reaction, with >99% of the Eu removed following the subsequent chromatographic separation. Overall recovery of the Tb radiotracer in 0.05 M HCl was 92%. These studies demonstrated the successful separation of a Tb(III) radiotracer from production-scale masses of Eu_2O_3. Further method optimization as well as quality testing of the radioterbium product are ongoing.

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NUCL 3987819

Surface-specific selectivity during lanthanide adsorption at aluminum oxide-water interfaces

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Regolith-hosted deposits serve as major lanthanide resources. These form via chemical weathering of granites and often display relative enrichment in the heavy lanthanides. Retention of these critical elements occurs via adsorption to clay minerals, such as kaolinite and gibbsite, with recovery possible using mild chemical extractions. The underlying interfacial chemistry that controls lanthanide retention, fractionation, and extractability in these deposits remains unresolved. Strong retention suggests a ligand-exchange binding mechanism, yet the ease of extractability implies weak binding. Molecular-scale information on interfacial reaction mechanisms of lanthanides is challenging to access via traditional approaches, such as X-ray absorption

spectroscopy, because of the disordered nature of the first coordination shells of these elements and the weak spectral contributions of structural cations in clays. We have applied resonant anomalous X-ray reflectivity to probe the comparative binding of a light (Nd), middle (Dy), and heavy (Yb) lanthanide to the (001) and (012) surfaces of aluminum oxide, structural analogs of the basal and edge surfaces, respectively, of both gibbsite and kaolinite. When reacting individually with the (001) surface, these three lanthanides show similar total binding but transition from predominantly inner-sphere complexation by Nd to predominantly outer-sphere binding by Yb. In addition, the inner-sphere complexes become more disordered moving from light to middle to heavy lanthanide. These trends correlate with the increasing hydration enthalpy across the lanthanide series. When all three elements co-adsorb to alumina (001) in a single system, competitive effects create strong selectivity for Nd over Dy and Yb as well as the complete disappearance of all outer-sphere species. In contrast, co-adsorption of Nd, Dy, and Yb to the alumina (012) surface shows minimal selective adsorption behavior and the formation of similar proportions of inner- and outer-sphere complexes for all three lanthanides. This study reveals that specific mineral surfaces display distinct selective adsorption behavior, implying that chemical fractionation of lanthanides in natural environments are affected by clay particle morphology.

NUCL 3987868

Understanding the Pu(VI)-oxalate system: Aqueous and solid-state complexation and degradation

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Aqueous-phase interactions between Pu(VI) and oxalate have been historically underrepresented in the literature in contrast to the use of Pu(IV)-oxalate precipitation in the processing of waste. The latter has led to a wide litany of studies focused on optimizing the process and understanding the calcination pathway from $Pu(C_2O_4)_2{\bullet}6H_2O(s)$ to $PuO_2(s)$. The prevalence of oxalate across the fuel cycle necessitates a better understanding of how oxalate can impact Pu behavior under conditions and Pu oxidation states beyond those utilized for Pu-oxalate precipitation. The present work focuses on Pu(VI), which is a product of Pu(IV) disproportionation and a Pu oxidation state that is expected to have a higher environment mobility than Pu(IV). It is, thus, a significant concern for waste storage.

We observed the formation of at least two aqueous Pu(IV)-oxalate complexes that form at $1 \leq pH_c \leq 7$ across a range of metal-to-ligand ratios. The formation and degradation of these complexes were monitored by UV-vis-NIR spectrophotometry. Over time, the reduction of the Pu(VI) to Pu(IV), followed by precipitation, led to the isolation of the first single-crystals of $Pu(C_2O_4)_2{\bullet}6H_2O(cr)$. Additionally, we observed and studied the photocatalytic component of the reduction mechanism.

We have also isolated and characterized the first single-crystal Pu(VI)-oxalate compound, $[PuO_2(C_2O_4)(H_2O)]\bullet 2(H_2O)$(cr). Photocatalytic reduction of these crystals resulted in the formation of a new crystal habit. While this structure has not been successfully isolated, preliminary data suggests it is not the same Pu(IV)-oxalate compound that forms upon reduction of the aqueous Pu(VI)-oxalate complexes.

Spectrophotometric and solid-state studies have provided some insight into the Pu(VI)-oxalate system. We observed the formation of multiple Pu(VI)-oxalate complexes and the possibility of multiple degradation pathways. The presence of Pu(VI)-oxalate complexes in solution demonstrates why a more thorough understanding of this system is needed.

NUCL 3987869

Theranostic ^{225}Ac/^{89}Zr-superparamagnetic iron oxide nanoparticles (SPIONs) to combine targeted alpha therapy and PET imaging

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Targeted alpha-therapy (TAT) with ^{225}Ac-radiotherapeutics has recently shown excellent clinical outcomes in several cancer types, including patients with late-stage metastatic disease. While much effort has been focused on directly imaging ^{225}Ac's daughters with SPECT, most ^{225}Ac-radiotherapeutics require a companion diagnostic agent. Herein, we report the development of a nanotheranostic agent, ^{225}Ac/^{89}Zr- superparamagnetic iron oxide nanoparticles (SPIONs), to combine the therapeutic and diagnostic benefits of TAT and PET, respectively. SPIONs also give the benefit of potential magnetic targeting, dual therapy with hyperthermia, use as an MRI contrast agent and well-studied methods for surface functionalization. ^{225}Ac and ^{89}Zr were co-precipitated during the SPION synthesis, achieving a radiolabeling yield > 90%, and were assessed for ^{225}Ac chemical stability and daughter retention. Additionally, the surface of the SPIONs was sequentially coated with oleic acid, glutathione, and then PEG to prevent macrophage sequestration and non-specific uptake in the reticuloendothelial system. The successful development of PEGylated ^{225}Ac/^{89}Zr-SPIONs will yield a nanotheranostic template that may be targeted to a variety of different receptors for cancer therapy.

NUCL 3988091

Thermal stability and decomposition mechanisms of uranyl nitrate hexahydrate

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Uranyl Nitrate Hexahydrate (UNH) is a key material in the nuclear fuel cycle and has been used for decades as a precursor in the preparation of many technogenic uranium bearing compounds such as UO_3, $UO_2O_2x4H_2O$, and U_3O_8. Despite the importance of UNH, published literature features many discrepancies about its thermal decomposition. For example, temperatures of dehydration vary greatly across reports, and intermediate species are not agreed upon, thus necessitating further research into the decomposition products of UNH and the mechanisms responsible for their formation. Understanding the complex behavior of UNH at elevated temperatures has the potential to provide insights into a sample's history, including storage conditions and processing methods. Consequently, this bears significant implications for the field of nuclear forensics. In this work, the relation between the heating rate of UNH and the formation of uranium trioxide has been studied. Structural changes during decomposition have been monitored via in-situ Raman spectroscopy and powder X-ray diffraction, and reaction kinetics have been characterized using thermogravimetric analysis, differential scanning calorimetry, and evolved gas analysis. Our study reports evidence of a stepwise decomposition unaffected by heating rate until 160°C, at which point separate decomposition pathways are observed when comparing fast and slow heating rates. Results from this study form a foundation for a continuing investigation into the many polymorphs of uranium trioxide.

NUCL 3988667

Synthetic access to unsymmetric, pyridyl-1,2,4-triazine complexant scaffolds via telescoped condensation of heteroaryl carbonitriles

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The remediation of spent nuclear fuel (SNF) obtained as a result of nuclear energy production is still a major environmental challenge. Over the last three decades, considerable work has been directed toward the design and synthesis of soft-Lewis basic complexant scaffolds for potential use in chemoselective liquid-liquid separations of trivalent actinides (An^{3+}) from trivalent lanthanides (Ln^{3+}) in spent nuclear fuel. Following Kolarik's demonstration of the usefulness of 1,2,4-triazinyl moiety for chemoselective separations with the synthesis of the 1,2,4-bis-triazinylpyridine (BTP) scaffolds as selective complexants for Am^{3+} over Ln^{3+}, conventional ligand design has centered on symmetric moieties of these BTP class of compounds. However, the solubility of these complexants in inexpensive, process-relevant nonpolar diluents, such as octanol and kerosene, remains a concern. Recent efforts in this lab have focused on ascertaining the impact of unsymmetric BTP complexants toward good solubility and complexation performance in separations processes. In this study, synthetic access to about 20 examples of the proposed unsymmetric BTPs in good yields was achieved via telescoped condensation of heteroaryl carbonitriles with diversely functionalized 1,2-

dicarbonyls. Further separation studies from simulated SNF will be possible with access to these unsymmetric BTPs. Method optimization and synthetic strategies toward relevant substrates will be presented.

NUCL 3988694

Astatine-211 for targeted alpha therapy: Target dissolution optimization and new methods of recovery in nitric acid media

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The successful clinical trial performance of alpha-emitters, such as ^{225}Ac-PMSA, has increased interest in targeted alpha therapy (TAT). ^{211}At is a promising candidate for TAT due to its short 7.2-hour half-life and its simple, quantitative alpha decay. This makes it exceptionally well-suited for clinical applications, but with little known about astatine's fundamental chemistry, further exploration is necessary to advance its potential as a TAT candidate. Current production of ^{211}At is primarily performed using the ^{209}Bi(α,2n)^{211}At nuclear reaction, with only a select few facilities capable of generating the required beam species and energy. Due to its limited availability, maximizing the recovery of ^{211}At from the metallic bismuth targets is critical to expanding the research effort. To investigate the dissolution of irradiated targets in nitric acid, various target-making and dissolution system parameters were tested on unirradiated bismuth targets. Separation of astatine from the metallic bismuth target is commonly achieved through liquid-liquid extraction, dry distillation, and extraction chromatography methods. However, ion-exchange chromatographic systems for astatine recovery have not yet been fully explored. Several methods of chromatographic separation are here proposed and investigated through batch studies. Affinities for several commercially available ion-exchange resins were then determined for bismuth and astatine in a nitric acid media.

NUCL 3988837

Small-molecule antagonist radiotracers for positron emission tomography imaging of the mu opioid receptor

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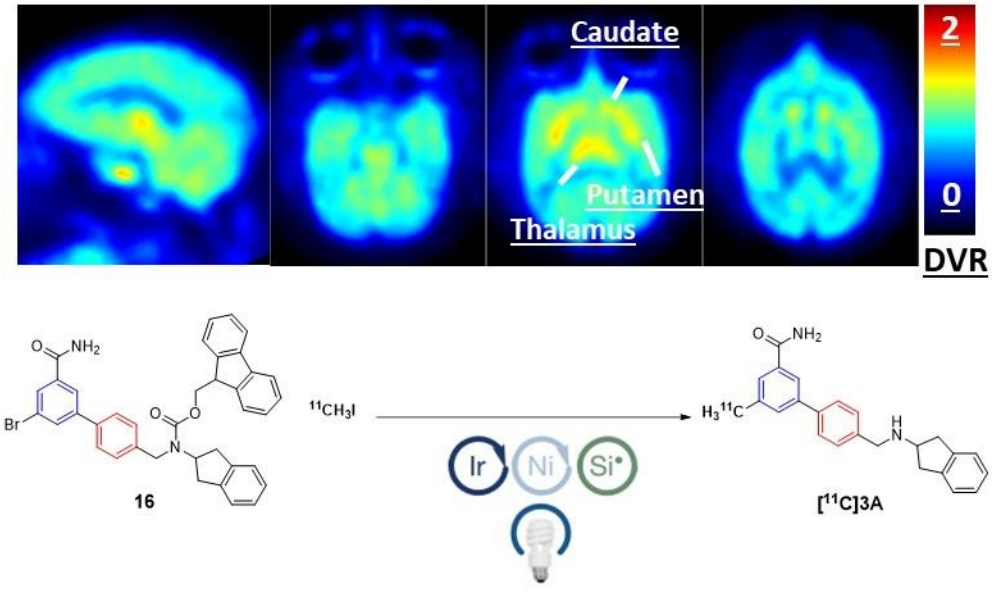
The mu opioid receptor (MOR) is a drug target for the treatment of pain and dysregulation of the MOR is common in neuropsychiatric disorders. PET analysis of the MOR utlilizes agonist [^{11}C]CFN, which carries risk and can cause respiratory depression at tracer doses. Therefore, there is an unmet need for the development of MOR antagonists to carry out PET imaging of the MOR. Herein, we describe the synthesis and evaluation of 24 MOR antagonists with affinity and selectivity towards the MOR. This library is based on MOR antagonist GSK1521498 and was designed to be compatible with metallophotoredox radiomethylation. **3A** displayed potent activity towards the MOR and selectivity over other opioid receptors. Competition curves were generated to determine Ki values for the opioid receptors. Radiolabeling utilized [^{11}C] MeI prepared on a Synthra MeI module. Nascent [^{11}C] MeI was coupled with the appropriate aryl-bromide precursor utilizing a Penn PhD Photoreactor with 425 nm LED irradiation. A library of 24 MOR antagonists were synthesized and evaluated for their affinity and selectivity for the family of opioid receptors. **3A** displayed an affinity of 7.8 nM for the MOR and was devoid of pharmacological activity at the MOR, thus classifying it as an antagonist. **3A** was subsequently radiolabeled and evaluated for use a PET tracer for *in vivo* MOR imaging. [^{11}C] **3A** was prepared in 4.0% ± 2.0 radiochemical yield, 96.8% ± 2.2 radiochemical purity, and possessed a molar activity of 800 ± 9.2 (n=3) at end of synthesis. Time-activity curves were generated and in a non-human primate model, [^{11}C] **3A** showed highest uptake in the thalamus and putamen, regions of the brain that exhibit high MOR density. A library of MOR antagonists were synthesized and radiolabeled utilizing metallophotoredox-radiomethylation. This is the first use of this methodology towards the radiosynthesis of previously undescribed radiopharmaceuticals. This represents a paradigm shift towards enabling study of the MOR through safer radiopharmaceuticals. Ongoing medicinal chemistry efforts are aimed at improving ligand affinity.

[^{11}C] 3A



NUCL 3988861

Radiopharmaceutical separations: Cradle to grave

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Development of radiopharmaceuticals requires purity considerations from the radionuclide onward. The isotopic and chemical purity of the target to be irradiated at either a nuclear reactor or an accelerator is critical to minimize radiation doses and purification following irradiation to isolate the radionuclide of interest. Isolation of high specific activity radionuclide from its target material in high chemical and isotopic purity is essential for use in radiolabeling the product radiopharmaceutical. Purification of the radiolabeled product may be necessary if isolation from unlabeled targeting vector is required. Recovery and recycling of highly enriched target material is necessary for cost effectiveness. Examples will be used to illustrate the importance of separations to the various processes involved.

NUCL 3988882

Design and synthesis of candidate fluorine-18 labeled radioligands for PET imaging of brain COX-1

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Cyclooxygenase-1 (COX-1) is constitutively expressed in brain and plays a major role in the biosynthesis of proinflammatory mediators in the CNS. COX-1 expression is upregulated in activated microglia in monkey neuroinflammatory models, suggesting COX-1 could be a useful biomarker for neuroinflammation. We have developed a highly selective COX-1 radioligand, [^{11}C]PS13, (*h*COX-1 IC_{50} = 1 nM and *h*COX-2 >1000 nM), which is now used with positron emission tomography (PET) to quantify COX-1 in monkey and human brain. A COX-1 PET radioligand labeled with longer-lived fluorine-18 would be more appealing because of the potential for wider use through distribution to PET imaging centers that are considerably distant from central radiosynthesis sites. We have labeled PS13 with fluorine-18 in the *trifluoroethoxy* position in modest yield and with low molar activity and have shown that this tracer can well image COX-1 in monkey brain. However, it is desirable to suppress occupancy of COX-1 by carrier from low molar activity [^{18}F]PS13 to better comply with the tracer principle. We therefore embarked on the design and synthesis of a next generation of ^{18}F-labeled COX-1 PET ligands, where the new candidates retain or have improved COX-1 affinity and selectivity, and also provide a possibility for labeling with fluorine-18 in high yield and

molar activity.
Systematic SAR was performed on the 1,2,4-triazole core of PS13 with modifications exploring rational alterations to one or more of the two pendant aryl groups and/or alkoxy side-arm, resulting in 31 new COX-1 ligands. These ligands were assayed for COX-1 binding affinity with a method developed in-house, in which recombinant human COX-1 was immobilized onto 96-well plates and the new ligands competed with [^{3}H]PS13 binding. Initial screening revealed two promising candidates, ZQC7 and ZQC17 with COX-1 K_i values of 6.6 nM and 6.1 nM, respectively (c.f. a K_D value of 7.9 nM for PS13). Both compounds feature readily accessible sites for straightforward labeling with either carbon-11 or fluorine-18 at high molar activity. ZQC17 was labeled in the *fluoroethoxy* position with fluorine-18 in high yields and with high molar activity (241 GBq/μmol). The lipophilicity (log$D_{7.4)}$ of [^{18}F]ZQC17 was also measured to be desirably less than that for [^{11}C]PS13 (3.26 vs 4.26) with potential for less unwanted non-specific binding in vivo. Evaluation of [^{18}F]ZQC7 and [^{18}F]ZQC17 for PET imaging of COX-1 in monkey brain is now being pursued.

NUCL 3989116

Group hexavalent actinide separation via co-crystallization of elements found in used nuclear fuel

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The burning of fossil fuels has been the primary source of energy for modern civilization. However, recently, the negative environmental impacts from these processes including the emission of pollutants and greenhouse gases, which accelerate climate change, have garnered much attention. This has necessitated the development of green, renewable energy, with one of the few energy sources that can be scaled to meet the growing demand being nuclear power. To enable the expansion of nuclear power several challenges need to be addressed. One of the main challenges is developing a separation/recycling scheme for used nuclear fuel (UNF) that enhances the recovery of the U, Pu, and other actinide (An) species. Sequentially, the ideal separation process should minimize the impact of waste bound for a geological repository, maintain the nonproliferation standards, and have the ability to scale the process for a diverse fleet of reactor fuels.
The aim of this research explores a single-step separation technology for the recovery of the actinides ranging from U-Am as a group, utilizing a co-crystallization with uranyl nitrate hexahydrate (UNH). Recent studies have shown the transuranic (TRU) species in their hexavalent state, Np(VI), Pu(VI), or Am(VI), which exist as the dioxo actinyl molecular ion, AnO_2^{2+}, have near proportional removal from solution to that of U(VI). The co-crystallization approach has extremely high selectivity for the An(VI) species, while completely discriminating against fission products. Aspects of the separation of

the hexavalent actinides from fission products will be discussed, at the 1-g and 10-g of U(VI) scales with special attention on the problematic fission product species like Mo, Tc, and Ru. These experiments will be analyzed by UV-Vis and ICP-MS to determine the separation of each element. Samples for analysis will be taken from pre-crystallization, post-crystallization supernatant, and from a solution of the dissolved crystalline product.
Am(III) will be added to the system in order to explore the optimal conditions of oxidation to Am(VI) using sodium bismuthate ($NaBiO_3$). Am and the other TRUs need to be in the 6+ state for this technology to properly incorporate them into the crystal lattice formed for separation from the fission products. Variables such as concentration of nitric acid, uranium, and sodium bismuthate and temperature will be investigated. The transition from Am(III) to Am(VI) will be monitored by UV-Vis over time.

NUCL 3989224

Evaluation, post-elution processing, and radiolabeling of an upscaled SnO2-based 44ti/44sc generator

Christine E. Schmidt[1,2,3]*, cschmidt1@gradcenter.cuny.edu, Vanessa A. Sanders*[4]*, Cathy S. Cutler*[4]*, Jennifer Shusterman*[3,5]*, Melissa A. Deri*[2,1]*. (1) Chemistry, CUNY Graduate Center, New York, New York, United States(2) Chemistry, Lehman College, Bronx, New York, United States(3) Chemistry, Hunter College, New York, New York, United States(4) Collider-Accelerator, Brookhaven National Laboratory, Upton, New York, United States(5) Lawrence Livermore National Laboratory Nuclear and Chemical Sciences Division, Livermore, California, United States*

^{44}Sc is emerging as an attractive PET imaging isotope due to its convenient 4 hour half-life and high 94% branching ratio. Additionally, it can be independently produced without the need for an on-site cyclotron by the decay of the long-lived ^{44}Ti parent ($t_{1/2}$ = 59.1 y) via a $^{44}Ti/^{44}Sc$ radionuclide generator, making it an exceptional choice for clinical use. A significant challenge with current generator systems is ^{44}Ti breakthrough during elution, potentially due to deterioration of the organic-based resins overtime. As an alternative, we have designed a $^{44}Ti/^{44}Sc$ generator using an inorganic-based resin, tin dioxide (SnO_2). Preliminary column study results show high ^{44}Sc elution yields with increased acid concentration, and increased ^{44}Ti breakthrough at >9 M, with HNO_3 outperforming HCl. A pilot 100 µL bed volume (BV) generator loaded with 7.4 kBq (0.2 µCi) demonstrated >80% ^{44}Sc elution yields and <1% ^{44}Ti breakthrough in 5 M HNO_3 over the course of a year. A scaled-up 200 µL BV 7.4 MBq (200 µCi) generator displayed a comparable average ^{44}Sc elution yield of >83% with no increase of ^{44}Ti over the course of 50 elutions. A post-elution processing procedure using DGA-normal resin has been established to fully remove trace levels of ^{44}Ti in dilute HCl. The purified ^{44}Sc was used to radiolabel DOTA, resulting in a >93% radioyield.

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NUCL 3989280

Flocculation and coagulation of uranium hydroxide for improved filtration

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Precipitation and filtration processes are used throughout the nuclear fuel industry to remove radioactive materials from water. Batch processing and membrane filtration require considerable worker oversight and involvement, and even though these operations are performed in a glove box, they still present dosage hazards to workers. This is partially due to the problematic hydroxide precipitates formed when pH is increased to above 7. These precipitates strongly associate with water, which not only reduces their effective density but also restricts the water removal rate. The use of flocculants and coagulants in nuclear material waste waters could reduce filtration time

and worker dosage in large-scale nuclear processing. This hypothesis has been explored by observing the settling behavior of precipitated uranium hydroxide with and without flocculants. We present here some of the first studies of the settling velocity of uranium hydroxides using a LUMiSizer, and how it changes with the addition of iron nitrate or polyacrylamide as flocculants/coagulants. The settling behavior of solids illuminates phenomena that foretells of filtration ease or issues and we have begun testing the effects of the added flocculants on the filtration of uranyl hydroxide.

NUCL 3989305 - Withdrawn

NUCL 3989469

Synthesis and evaluation of ^{177}lu-Dotaga-*p*iba-Llp2a analogues with different click chemistry linkages as agents for metastatic melanoma

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Melanoma is the deadliest form of skin cancer. Transmembrane integrin-very late antigen-4 (VLA-4), which plays an important role in tumor growth, angiogenesis, and metastasis, is overexpressed in metastatic melanoma. The peptidomimetic LLP2A has a high binding affinity to VLA-4 and is used as a targeting and therapeutic delivery agent. Previous studies demonstrated that ^{177}Lu-DOTA-LLP2A is not an effective therapeutic agent against metastatic melanoma in mice due to its rapid clearance from tumor and blood. To improve the tumor retention time of the potential therapeutic agent, we first designed a complex ^{177}Lu-DOTAGA-*p*IBA-PEG$_4$-LLP2A (compound **1**) where an albumin binding moiety, (4-(*p*-iodophenyl)butyric acid (*p*IBA)) was covalently attached. *In vivo* data demonstrated that the albumin binder (*p*IBA) improved tumor retention. To help further screen high efficacy therapeutic agents from libraries of compounds containing different VLA-4 ligands, albumin binders, and chelators, we investigated different click chemistries, including DBCO-azide (^{177}Lu-DOTAGA-*p*IBA-DBCO-PEG$_3$-LLP2A, compound **2**), BCN-azide (^{177}Lu-DOTAGA-*p*IBA-BCN-PEG$_4$-LLP2A, compound **3**), and TCO-tetrazine (^{177}Lu-DOTAGA-*p*IBA-TCO-PEG$_4$-LLP2A, compound **4**). *In vivo* biodistribution data (out to 168 h) demonstrated that compared to compound **1** (amide linkage), click compounds **2**-**4** resulted in slightly higher tumor uptake past 48 h. At 48 h, the tumor to blood ratio of compound **1** is higher than that of compound **3** and compound **4**. At 96 h and 168 h, the tumor to blood ratio of compound **4** is higher than that of compound **3**. Compound **3** showed enhanced kidney clearance as well as lower spleen uptake compared to compound **4**. Other than ease of synthesis, there are no significant advantages of click linkages for *in vivo* behavior. SPECT imaging was performed for compounds **3**-**4**. Compound **3** demonstrated a better tumor contrast compared to compound **4** (168h).

NUCL 3989644

o-(Sulfonamido)phenol ligands as f-element extractants for combined Cs and actinide separations in caustic high-level waste

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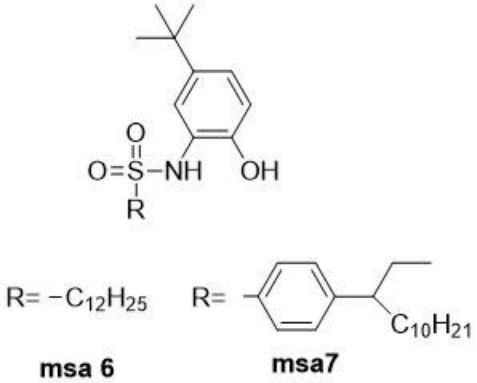
As part of an effort to develop a combined Cs and actinide (An) extraction process for Caustic High-Level Waste (HLW) for improvement of the Next-Generation Caustic Side Solvent Extraction (NG-CSSX) process, our group has reported *o*-phenylenediamine-derived sulfonamide (**dsa**) and *o*-(sulfonamido)phenol (**msa**) ligands, as effective Sm(III) extractants from alkaline aqueous solutions. Specifically, recoveries up to 81% at pH 13.0–13.5 (for **dsa**) and up to 90% at pH = 14.0 (for **msa**), into chlorinated solvents were achieved after a single loading/stripping cycle. In this study, the highly-lipophilic **msa** derivatives **msa6** and **msa7** were synthesized, characterized, and evaluated for Sm(III) extraction from up to 2.5 M NaOH aqueous solutions using a formulated NG-CSSX simulant and the actual NG-CSSX solvent, showing up to 25% recovery of Sm(II) after a single loading/stripping cycle. Extraction experiments with both extractants were also conducted in the presence of the most abundant ions in tank waste; K^+(0.045 M), Na^+ (5.6 M), CO_3^{2-} (0.2 M), NO_2^- (0.5 M), NO_3^- (2.06 M), OH^-(2.06 M), Cl^- (0.01 M) and SO_4^{2-} (0.14 M), showing up to 8% recovery of Sm(III) and 15% recovery of Cs(I) for **msa6** in the listed ion matrix. The extraction efficiency of Am-241 and Eu-154 with **msa7** showed D_{Eu} = 3.0, D_{Am} = 1.08, and D_{Cs} = 254.9 when irradiated at 202 kGy, while **msa6** showed D_{Eu} = 1.64, D_{Am} = 0.79, and D_{Cs} = 212.83 at 202 kGy. Studies with slope analysis using Sm(III) and other Ln(III) and spectroscopic studies by ^{1}H-NMR for determination of binding constants will also be presented



NUCL 3989644

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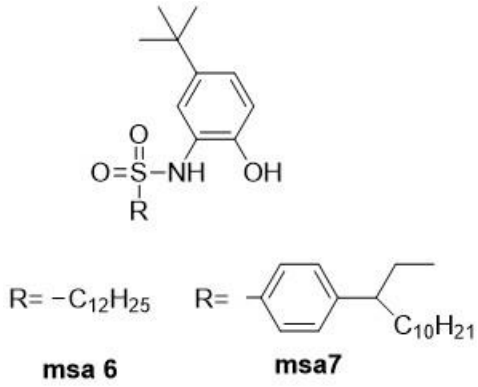

NUCL 3989679

Synthesis of [^{11}C]-*carbonyl*-RO6899880 using [^{11}C]CO: An alternative agonist radiotracer for imaging the GABA$_A$ receptor

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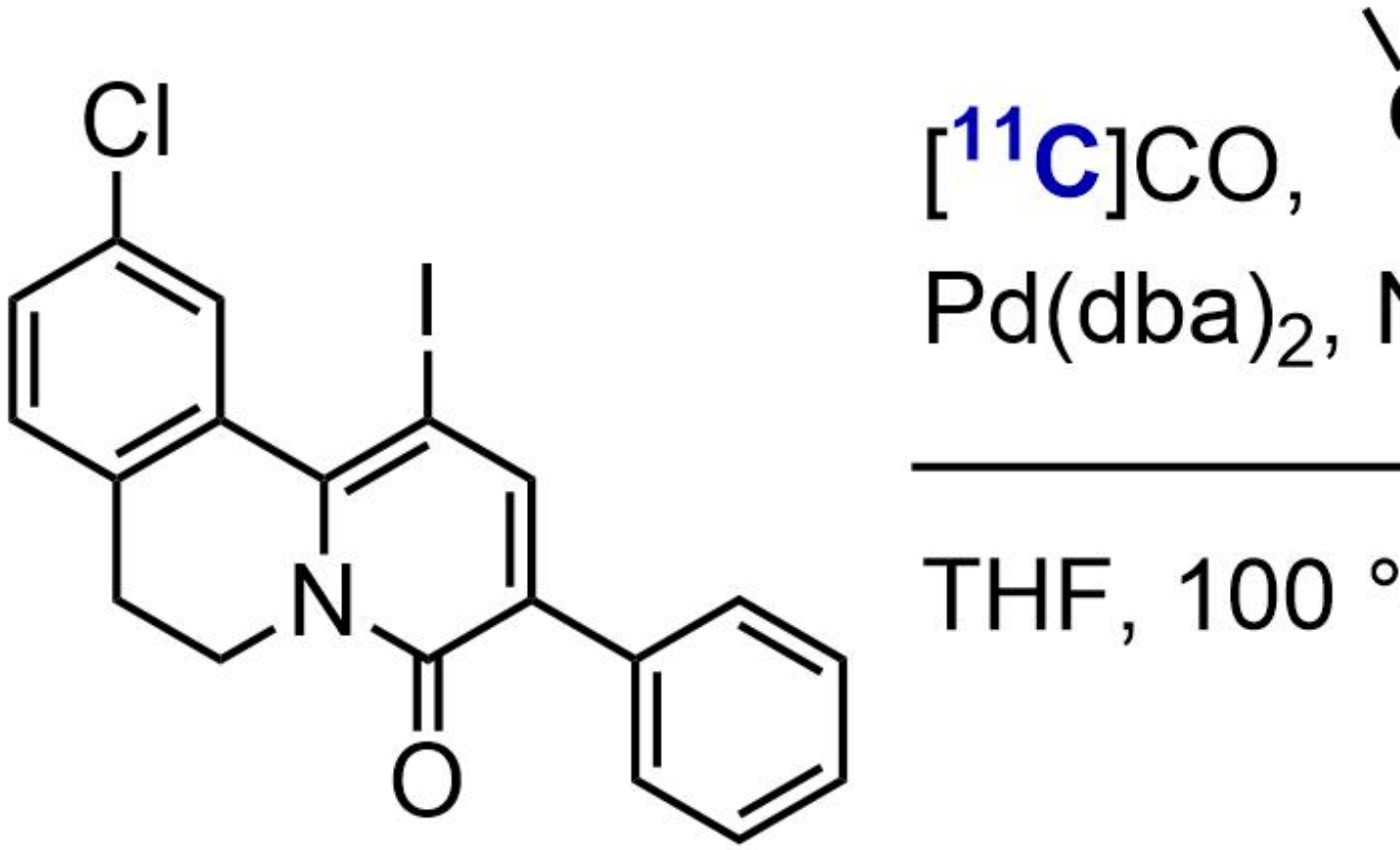
Background: ^{11}C-Carbonylation reactions have proven to be useful for the synthesis of ^{11}C-amides and offering alternatively labeled compounds with optimal radiometabolism. The recent development of radiolabeling methods using [^{11}C]CO have provided access to new radiosynthesis pathways for ^{11}C-carbonylation. [^{11}C]RO6899880 is a PET radioligand with high sensitivity to changes in endogenous GABA$_A$ levels, which could allow close monitoring of the GABAergic system in response to diseases. The goal of the present work is to synthesize a unique isotopolog of RO6899880 labeled at the carbonyl position using [^{11}C]CO as an alternative agonist radiotracer for PET imaging of the GABA$_A$ receptor.
Methods: [^{11}C]RO6899880 was prepared from the precursors 1-iodo-10-chloro-4-oxo-3-phenyl-6,7-dihydro-4H-benzo[a]quinolizinone and (*S*)-3-methoxy-pyrrolidine by ^{11}C-carbonylation using [^{11}C]CO in the presence of bis(dibenzylideneacetone)palladium(0) and NiXantphos in THF, at 100 ^{o}C for 5 min, on a TracerMaker^{TM} (Scansys Laboratorieteknik) synthesis platform. The crude material was purified by semi-preparative HPLC and formulated in saline for an overall synthesis time from end of bombardment of 45 min.
Results: Previously prepared from its corresponding desmethyl precursor *via* [^{11}C]CH_3I methylation, we report the labeling of the amide moiety of [^{11}C]RO6899880 by ^{11}C-carbonylation *via* [^{11}C]CO of the iodo-precursor with (*S*)-3-methoxy-pyrrolidine using a NiXantphos-mediated protocol under atmospheric pressure with no-carrier-added [^{11}C]CO (Figure 1). Optimization of the reaction conditions and evaluation of brain and plasma radiometabolites compared to the ^{11}C-methylated analog are underway and will be presented.
Conclusion: [^{11}C]*carbonyl*-RO6899880 was successfully synthesized by ^{11}C-carbonylation in a fully automated radiosynthesis as an alternative GABA$_A$ receptor agonist radiotracer. Pending the radiometabolite analysis, we plan to validate the radiochemistry and translate this unique isotopolog for first in human PET imaging studies.
Figure 1. Radiosynthesis of [^{11}C]RO6899880 by ^{11}C-carbonylation *via* [^{11}C]CO.



NUCL 3990246

Isotope harvesting at FRIB: Upcoming opportunities for Nuclear Medicine

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At the Facility for Rare Isotope Beams (FRIB), exotic secondary beams are created by the fragmentation of a high-power primary beam in support of our quest to elucidate fundamental questions in nuclear sciences. In this process, only a small fraction of the beam products are selected and co-produced fragments are intercepted by accelerator components, while the unreacted primary beam will be stopped in a water-traversed beam dump. The accumulated radionuclides in all these components represent an

invaluable resource. Their collection through a targeted isotope harvesting program will galvanize the advancement of fundamental and applied research opportunities, among them nuclear medicine.
In this talk, I will give an overview of the isotope harvesting process, first with a focus on the aqueous-phase collection of ^{62}Zn from a stopped ^{78}Kr beam. Together with its radioactive daughter ^{62}Cu, the pair finds applications as a radionuclide generator for nuclear medicine. The here-developed harvesting and purification methods facilitated the recovery of pure ^{62}Zn, which was used to set up a preliminary radionuclide generator. However, in FRIB's normal operation mode, a broad variety of multiple isotopes of each element will be created, and often direct harvesting efforts will not yield radioisotopically pure samples. To increase the spectrum of pure radioisotopes, we envision the implementation of a mass-separation step. At FRIB, a suitable mass analyzer magnet is already part of the existing infrastructure and could be utilized to establish a prototype mass separator. In this way, radioisotopically pure samples will be collected and also serve as a source for non-standard isotopes for nuclear medicine research. I will give an overview of some first mass-separation experiments where we investigated the release and extraction properties of stable Ni isotopes in the ion source.

NUCL 3990474

Development of a bismuth-213 labeled pyridyl benzofuran for targeted alpha therapy of amyloid beta aggregates

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Alzheimer's Disease (AD) is a prevalent neurodegenerative disease which has very few treatment options, of which there is no cure. It has been shown that whole-brain ionizing radiation can generate an immune response toward, and reduce the presence of, amyloid-beta plaques, a key biomarker in AD. We hypothesize that targeted alpha therapy (TAT) may generate a similar immune response and a greater reduction in amyloid-beta, while reducing dose to healthy tissue. A pyridyl benzofuran-based targeting agent (BiBPy) was synthesized for TAT of AD and radiolabeled with ^{213}Bi obtained from a small ^{225}Ac/^{213}Bi radionuclide generator. The specific activity was found to be 121 GBq/μg utilizing a titration method. The binding affinity to amyloid beta was measured to be K = 11 nM employing a competition assay with Thioflavin T on amyloid beta aggregates. Brain homogenate from transgenic APP/PS1 double mutant AD mice was incubated with varying doses of [^{213}Bi]-BIBPY and displayed a clear reduction in plaque concentration with increasing activity, resulting in an IC_{50} of 0.337 MBq. When our treatment was blocked with Thioflavin T, reduction of amyloid beta was significantly reduced (p=0.002). The concentration of plaques *in vitro* could be reduced below the minimum detectable limit of both ELISA and Western Blot at activities above 0.74 MBq. At the same time, the concentration of control protein GAPDH in the samples did not vary, suggesting that the targeted approach minimizes off-target dose. Targeted alpha

therapy has been demonstrated to reduce amyloid-beta plaque burden *in vitro* for the first time. Future work includes *in vivo* biodistribution in AD and WT control mice to confirm uptake in the brain and stability of our compound. This biodistribution will be accompanied by autoradiography of brain tissue to confirm *in vivo* binding, as well as immunohistochemistry to investigate the immune response to TAT.

NUCL 3990487

Separation of high specific activity ^{161}Tb and ^{155}Tb from proton irradiated ^{nat}Dy foils

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One critical area of radiopharmaceutical research and development is the production of high specific activity theragnostic radionuclides due to their potential to advance personalized medicine. Terbium is an emerging theragnostic element that has four medically relevant radioisotopes:^{149}Tb, ^{152}Tb, ^{155}Tb, and ^{161}Tb. Terbium-161 ($t_{1/2}$ = 6.89 d, β^- 100%, $E_{\beta max}$ 594 keV) is a highly promising radioisotope for targeted cancer treatment due to its emitted radiation, which consists of both Auger electrons and short-range beta particles. This allows for a higher total electron to photon dose ratio compared to the clinically established ^{177}Lu, potentially enhancing tumor cell killing for a given injected dose. Production of ^{161}Tb via the ^{nat}Dy(p,x)^{161}Tb pathway by irradiation of ~120 mg of natural dysprosium metal foils with~60 MeV protons at 3 µA for 24 hours, has been conducted at the Brookhaven LINAC Isotope Producer (BLIP). The resulting Tb radioisotope yields of ~3 µCi of ^{152}Tb ($t_{1/2}$ = 17.5 h), ~45 µCi of ^{155}Tb ($t_{1/2}$ = 5.32 d), ~32 µCi of ^{156}Tb ($t_{1/2}$ = 5.35 d), and ~88 µCi of ^{161}Tb was observed by gamma spectroscopy. A chromatographic separation method using Eichrom's LN resin for the isolation of Tb from a portion containing ~35 mg of irradiated ^{nat}Dy has been performed with the use of two sequential columns, the first containing ~4.5 g of LN resin and the second containing ~1 g of LN resin. This separation achieved overall Tb recoveries of between 65-81% whilst removing ~90% of the Dy. Studies to further optimize the separation of Tb from Dy are ongoing. Results will be presented on the effect of varying concentrations, flow rates, column size, and other parameters for the purpose of optimizing the separation.

NUCL 3990856

Thick target yields and cross section measurements of ^{43,44g,44m}sc via ^{19}f + ^{27}al

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Positron-emitting scandium radioisotopes ^{43}Sc ($t_{1/2}$ = 3.891 h) and ^{44g}Sc ($t_{1/2}$ = 3.97 h) have been recently proposed for diagnostic radiopharmaceutical use due to their favorable half-lives and chemistry of scandium. The primary sources of these scandium radioisotopes include proton or deuteron bombardment of isotopically enriched calcium or titanium targets. Using natural target materials leads to the coproduction of ^{46}Sc ($t_{1/2}$ = 83.79 d)—an unacceptably long-lived contaminant. The bombardment of ^{27}Al with ^{19}F produces ^{43,44g,44m}Sc among other stable or long-lived chemically separable products, but this reaction cannot form ^{46}Sc. The objective of this work was to measure relevant cross sections. PACE4 cross section predictions were used in the preparation of this experiment and compared to these experimental measurements.

Cross section measurements were performed using 580 ± 80 (0.95) nm ^{27}Al foils. Using an MC-SNICS and FN 10 MV Tandem Accelerator, ^{19}F beams at 35, 40, 45, 50, 55, and 60 MeV were produced with beam currents between 40–80 pnA. Thick target yields to complement these measurements were performed using 1 mm thick ^{27}Al targets.

Activation products were characterized using offline gamma spectroscopy with an HPGe system. End-of-bombardment activities were determined by fitting decay equations to the gamma spectroscopy data. The measured cross sections indicate an overestimation by PACE4 for the scandium radioisotopes. This is corroborated by the measured thick target production rates. This may be due to differences in entrance-channel angular momentum of a heavy ion beam compared to light-ion production, but additional work is required to understand this discrepancy.

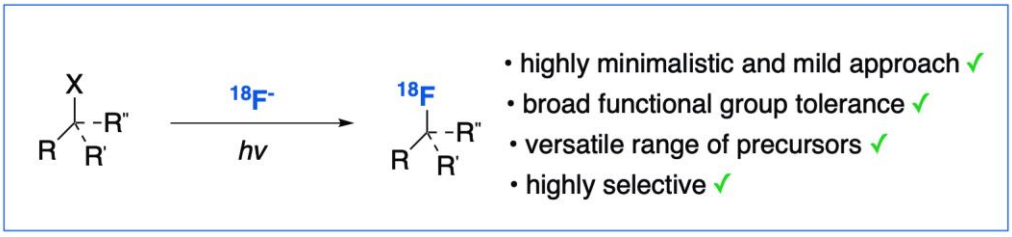
This work reports nuclear reaction cross sections ^{27}Al (^{19}F, *x*) ^{43}Sc, ^{27}Al (^{19}F, *pn*) ^{44g}Sc, and ^{27}Al (^{19}F, *pn*) ^{44m}Sc at six energies between 35 and 60 MeV lab energy. Limited by low count-rates, cross sections within the same energy range are provided for ^{27}Al (^{19}F, *3pn*) ^{42}K, ^{27}Al (^{19}F, *3p*) ^{43}K.

NUCL 3991063

Synthesis of 18F-alkyl fluorides via the photoredox mediated nucleophilic radiofluorination of a novel class of precursors in radiochemistry

Sebastiano Ortalli[1]*, sebastiano.ortalli@chem.ox.ac.uk, Joseph Ford*[1]*, Andrés A. Trabanco*[2]*, Matthew Tredwell*[3,4]*, Veronique Gouverneur*[1]*. (1) University of Oxford, Oxford, United Kingdom(2) Janssen Research and Development Toledo, Toledo, Spain(3) Cardiff University School of Chemistry, Cardiff, United Kingdom(4) Cardiff University School of Medicine, Cardiff, United Kingdom*

The radioactive isotope of fluorine ^{18}F finds ample applications in Positron Emission Tomography (PET), a functional and quantitative molecular imaging technique relying on the detection of gamma rays from positron-emitting radionuclides administered in the form of radiotracers. PET stands out amongst other imaging modalities as this non-invasive and highly sensitive technique interrogates biological processes *in vivo* and in real time. In this context, ^{18}F serves as a radionuclide of choice in light of its uniquely favourable decay properties (97% b+ decay, 109.8 min half-life, 635 keV positron energy), and therefore predominates amongst all radiotracers employed in the clinic. Nevertheless, the bottleneck for PET undeniably remains the development of robust radiosynthetic methodologies enabling the mild and selective incorporation of ^{18}F into potential radiotracers. In particular, access to ^{18}F-labelled secondary and tertiary alkyl fluorides still poses an unmet challenge in ^{18}F-radiochemistry. These motifs are traditionally synthesized *via* the displacement of reactive leaving groups by [^{18}F]fluoride. Such approach often requires extensive synthetic sequences to prepare complex prefunctionalised precursors, and necessitates harsh radiofluorination conditions, which pose drastic limitations on functional group tolerance. In addition, poor or no reactivity is often observed alongside the formation of elimination by-products that are challenging to separate. Herein, we report a novel approach for the synthesis of ^{18}F-alkyl fluorides with [^{18}F]fluoride *via* the photoredox-mediated radiofluorination of a previously unexplored class of precursors in radiochemistry, conveniently accessible from a striking variety of functional groups. The value of this methodology is demonstrated on a vast collection of structurally diverse and complex motifs. This mild and direct transformation stands out for its broad functional group tolerance and operational simplicity.



NUCL 3991063

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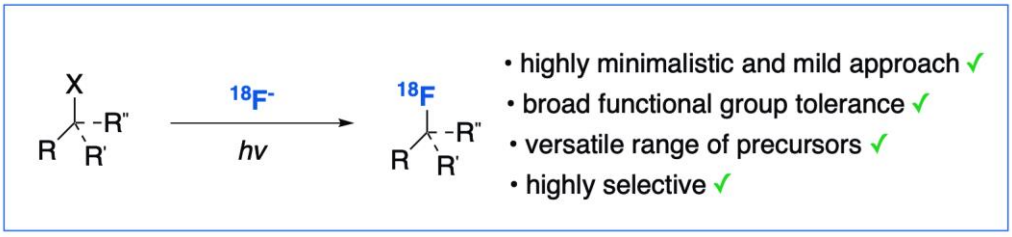

NUCL 3991130

Computational tools for the study of heavy elements and radionuclides in condensed phase

Malgorzata Makos[1], Brett A. Smith[1], Riddhi R. Golwankar[2], Alexander C. Ervin[2], Emily R. Mikeska[2], James D. Blakemore[2], Roger Rousseau[1], ***Vanda Glezakou[1]****, glezakouva@ornl.gov. (1) Chemical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee, United States(2) Department of Chemistry, University of Kansas College of Liberal Arts and Sciences, Lawrence, Kansas, United States*

The chemical properties of the *4f* and *5f* elements have long captured our attention, due to both experimental and computational challenges surrounding their studies. Modeling of these elements in the condensed phase is compounded by the long time and length scales that need to be accessed. In my presentation, I will review recent contributions in the study of heavy elements in condensed phase. The development of pseudopotentials and companion basis sets for the whole lanthanide and actinide series offers a computational tool for reliable ab initio molecular dynamics (AIMD) studies of these elements. In addition, I will show how the combination of AIMD with data science allows us to extend simulation times and extract descriptors that can serve as structural fingerprints of actinides in a molten salt matrix.

NUCL 3991245

Extracting chemistry from core-level spectroscopies: Combining theory and experiment

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The goal of X-Ray Photoelectron Spectroscopy, XPS, and X-Ray Adsorption Near Edge Spectroscopy, XANES, is to obtain information about the chemical interactions and bonding in the compound studied. With modern computational resources, theorists can obtain XPS and XANES energies and intensities that compare favorably with measured spectra. Experimentalists can obtain XPS and XAS spectra for a variety of samples, sometimes to be compared with theoretical results. However, rather than examine the XPS and XAS of individual systems, another approach involves varying materials and, especially for theorists, varying parameters since this may allow the physical and chemical mechanisms responsible for the observed features to be identified and related to the chemistry of the material. Theorists have a special advantage in that it is straightforward to vary bond distances and electronic states and to vary the level of the theoretical treatment of the wavefunctions. However, it is necessary to use special methods for the analysis of the molecular orbitals and wavefunctions that go beyond the usual Mulliken Population Analysis. There are several critical contributions from experimentalists including identifying suitable systems for joint studies, making suitable measurements, and assessing the reliability of the measurements. The type of information that can be obtained will be discussed for representative systems that have been studied in collaborations between the authors and their experimental colleagues. This will include analysis of XPS BE shifts and the chemical significance of the shifts, the XPS of ionic Ni(II) compounds with different ligands, and the XANES of Actinyls. In all cases, how the XPS and XANES features measured can provide information about the chemical interactions will be described.

NUCL 3991331

Silica nanoparticles as a vehicle for a ^{230}pa/^{230}U/^{226}Th radionuclide generator system

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Targeted alpha therapy (TAT) is a treatment modality that employs the high linear energy transfer (LET) of alpha particles to generate double stranded DNA breaks resulting in a lethal dose to targeted cancer cells. Radionuclide generators are used to supply short-lived radionuclides for imaging and therapy typically by affixing the long-lived parent radionuclide onto a solid support and “milking” the short-lived daughter off. Several short-lived alpha emitters are of interest to TAT and are available from their longer-lived parents, such as ^{225}Ac/^{213}Bi, ^{230}Pa/^{230}U/^{226}Th, and ^{212}Pb/^{212}Bi. A limiting factor in the use of traditional resin-based radionuclide generators for alpha emitting radionuclides is that the same LET, which is so useful for cancer treatment, is highly destructive to the resins used in these systems resulting in failure at the high curie level activities needed for clinical applications. We are investigating a silica-based nanoparticle system for the routine supply of ^{226}Th from its grandparent ^{230}Pa via the following decay chain: ^{230}Pa(17.4 d, β^- 7.8%)^{230}U(20.23 d, α)^{226}Th. ^{226}Th (30.6 m) decays with 4 alpha particles in rapid succession allowing for maximal dose to targeted cells. Silica is a promising material to investigate for radionuclide generators employing alpha emitting radionuclides due to its high radiation resistance, facile synthesis and high affinity for ^{230}Pa. Incorporating ^{230}Pa, as opposed to ^{230}U, is advantageous as it prolongs the life of the radionuclide generator since ^{230}U is expected to remain in the nanoparticle upon beta decay from ^{230}Pa. However, the alpha decay to ^{226}Th will result in a daughter recoil of ~38 nm liberating ^{226}Th from the nanoparticle leading to in a physical separation as opposed to a chemical separation. We have successfully synthesized silica nanoparticles, utilizing the Stöber method, controlling the size of the nanoparticles to create uniform nanoparticles ranging from 20-250 nm in diameter. For our current application, nanoparticles ranging from 50-75 nm would be the most useful as this allows >90% of the ^{226}Th to escape the particle. Direct incorporation of protactinium into our nanoparticles during the Stöber synthesis resulted in radiosynthetic yields of 98 ± 3%. Experiments are ongoing to investigate chemical and radiolytic stability in addition to efficiency of ^{226}Th daughter release.

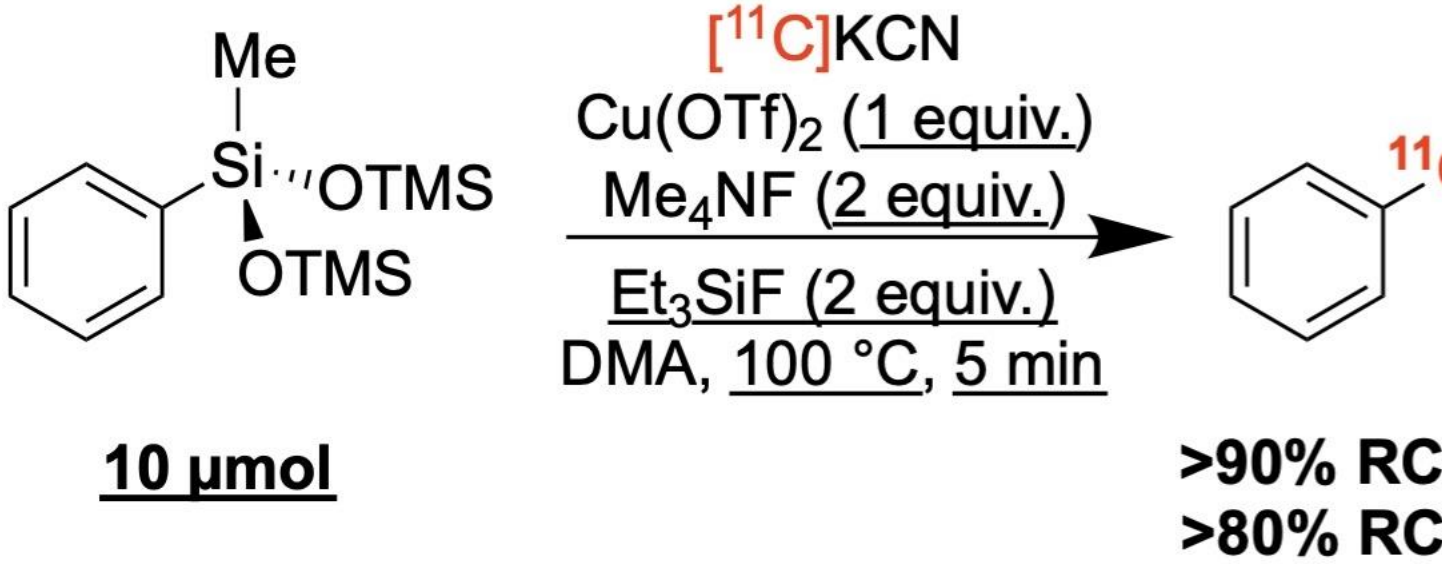
NUCL 3991478

Stable aromatic Heptamethyltrisiloxanes for novel copper-mediated radiocyanation

***Jay Wright**[1], jawr@umich.edu, Richard Ma[1], Joshua Priest[1], Allen F. Brooks[1], Eric W. Webb[1], Melanie S. Sanford[2], Peter J. Scott[1]. (1) Radiology, University of Michigan, Ann Arbor, Michigan, United States(2) Chemistry, University of Michigan, Ann Arbor, Michigan, United States*

Copper-mediated radiolabeling reactions are state-of-the-art methodologies for radiolabeling aromatic organic molecules for PET imaging. Using a variety of precursors, such as aryl boronate esters, stannanes, iodonium salts, halides, diazonium salts, and sulfonium salts (amongst others), multiple labelled systems, including electron-rich arenes, can now be accessed that are otherwise challenging to construct with other techniques

However, many of these compounds have inherent drawbacks, including bench-top stability, toxicity, and reactivity issues. We present aryl heptamethyltrisiloxanes as a new addition to the existing profile of copper-mediated radiolabeling precursors that operate via the prototypical Cu(I)/Cu(III) redox couple. Specifically, we describe efficient radiocyanation reactions of these precursors that carry comparable or enhanced reactivity to existing precursors whilst offering enhanced stability and reduced toxicity.



NUCL 3991660

Plutonium redox chemistry and reaction mechanisms controlling its migration in the environment

***Annie Kersting**, kersting1@llnl.gov. Visiting Scientist, Seaborg Institute, Lawrence Livermore Natonal Laboratory, Livermore, California, United States*

Actinides, such as plutonium (Pu), have been introduced into the environment in large quantities due to world-wide nuclear weapons production and testing, nuclear energy production, and associated environmental accidents. Due to plutonium's toxicity and long half-life ($t_{1/2}$ ^{239}Pu 2.4 x10^4 yrs), it represents a long-term environmental and human

health risk that requires us to both effectively manage Pu-contaminated sites and develop safe, long-term nuclear waste storage strategies. Over time, all engineered barriers designed for either long-term nuclear waste storage or contaminated sites will degrade and ultimately fail, resulting in the host geologic environment becoming the primary defense against migration to the biosphere. For this reason, understanding the surface structure and reactivity of coupled Pu–mineral, Pu–organic ligand, and Pu–microbe interfacial processes is needed to advance our understanding and ultimately effectively manage the long-term risk of nuclear waste. Almost 25 years ago, Pu was shown to have migrated over a kilometer associated with pseudocolloids at the Nevada National Security Site, Nevada. Although this mechanism was subsequently confirmed for other contaminated sites, more recent work has highlighted additional potential mechanisms for Pu migration. At Rocky Flats (CO), surface transport of Pu was associated with organic bio-colloids or macromolecules. Under more extreme acidic conditions mimicking the process waste stream at the Hanford Site (WA), Pu was shown to be mobilized when complexed in an organic phase with TBP-nitrate. The presence of Fe(II), natural organic matter, and H2O2 has been shown to oxidize Pu(IV) to more mobile Pu (V/VI). In contrast to these potential mechanisms that may act to enhance Pu mobility in the environment, Pu was recently shown to be incorporated into both calcite and iron oxide precipitates, a process that may lead to long-term immobilization of Pu. Although colloid-facilitated transport was invoked early on as one possible mechanism for transporting Pu in the environment, it is clearly not the only mechanism and competition among multiple mechanisms needs to be evaluated. Progress in evaluating Pu behavior in more complex systems will be presented with a focus on better assessing our ability to safely store nuclear waste.

NUCL 3991987

Radiosynthesis and evaluation of a novel ^{18}F labeled PET ligand for imaging monoacylglycerol lipase

***Yinlong Li**, yinlong.li@emory.edu, Jiahui Chen, Jian Rong, Chunyu Zhao, Ahmad Chaudhary, Xin Zhou, Jimmy Patel, Kuo Zhang, Steven Liang. radiology, Emory University, Atlanta, Georgia, United States*

Monoacylglycerol lipase (MAGL) is a 33 kDa cytosolic serine hydrolase that hydrolyzes monoacylglycerols to corresponding fatty acid and glycerol. MAGL is highly expressed in central nervous system (CNS) and peripheral tissues, such as liver, lung, and adipose tissue. Typically, MAGL is responsible for the degradation of 2-arachidonoylglycerol (2-AG), which is a primary transmitter for modulating several physiological processes of endogenous cannabinoid system, including pain, inflammation, appetite, memory, and emotion. Inhibition of MAGL in the brain could increase the level of 2-AG and leads to decreased levels of pro-inflammatory prostaglandin and thromboxane. Therefore, MAGL is considered as a promising therapeutic target for the treatment of neuropsychiatric disorders, metabolic syndromes, and cancer. Considering positron emission tomography (PET) is a non-invasive molecular imaging technology to quantify physiological processes in living systems, we

developed a novel PET tracer for assessing the abundance of MAGL and the drug-target interaction. We synthesized two fluorinated MAGL inhibitors (epimers: MAGL-2304 and MAGL-2305) in four steps from commercially available reagents. The corresponding precursors MAGL-2304-Bpin and MAGL2305-Bpin were prepared through a similar pathway. The results of *in vitro* MAGL inhibitory activity showed MAGL-2304 (IC_{50} = 18.6 nM) and MAGL2305 (IC_{50} = 1.6 nM) possess potent MAGL inhibitory activity. Next, we achieved successful ^{18}F-labeling reactions via copper-mediated radiofluorination to afford [^{18}F]MAGL-2304 and [^{18}F]MAGL2305 in 13% and 9% radiochemical yields, respectively (non-decay corrected). The *in vitro* autoradiography and *in vivo* PET imaging studies of [^{18}F]MAGL-2304 and [^{18}F]MAGL2305 showed that both tracers had specific binding towards MAGL and readily penetrated the blood−brain barrier (BBB) in the brain of rodents (mice and rats). Further validation of radiometabolite analysis and *ex vivo* biodistribution are currently underway.

NUCL 3991987

Radiosynthesis and evaluation of a novel ^{18}F labeled PET ligand for imaging monoacylglycerol lipase

***Yinlong Li**, yinlong.li@emory.edu, Jiahui Chen, Jian Rong, Chunyu Zhao, Ahmad Chaudhary, Xin Zhou, Jimmy Patel, Kuo Zhang, Steven Liang. radiology, Emory University, Atlanta, Georgia, United States*

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[^{18}F]MAGL2305 showed that both tracers had specific binding towards MAGL and readily penetrated the blood−brain barrier (BBB) in the brain of rodents (mice and rats). Further validation of radiometabolite analysis and *ex vivo* biodistribution are currently underway.

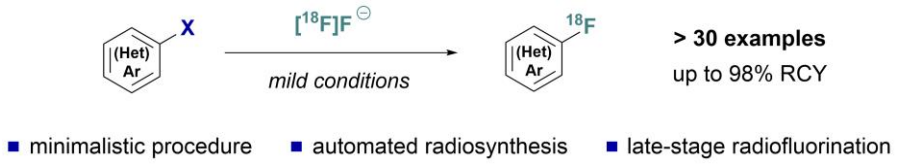
NUCL 3992179

New routes to ^{18}F-fluorinated heteroarenes

Joseph Ford[1], *joseph.ford@chem.ox.ac.uk, Jeroen B. Sap*[5,1], *Sebastiano Ortalli*[1], *David Hewings*[4], *Matthew Tredwell*[2,3], *Veronique Gouverneur*[1]. *(1) University of Oxford, Oxford, United Kingdom(2) Cardiff University School of Medicine, Cardiff, United Kingdom(3) Cardiff University School of Chemistry, Cardiff, United Kingdom(4) Vertex Pharmaceuticals Europe Limited, Abingdon, United Kingdom(5) Genentech Inc, South San Francisco, California, United States*

Positron emission tomography (PET) is a powerful molecular imaging technique, allowing for the visualization of metabolic processes *in vivo*. The decay properties of the radioisotope fluorine-18 render its incorporation into small molecule tracers for PET applications particularly advantageous. This has led to the development of a wide array of novel methodologies to introduce fluorine-18 into small molecules. Nucleophilic aromatic substitution with [^{18}F]fluoride remains one of the most popular and well-established approaches to ^{18}F-fluorinated molecules and is often applied by practitioners for the synthesis of radiotracers. Several of these methods display excellent versatility and offer highly effective routes to ^{18}F-fluoroheteroarenes. However, outstanding challenges concerning precursor synthesis, purification and reactivity mean there is significant interest in new methods, particularly those utilizing native functional handles for selective and late-stage radiofluorination.

We disclose a new precursor type for ^{18}F-fluorination of heterocyclic compounds, which has allowed for the late-stage radiofluorination of substrates derived from various heteroaromatic scaffold types in good to excellent radiochemical yield. The reaction operates under mild conditions, in over 30 examples. This methodology has been demonstrated to be amenable to scale-up and automation using a robotic synthesizer, allowing for the preparation of ^{18}F-radiotracers suitable for preclinical imaging studies.



NUCL 3992276

Production and separation of radioplatinum for radiotheragnostic applications

***Deepika Davuluri**, davulur8@msu.edu, Katharina Domnanich. Chemistry, Michigan State University, East Lansing, Michigan, United States*

The Facility of Rare Isotope Beams (FRIB) generates exotic isotopes which are produced by the fragmentation of primary beams. When the purified secondary beams are delivered to the user end stations, co-generates fragments, are intercepted by accelerator components, like mass slits and fragment catchers. The deposited radioisotopes can be collected from these components via 'solid isotope harvesting' and represent an invaluable resource for nuclear medicine research.

This study focusses on harvesting the novel radioisotopes ^{189}Pt and ^{197}Pt, which are considered suitable candidates for diagnostic and therapeutic applications in nuclear medicine.^{197}Pt with β^- decay properties, complimented with auger electrons emissions is considered suitable for targeted radionuclide therapy. The positron emission capabilities of ^{189}Pt make it an exemplary candidate for diagnostic Positron Emission Tomography (PET) imaging. Both Pt radioisotopes are exciting for nuclear medicine applications because their characteristics render a theragnostic approach possible. In radiotheragnostics, the same pharmaceutical is labeled either with a diagnostic or therapeutic radioisotope, thereby exhibiting an analogous in vivo behavior which allows for more accurate diagnosis and improved therapy.

The isotopes will be collected using a solid collector, installed as end station at a user beamline at FRIB. This collector encompasses a stack of aluminum foils, mounted to a KF40 flange blank, with a tantalum plate at the back. To separate the harvested ^{189}Pt and ^{197}Pt from the co-implanted impurities, like Au, Ir, Os, and potentially Lu, Re, Ta, Yb, and W along with the bulk Al, a series of experiments are planned. Initially, the aluminum foils will be dissolved in hydrochloric acid. The first separation step foresees the use of anion exchange resin, followed by further purification on tri-butyl phosphate (TBP) resin. This methodology has been proposed after running a series of simulation experiments.

To perform the test separations, synthetic mixtures with standard solutions are prepared and analyzed by Inductively coupled plasma - optical emission spectroscopy (ICP-OES). To guide the determination of the optimal process conditions, the 'Design of the Experiments' approach shall be used.

NUCL 3992649

Establishing radioantimony(V) chemistry for Sb-119 targeted Auger therapy

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Auger electrons are low-energy electrons emitted from core atomic orbitals following electron capture. Although Auger emitters have been largely overshadowed by the popularity of alpha- and beta-emitting radionuclides for targeted radiotherapy of cancer, the ultra-short penetration range and high linear energy transfer (LET) of Auger electrons offer unparalleled potential for targeting and destroying micrometastases and single cancer cells with minimal damage to surrounding healthy tissue. Among the Auger electron-emitting radionuclides that are suitable for biomedical applications, antimony-119 (Sb-119, half-life = 38.2 h) has emerged as highly promising because of its favorable nuclear properties. Specifically, it emits an average of 23.7 electrons with a kinetic energy of approximately 8.9 keV per decay, which is ideal for cellular and subcellular targeting applications, and only a single gamma photon of low energy (23.9 keV, 16%), which is highly desirable to minimize the radiation burden to patients arising from penetrating gamma rays. It also has a diagnostic partner, Sb-117 (half-life = 2.8 h), that has the potential to be used for SPECT and PET imaging. One outstanding challenge hindering the advancement of Sb-119 for targeted Auger therapy resides in the poor understanding of the coordination chemistry of this radionuclide, which is rendered complicated by its metalloid character, the existence of multiple stable oxidation states, and its tendency to form hydroxide species in aqueous solution. In this presentation, we report our efforts to develop chelators that stabilize the oxophilic Sb(V) ion and we provide insight into the chemical and radiochemical challenges that arise from handling this metalloid. Our methods to assess the radiolabeling of chelators with radio-Sb(V) and the resulting stability of the complexes in human serum are also described. Finally, we share our encouraging results from in vivo imaging and biodistribution studies in mice of radio-Sb complexed by a catechol-rich chelator and our steps towards the development of a bifunctional targeted construct. Collectively, these studies provide a foundation upon which to advance Sb-119 in nuclear medicine.

NUCL 3992724

Community FAIR data approach to simulating actinide sorption to mineral surfaces

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The Lawrence Livermore National Laboratory-Surface Complexation/Ion Exchange (L-SCIE) database is a recent effort to unify community sorption experiments and metadata in a findable, accessible, interoperable, and reusable (FAIR) format. To date, it has mined 10’s of thousands of raw sorption data from the literature and provides a platform to test novel approaches to surface complexation/ion exchange modeling and database development. Briefly, L-SCIE mines sorption data (K_d, % sorbed, surface excess) and dataset experimental conditions (background electrolyte, mineral surface area, gas composition, etc.) from journal manuscripts and loads them into a database. The sorption data undergo a series of unit conversions to yield a unified database which

includes propagated conversion errors from the original extracted data. The database can then be filtered for a metal-mineral pair of interest in order to display a corresponding experimental dataset. The database is linked to the PHREEQC geochemical modeling code that can be used to identify reactions and associated reaction constants that effectively reproduce the available community data.
We will present an update to both traditional surface complexation/ion exchange modeling and hybrid machine learning (ML) that achieve high-quality predictions of actinide sorption to mineral surfaces using this community data approach. Both the traditional and hybrid ML approaches rely on PHREEQC geochemical modeling. However, the traditional approach relies on PHREEQC to simulate reactions at the mineral-water interface while the hybrid ML approach relies on a random forest (RF) algorithm to quantify adsorption and avoids SCM modeling constraints entirely. Here, will demonstrate both approaches and describe the next steps in the evolution of LLNL's community FAIR data effort.

NUCL 3992867

Conversion of synergistic solvent extraction systems to novel solid phase extractions systems for the separation of lanthanides ^{161}tb from enriched ^{160}Gd targets

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Trivalent *f*-block element separations remain a central challenge due to their similar ionic radii and chemical behavior. Intragroup lanthanide separations, such as in the production of Terbium-161 ($t_{1/2}$ = 6.95 days) using nuclear reactors and enriched ^{160}Gd targets, are important in targeted radiotherapy applications where a no carrier added, and high molar activity product is crucial. Synergistic solvent extraction systems using 2-Thenoyltrifluoroacetone (HTTA) and Dibutyl N,N-Diethylcarbamylmethylenephosphonate (DBDECMP) in 1,2-dichloroethane previously suggested promising separation potential with a high separation factor ($SF_{Tb/Gd}$) of 3.68 ± 0.14 demonstrated at pH = 2.00, HNO_3. Solvent extraction systems are often avoided in nuclear medicine because of potential contamination with organic solvents and the difficulties of automation in large-scale production. Solid phase extraction chromatography (EXC) resins are a promising alternative that ensures significantly less residual solvent in the isolated radioisotope and are more amenable to large-scale productions This synergistic solvent extraction system was converted to EXC resins using 20 – 50 µm Prefilter Resin (*TrisKem International*) and rotary evaporator methods. A variety of extractant ratios (grams of HTTA per gram of DBDECMP) and extractant loadings (total grams of HTTA + DBDECMP per gram of support) were studied as a function of acid concentration (pH 0.00 – 3.00, HNO_3) using batch experiments with radiolytic and spectrophotometric techniques. When translated to solid-phase EXC

resins, the synergistic properties of HTTA and DBDECMP in the solvent extraction systems are also present when loaded onto an EXC resin. As the amount of DBDECMP loaded on the resin increased, the k' values decreased for a given pH value. The highest k' values had the lowest amounts of DBDEMCP, suggesting only a small amount of neutral extractant is needed to elicit a synergistic effect. Initial k' ratios suggest that the solid phase resins could effectively separate terbium and gadolinium for nuclear medicine applications. However, further optimization of pH and column characteristics are still being investigated.

NUCL 3992982

Statistical design of experiments (DoE) as an essential tool for efficient radiochemical data acquisition, response surface modeling, and radiosynthesis optimization

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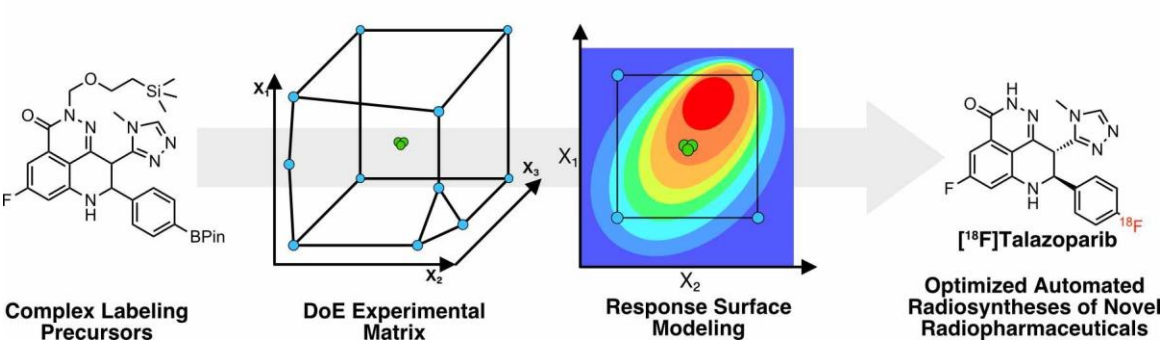
Advances in radiochemistry, like the copper-mediated radiofluorination (CMRF) reaction, are transforming radiopharmaceutical development for nuclear medical applications. However, translating these complex multicomponent reactions into reliable, fully automated cGMP-regulated production protocols for physiologically relevant radiopharmaceuticals remains a significant challenge. This task has proved notoriously difficult via the traditional "One Variable at a Time" (OVAT) optimization approach, which is experimentally inefficient and prone to finding local optima, adding significant cost and time to developing novel radiopharmaceuticals. There is an unmet need to bring data-driven solutions to the complex optimization problems of radiopharmaceutical research and development. We have thus worked to implement "Design of Experiments" (DoE) into our radiopharmaceutical development program. DoE is a statistical toolkit that aims to select an optimal set of experiments to maximize the amount of information obtained within a defined region of experimental space. This data is then used to map a given region of experimental space across multiple variables and responses simultaneously, identify significant process variables, or model a detailed response surface. This information facilitates the identification of optimal reaction conditions, can guide further optimization studies, or aid in general decision-making.
Using DoE, we have improved the synthesis performance of several established radiotracers of clinical importance, making cGMP syntheses both higher yielding and more reliable through increased margin for error. The increased margin also enables longer and more complicated automated protocols, expanding accessible radiopharmaceutical space through synthetic flexibility. Moreover, DoE has allowed us to identify nonintuitive substrate-specific radiolabeling conditions that would not have

been observed via OVAT. By combining DoE experimental design efficiency with high-throughput radiochemical analysis methods, we can acquire information-rich datasets for a wide breadth of chemical space. These datasets will form the foundation needed to bring predictive AI/ML models to radiopharmaceutical development. This presentation will explore the future role of the DoE in data-driven radiopharmacy.



NUCL 3993068

Radiosynthesis and preclinical evaluation of a PET radioligand for transmembrane AMPA receptor regulatory protein

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Objectives: The amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) type glutamate receptor (AMPARs), as a subtype of ionotropic glutamate receptors (iGluRs), is the predominant excitatory neurotransmitter receptors in the central nervous system (CNS) and mediate plasticity and fast synaptic transmission. Recent studies indicated that the abnormal expression and regulation of AMPARs are associated with multiple neurological disorders and neurodegenerative diseases. Therefore, these receptors could represent an exciting target for therapeutics of diseases. Imaging and quantification of AMPA receptors is critical in advancing the understanding of AMPA receptor-related disorders in the CNS. Here, we developed a novel 18F-labeled radioligand **[^{18}F]AMPA-2306** for AMPA receptor imaging.
Methods: We used a three-step synthetic approach involving nucleophilic substitution between the amino group and a sulfonyl chloride, followed by Suzuki coupling with boric acid derivatives, to generate target molecule **AMPA-2306** and the corresponding precursor for F-18 labeling. The radiosynthesis of **[^{18}F]AMPA-2306** was carried out by heating precursor (2 mg) and [^{18}F]fluoride/Kryptofix222 in DMSO at 130 centigrade for 30 min via nucleophilic aromatic substitution of nitro group. The dynamic micro PET imaging was then performed with radioligand **[^{18}F]AMPA-2306** in mice.
Results: The reference **AMPA-2306** was synthesized in 47% overall yield over three

steps and the corresponding nitro-containing precursor was obtained in 26% yield. The desired PET ligand **[^{18}F]AMPA-2306** was achieved in 12% (non-decay corrected). The radiochemical purity detected by radio-HPLC was greater than 99%, and the molar activity of **[^{18}F]AMPA-2306** was higher than 37 GBq/µmol. No radiolysis was observed within 90 min in two different sets of formulations, namely saline containing 0.8% ascorbic acid and PBS containing 10% EtOH. The performance of **[^{18}F]AMPA-2306** was evaluated by microPET imaging to confirm the penetration of the blood-brain barrier (SUV_{max} = 3).
Conclusion: We developed an efficient synthetic route of AMPA-2306, the nitro-containing precursor, and **[^{18}F]AMPA-2306**. We also examined the effect of the parameters on the radiochemical yield and the specific activity of **[^{18}F]EM29D**. The radioligand demonstrated excellent blood-brain barrier permeability in mouse PET imaging. Results from this study are of interest for future development and evaluation of AMPA-targeted PET tracers.

NUCL 3993154

Uranium and cobalt separation from U/LNS and co/LNS ionic liquids solutions by means of current modulated electrolysis

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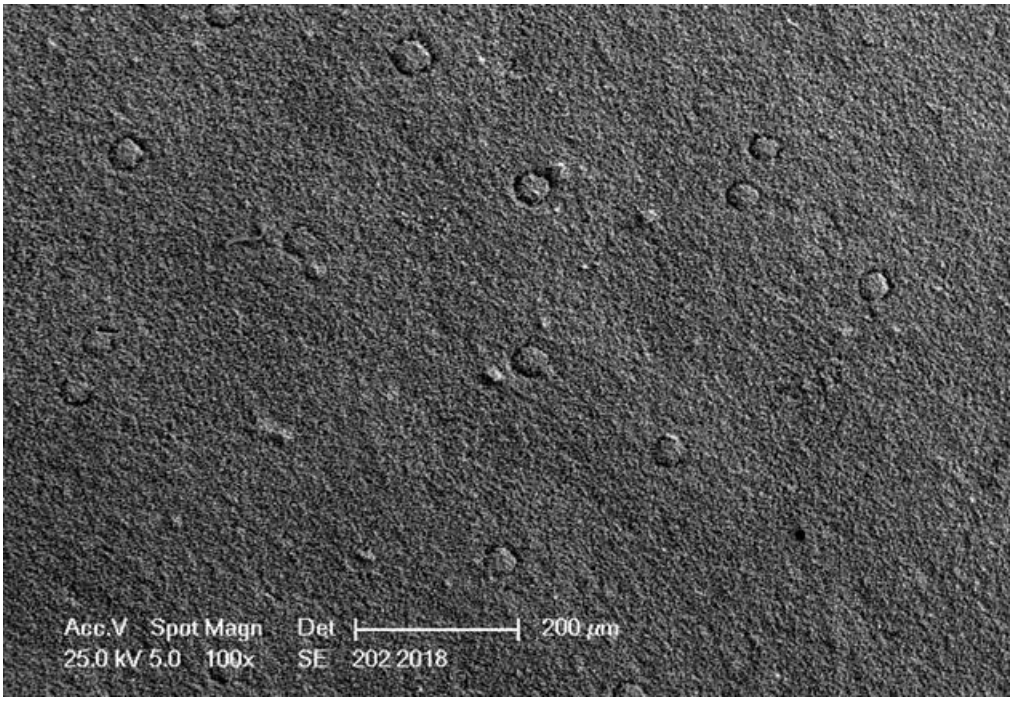
The electrochemical separations from non-aqeuous systems are highlighted processes in the field of SNF reprocessing and other waste recycling schemes as well. Next to high-temperature molten salts, ionic liquids and some of their unique properties are definitely attractive also for areas of SNF reprocessing and solid waste decontamination processes. Most reprocessing or decontamination schemes will need to include separation of individual contaminants from each other. Typically, this will include separation of uranium from other elements like fission products or cobalt as the other important contaminant necessary to be dealt with during the decommissioning. The measurement of electrochemical characteristics of uranium, cobalt and samples of lanthanides in TSFI-based ionic liquids have shown that all elements undergo reduction to its basic metallic state within the electrochemical window. The stability of studied ILs is sufficient to achieve an electrolytic separation of all studied elements. The possibility of uranium and cobalt recovery from the complex ionic liquid solution was demonstrated and current-modulated electrolysis was used to achieve the deposition of pure (99.9 %) and compact deposit of cobalt or uranium.



SEM picture of Co layer deposited from the Co/IL solution

NUCL 3993393

Overview of the accelerating radiotherapeutics through advanced molecular constructs initiative at Oak Ridge National Laboratory

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Oak Ridge National Laboratory (ORNL) produces medically important radionuclides in support of the US Department of Energy's Isotope Program. This production is enabled by the High Flux Isotope Reactor and the Radiochemical and Engineering Development Center, as well as other hot cell and radiological facilities. ORNL is building capabilities to explore fundamental science and applications related to the medical radionuclides produced. The Accelerating Radiotherapeutics through Advanced Molecular Constructs (ARM) Initiative was established to enable technological advances in the design, synthesis, and characterization of molecular cages to facilitate targeted transport of therapeutic radioisotopes to cancer sites. The synthesis of novel molecular constructs for their targeted delivery is guided by in silico design and by the knowledge obtained from conducting fundamental research into the coordination chemistry of actinide, lanthanide, and alkaline earth radioisotopes, such as ^{225}Ac, ^{177}Lu, and ^{223}Ra. This initiative aims to extend to the elucidation and understanding of the mechanism of action of these targeted radioisotopes alone and as combination therapies to help set the stage for advances in precision medicine for cancer and drug-resistant metastatic disease. The initiative is focused on four thrust areas: (1) designing ultrachelators for targeted radiotherapy, (2) developing targeted nanoconstructs for theranostics and

combination therapy approaches, (3) exploring nanobodies as novel targeting vectors to deliver molecularly caged radionuclides directly to cancer cells, and (4) understanding dosimetry at scale from the subcellular and cellular levels to the whole-organ and individual levels. Each of these thrusts aim to maximize therapeutic effect while minimizing side effects. This research initiative aims to complement the radioisotope production at ORNL and establish ORNL's capabilities in the field of radiotherapeutics.

NUCL 3993551

Multimodal approach to understanding uranium oxides

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Uranium oxides are ubiquitous in the nuclear fuel cycle. Their importance ranges from their use in nuclear fuels to environmental chemistry and waste product handling. At the same time, uranium oxides often appear as open *f* shell systems and thus their electronic properties are fundamentally interesting. In this discussion, we will explore the combined use of experimental and computational methods to study the physical properties of uranium trioxides and triuranium octoxide, with a specific interest in magnetic and lattice excitations. We will show how the combined use of inelastic light and neutron spectroscopy with density functional theory can provide synergistic information, providing more scientific insight together than their independent contributions.

NUCL 3993773

Interfacially controlled molecular transport in solvent extraction

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Structure and function of oil/aqueous interfaces play a key role in a range of applications spanning sample purification, rare-earth element recovery to nuclear waste remediation. Information on the self-assembly and transport of supramolecular assemblies at these buried interfaces is therefore of significance for designing new interfaces with improved function. Here we discuss dynamic interfacial restructuring that takes place when sparingly soluble ligands used in solvent extraction transport into neighboring aqueous phase in a concertation-dependent manner. We monitor these time-evolving interfaces using vibrational sum frequency generation combined with neutron and X-ray scattering methods. The results support an "antagonistic" role of

ligand complexation in the aqueous phase that could serve as a holdback reagent in kinetic separations. Our findings enable new insights into solvation, interfacially controlled chemical transport, and present potential avenues to design interfaces with enhanced selectivity and efficiency for targeted extractions.

NUCL 3993971

Expanding the flavor of radium

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Radiopharmaceutical chemistry is a hot (pun-intended) field. One currently used radiopharmaceutical isotope is radium-223. As a natural bone-seeker, radium is unsurprisingly used to treat bone metastasized cancers as soluble radium chloride. Due to the dearth of knowledge surrounding radium's coordination chemistry, it is *only* used for bone metastasized cancers despite having a promising radiolytic decay pathway for treating cancerous tissue. The Gaiser group has begun designing and developing novel chelators specifically for encapsulating radium to deliver it to other parts of the body to harness and subsequently direct the treatment power of radium. Using the more stable radium isotope, 226, allows for reliable solution and solid state characterization techniques to probe the preferred coordination environment of radium. This coupled with advanced organic synthesis to make a novel radium-specific chelator holds great promise to revolutionize current radium radiopharmaceuticals.

NUCL 3994012

Probing solid-state hydronium cation and irradiation stability of the synthetic analog of the uranium mineral chernikovite

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The synthetic analog of chernikovite, $(H_3O)(UO_2)(PO_4) \bullet 4H_2O$ also known as hydronium uranyl phosphate (HUP), was studied using a variety of experimental and computational methods, including the first neutron diffraction study to gain insight into structural features of the hydronium cation in the solid state. Raman and attenuated total reflectance infrared spectroscopic measurements were informed by density functional perturbation theory calculations and phonon eigenvector visualizations for spectral assignments. In addition, HUP was studied using He^{2+} irradiation as an analog for a radiolysis to investigate the irradiation stability of this material and, in particular, hydronium cations in the solid state. Dose studies irradiated each sample to 5, 10, 15,

25, and 50 MGy and structural insight was gained using optical vibrational spectroscopy and powder X-ray diffraction. Surprising irradiation stability of hydronium was observed up to a dose of 5 MGy.

NUCL 3994453

Cross section measurement of the ^{70}Ge(d,n)^{71}As nuclear reaction

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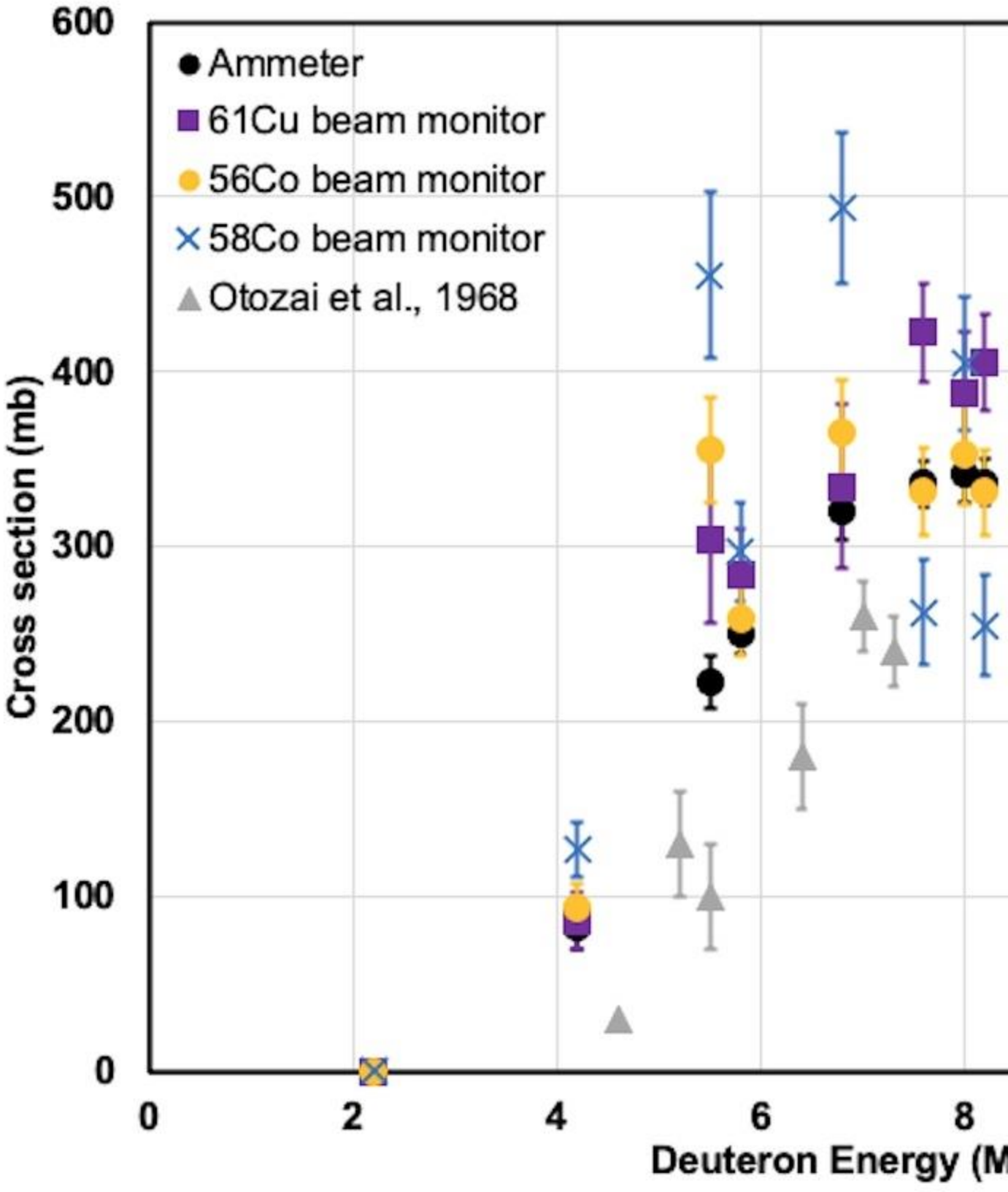
Positron-emitting ^{71}As ($t_{1/2}$ = 65.3 h, 28.3% β^+) has potential as diagnostic analogue to beta-emitting ^{77}As-labeled therapeutic radiopharmaceuticals. We developed novel metallic germanium coin targets for the production of ^{71}As via the ^{70}Ge(*d,n*)^{71}As nuclear reaction. However, the measured experimental yields consistently disagreed with yields calculated from literature cross sections (Otozai *et al* Nucl Phys A107: 427 (1968)).. Thus we have measured the experimental cross section of ^{70}Ge(*d,n*)^{71}As.

Five stacks, each containing two target foils (0.41±0.02 µm ^{nat}Ge on 25.4 µm Kapton), a beam monitor foil (15.6 ± 0.4 µm ^{nat}Ni), and an energy degrader foil (50 µm ^{nat}Al) were assembled in aluminum frames. These target stacks were irradiated for 4 – 6 h with 100 – 150 nA of deuterons with incident energies of 4, 7, 8 and 10 MeV with the University of Notre Dame's FN tandem accelerator. ^{71}As from ^{70}Ge(*d,n*) and ^{61}Cu, ^{56}Co and ^{58}Co via ^{nat}Ni*(d,x)* produced in the foils were subsequently quantified by high purity germanium gamma spectrometry and the production cross-sections calculated using $A(t) = n\sigma I(1-e^{-\lambda t})$, where *A(t)* is the end of bombardment activity, *I* is the deuteron intensity, *n* is the target thickness in nuclei per unit area, σ is the reaction cross section. Ammeter measurements of the electrically isolated, magnetically-suppressed beamline quantified deuteron irradiation intensities for comparison with the intensities calculated from Ni foil activation.

The measured cross sections shown in Fig 1 are higher than previous literature measurement. However, the deuteron intensities measured from beam monitor reactions are not self-consistent. Additionally, at the lowest irradiated energies, the deuteron intensity measured by beam monitor foils was significantly lower than that measured by the online ammeter. This work reports the experimental measurement of the ^{70}Ge(*d,n*)^{71}As nuclear reaction cross section, which is well suited for the production of ^{71}As for preclinical quantities of diagnostic radiopharmaceuticals.

Figure 1. Comparison of 70Ge(d,n)71As excitation function
measured data utilizing Ammeter- and beam-monitor-foil-



NUCL 3994462

Advanced BTPs for chemoselective minor actinide separations

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Expansion of nuclear power to meet the growing demand for carbon neutral energy is predicated, in part, on nonproliferative and effective waste mitigation strategies. Selective separation of the minor actinides, Am and Cm, from the neutron-poisoning lanthanides can decrease the heat load, volume, and radiotoxicity of spent nuclear fuel (SNF) stored in a geologic repository. Biphasic approaches leveraging 2,6-bis-1,2,4-triazinylpyridine (BTP) soft-donor complexants for this grand challenge in separation science have been known in the primary literature for over two decades, but substantive performance limitations remain. Recent results have underscored the potential for advanced BTPs, polar heteroaromatic molecules, to effectively dissolve in process-relevant, nonpolar diluents including constitutional isomers of octanol as well as kerosene without phase modifiers. These complexants are able to achieve high separation factors for Am over Eu in simulated SNF and effectively decomplex the chelated An without competitive ligand exchange. Convergent synthetic strategies for complexant construction, performance validation in biphasic separations assays, and supporting spectroscopic evidence for metal:complexant binding will be presented.

NUCL 3994466

Arrhenius behavior of the dodecane radical cation reaction with lanthanide-ion complexes of *N,N,N',N'*-tetraocyl diglocolamide (TODGA)

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Designer ligands used to selectively complex metal ions for their extraction and recovery are of vital importance for improving nuclear fuel cycle technologies. Unfortunately, both free ligands and their metal-ion complexes are subject to the detrimental impacts of ionizing radiation. Typically, the degradation of these solutes is due to secondary, indirect, processes, where the radiation mainly interacts with the solvent and these radical species produced then react with the ligands present. In this study, the temperature-dependent reaction of the dodecane radical cation with *N,N,N',N'*-tetraoctyldiglocolamide (TODGA) complexed with lanthanide ions in dodecane has been re-evaluated. TODGA was originally designed for the separation of the trivalent minor actinides, particularly americium and curium, from the trivalent

lanthanides, but also forms Ln complexes. Utilizing fast electron-pulse radiolysis and transient absorption spectroscopy the kinetics of the dodecane radical cation ($RH^{+\bullet}$) with TODGA, and TODGA-Ln complexes have been directly measured. From the measured pseudo-first-order kinetics of $RH^{+\bullet}$ decay, absolute second-order rate constants were calculated. The room-temperature values for the lanthanides showed consistently faster reactivity for the larger complexes. Arrhenius parameters for La, Gd, and Lu-TODGA complexes have also been determined over the range 10-40^{o}C. These are the first temperature-dependent rate constants measured for these Ln^{III+}/ligand complexes in irradiated organic media.

NUCL 3994617

Nanoscale interrogation of metallic nuclear materials: Atomic force microscopy and magnetic force microscopy

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Relationships linking chemical and physical material properties with formation conditions is the scientific basis for nuclear nonproliferation materials analysis. Metallic nuclear materials present unique challenges for physical property measurement, specifically their unsuitability for optical spectroscopy. In this work, we deploy a new measurement modality, atomic force microscopy/magnetic force microscopy (AFM/MFM), for the analysis of uranium steel alloys. We show that surface topography, relative hardness, and magnetic properties of the constituent phases can be separated using AFM/MFM. In addition to finding two novel uranium–transition metal (M = Fe, Cr, Ni) intermetallic phases, differences in surface oxide topography for four distinct UM_x phases are characterized, and changes in ferromagnetic steel fraction as a function of uranium content is described. These physical properties could be used to discern material formation history, cooling rates, or other pertinent nonproliferation process parameters.

NUCL 3994783

Development of neptunium nanoparticle feedstocks for target preparation

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While thin actinide target preparation methodologies are well established, thick actinide targets for greater isotope production yields remain elusive. Feasibility studies, with cerium as an analogue, reveal electrophoretic deposition (EPD) to be a promising candidate for actinide target development. EPD uses metal-oxide nanoparticle suspensions as feedstocks. The first actinide target of interest requires a neptunium nanoparticle feedstock, however, there have been few systematic studies addressing

intentional formation of such nanoparticles. In this presentation, synthetic approaches for neptunium nanoparticle EPD feedstocks will be discussed with subsequent characterization to evaluate oxidation states, speciation, particle size, aggregation behavior, and potential for electrophoretic deposition. Variables — concentration, solvent selection, pH, and additives — will be examined to establish and optimize the degree of control over neptunium nanoparticle suspension characteristics.

NUCL 3994803

Investigating the mechanism of aluminum fluoride chelation

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Since the emergence of ^{18}F as a radioisotope, there has been a drive towards new methodologies for incorporating [^{18}F]fluoride into complex structures that are often susceptible to degradation *via* the routine conditions used for nucleophilic substitution. Aluminum fluoride (AlF) radiolabeling has been used over the past decade to incorporate [^{18}F]fluoride into large biomolecules in a highly selective fashion using relatively facile conditions (eg no fluoride drying), utilizing the strong bond formed between aluminium and fluoride in acidic media. It has been used in a range of pre-clinical and clinical compounds to great success, such as for PSMA and FAP imaging in humans.
However, despite its widespread usage, there are a large number of variations in the reaction conditions throughout the literature, without a definitive discussion provided on the mechanism of the reaction, to understand how these minor changes in the reaction would alter the end product, if at all. To attempt to delineate this process, we have looked at the AlF reaction from three complementary directions - theoretical modeling studies, fluorine-19 chemistry and fluorine-18 radiochemistry - and taken key modifiers seen from the literature, examining their effect on the overall AlF mechanism.

NUCL 3994859 - Withdrawn

NUCL 3995069

Impact of node structure on ionizing radiation stability of thorium-terephthalate metal organic frameworks

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The radiation stability of three thorium terephthalate (benzene dicarboxylic acid, BDC) metal organic frameworks (MOFs) was studied using He^{2+} ions to mimic alpha-

radiolysis. The structures differ in polyhedral connectivity of the node-linker connection, despite identical node and linker identity. Th-UiO-66, isostructural to Zr-UiO-66, contains hexameric thorium oxide nodes that are 12-connected to six ditopic BDC linkers. The two additional materials investigated were $Th(BDC)_2(DMF)_2$ and $Th(BDC)_2$, which contain mononuclear nodes that are eight-connected by four ditopic BDC linkers. The materials were exposed to doses of approximately 5, 10, 15, 20, 25 and 50 MGy. Material degradation was characterized using X-ray powder diffraction (PXRD), Raman spectroscopy, and diffuse reflectance Fourier Transform infrared spectroscopy. The structures containing fewer node-linker connections presented enhanced radiation resistance. PXRD data showed residual crystallinity of $Th(BDC)_2(DMF)_2$ at 50 MGy whereas Th-UiO-66 exhibited amorphization at 25 MGy.

NUCL 3995128

Influence of Al on the retention of trivalent actinides and their homologues in feldspar

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Final disposal in a stable, deep geological formation in crystalline rock is considered to be the safest concept for disposal of radioactive waste. Retention of minor actinides on granitic minerals like feldspar are described in the literature, but differences within the feldspar group are not well understood. For instance, different solubility leads to different amounts of dissolved cations in solution, which will affect the mineral's surface chemistry. The most important cation in this context is Al^{3+}, which is produced by dissolution and may adsorb strongly on the feldspar surface.
Here, we study the effect of aqueous aluminum species on the sorption behavior of trivalent actinides and lanthanides on orthoclase, a K-bearing feldspar, in order to understand the differences in the sorption behavior of minor actinides on K- and Ca-feldspar. Surface charge characterization reveals a strong increase of the zeta potential and even charge reversal between pH 4.5 – 7 for Ca-feldspars. This behavior is not observed for pristine K-feldspar, but can be reproduced by adding Al^{3+} to the aqueous phase. The formation of a potential secondary phase is investigated by a Raman analysis, synchrotron powder X-ray diffraction (XRD), and high-resolution X-ray reflectivity. The data indicate that no crystalline Al^{3+} precipitate is formed on the surface. Instead, Al^{3+} is adsorbed on the surface of the mineral, thus increasing uptake of the actinides.

NUCL 3995200

Development of *in vivo* compatible ^{44}Sc complexes for targeted PET imaging

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Targeted nuclear medicine is an emerging clinical paradigm that harnesses radioactive isotopes for imaging and therapy by capitalizing on differential target expression of diseased and healthy cells. Development of clinically applicable radiopharmaceuticals requires carefully matching the physical half-life of the radioisotope with the biological half-life of the targeting vector to ensure optimal target accumulation within a relevant timeframe. Radioisotopes of scandium exhibit decay properties ideally suited for targeted imaging and therapy with small biologics, such as antibody fragments. Namely, ^{43}Sc ($E\beta^{+}_{avg}$ = 476 keV, $t_{1/2}$= 3.9 h) and ^{44}Sc ($E\beta^{+}_{avg}$ = 632 keV, $t_{1/2}$= 4 h) enable prolonged positron emission tomography (PET) imaging up to 24 hours post injection, while the emission properties of ^{47}Sc ($E\beta^{-}_{avg}$ = 162 keV, $t_{1/2}$ = 80.4 h) are well-suited for subsequent therapeutic intervention. However, strategies to chelate scandium isotopes under conditions compatible with thermally sensitive biologics to afford inert complexes is critically lacking.

Currently, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (**DOTA)** is considered the gold standard Sc^{3+} chelator, but the slow complexation kinetics require radiolabeling at 80 C for at least 30 minutes. To address this, we rationally designed a triaza-macrocycle derived chelator, **L2**, that is well-matched to the ionic radii and coordination preferences of Sc^{3+}, as supported by density functional theory (DFT) calculations and pH-dependent UV speciation. Radiolabeling studies with ^{44}Sc at room temperature indicate that **L2** affords a 250-fold increase in apparent molar activity relative to our first-generation chelator, mpatcn (**L1)**, and a 3-fold increase relative to DOTA at 80 C. Proof-of-concept radiolabeling of peptide and antibody conjugates for prostate and breast cancer targeting, respectively, demonstrate compatibility with a wide range of targeting vectors and underscore the potential to expand our scope of imageable and treatable disease targets. Toward this goal, a ^{44}Sc-PET imaging and biodistribution study in a pre-clinical model of prostate cancer will be discussed.

NUCL 3995447

Reactions of the nitrate radical ($NO_3^{\bullet}$) in condensed organic media: Kinetics and reaction mechanisms

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The nitrate radical ($NO_3^\bullet$) is well-explored in atmospheric chemistry both in the gas phase and aqueous condensed phase. However, its reactivity in the organic phase has only minimally been investigated. In particular, in nuclear waste reprocessing the solvent-extraction of metal ions from acidic aqueous media into an organic phase also allows uncharged nitric acid to be co-extracted. In the presence of radiation, radical species such as $NO_3^\bullet$ can be formed, either by direct radiolysis or through reactions of other ions and radicals. The nitrate radical can subsequently react with other solutes present, which could potentially lead to the degradation of extraction ligands and metal-ligand complexes, thus reducing overall extraction efficiency. Here we report on our studies on the reactivity of the $NO_3^\bullet$ radical in *n*-dodecane, utilizing the flash photolysis of cerium (IV) ammonium nitrate to uniquely generate this species. The $NO_3^\bullet$ reactions with common solvent extraction ligands containing nitrogen and phosphorus were explored, with second-order rate constants obtained for a suite of ligands. Organophosphorus ligands exhibited slower reactions, primarily through hydrogen atom abstraction, with reaction rate constants influenced by the number of electron-withdrawing groups attached to the phosphorus atom. Nitrogen-containing ligands showed higher reactivity due to possible electron transfer pathways. The kinetics of the $NO_3^\bullet$ radical with lanthanide-metal loaded HEH[EHP] complexes showed a consistent correlation, with faster reactivity for the lanthanide metal ions of larger radii.

NUCL 3995531 - Withdrawn

NUCL 3995531 - Withdrawn

NUCL 3995536

Many flavors of radiopharmaceutical separations: Preparation of safe and effective molecular imaging radiotracers

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Radiopharmaceuticals play a key role in the assessment of normal aging and disease processes in animal models and humans. There are many radiopharmaceuticals that have been approved for use in humans as diagnostic agents. Radiotracers are also critical tools for the development of new drugs, through assessment of pharmacokinetics and orthogonally pharmacodynamics, and underpin the rapidly growing field of radiotherapeutic agents including radiotheranostics. Radiochemical and chemical purity are critically important to assure that a single radioactive molecular entity is being prepared and applied in in vitro assays and in vivo imaging. Several methods of separation have been employed to purify the various types of radiopharmaceuticals including solid phase extraction, HPLC, GC, and size exclusion chromatography, to name a few. The fundamental importance of radiopharmaceutical purity along with the potential consequences of poor separations, and the methods used to achieve high purity agents will be addressed in this presentation.

NUCL 3995581

X-ray measurements of lanthanide coordination at liquid surfaces

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The purification and separation of lanthanides often relies upon their complexation to extractant molecules. EXAFS (extended x-ray absorption fine structure) is the “go-to” technique for measuring elemental speciation, including the identity, number, and distance of coordinating ligands within a roughly 5 Å radial distance. Complementary to EXAFS is high energy X-ray scattering (HEXS) which measures the pair distribution function. These techniques have been used to characterize lanthanide-extractant complexation and lanthanide coordination in bulk liquid environments, including aqueous and organic solutions. It is believed that ion-extractant complexation at liquid interfaces also plays an important role in separations techniques such as solvent extraction and ion foam flotation. The geometric constraints and dielectric and chemical heterogeneities present at liquid interfaces may influence ion-extractant complexation, though the challenges in measuring elemental speciation at liquid surfaces and interfaces has impeded our understanding of these effects. We report the implementation of X-ray absorption spectroscopy (EXAFS and XANES) and grazing-incidence HEXS at NSF’s ChemMatCARS at the Advanced Photon Source to investigate lanthanide-extractant complexation at aqueous-vapor interfaces and to study the surfaces of concentrated electrolyte solutions of lanthanides. Examples of extractants that will be discussed include organophosphoric acid extractants, such as HDEHP and DHDP, and bio-inspired lanthanide binding peptides.

NUCL 3995610

225Ac radiolabeling and biological studies of novel pancreatic monoclonal antibodies

***Vanessa A. Sanders**[1], vsanders@bnl.gov, Joseph Merrill[2], Scott Lyons[2], Cathy S. Cutler[1]. (1) Isotope Production, Brookhaven National Laboratory, Upton, New York, United States(2) Cancer Center, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, United States*

Actinium-225 (^{225}Ac; $t_{1/2}$=9.92 d) has shown impressive preliminary results in the treatment of advanced stage prostate cancer, showing regression of metastases and reduction in PSA levels, mainly due to the emission of 4 alpha particles in the actinium decay chain. The success of this treatment has led to investigations of promising ^{225}Ac treatment for other challenging diseases. One is pancreatic ductal adenocarcinoma (PDAC) which has increasing occurrence due to poor diagnosis and is difficult to treat as the microenvironment leads to the poor uptake of treatment drugs. In addition to the poor microenvironment the pancreas is located near many radiosensitive organs increasing the need for precise targeting in the treatment of PDAC. Monoclonal

antibodies have been shown to possess excellent *in vivo* characteristics for targeting tumors. Therefore, the development of an antibody which targets PDAC in conjunction with the use of powerful emitted alpha particles from ^{225}Ac could provide a means to treat patients with PDAC. In this work we have developed a series of TOBI antibodies that are being evaluated against patient derived organoids to investigate the efficacy of the resulting ^{225}Ac-TOBI system. This work stems from previous work where zirconium-89 was used to visualize the *in vivo* uptake of TOBI antibodies in PDAC tumors. Our preliminary ^{225}Ac radiolabeling results show less than optimal yields indicating the need for optimized strategies. Stability studies were conducted using minimal amounts of common radioprotectants (gentisic, ascorbic, or a combination) Stability studies of the radiolabeled ^{225}Ac-TOBI antibody showed significant degradation (<10% intact) 1 day post radiolabeling. Here the results of ^{225}Ac-TOBI antibody radiolabeling strategies, subsequent immunoreactivity and *in vivo* studies will be presented.

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NUCL 3995821

Radionuclide interaction with hydrothermally altered repository materials

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One of the more widely accepted concepts for the disposal of high-level nuclear waste involves placing steel waste canisters within a geological repository, separated from the host rock by a barrier made of bentonite/clay. Bentonite serves a dual purpose: it acts as a physical shield, preventing the infiltration of fluids from the natural environment and their interaction with the waste canisters, and it serves as a chemical barrier by slowing down the migration of radionuclides in case of a release. The elevated temperatures (ranging from 100 to 200 °C) near the waste canisters due to radioactive decay can potentially alter the ability of bentonite clay to adsorb contaminants. Therefore, it is crucial to consider the impact of increased temperature on the engineered barrier when designing a nuclear waste repository. In this study, we investigate the adsorption capacity of clay samples that have been altered by hydrothermal processes in batch sorption experiments involving various radionuclides (137Cs, 90Sr, 243Am) at different ionic strengths (0.01M NaCl and 1M NaCl). These hydrothermally altered samples underwent short-term (days to months) exposure to high temperatures (200-300 °C) in laboratory setting. Our findings indicate that both the hydrothermal alteration of clays and the ionic strength of the solutions significantly impact the sorption capacity of 90Sr and 137Cs. However, the sorption of 243Am is relatively unaffected. These outcomes highlight inherent differences in how cesium, strontium, and americium interact during sorption (such as cation exchange or surface complexation) and have implications for the diffusive transport of radionuclides through engineered barriers. These factors must be taken into consideration when designing waste disposal repositories.

NUCL 3995952

Covalent triazine frameworks for the separation of lanthanides and actinides

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Covalent triazine frameworks (CTFs) are a type of porous organic polymer, cross-linked by the chemically stable triazine ring. Despite their rich chemistry, robustness, and high porosity, CTFs remain largely unexplored as a sorbent for chromatographic ion separation. In this study, a previously demonstrated dicyanopyridine-based CTF is characterized as a metal ion adsorbent and optimized for the chromatographic separation of lanthanides and actinides in acidic solution.

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NUCL 3996174

Panel: Early career LGBTQ+ voices in nuclear chemistry and Technology

Tyler L. Spano[1]*, spanotl@ornl.gov, Brodie Barth*[2]*. (1) Oak Ridge National Laboratory, Oak Ridge, Tennessee, United States(2) University of Notre Dame, Notre Dame, Indiana, United States*

This panel discussion will feature a diverse group of early career professionals in nuclear chemistry who are members of the LGBTQ+ community and will explore:

Personal journeys of LGBTQ+ scientists in nuclear chemistry.
The importance of LGBTQ+ representation in STEM fields.
Strategies for promoting diversity and inclusion in nuclear chemistry and technology.
Overcoming challenges faced by LGBTQ+ individuals in the workplace.
How embracing diversity can drive innovation and collaboration in nuclear chemistry.

NUCL 3996227

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How embracing diversity can drive innovation and collaboration in nuclear chemistry.

NUCL 3996489

Development of a methodology for the nuclear forensic analysis of a historical ^{226}Ra pigment sample

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Radium pigments and paints were used in the early 1900s for the watch dial industry due to their attractive, self-luminescent properties. These pigments and paints are no longer used as they pose many health hazards; the International Atomic Energy Agency (IAEA) has identified ^{226}Ra, the main radioactive component within the sample, as a potential threat in the use of radiological dispersive devices (RDDs). To combat nuclear terrorism events, nuclear forensic analytical techniques are used for origin attribution in interdicted samples. Many techniques used to analyze nuclear materials are well documented in the literature; however, literature regarding forensic signatures or forensic techniques used to analyze ^{226}Ra radiological materials are nonexistent. Therefore, this work focuses on developing a methodology for the determination of radiochronometric ages of ^{226}Ra-containing radiological materials. This talk will discuss the production of a representative, mock ^{224}Ra pigment sample used to develop dissolution and separation procedures necessary for a radiochronometric analysis. In all, these results aim to pioneer future nuclear forensic analyses for ^{226}Ra radiological samples and ultimately aim to combat events of nuclear terrorism.

NUCL 3996617

Efficient separation method for terbium and gadolinium using LN2 resin

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Introduction: Terbium-161-based radiopharmaceuticals currently show potential as theranostic agents. Specifically, ^{152}Tb ($t_{½}$= 17.4 h, 20% β+, ec decay) and ^{155}Tb ($t_{½}$= 5.34 d, ec decay) for diagnosis and ^{161}Tb ($t_{½}$= 6.89 d, β^- decay) and ^{149}Tb ($t_{½}$= 4.12 h, 17% α, ec, β+ decay) for therapy are sought for their ability as a theranostic quartet. To produce pharmaceuticals containing these radiometals , efficient isolation from Tb is necessary. No-carrier-added ^{161}Tb is produced through the ^{160}Gd(n,γ)^{161}Gd(β^-)^{161}Tb reaction in nuclear reactors. This abstract evaluates extraction chromatography (EXC) with the LN2 resin (Triskem, France) to purify terbium from 10 – 100 mg quantities of gadolinium.

Methods: LN2 EXC resin was dry-packed into columns prepped with 1 M HNO_3 and 0.1 M HNO_3 and flowed through a peristaltic pump at 1 mL/min. Column performance was assessed for isolation of 0.5 mg of Tb from varying masses of Gd: 0.5 mg, 2.5 mg, 9.5 mg, 19.5 using 300 mg columns and 87 mg using a 2.7 g column. Columns were loaded with Tb/Gd in 5.6 mL 0.1 M HNO_3, rinsed with 14 – 17 column volumes (CVs) of 0.2 M HNO_3 to remove Gd, and finally Tb was eluted in 4 CVs of 1 M HNO_3. Terbium and gadolinium concentrations were analyzed with Microwave Plasma Atomic Emission Spectroscopy (MP-AES).

Results: Ideal Gd/Tb separation entails a efficient recovery of Tb and a high Gd/Tb separation factor. These parameters are summarized in Table 1 below for varying LN2 resin mass. As Gd load mass increases in the 300 mg column, diminishing Tb recovery was observed. The 20 mg Gd mass experiment corresponds to 50% of the column's theoretical capacity, where we observed moderate but diminishing Tb recovery (67%) and Gd/Tb SF (1600). Scaling up to more realistic Gd masses with excess column capacity, the 87 mg Gd, 2.7 g LN2 experiment demonstrated the maximum observed Tb recovery (98%) and SF (3.8k).

Conclusion: An LN2-resin-based EXC method for isolating terbium from gadolinium was evaluated. The procedure is simple, automatable, and well suited for isolating ^{161}Tb from neutron-irradiated ^{160}Gd.

Table 1. Experimental conditions and results of Tb isolation from Gd using LN2 columns

Loaded Gd/Tb mass (mg)	LN2 resin mass (g)	%Tb recovery	Gd/Tb Separation factor	n =
1	0.3	96% ± 2%	1262 ± 977	2
3	0.3	90% ± 1%	863 ± 120	2
10	0.3	83% ± 3%	1460 ± 1742	2
20	0.3	67.4% ± 0.3%	1605 ± 269	2
87	2.7	98% ± n/a	3867 ± n/a	1

NUCL 3996648

Liquid-liquid extraction and spectroscopic studies of 3,3'-dialkoxy BTP bipolar complexants for minor actinide separations

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In an attempt to combat climate change and achieve the goal of net-zero emissions by 2050, nuclear energy capacity is projected to dramatically increase in the near future. An inevitable rise of spent nuclear fuel (SNF), on top of the approximate 83,000 metric tons of legacy waste, places urgency on an environmentally safe management plan. Separations of the long-lived minor actinides (MA) from the lanthanide fission products in SNF is of particular interest as the MA are the main targets for transmutation due to their major contributions to the heat load and radiotoxicity of the long-term waste. This task can be achieved if an ideal complexant is realized for the chemoselective extraction of the MA from the lanthanides under conditions pertinent to post-PUREX SNF. In this presentation, a comprehensive performance evaluation of a new alkoxy-BTP complexant will be presented and the impact of structural modifications to the functionalized alkoxy-aryl-1,2,4-triazene substituents will be highlighted. Current $^{241}Am^{3+}/^{154}Eu^{3+}$ separations, decomplexation ($^{241}Am^{3+}$ stripping), spectroscopic analysis, and full lanthanide series extractions will be described.

NUCL 3996815

Imaging infectious diseases: Molecular imaging approaches to visualizing HIV and Long COVID

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Infectious disease poses a major threat to global human health as highlighted by the recent COVID19 pandemic. Assessment, treatment and curative interventions of infectious diseases, including but not limited to, COVID19, tuberculosis and HIV may benefit from the development of radiopharmaceuticals. These radiopharmaceuticals may be able to quantitate the extent of the infection, the presence of viral reservoirs, be useful in drug development and ultimately in the assessment of treatment response and curative strategies. Two radiopharmaceutical imaging approaches have been developed to assess viral reservoirs in HIV and Long COVID patients based on targeted antibodies labeled with zirconium-89 and a small molecule PET imaging agent targeting activated T cells, [18F]FAraG. These agents have advanced from preclinical studies to early human studies under FDA approved investigational new drug applications. This presentation will highlight the radiochemical and preclinical development of these tracers, the pathway to first-in-human evaluation and early results from the clinical research studies. These radiopharmaceuticals may be powerful tools for the characterization of viral infection and immune activation.

NUCL 3996879

Interfacial precipitation of Uf_6 from room temperature ionic liquid using water or propionitrile

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The enrichment of uranium has generated over 700,000 metric tons of depleted uranium hexafluoride (UF_6) stored as nuclear waste in the United States. Storage of this material is costly and burdensome, as this form of uranium is highly corrosive and volatile. Recent research has demonstrated that UF_6 can be stabilized through the direct dissolution into room temperature ionic liquid (IL). The process utilizes the inherent properties of the IL to facilitate the rapid reduction of UF_6 to UF_6^-. Additional reduction of the UF_6^- to form UF_6^{2-} is also possible resulting in mixed valency of the dissolved uranium. With the addition of water, two competing reactions occur which results in the precipitation of uranium tetrafluoride (UF_4) from the IL and the formation of uranyl (UO_2^{2+}) in the aqueous phase. The results indicate that the competing reactions can be influenced by the mixing of the IL and water phases. The precipitation reaction was also examined using propionitrile, a non-aqueous solvent with an affinity for fluoride. The UF_4 precipitate builds up at the IL interface when left unagitated. The reaction kinetics and UF_4 percent yield were evaluated for both water and propionitrile. The rate of reaction was also examined at room temperature and at elevated temperatures. The methods discussed provide a pathway for uranium recovery and illuminate the behavior of UF_6 in ionic liquid to undergo interfacial precipitation.

NUCL 3997042

Interfacial redox chemistry of molecular uranyl complexes immobilized on carbon electrodes

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The interfacial behavior of actinides can influence the speciation of these important elements, but the development of ligand systems that can be associated with surfaces for selective capture of actinides from solution has received little attention. In this presentation, the design, synthesis, and interfacial electrochemical properties of tailored uranyl (UO_2^{2+}) complexes that can be immobilized on carbon electrode surfaces will be described. Immobilization of a key uranium-binding ligand motif is driven in our system by noncovalent interaction of pendant polycyclic aromatic hydrocarbons (PAHs) with graphitic electrode surfaces. X-ray photoelectron spectroscopy and electrochemical studies have been used to probe the properties of the immobilized complexes, revealing

that they appear discrete and well-defined at electrochemical interfaces. Our latest results will be discussed, including studies of quantitative capture of UO_2^{2+} from solution using electrodes functionalized with our ligands and studies comparing the effectiveness of various PAHs toward immobilization.

NUCL 3997094

Solvent extraction system-level modeling and simulation with radiolysis

***Valmor F. de Almeida**, valmor_dealmeida@uml.edu. Chemical Engineering (Nuclear Program), University of Massachusetts Lowell, Lowell, Massachusetts, United States*

Hydrometallurgical solvent extraction is often used in nuclear fuel cycle applications where primary and secondary radiolysis of water adversely affect the kinetics of separation. Nevertheless, detailed radiolysis reaction mechanisms are seldom considered in modeling and simulation. An example of how this can be accomplished for nuclear fuel recycling with multiple stages will be covered.

NUCL 3997480

Developing an understanding of the role of free radicals in actinide separations processes

*Brett Lottes, **Korey Carter**, korey.p.carter@gmail.com. Chemistry, The University of Iowa, Iowa City, Iowa, United States*

The development of carbon-free energy technologies is critical for the world's decarbonized energy future, and nuclear energy currently provides the majority of zero-carbon electricity generated worldwide. One of the major challenges that remain and that is also critical for the development of new more fuel efficient and economical technologies is developing an understanding of chemical behavior of systems under high radiation fields where a- and g-radiolysis is known to occur. While there are significant ongoing efforts evaluating the radiolysis of solvents and extractants in separations schemes, much less is known about how the presence of actinides impact radiolysis and degradation pathways. We have initiated a research program to investigate actinide-free radical interactions in both small molecule complexes and polyoxometalate clusters and results thus far include families of uranyl peroxide clusters (UPCs) that can stabilize reaction oxygen species and trap fission product metals in CARBEX related conditions. We have also identified and photochemically synthesized a whole series of small molecule actinide free radical complexes that feature superoxide radical anions in conditions that mimic radiation fields generated by g-emissions. All materials have been characterized via single crystal X-ray diffraction (XRD) and vibrational spectroscopy, with solid- and solution-state EPR and ^{13}C and ^{19}F NMR spectroscopies used to definitively confirm and understand the behavior of free radicals included in actinide complexes and clusters. Results related to CARBEX related conditions will be the focus of this presentation and overall improvements in

understanding of actinide-free radical interactions in f-element separations processes will be highlighted as well.

NUCL 3997505

Nuclear forensics, Radioanalytical and environmental radiochemistry: The many flavors of nuclear chemistry at the University of Central Florida

***Vasileios Anagnostopoulos**, Vasileios.Anagnostopoulos@ucf.edu. Chemistry, University of Central Florida, Orlando, Florida, United States*

In this talk, Dr. Vasileios Anagnostopoulos will present an overview of the radiochemistry program at the University of Central Florida and its many different flavors: nuclear forensics and environmental radiochemistry, as well as radioanalytical chemistry. The most recent, exciting findigns will be presented along with the challenges that are part of this field, as well as future doncideration and needs. Dr. Anagnostopoulos is an Assistant Professor with the Department of Chemistry at the University of Central Florida and currently leads the Radiochemistry program in this institution.

NUCL 3997659

Effect of gamma irradiation on efficacy of extraction chromatography materials

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Abstract – Extraction chromatographic resins have developed considerably since their introduction as commercially available materials in the early 1990s. They play an important role in radiochemical separations due to their high retention for elements of interest, excellent separation performance, as well as the small amount of waste created. An issue that remains prevalent within the study of such materials is their durability under intense radiation exposure. Radiolytic degradation of the organic molecules used as extractants as well as the polymer backbone can have massive impacts on the efficiency of the radiochemical separation attained. Extraction chromatography provides rapid, efficient separations in analytical scale radiochemical separations. However, procedures such as those used for preparing radioisotopes for radiopharmaceutical applications or separations involving used nuclear fuel can result in these resins being exposed to incredibly intense radiation fields. We exposed extraction chromatography resins (DGA, TEVA, UTEVA, SR, PB) to an strong cesium-137 (Cs-137) source to achieve a wide range of total doses (10 Gy to 250 kGy). The impacts of radiation dose on material properties as well as the separation efficiency were quantified and are presented here.

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Effect of gamma irradiation on efficacy of extraction chromatography materials

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NUCL 3997738

Antibody-based positron emission tomography in the brain

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Positron emission tomography (PET) has become a mainstay of medical imaging due to its ability to not only identify structural features but also to derive functional information non-invasively. PET of the brain and central nervous system allows us to learn about CNS cancers, psychological conditions, and neurodegeneration, but limitations arise when operating within the confined chemical space that is small molecules. Antibodies provide solutions to many of these limitations, including an exquisite ability to distinguish chemically-similar species (such as highly homologous receptor subtypes) and to target specific forms of proteins (for example, only binding a disease-correlated, phosphorylated species and not the healthy, non-phosphorylated form). Antibodies of course have limitations, perhaps the greatest of which being their nearly absent blood-brain barrier (BBB) penetration, but numerous strategies to increase brain uptake have been developed.

Efforts to image brain targets with antibody-based PET radiopharmaceuticals have begun and found success where small molecules have struggled, including selective imaging of α-synuclein selectively versus amyloid-β as well as imaging of amyloid-β

precursor proteins instead of only imaging fully formed plaques. We have identified two features that we believe are the next critical steps for CNS PET with antibodies to advance towards the goal of clinical reality: 1) antibodies should be labeled with readily available PET isotopes, particularly radiometals such as ^{64}Cu and ^{89}Zr; 2) the ability of antibodies to image brain targets at physiologically-relevant levels must be demonstrated. The goal of this project was to image an extracellular brain target at endogenous levels in rats using radiometal-labeled bispecific antibodies and to compare these data with a small molecule standard. We have initiated our efforts by targeting the serotonin transporter (SERT), and we will use [^{11}C]DASB as our small molecule comparison. Anti-SERT antibodies with anti-transferrin receptor targeting units, for permeation across the blood-brain barrier, are used to evaluate brain uptake versus a control antibody that lacks the anti-transferrin receptor moiety. Our results include evaluation of antibody design and expression, radiolabeling, and initial studies in rats.

NUCL 3999505

Moving from extractive resins to adsorptive filters: The impact of ligand immobilization on f-element adsorption and desorption

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Extractive resins have long been a workhorse in the f-element separations community with wide ranging applications in nuclear medicine, nuclear forensics, and radioanalytical chemistry. These resins are synthesized by physically absorbing a selective ligand into the ~10-50 nm pores of polymer resin beads. The resulting 100-micron diameter resins are packed into columns and used for separations. Due to the transport limitations of the resin geometry, separations are often performed at low flowrates of 1 mL/min. Rapid, selective separations would improve yields in nuclear medicine, reduce the nuclear forensics timeline, and broadly enable more efficient radioanalytical separations.

To fill these needs, we synthesized chelating membrane adsorbers—a scalable, high-throughput alternative to extractive resins. This work spans membrane synthesis (electrospinning), diglycolamide (DGA) ligand synthesis, covalent functionalization of the electrospun membranes, and adsorption/desorption experiments with Ac-225, La, and Ce in 4 M, 6 M, and 10 M nitric acid. The resulting membrane adsorbers contained 36 wt% DGA which is consistent with commercially available extractive resins containing physisorbed DGA ligands. Importantly, the DGA-functionalized membranes maintain a high permeance of ~ 500 LMH/bar. Rapid desorption kinetics with 10 M nitric acid suggest that these DGA-functionalized membranes have the potential to accelerate the product capture step in elution chromatography. The membrane adsorber performance are directly benchmarked against the commercial DGA resins. This

comparison showcases the differences in ligand performance using two immobilization methods (physically absorbed as a liquid) vs. covalently tethered to a polymer surface. While these chelating membranes were originally studied in the context of nuclear medicine, they serve as a promising platform for other applications which require lanthanide and actinide separations.

NUCL 4000893

The use of surrogates in radionuclide separations method development

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In the course of method development for the separation of a specific radionuclide, it is sometimes necessary or advantageous to use a surrogate due to difficulty in obtaining the specific radionuclide, difficulties in measurement due to complex decay chains, radionuclide license issues, or other considerations. The surrogate could be a stable isotope or different radioactive isotope of the same element or a stable or radioactive nuclide of a different element with similar chemistry. The use of a surrogate can often predict the behavior of the desired radionuclide; however, there may be differences, understood or unforeseen, that lead to significant deviations in the behavior of the surrogate. Examples of successful and unsuccessful applications of surrogates in radionuclide separation schemes will be provided in applications including using rare earth elements to develop minor actinide separations, chromatographic separations of medical radioisotopes in buffer solutions (^{225}Ac, ^{68}Ga, $^{203/212}$Pb), and using stable Ba to predict the behavior of ^{226}Ra used as target material to produce ^{225}Ac.

NUCL 4002770

Mitigating the corrosive effects of molten salts through multi-layer ALD coatings for optimal material passivation

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Molten salts are extremely efficient heat exchange fluids, and have uses in applications such as molten salt nuclear reactors (MSRs) and concentrated solar power generators (CSPs). Because molten salts form stable ionic electrolytes at high temperatures, they also foster corrosion through electrolytic oxidation and dissolution. This makes safe, secure molten salt containment a challenge. Thin passivating layers are often employed to mitigate corrosion, however no perfect solution currently exists. The goal of this research is to intentionally employ multiple layered materials to achieve optimal corrosion resistance in highly corrosive environments, such as those in MSRs and CSP generators. This goal will be achieved through the systematic study of 1) layer material composition, 2) layer material thickness, and 3) number and order of layers. Using

atomic layer deposition (ALD), multi-component, atomically precise anti-corrosive coatings are prepared for iterative studies of early stages of corrosion at the interfacial scale. In situ analytical techniques such as attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR) and in situ SEM using WETSEM™ atmospheric control capsules are employed to characterize the chemical, compositional and morphological changes that occur during corrosion, to identify and eventually mitigate the deficiencies of these coatings. In summary, the proposed work has the potential to significantly enhance the resistance of materials used in manufacturing and infrastructure; not only for MSRs and CSPs generators, but more generally for materials at risk of exposure to highly corrosive environments.

NUCL 4005161

A micromanipulation platform to enable nuclear forensics studies at the single particle level

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Many applications in the field of nuclear forensics would benefit from the ability to carry out analyses at the single particle level, but the identification and manipulation of particles of interest remains a fundamental challenge. Here, we describe a non-destructive, non-contaminating micromanipulation platform which can enable the capture, manipulation, and analysis of individual particles or clusters of particles. A series of case studies are described where the platform is used to enable single particle selection and analysis via methods such as Scanning Electron Microscopy-Energy Dispersive X-Ray Spectroscopy (SEM-EDS) and Inductively Coupled Plasma Mass Spectrometry (ICP-MS). The results from these studies demonstrate the developed platform can empower researchers in the field to carry out critical single particle elemental/isotopic analyses with implications for current and future national security.

NUCL 4005405

Engaging LGBTQ+ researchers in nuclear & radiochemistry: lessons & ideas from academia to industry

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As we discuss increasing diversity, equity, inclusion and belonging (DEIB) to research teams and corporations, many research team leaders want to know what techniques actually work. This talk will be centered on concrete ideas from lessons learned about what could work to help engage LGBTQ+ (Lesbian, Gay, Bisexual, Transgender, queer, and other sexual and gender minorities) researchers. Although LGBTQ+ is largely grouped together, each group not only is diverse, but also includes individuals with intersectional identities that may change what works with one researcher and disengages another. Through the lenses of our different research experiences, this presentation should help resolve some misunderstandings and provide resources and ideas that anyone could implement to engage researchers in nuclear and radiochemistry.

NUCL 4026104

DFT analysis for the binding of rare-earth nitrates to MCM-22 cluster models

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MCM-22 type zeolites are a class of aluminosilicates suitable for exploring the fundamental aspects of the binding of rare earth elements (REEs). The aim of the present study is to explore the RE nitrate binding to the silanol and Bronsted-Acid Sites (BAS) of MCM-22 and compare the binding efficiency of the sites based on the calculated binding energy values. A cluster model of MCM-22 was constructed to represent the external and internal surfaces having twenty-four and thirty-seven Si sites (denoted as T sites), respectively (Figure 1). To generate the BAS in both external and internal surfaces, suitable Si atoms are replaced with Al and H was added to the O atom that bridges the Al with an adjacent Si. The choice of the Si atoms for the replacement to generate BAS is performed based on the accessibility of the RE nitrates for binding - T1, T2 and T3 sites. The binding energy for the bonding between RE nitrate and silanol/BAS is calculated using the following equation:
Cluster-model + $Nd(NO_3)_3$ à Cluster-$Nd(NO_3)_2$ + HNO_3
BE = E[Cluster-model] + E[$Nd(NO_3)_3$] – E[Cluster-$Nd(NO_3)_2$] – E[HNO_3]
As the presence of Na^+ in the MCM-22 structures was noticed experimentally, we have removed the H atom from our -Si-O(H)-Al- cluster models and placed a Na^+ in the vicinity leading to the formation of -Si-O(Na)-Al- clusters.
For the cluster models with Na^+, the binding energies are calculated as follows:
Cluster-model-Na + $Nd(NO_3)_3$ à Cluster-$Nd(NO_3)_2$ + $NaNO_3$
BE = E[Cluster-model-Na] + E[$Nd(NO_3)_3$] – E[Cluster-$Nd(NO_3)_2$] – E[$NaNO_3$]
The calculated results reveal stronger binding at BAS sites for both external and internal BAS sites, but much weaker binding at silanol sites. This is consistent with the picture deduced from recent experiments. Moreover, it is also evident that the -Si-O(H)-Al- shows stronger binding with $Nd(NO_3)_3$ than -Si-O(Na)-Al- clusters.

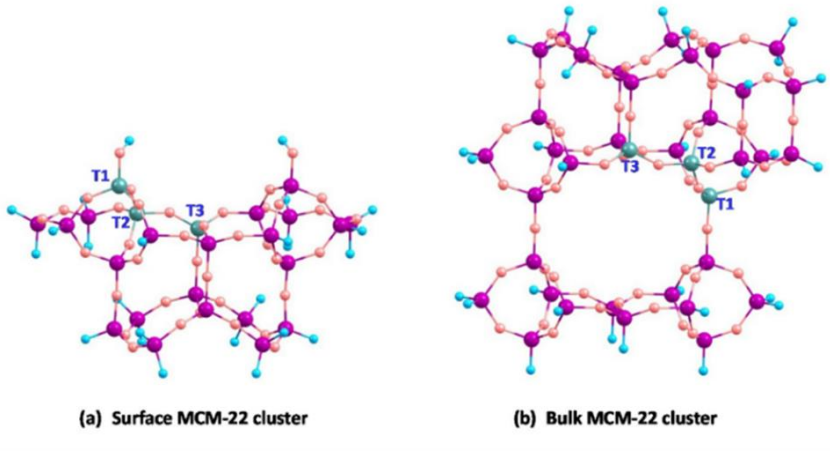

Figure 1. MCM-22 surface and bulk cluster models.

NUCL 4026107 - Withdrawn

NUCL 4026112

Presentation title: REACKT: Advancements in Computational Protocols for Lanthanide and Actinide Systems

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The elucidation of the binding selectivity of lanthanides and actinides is quintessential for advancing nuclear and radiochemical applications, encompassing nuclear forensics, the design of separation agents, and the interpretation of spectra. Theoretical investigations employing molecular modeling methods, such as ab initio and Density Functional Theory (DFT), have been instrumental in simulating binding interactions, with computational protocols being refined for superior accuracy encompassing relativity, spin-orbit coupling, and core correlation effects. The integration of contemporary data modeling approaches, like Artificial Intelligence (AI) and Machine Learning (ML), further augments our understanding of binding selectivity properties. A notable stride in this domain is the advent of the REACKT program, which endeavors to bolster the precision and efficiency of computational methodologies. This presentation delineates the development and integration of computational protocols within the REACKT framework, illustrating how this program propels the frontier of lanthanide and actinide chemistry modeling. By leveraging the REACKT program, we elucidate how a synergistic blend of traditional computational chemistry methods and modern data analytics can significantly enhance predictive accuracy and provide deeper insights into the complex behavior of lanthanide and actinide systems.

NUCL 4026114 - Withdrawn

NUCL 4044364

Panel Session on Artificial Intelligence and its Applications in Nuclear and Radiochemistry

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This panel discussion features experts in the field of artificial intelligence (AI) as it applies to nuclear and radiochemistry. The panel includes specialists who are at the forefront of integrating advanced data science techniques into the realm of radiochemistry. The discussion will welcome a wide range of topics, encompassing the broad spectrum of AI such as machine learning, neural networks, algorithm design, and data science and analytics. Advances and challenges fostered by these technologies will be addressed, including the evaluation of key properties in material design, morphology analysis, molecular systems, detection, spectroscopy, and setting new accuracy standards. The panelists will also explore how breakthroughs in high performance computing are enabling AI to provide unprecedented insights, thereby enhancing chemistry's role in addressing national and global challenges and contributing to its resilience and sustainability.