DE-SC0019565
Dr. Michelle Shinn,
Dr. Ethan Balkin

Purification of Lutetium-177

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Technical Objective

Objective

- Rapid chromatography for purification of lutetium-177
- Lutetium-177 used in targeted radionuclide therapy

Why?

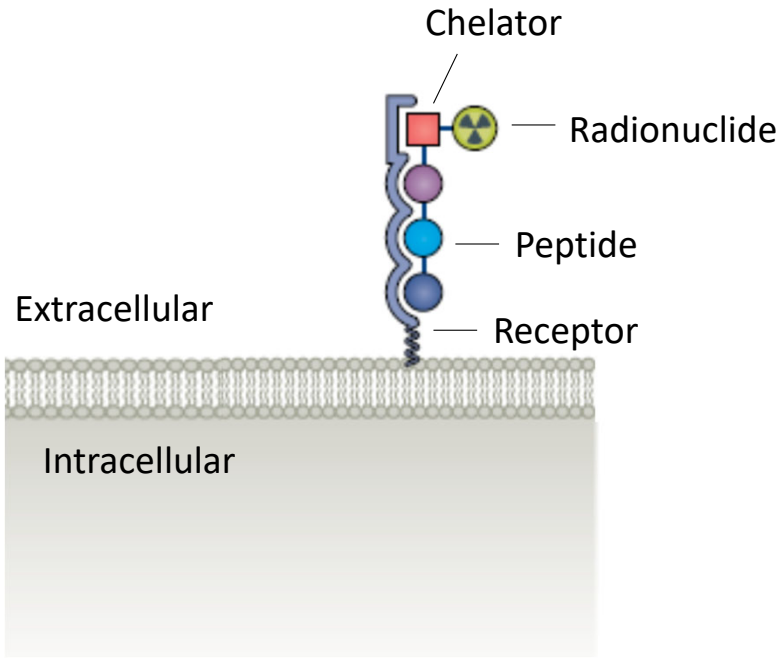
- Current state of the art is time consuming and limited to small batch sizes

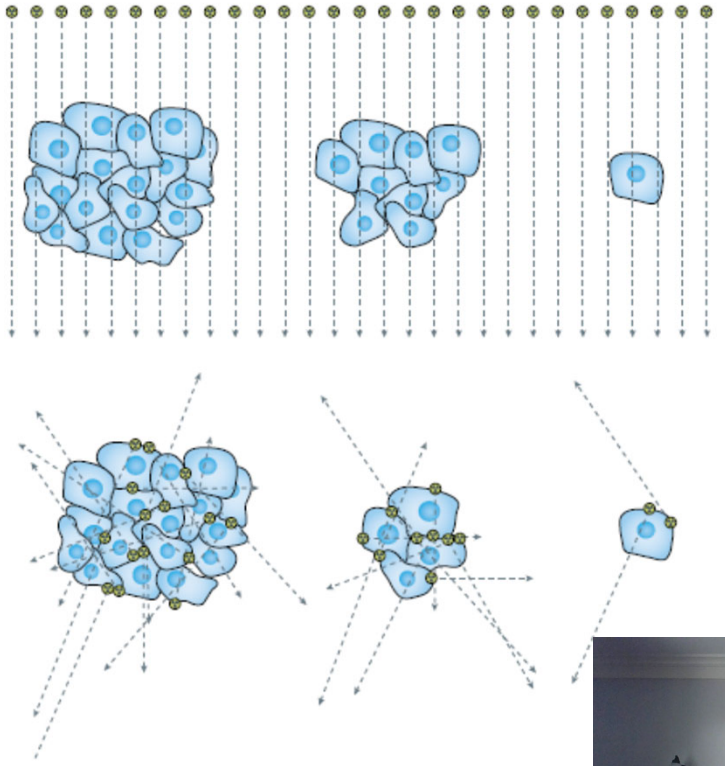
How?

- New solvents allows for new chemistries

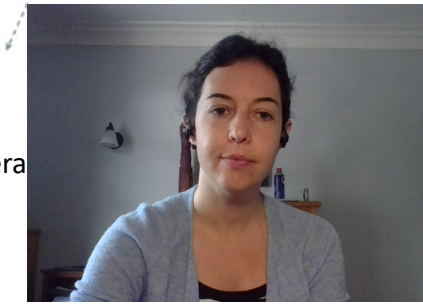
Image: ITM

Peptide Receptor Radionuclide Therapy



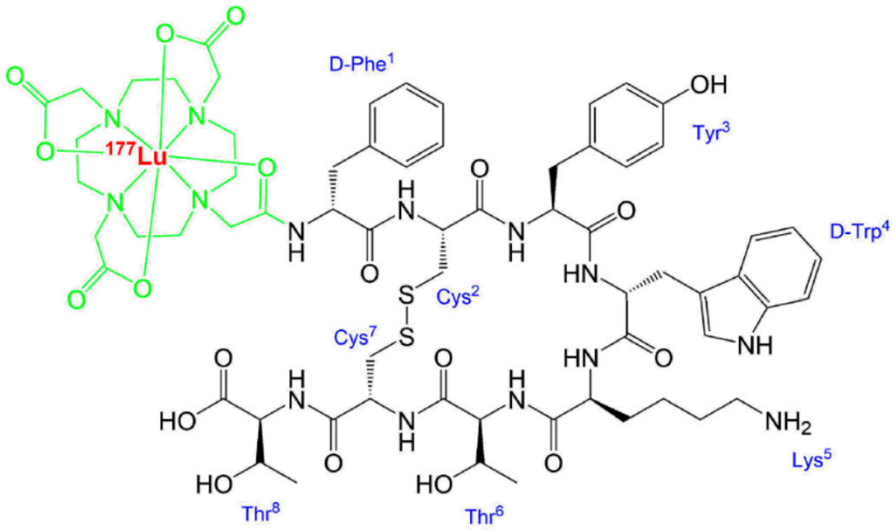


Images from Sgouros, George, Lisa Bodei, Michael R Mcdevitt, and Jessie R Nedrow. 2020. "Radiopharmaceutical Thera
Drug Discovery 19 (September). https://doi.org/10.1038/s41573-020-0073-9.



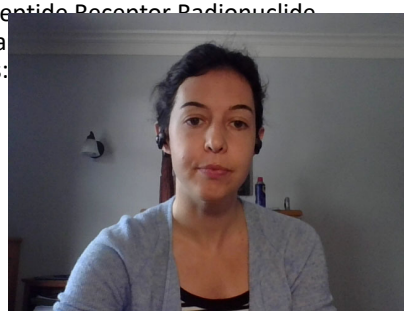
Lutetium-177

- ^{177}Lu-DOTATATE, approved for neuroendocrine tumors
- ^{177}Lu-lilotomab satetraxetan for non-Hodgkin's lymphoma (Phase I/II)
- ^{177}Lu-DOTATOC for neuroendocrine tumors (Phase III, expected approval in 2024).
- ^{177}Lu-PSMA-617 for prostate cancer (Phase III, expected approval in 2022)



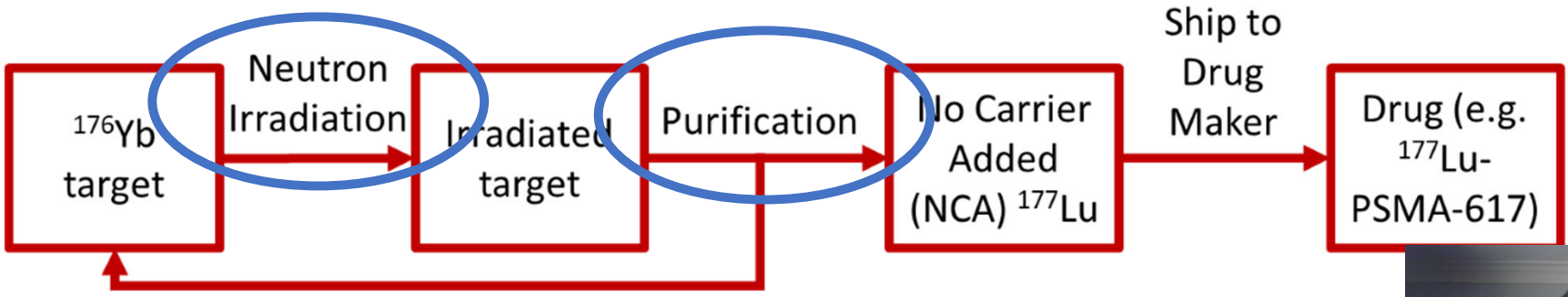
radionuclide (^{177}Lu) + chelator (DOTA) + targeting peptide (octreotate)

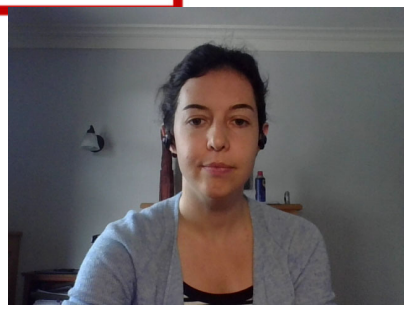
Image from Hennrich, Ute, and Klaus Kopka. 2019. "Lutathera®: The First FDA- and EMA-Approved Radiopharmaceutical for Peptide Receptor Radionuclide Thera https:



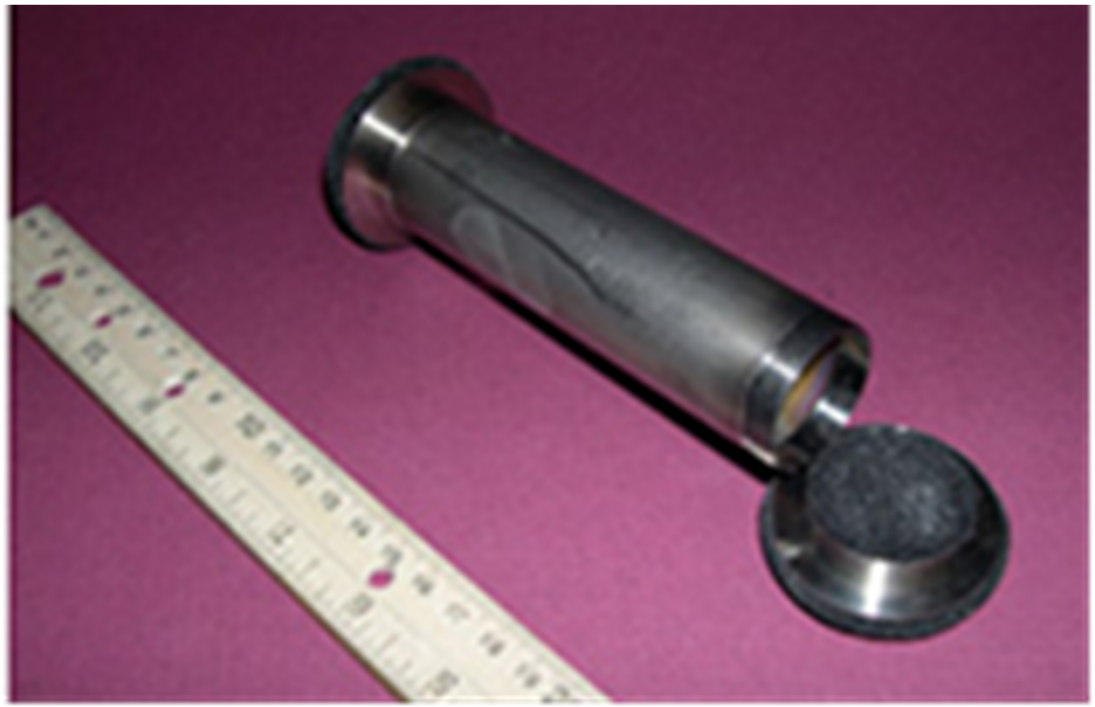
Supply Chain

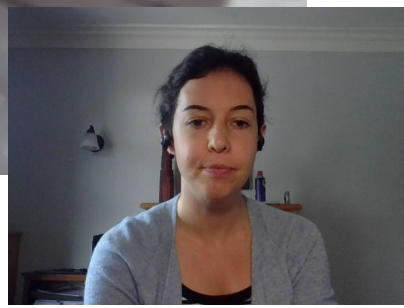
- Target customers are isotope manufacturers
- Irradiate and purify lutetium-177, sells to drug makers
- Examples: IDB Holland (subsidiary of Novartis), Isotope Technologies Munich (ITM), Isotopia, Eckert & Ziegler, Bhabha Atomic Research Centre, etc.





Irradiation of ytterbium-176





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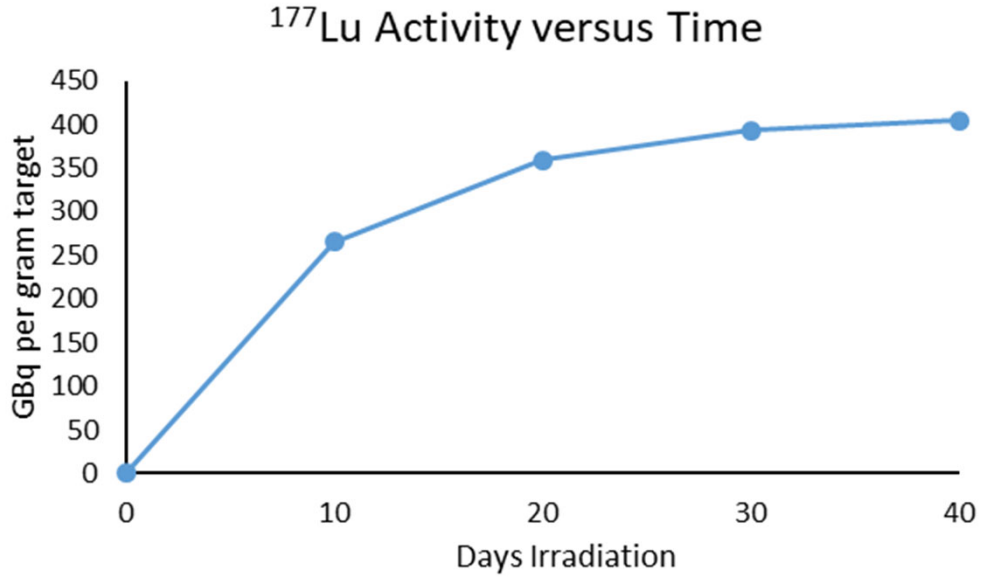
Irradiated Target



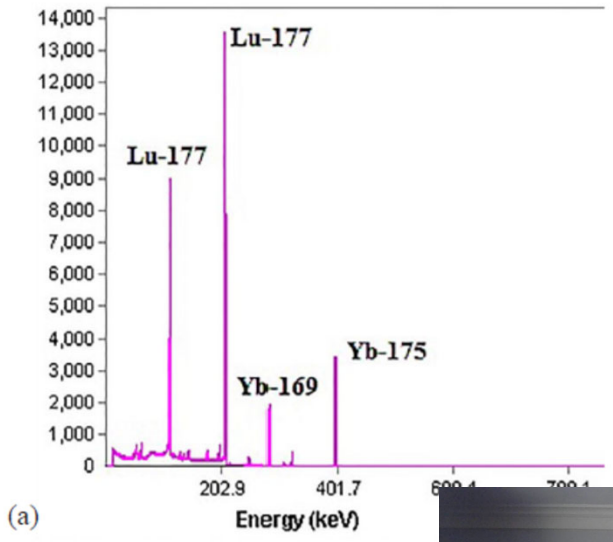
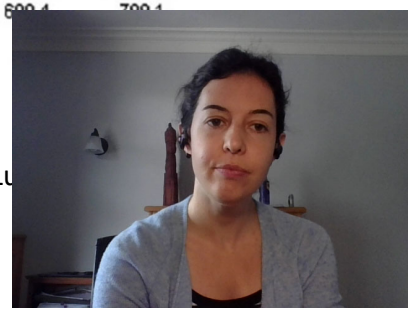


Image from Salek, Nafise, Mojtaba Shamsaei, and Mohammad Ghannadi Maragheh. 2016. "Production and Quality Control 177 Lu
Potential Agent for Bone Pain Palliation" 17 (6): 128–39.



Current Purification Technologies

Alternative	Advantages and Disadvantages
Aqueous ion exchange chromatography	**Advantages:** Chemicals are cheap and readily available **Disadvantages:** Requires multiple stages, long processing times (6-8 hours) Methods can be limited to small target sizes (~150 mg)
Extraction chromatography	**Advantages:** Suitable for large targets (>300 mg) **Disadvantages:** Complex, many stages and resin types required The process is ~16 hours and may need to be repeated multiple times
Cementation	**Advantages:** Applicable to medium-sized targets (at least 200 mg) Processing times are relatively short (3-4 hours), but may require extraction chromatography to clean up product **Disadvantages:** Residual mercury can be present which is a health risk for patients

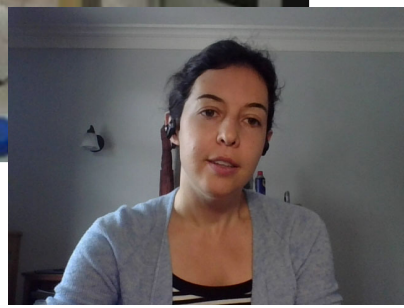


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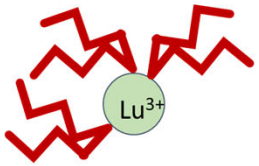
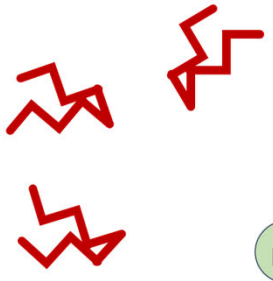
Image from Barkhausen, Christoph. 2011. “Production of Non Carrier Added (n.c.a.) 177 Lu for Radiopharmaceutical Applications.” Technical University of Munich.

Process

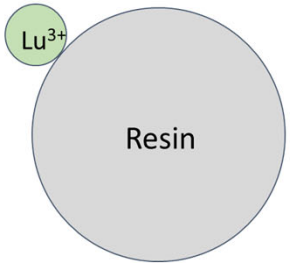
Loading

1. Chemical with metal



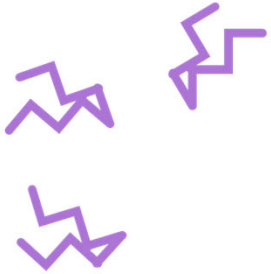


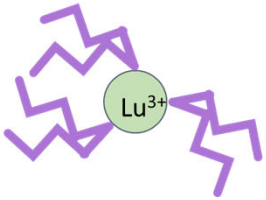
2. Metal has been loaded onto resin



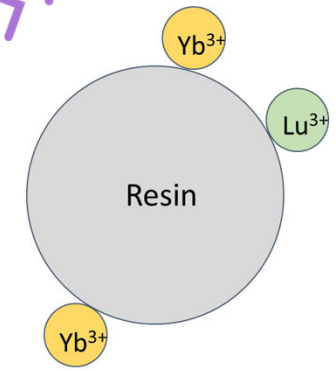
Stripping

1. Chemical





2. Metal has been stripped from resin



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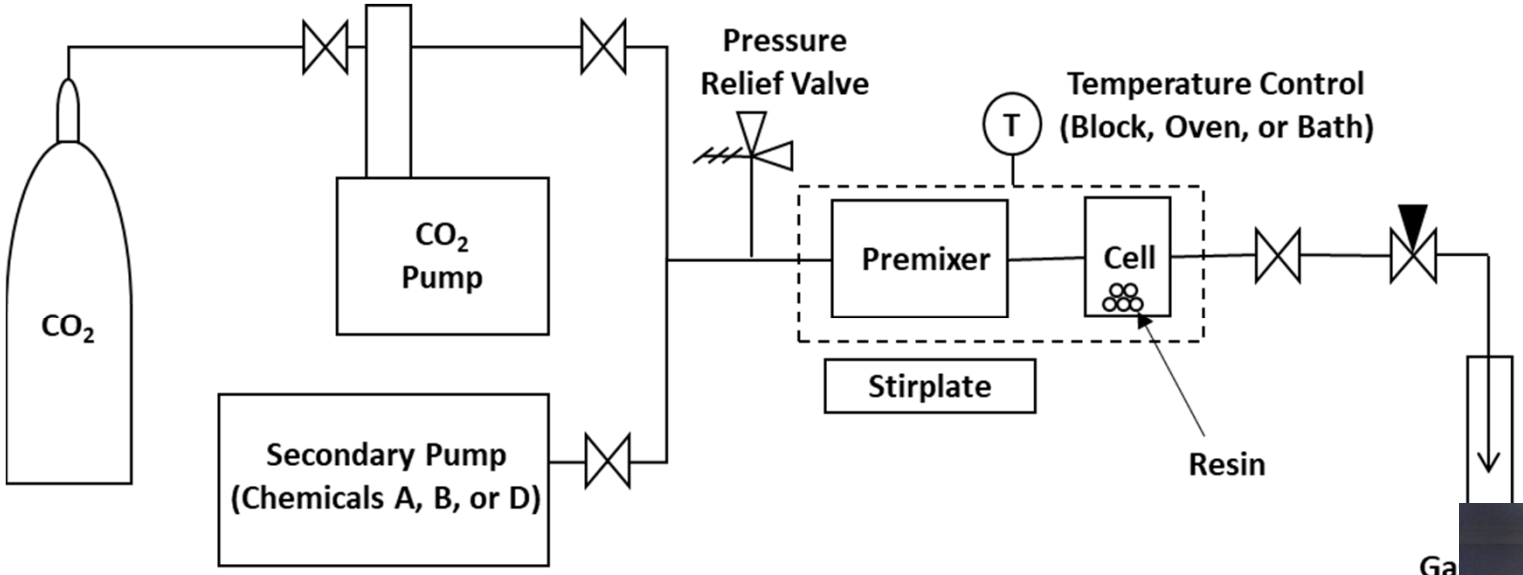
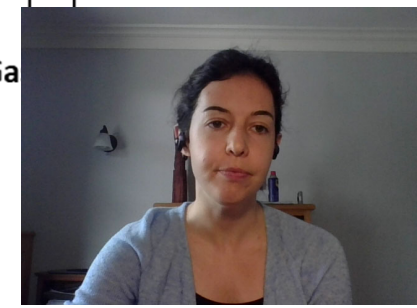
Phase I – Testing Separation Factors

- Tested extraction of Lu and Yb from Resin A





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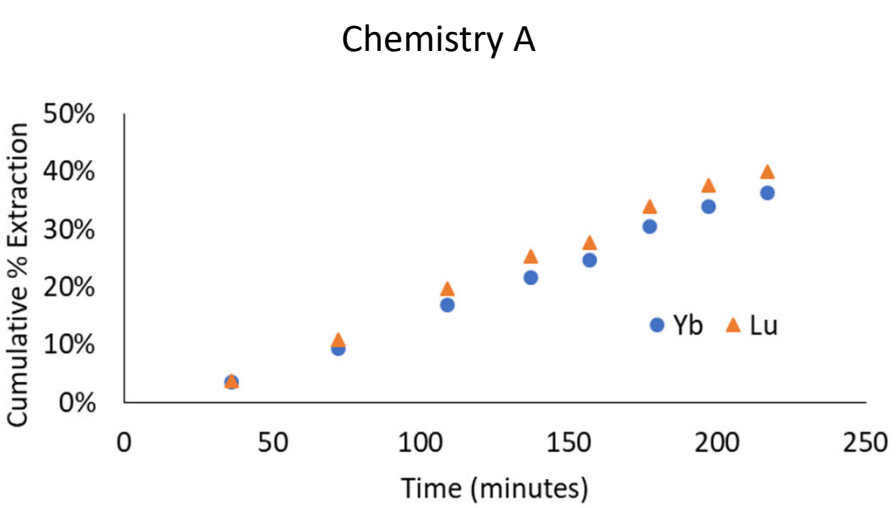
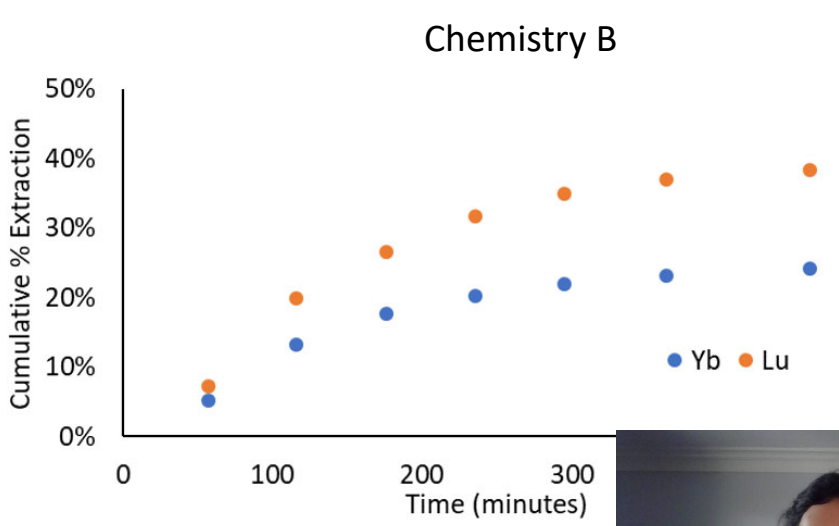
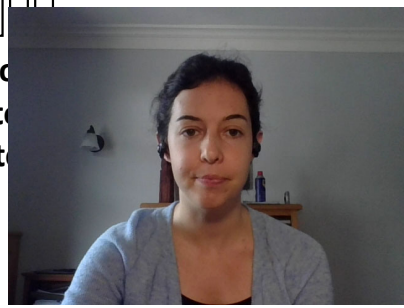




Chromat



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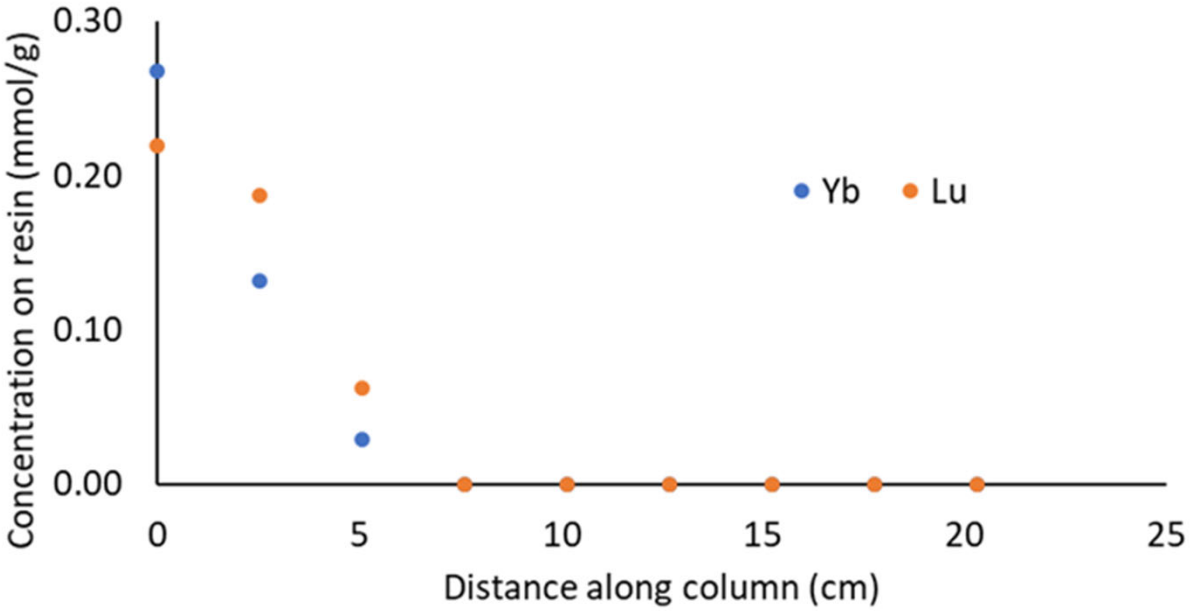
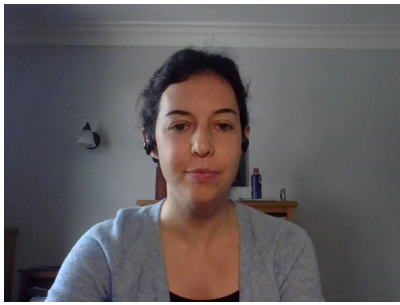
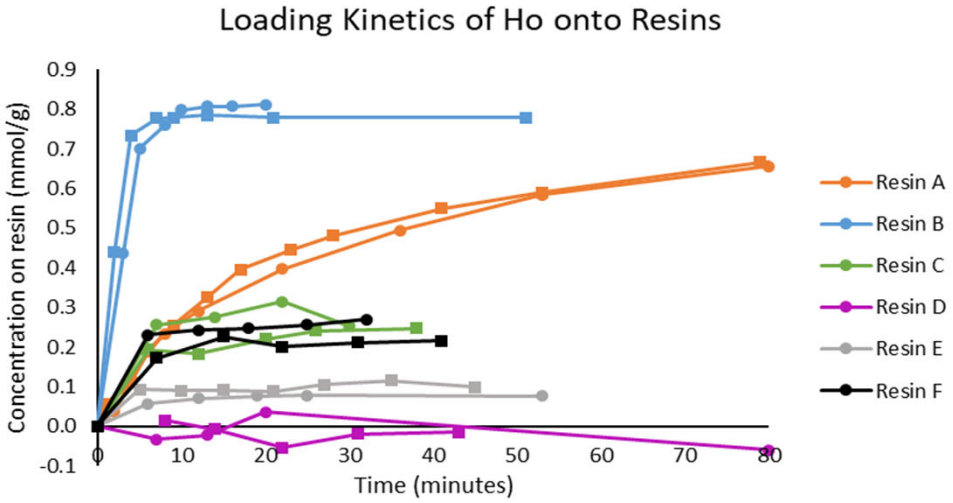
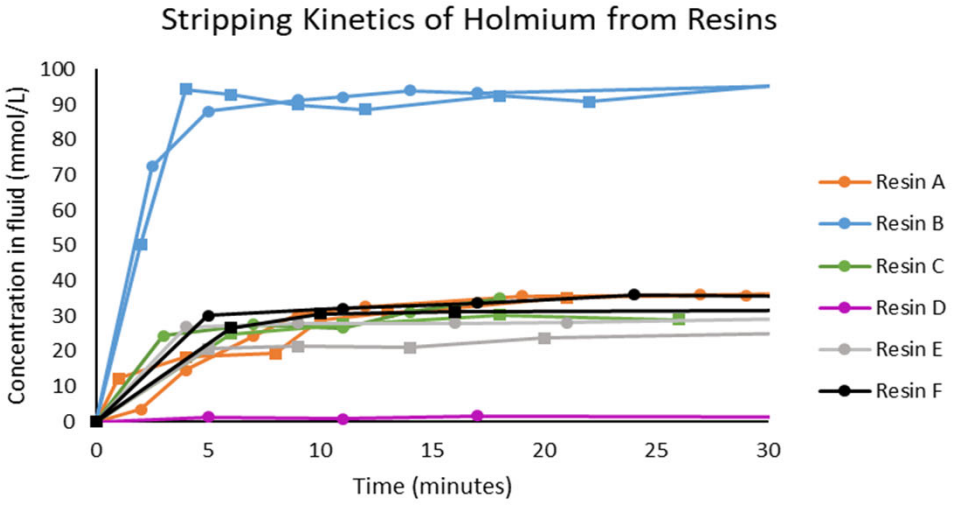
Initial Chromatography Effort



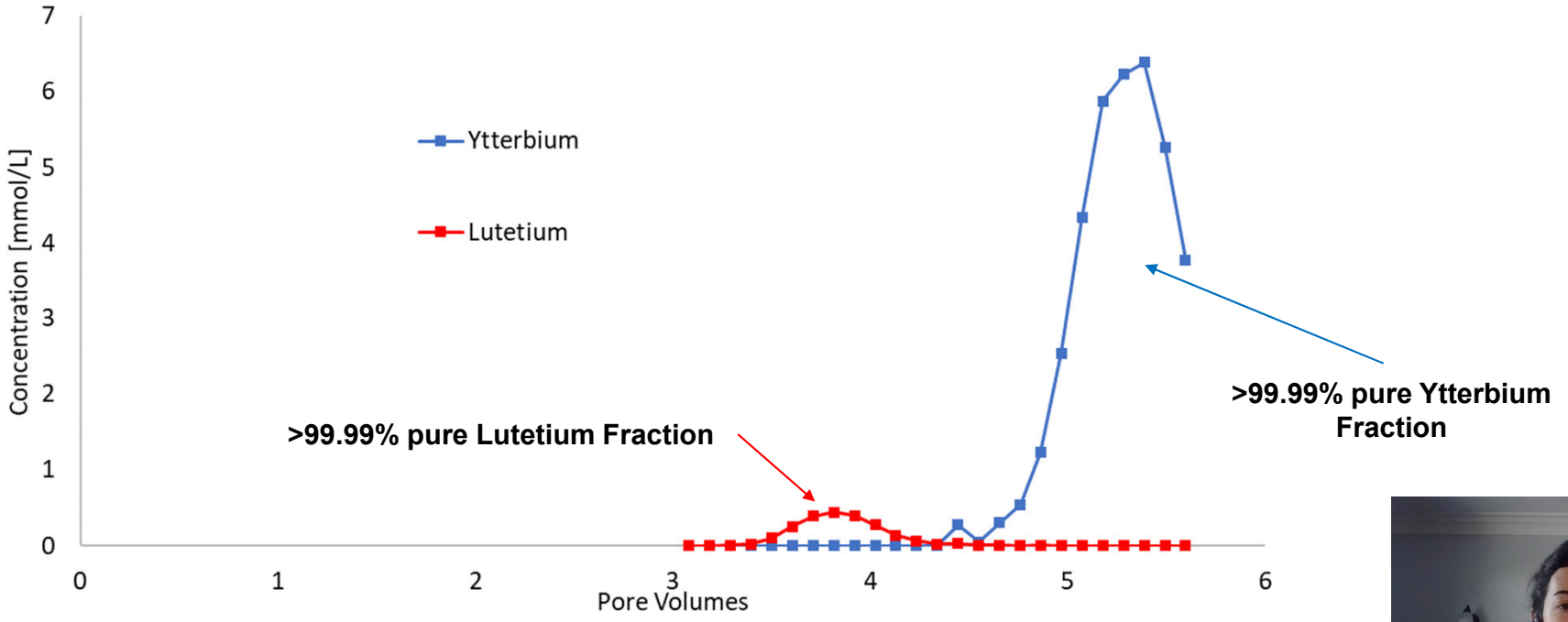


Resin Screening



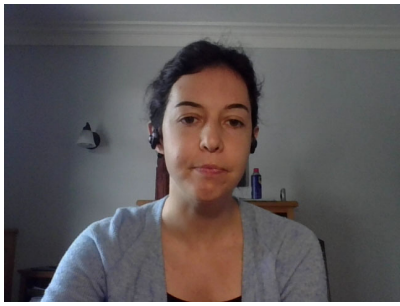


Sample Chromatogram



Next Steps

- Purification of irradiated target (October 2021 – April 2022)
- Confirmation of radionuclidic and chemical purity
- Patent review
- Ongoing customer discovery and reach-out
- Ongoing kinetics work at Idaho National Laboratory



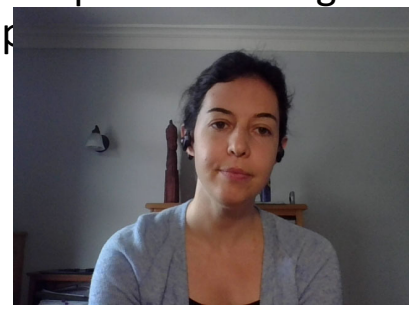
The Team

Research Institute:
Idaho National Laboratory
Dr. Robert Fox
Distinguished Staff Scientist

- 30 years experience with radiological materials, lanthanide and actinide separations, and supercritical CO_2
- Existing relationship with HFIR at Oak Ridge National Laboratory
- Previous and current partnerships with CF Tech

Small Business Concern:
CF Technologies, Inc.
Dr. Laura Sinclair
Mr. John Moses

- 30 years experience in supercritical, chromatography and high pressure processes
- In-house laboratory, pilot, engineering, and machining capabilities
- CF Tech's Dr. Sinclair has 10 years experience in high pressure processes and metal sep



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