An Efficient Separation Method for Terbium and Gadolinium

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Introduction

Terbium-based radiopharmaceuticals currently show good potential within the field of theragnostics [1]. 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 "theragnostic quartet." To produce pharmaceuticals containing these radiometals, an efficient separation and isolation process is necessary for Tb. Pure, no-carrier added ^{161}Tb is produced through the ^{160}Gd(n,γ)^{161}Gd(β^-)^{161}Tb reaction in nuclear fission reactors. Thus, separating terbium from massive gadolinium targets is currently a barrier to producing high specific activity terbium pharmaceuticals. This abstract proposes a separation method using LN2 extraction chromatography (EXC) resin, which has been tailored for adjacent lanthanide separation.

Results

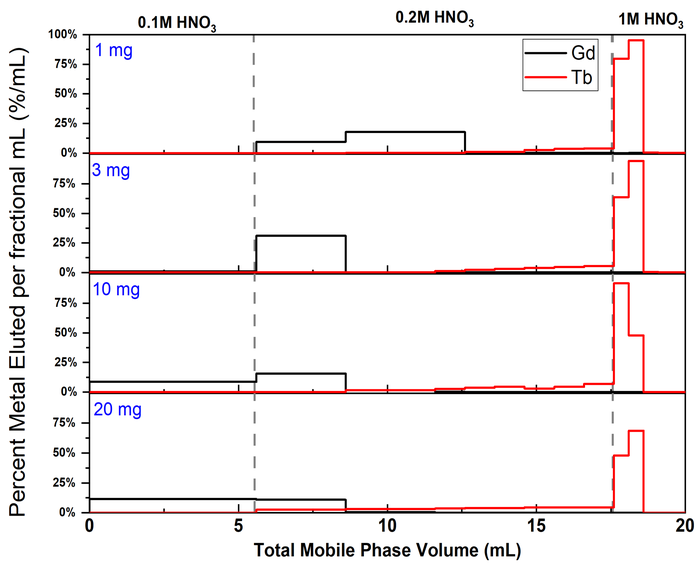

Figure 1: Elution profiles of different columns.

- For columns loaded with 1 mg Gd/Tb, no Gd or Tb can be seen passing through the column prior in the loading solution
- As column size increases to 20 mg, the Terbium peak shrinks and the Gadolinium peak is observably less defined
- In the 10 mg and 20 mg columns, more Terbium elutes earlier, resulting in more overlapping of Gd and Tb peaks

Gadolinium Recycling

Motivations

- Production of no-carrier-added Tb-161 would require the use of enriched Gd-160, which is expensive. A recycling process of target material from $Gd(NO_3)_3$ to Gd_2O_3 would be required to optimize the Tb-161 production process.

Methods

- The load and rinse fractions of an LN2 column loaded with 19.5 mg Gd were collected and dried with argon gas (60 mL/min) at 130 C yielding $Gd(NO_3)_3 \cdot 6H_2O$.
- Residue was heated to 400 C to decompose the nitrate to oxide (Gd_2O_3).
- Masses of the recovered Gd were measured at various steps and compared with expected mass loaded onto the LN2 column.
- This trial has promising indications for Gd target recycling

	$Gd(NO_3)_3 \cdot 6H_2O$	Gd_2O_3
Theoretical Yield (mg)	45.94	21.15
Actual Yield (mg)	48.15	20.7
Percent Yield	105%	98%

Figure 3: Yields of different forms of recycled Gd

Future Production

Calculations based on literature yields [3] were made to determine theoretical yield of Tb-161 from enriched Gd-160 targets at the UW-Madison Nuclear Reactor Facility.

UW Nuclear Reactor Considerations
- 1.1 x 10^{13} n/cm^2/s neutron flux
- Possible irradiation time – any lengths over 1 day are likely not feasible. Due to time constraints, the Physical Yield of 5.5 μCi/mg/h is more applicable than the Saturation Yield of 1.3 mCi/mg.

Theoretical Yield
- A 4-hour irradiation of 100 mg $^{160}Gd_2O_3$ would produce 2.2 mCi ^{161}Tb
  - Sufficient for *in vitro* ^{161}Tb-based radiopharmaceutical evaluation

Separation Process

Resin

- 20-50 μm bead size LN2 extraction chromatography resin; dry packed into 300 mg column and mobile phase was flowed through column at 1 mL per minute

Loading Mass Determination

- All trials utilized 500 μg Tb
- Gd mass was tested at 500 μg, 2.5 mg, 9.5 mg, and 19.5 mg

Mobile Phase Volume Optimizations

- Prep: 3 mL of 1 M HNO_3 followed by 14 mL of 0.1M HNO3
- Loading: 5.6 mL of 0.1 M HNO_3. Gd and Tb standards were dried down to fit into this mass
- Rinse: 12 mL of 0.2 M HNO_3 collected in fractions of 1– 3 mL fractions
- Elute: 3 mL of 1 M HNO_3 collected in 0.5 mL fractions.

Analysis

- All trace-metal analysis was performed on Agilent's microwave plasma atomic emission spectrometer (MP-AES)

30 mm x 5.5 mm ⌀ column
300 mg LN2, 20-50 μm

Figure 2: A representation of the LN2 column and peristaltic pump used in all separation trials. Liquid was flowed through at 1 mL/min

Gd/Tb Separation Factor equation:

$$Sf_{Gd/Tb} = \frac{\frac{Gd\ Before}{Gd\ After}}{\frac{Tb\ Before}{Tb\ After}}$$

Results and Discussion

	Gd/Tb Separation Factor (%Tb recovery)		
Loaded Gd/Tb mass	9 mL of 0.2 M HNO_3	10 mL of 0.2 M HNO_3	12 mL of 0.2 M HNO_3
1 mg	900 (98%)	2000 (95%)	6100 (88%)
3 mg	700 (95%)	900 (91%)	1100 (82%)
10 mg	1900 (84%)	2700 (81%)	10000 (70 %)
20 mg	1300 (72%)	1400 (68%)	1500 (58%)

Table 1: Separation factor and terbium percent recovery calculated after 9 mL rinse, 10 mL rinse, and 12 mL rinse.

Objective: Maintaining both a high Gd/Tb separation factor (>1000) and a high Tb % recovery (>90%)
- Tb percent recovery drops as Gd mass increases
- Separation factor for a given Tb recovery drops as Gd mass increases
- Separation must optimize both of these factors

However …
- The 300 mg LN2 column still adequately separated Tb and Gd up to 20 mg total (~90% of its theoretical capacity)
- Eluting Terbium between 9 and 12 mL 0.2 M HNO_3 in all trials maintains the highest Sf and % recovery

References

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