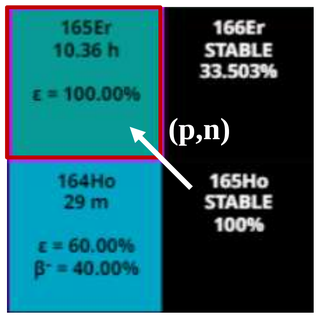
Toward Automating the Separation of Adjacent Lanthanides: ^{165}Er from ^{Nat}Ho

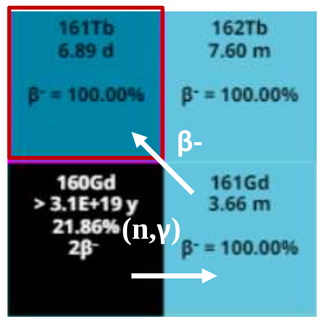
Taylor R. Johnson[1], Todd E. Barnhart[1], Jonathan W. Engle[1,2], Paul A. Ellison[1]

[1]Department of Medical Physics and [2]Department of Radiology, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

Objectives

- ^{177}Lu dotatate and ^{177}Lu PSMA-617 have been FDA approved
- Other radio-lanthanides of interest for medical use:





  - **Requires the separation of adjacent lanthanides**
    - Difficult to accomplish
    - Achieved with a cation exchange (CX) and two extraction chromatography (EXC) steps for Ho/Er

- Goals
  - Automate separation of ^{165}Er from Ho
  - Separate ^{161}Tb from ^{160}Gd using LN2 EXC resin

Methods

- Previous method:
  - Collect off CX, acidify, then load on LN2 column
- Proposed method:
  - Load eluent from CX onto LN2 column as it elutes
  - **Requires LN2 column to separate the lanthanides under less acidic conditions**

Assessing separation factor and yield of proposed method

- Separation testing

  - 500 mg LN2 column (Triskem LN2, 20-50 µm, 5.5 mm ⌀ x 50 mm)
  - Load solution:
    - 70 mM alpha hydroxy isobutyrate, pH 4.7, ~225 mL
    - 4-100 µCi ^{165}Er or ^{161}Tb
    - 0.5-2 mg ^{Nat}Ho or ^{160}Gd
  - Load column at 5mL/min
  - Rinse column with 60-100 mL 0.2-0.4 M nitric acid at 1mL/min into 5 mL fractions

- Activity quantification
  - ^{165}Er: dose calibrator measurement (Capintec CRC-15R, setting #260)
  - ^{161}Tb: NaI detector, 2-minute counts
- Target material quantification
  - ^{Nat}Ho: Microwave Plasma Atomic Emission Spectrometry (Agilent MP4200)
  - ^{160}Gd: Arsenazo III spectrophotometry (pH = 3, 0.02 M nitric acid base)

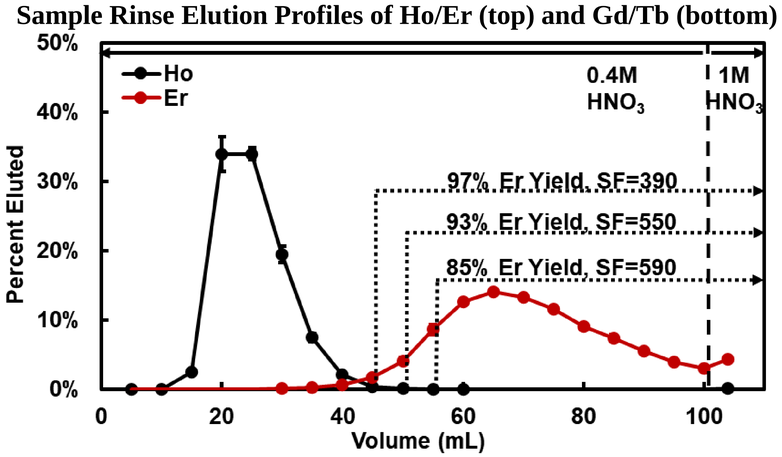
Results

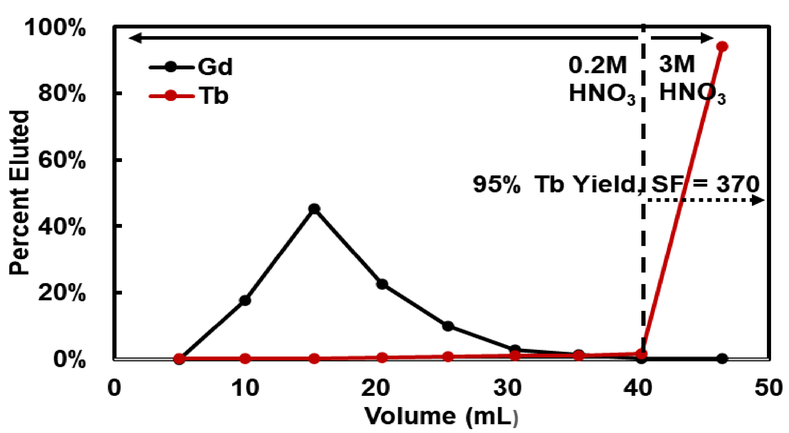
- The direct loading procedure decreased the overall length of the ^{165}Er radiochemical isolation from ~5 to ~4 hours

[^{165}Er]PSMA-617

- Ho/Er separation factor (SF) increases as rinse volume increases, though with decreasing radiochemical yield (RCY)
- Separation products were reacted with PSMA-617 (80°C for 30 min, pH 4.0-4.2) to find end-of-bombardment [^{165}Er]PSMA-617 molar activity
- The maximal Gd/Tb separation tested was achieved with 0.2 M nitric acid rinse, with 95% ^{161}Tb RCY and SF of 370

Sample Rinse Elution Profiles of Ho/Er (top) and Gd/Tb (bottom)





- The SF and RCY of the proposed method for the Ho/Er was within the uncertainties of the published procedure

Method	SF	RCY	Molar Activity	n
Proposed	419 ± 47	82 ± 9	0.57 ± 0.52 Ci/µmol	3
Published	594 ± 450	80 ± 7	1.6 ± 1.0 Ci/µmol	9

Conclusion

- **Possible to load the CX eluent onto LN2 column while retaining separation factor and yields for ^{165}Er as previous method**
- Partial automation of the ^{165}Er-Ho separation reduces operator exposure and scientist workload
- **Can separate other adjacent lanthanides, such as Gd/Tb using LN2 with proper choice of rinse**
- Future work
  - Apply to other radio-lanthanides of use
  - Refine procedure for more consistent results
  - Advance automation technique through valve and pump systems

References

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Acknowledgements

This research is supported by the U.S. Department of Energy (DOE) Isotope Program, managed by the Office of Science for Isotope R&D and Production, grant number DE-SC0020955. High purity holmium target material was provided by Materials Preparation Center, Ames Laboratory, US DOE Basic Energy Sciences, Ames, IA, USA. Work using the reactor-produced ^{161}Tb will be with the cooperation of the University of Utah through the Horizon-broadening Isotope Production Pipeline Opportunity funded by the DOE.