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SECURE

Strengthening the European Chain of sUpply for next generation medical RadionuclidEs

Separation of Terbium from Gadolinium target using cation exchange chromatography

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ENEA in SECURE Project

The EU funded SECURE Project, coordinated by POLATOM and involving a consortium of 17 European partners, aims to identify and utilize research infrastructures and raw materials in Europe to produce new radionuclides for theranostic applications in nuclear medicine, particularly alpha and beta emitters. ENEA is specifically tasked with conducting studies and experimental tests on physical and chemical processes to produce new radionuclides, including ^{161}Tb. The ENEA team is investigating the possibility to produce ^{161}Tb by neutron activation of a ^{160}Gd highly enriched gadolinium target, specifically by utilizing the reaction channel $^{160}Gd(n,\gamma)^{161}Gd(\beta^-)^{161}Tb$ in a nuclear reactor (ENEA TRIGA RC-1).

Figure.1 The TRIGA RC-1 at the ENEA Casaccia Research Centre

^{161}Tb is a promising radionuclide in cancer treatment, showing similar decay characteristics and chemical behaviour to clinically employes ^{177}Lu.
The therapeutic effect of ^{161}Tb may be enhanced due to the co-emission of a larger number of conversion and Auger electrons, which would be more effective in the treatment small metastases and single cancer cells.[1,2]
To produce pharmaceuticals containing this radionuclide, an efficient separation and isolation process is necessary. Thus, the separation of terbium from large gadolinium targets is currently a hurdle to producing terbium-based pharmaceuticals with high specific activity. In this contribution, the authors focus on optimizing the separation process of Tb from Gd, using cation exchange chromatography with various concentrations of α-hydroxyisobutyric acid as the eluent.

Separation Process

Mass target preparation

- Conversion of Gd_2O_3 in $GdCl_3$. Gd_2O_3 is dissolved in 2 mL of HCl 12 M, it is evaporated to dryness and it is again dissolved in 2 mL NH_4Cl 0.05 M and 1 mL di HCl 0.1 M and different amount of Tb are added.

Resin

- Dowex 50W-X8 (200-400 mesh) NH_4^+ form; ⌀ 5 mm, h 150 mm.

Loading Mass Determination

- All trials utilized 40 mg of Gd
- Tb mass is tested at 4 mg, 400 µg, 4 µg , 0.04 µg

Mobile Phase Volume Optimization[3]

- Elution: 0.13 M α-HIBA and 0.14 M α-HIBA collected in 10 mL fractions.
- Flow rate: 0.2 mL/min and 0.4 mL/min

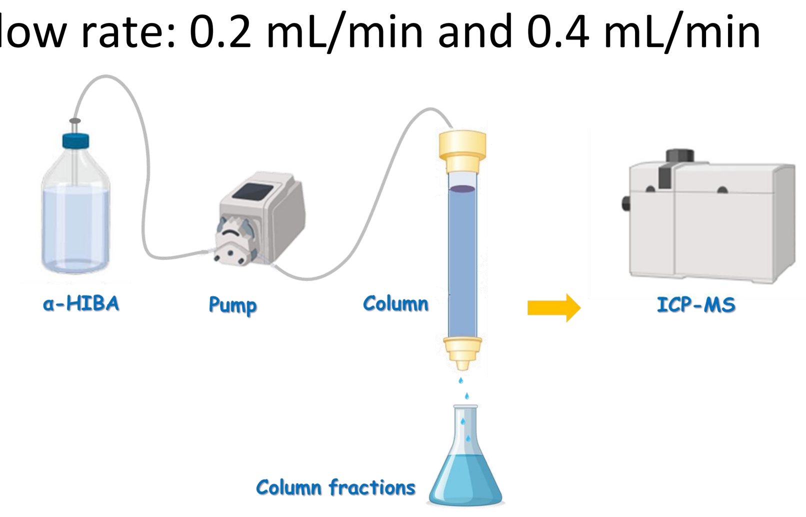
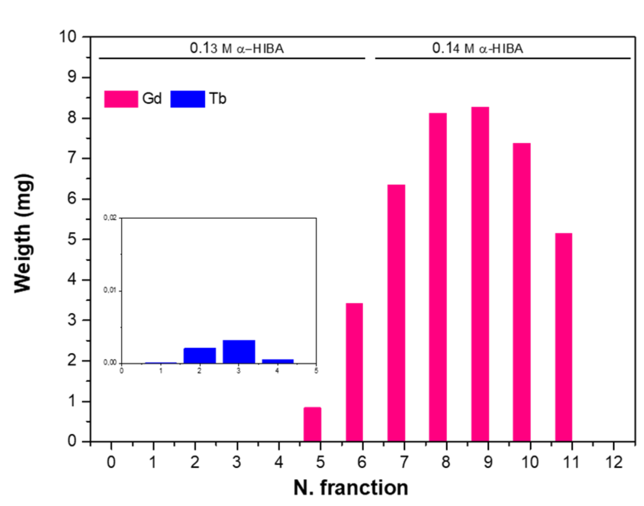


Figure.2 Representation of the Dowex 50W-X8 column and peristaltic pump used in all separation trials.

ICP-MS Analysis

- ICP-MS analysis confirms the separation of Tb (fractions 1-4) and Gd (fractions 5-11) with a recovery for Gd and Tb of 92% and 95% respectively.



	mg (before column)	mg (after column)	Recovery %
Gd	43	39.54	92%
Tb	0.004	0.0038	95%

Figure.3 Elution profile for the separation of Tb from Gd (Tb/Gd 1:10000)

Gadolinium Recycling

Motivation

Production of no-carrier-added ^{161}Tb would require the use of enriched ^{160}Gd, which is expensive. A recycling process of target material from Gd-Oxalate to Gd_2O_3 would be required to optimize the ^{161}Tb production process.

Method

- To remove α –HIBA, a fast final purification on a second Dowex 50W-X8 NH_4^+ form is done.
- Separated Gd fractions are collected and ammonium oxalate is added to obtain Gd-Oxalate precipitate, which is subsequently centrifugated.
- The precipitate is heated to 700 °C for 2h to decompose Gd-Oxalate to Gd_2O_3. The obtained Gd_2O_3 is stored for analysis.

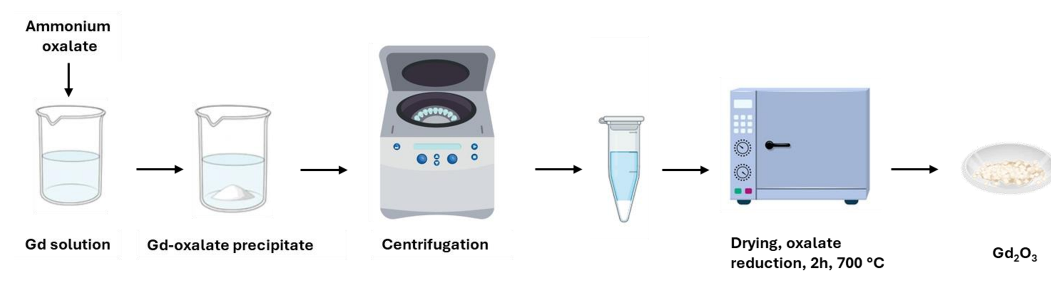


Figure.4 Preparation process of Gd_2O_3 compound

- Raman and XRD anlysis confirm the Gd_2O_3 structure with a cubic phase.[4]

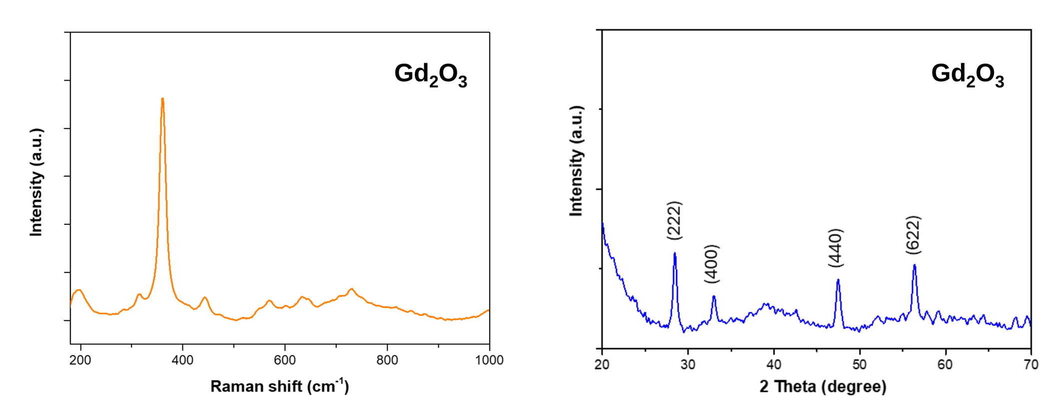


Figure.5 Raman (λ=532 nm) and XRD spectra of Gd_2O_3 compound

- This trial has promising indications for Gd target recycling → % yield obtained ~ 97%

References

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2. McNeil, S. et al., A simple and automated method for ^{161}Tb purification and ICP-MS analysis of ^{161}Tb, *EJNMMI Radiopharmacy and Chemistry*, **2022**.
3. Olszewski, G. et al., Development of ^{148}Gd analysis method using stable Gd,*Talanta*,**2021.**
4. Manigandan, R. et al., Structural, optical and magnetic properties of gadolinium sesquioxide nanobars synthesized via thermal decomposition of gadolinium oxalate, *Materials Research Bulletin*, **2020**.

Project partners

- **Narodowe Centrum Badań Jądrowych (NCBJ)** Poland
- **Nuclear Research and Consultancy Group (NRG)** Netherlands
- **Institut Max von Laue – Paul Langevin (ILL)** France
- **Institut Jožef Stefan (JSI)** Slovenia
- **European Nuclear Education Network (ENEN)** Belgium
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- **European Federation of Organisations for Medical Physics (EFOMP)** Netherlands
- **Agenzia nazionale per le nuove tecnologie, l'energia e lo sviluppo Economico sostenibile (ENEA)** Italy
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- **Clusterul Regional Inovativ de Imagistică Moleculară şi Structurală Nord-Est (IMAGO-MOL)** Romania
- **Istituto Romagnolo per lo Studio dei Tumori Dino Amadori (IRST)** Italy
- **Université de Bretagne Occidentale (UBREST)** France
- **Univerzitetni Kliničnl Center Ljubljana (UKCL)** Slovenia
- **Joint Research Centre (JRC)** Belgium
- **National Nuclear Laboratory (NNL)** United Kingdom

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