



High Purity Radiolanthanides

Abstract

A novel patented [USPTO 12,416,064 B2] chromatography process has been developed by CF Tech (Boston, MA, USA) and Battelle Energy Alliance (Idaho National Lab, Idaho Falls, ID, USA) for separation of lanthanides and elemental metals. The process was demonstrated in the production of no carrier added lutetium-177 (^{177}Lu) for cancer treatment. ^{176}Yb targets were irradiated in the MIT Nuclear Reactor generating ^{177}Lu with activity levels up to 10.3 Ci/g target. The chromatography process recovered more than 90% of the ^{177}Lu meeting all measured radionuclidic and radiochemical purity standards (^{175}Yb , ^{176}Yb , Cu, Zn, Pb). The chromatographic process takes less than 5 hours, uses off-the-shelf chemicals and resins, and requires only a single column pass to achieve decontamination factors of 10^6 or greater. This breakthrough technology offers simplicity and speed, with potential for quickly purifying many other lanthanides and short-lived radioisotopes.

CF Tech's patent was co-developed with leading researchers at Idaho National Laboratory, a leading nuclear technologies breakthrough facility. CF Tech's intellectual property portfolio includes pending exclusivity, licensing and sub-licensing rights to this invention and encompassing associated INL protected separation technologies. The MIT Nuclear Reactor is an available partner for irradiation and hot box services.

Chromatographic Purification of Radiolanthanides

Introduction

CF Technologies, Inc. (CF Tech) has developed a chromatography process for lanthanide separations. Decontamination factors of 10^6 or greater are achieved in just a single column pass in under 5 hours, comparing favorably to ion exchange chromatography and extraction chromatography, which can require multiple column passes and longer processing times to achieve the same decontamination factors.^{1,2}

The process was demonstrated for purification of no carrier added ^{177}Lu . This radioisotope is a key ingredient in cancer therapies Lutathera (^{177}Lu -DOTATATE), Pluvicto (^{177}Lu -PSMA-617), and numerous other cancer treatments undergoing clinical trial.³ ^{177}Lu is an attractive and rapidly growing radioisotope for targeted radionuclide therapy due to its favorable penetration range, emission of low-energy gamma photons for imaging, favorable half-life (6.65 days), and a favorable oxidation state for radiolabeling a variety of carriers.⁴ With a half-life of only 6.65 days, this isotope loses about 10% of its activity every day, making processing speed critical to its medical yield and efficacy.

The global market for ^{177}Lu is expected to grow significantly, to reach US\$10 billion by 2032, corresponding to 1.3 million patient treatments per year. Current growth rates in the sector are 22% from 2025 – 2032.^{5,6,7}

Process Description

In this purification process, the irradiated target is dissolved and injected into the chromatography column, and pure ^{177}Lu elutes in 3 – 4.5 hours, followed by ^{176}Yb . As the eluant leaves the column, it flows through an in-line UV-Vis detector for inline monitoring of Yb, and then to a fraction collector (Figure 1). Operation of major equipment is done remotely, minimizing worker radiation exposure.



The half-life of Lutetium-177 is only 6.65 days. Fast processing speeds, high yield, and high purity doses are absolutely critical for patients.



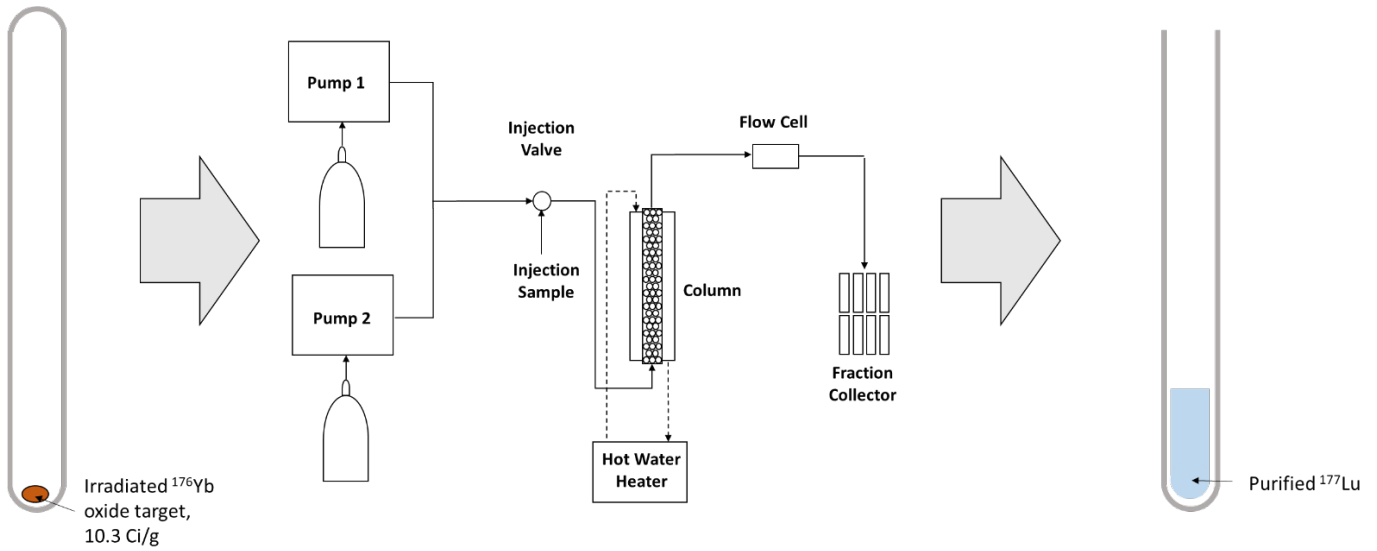


Figure 1 – System setup

Demonstration for ^{177}Lu Purification

^{176}Yb oxide targets were irradiated in the MIT Nuclear Reactor at a thermal neutron flux of $5.6 \times 10^{13} \text{ n/cm}^2\text{s}$ for 20 days. Activities ranged from 5.2 to 10.3 Ci/g. The Lu and Yb isotopes were separated in CF Tech's chromatography system in a single column pass. The ^{177}Lu fraction was analyzed for ^{177}Lu and ^{175}Yb using a High-Purity Germanium Gamma Spectrometer, then analyzed by ICP MS for Cu, Zn, Pb, and ^{176}Yb .

Figure 2 – Rabbit containing ^{176}Yb being inserted into MIT Nuclear Reactor



Process chromatograms from 2 runs are shown in Figure 3. Total Yb isotopes (measured by UV-Vis) are shown in pink, while the ^{175}Yb and ^{177}Lu (measured by gamma spectroscopy) are shown in blue and green respectively. In the first run, 65 mCi of ^{177}Lu in 12.3 mg of Yb was injected, with recovery of both the Lu and Yb fractions. In the second run, 313 mCi of Lu in 25.2 mg of Yb was injected with eluent collection stopped after the ^{177}Lu eluent was collected. This significantly larger batch of material, demonstrates scalability. All activities are back-calculated to the end of irradiation. Further testing with cold mixtures of Yb and Lu demonstrated the scalability of the chromatography process up to 120 mg in a ¼" column.

The distinct, sharp, well separated peaks are representative of the high purity material collected, $^{176}\text{Yb} < 0.1 \mu\text{g}/\text{GBq}$ after 9 days.

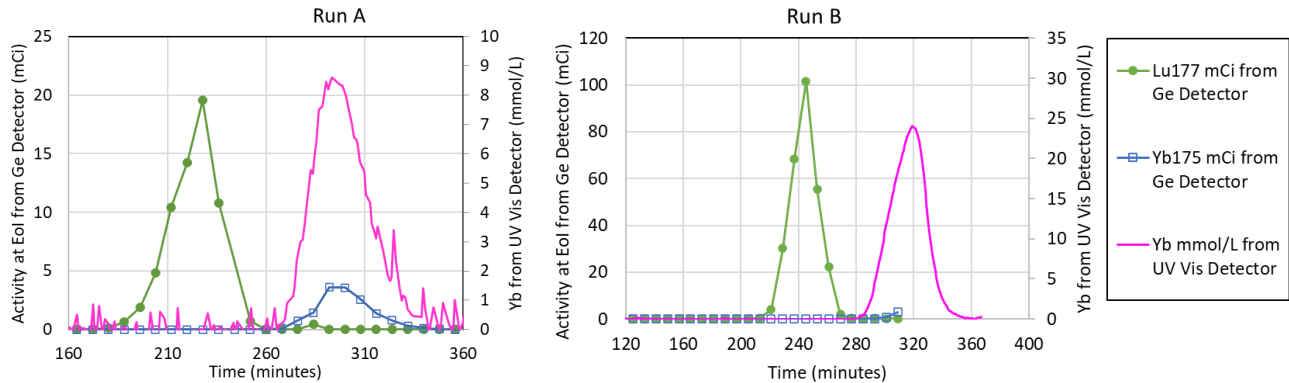


Figure 3 – Chromatograms (Eol=End of Irradiation)

Recoveries and purity metrics are listed in Table 1. High ^{177}Lu recoveries were achieved with a single column pass in 4 and 4.5 hours in these two runs. European Pharmacopeia purity standards were met. In Run A only, the ^{176}Yb fraction was recovered, with a measured recovery of 87%. Copper, zinc, lead, and ^{174}Yb levels were lower than the original irradiation target, confirming that the ^{176}Yb is suitable for re-irradiation as a target for future production of ^{177}Lu , with improved purity after each recycle.

Table 1 – Run parameters (all activities back-calculated to end of irradiation)

	Target	Run A	Run B
Injected Activity		64.6 mCi	313 mCi
^{177}Lu Recovery (^{177}Lu recovered/ ^{177}Lu injected)	>85%	107%*	91%
^{176}Yb Recovery	>85%	87%	N/A
Decontamination Factor	> 10^5	> 1.8×10^6	> 9.0×10^5
Time to Recover Lu	<8 hours	4 hours	4.5 hours
Recovered ^{177}Lu meets European Pharmacopeia purity standards?	$^{175}\text{Yb} < 0.07\%$ Cu < $1 \mu\text{g}/\text{GBq}$ Zn < $1 \mu\text{g}/\text{GBq}$ Pb < $0.5 \mu\text{g}/\text{GBq}$ $^{176}\text{Yb} < 0.1 \mu\text{g}/\text{GBq}$ after 9 days	Yes	Yes
Recovered ^{176}Yb suitable for re-irradiation?	$^{174}\text{Yb} < 0.44\%$ Cu < $43 \mu\text{g}/\text{g}$ Zn < $23 \mu\text{g}/\text{g}$ Pb < $43 \mu\text{g}/\text{g}$	Yes	^{176}Yb recovery not attempted

*The recovery greater than 100% in Run A is attributed to background radiation detected by the sodium iodide spectrometer used to measure the activity of the material injected, and of the Lu product fraction

Conclusion

Irradiation of ^{176}Yb targets at the MIT Reactor was successful in generating ^{177}Lu at up to 10.3 Ci/g. Greater than 90% recoveries were achieved in the chromatographic purification, while meeting all measured product purity requirements in a single column pass. In particular, ^{176}Yb levels met the industry standard of $<0.1 \mu\text{g}/\text{GBq}$ after 9 days. The ^{176}Yb recovery was 87%, while the ^{176}Yb had better purity than the original irradiation target, making it suitable for re-irradiation with improved purity after each recycle.

The results indicate that this novel chromatographic purification method is effective at separating commercial quantities of ^{177}Lu from irradiated ^{176}Yb targets. Decontamination factors for a single column pass were about 10^6 . This is an extremely efficient separation showing considerable promise for other lanthanide separations, including emerging isotopes for cancer treatment such as holmium-166, terbium-161, and others.

CF Tech's technology is available for licensing. Please reach out to us to discuss options for introducing this technology into your suite of products and services for radioisotope production, reactor production offerings, and to expand upon quantitative measurement.

Related Lanthanide Separation Developments

To further prepare for an expanded suite of stable and radioisotope separations, CF Tech has demonstrated high purity separations of heavy lanthanides from one another as seen in Figure 4 below – dysprosium, holmium, erbium, thulium, and ytterbium from each other in a single column pass.

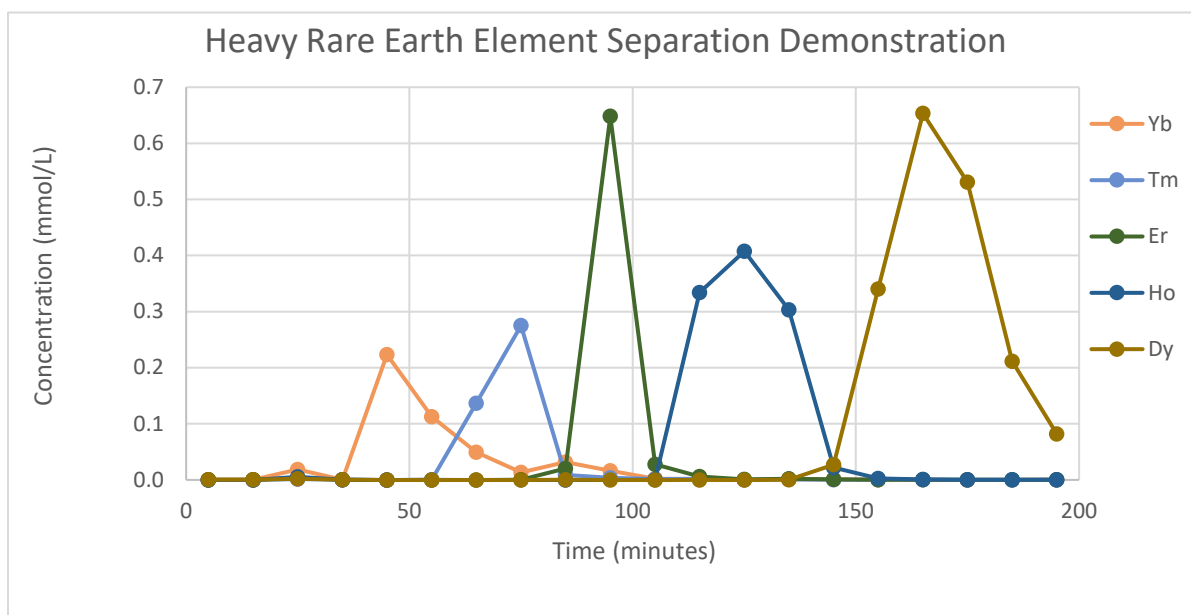


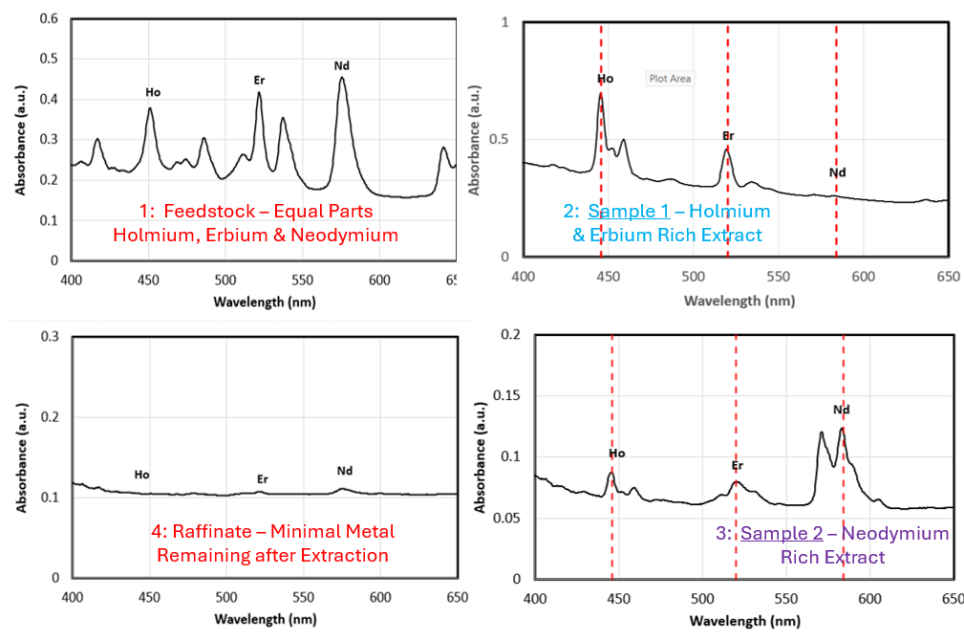
Figure 4 – Heavy rare earth element separation demonstration results

While chromatography is extremely useful for high purity separations, CF Technologies, Inc. has also demonstrated easy to implement continuous counter-current extraction and separation of rare earth elements using low-cost, highly available and recyclable supercritical carbon dioxide as a solvent. As represented in Figure 5, carbon dioxide provided a simple solution to separating a high yield product of holmium and erbium separate from neodymium, a highly useful process for mining and by-product streams for recovery of high value material at low costs from a mixed material feedstock.

Supercritical Fluid Selective Extraction of Holmium/Erbiun from Neodymium

Ho: Holmium
Er: Erbium
Nd: Neodymium

Analysis of Samples by UV-Vis Spectroscopy



Mining wastes can contain valuable light rare earth elements such as Holmium, Erbium and Neodymium. Neodymium, with a trade price of approximately \$45/pound is especially sought after, as a main component in powerful permanent magnets used in EV motors and wind turbines, among other industries.

In this thoughtfully designed experiment, CF Tech was able to first selectively extract the Holmium and Erbium from the Neodymium, and then extract the Neodymium in high yield.

CF Technologies, Inc. (Boston, MA) seeks partners as they continue to expand this economical process to extract and separate rare earth elements from natural matrices, such as compositions present in mining waste streams, at high purities.

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8921-PR1-2025

Figure 5 – Rare earth element separation by supercritical carbon dioxide demonstration results

About the Team

CF Tech has 30 years of experience in critical fluid and chromatography process development. Applications include chromatographic purification, extraction, fractionation, reaction, particle formation, aerogel production, cleaning, and decontamination. The Principal Investigator, Dr. Laura Sinclair, has made several important contributions in the extraction, purification, and separation of lanthanides. CF Tech's partner, the MIT Nuclear Reactor Laboratory is an interdepartmental center that operates a high performance 6 MW nuclear research reactor. This work was funded in part by the US Department of Energy (DE-SC0019565). ICP MS services were provided by a core center grant P30-ES002109 from the National Institute of Environmental Health Sciences, National Institutes of Health.

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