# The Conversion of Synergistic Solvent Extraction Systems to Novel Solid Phase Extractions Systems for the Separation of Lanthanides $^{161}$Tb from Enriched $^{160}$Gd Targets

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## Introduction

Theranostic (therapeutic and diagnostic) pairs are radioisotopes that can potentially be used in treating and diagnosing diseases. While true theranostic pairs are generally a combination of two or more radioisotopes, $^{161}$Tb has the potential to function on its own as a theranostic nuclide.

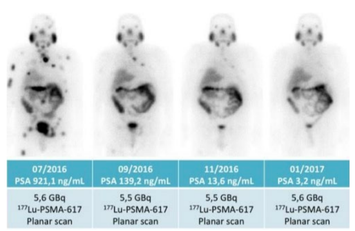


***Figure 1:*** *Imaging and treatment of castration-resistant prostate cancer using radioisotope $^{177}$Lu PSMA-617*[1].

- $^{161}$Tb decays by beta emission and has similar decay properties as $^{177}$Lu (FDA-approved as LUTATHERA ®).
- The $\beta^-$ particle ($\beta_{max} = 518\ keV$) emitted from $^{161}$Tb has low linear energy transfer (LET), depositing its energy over a long range (0.2 - 5 mm) in tissue, making it potentially effective for the treatment of bulky tumors.
- $^{161}$Tb has Auger electron emissions which have shorter ranges (0.1 - 50 µm) with a relatively high LET (1-10 keV/µm) that have the potential to target single-cell metastases with high cell toxicity.

One of the challenges with implementing $^{161}$Tb and other radioisotopes of terbium into nuclear medicine is separating target and product material to obtain high apparent molar activity. While separating these species was proven effective using a synergistic solvent extraction system with the extractants Diethylcarbamylmethylenephosphonate (DBDECMP) and 2-thenoyltrifluoroacetone (HTTA), an alternative method using a solid phase extraction chromatography (EXC) system would be better suited for nuclear medicine applications and large-scale separations.

$$^{160}_{64}Gd(n,\gamma)^{161}_{64}Gd \rightarrow (3.7\ min, \beta^-) \rightarrow {}^{161}_{65}Tb$$

*Conversion of enriched $^{160}$Gd target to radioisotope $^{161}$Tb via indirect neutron capture*

## Methods

- Novel EXC resins were synthesized by dissolving extractants (DBDECMP and HTTA) in methanol and mixing with 20 - 50 µm inert support. Residual solvent was removed using gradient vacuum conditions, leaving the extractant system impregnated in the inert support.
- The extraction behavior of the solid-phase systems were studied as a function of acid concentration (pH 0 – 3.00, $HNO_3$), extractant loading (gram of extractant per gram of support), and extractant ratio using batch experiments with radiolytic and spectrophotometric techniques.

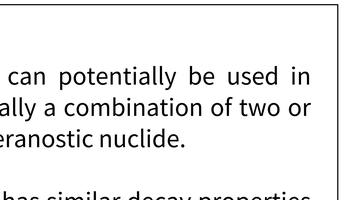

***Figure 2:*** *University of Utah TRIGA reactor used in the production of $^{161}$Tb, among many other radionuclides.*

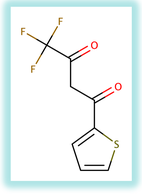

***Figure 3:*** *Chemical Structure of HTTA*

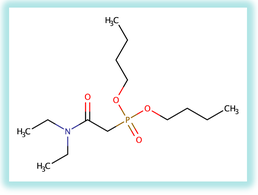

**Figure 4:** *Chemical Structure of DBDECMP*

- A $^{160}$Tb surrogate was used in place of $^{161}$Tb in radiolytic analysis.
- To study the application of these EXC resins in column separations, a selected resin was synthesized and analyzed via a wet-packed drip column.

## Results

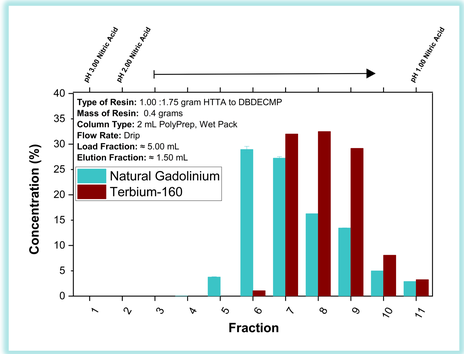


***Figure 5:*** *Elution profile of Tb and Gd on a wet-packed column. The column was eluted with a drip technique and a resin with a 1.00 : 1.75 ratio of extractants HTTA and DBDECMP.*

- Synergism was retained in the synthesized EXC resins but at a lower degree than in the liquid phase systems.
- The resins displayed the best separation factors within a pH range of 1.75 – 2.25.
- As the pH value approached 3.00, the extraction for both gadolinium and terbium approached 100%, resulting in poor separation factors.

A separation factor of 2.76 was obtained using a resin with a loading of 1.00 gram of HTTA to 1.5 grams of DBDECMP with an extractant loading of 25% and a 10% dodecane additive. The solid phase distribution coefficient (k') values for terbium and gadolinium for this resin at pH 1.75 were 7.65 and 2.77, respectively.

A different resin, (1.00 gram of HTTA to 1.75 grams DBDECMP with an extractant loading of 30%, and a 10% dodecane additive had a lower separation factor (pH = 2.00, SF = 1.54) but had a more amenable k' values (22.33 and 34.32 for Gd and Tb, respectively). The column elution profiles for gadolinium and terbium were reported using this resin.

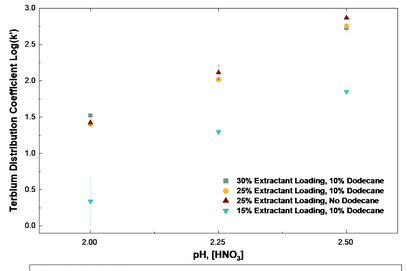


***Figure 6: Log(k') Values for Terbium as a function of pH for Various Extractant Loadings.*** *The trend in this graph shows that as extractant loading (in an inert resin with a 40% loading capacity) is increased, there is higher overall extraction for all pH values.*

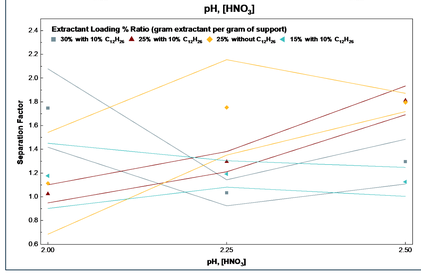


***Figure 7: Separation Factors for Gadolinium and Terbium as a function of pH for Various Extractant Loadings.*** *The thickness of the lines represents the standard deviation. There does not appear to be a clear relationship between extractant loading and SF. At 25% loading with 10% dodecane, as the pH increased the SF also increases.*

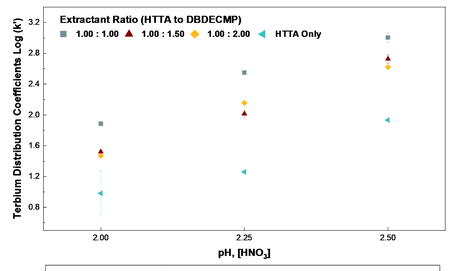


***Figure 8: Log(k') Values for Terbium as a function of pH for Various Extractant Ratios.*** *Compared to the k' of the combined extractants HTTA and DBDECMP, the k' of HTTA alone is consistently lower. This is indicative that synergism in the solvent extraction is being retained in the EXC resins*

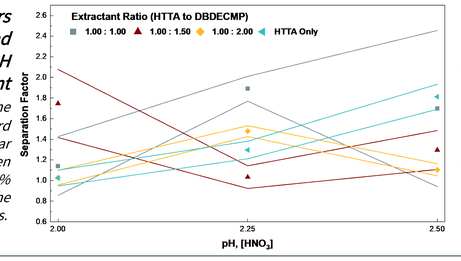


***Figure 9: Separation Factors for Gadolinium and Terbium as a function of pH for Various Extractant Ratios.*** *Because of the large error associated with some of the resin's separation factors, it cannot be said that the separation factors follow a particular trend as pH increases.*

## Conclusion

- Batch experiments conducted with the novel synthesized resins showed that the synergistic effects on separation and extraction of combining HTTA and DBDECMP in solvent extraction systems could be retained upon conversion to a solid phase system.
- Initial separation factors suggest that the solid phase resins could effectively separate terbium and gadolinium for nuclear medicine applications.
- Future studies will continue to investigate extractant loading percentages and extractant ratios with different column diameters and lengths, resin amounts, and flow rates to obtain optimal parameters for separations.

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**References**

1. H. Nicolai, P054 – 177 Lutecium PSMA -617 in metastatic castration-resistant prostate cancer: Initial clinical experience, European Urology Supplements, Volume 16, Issue 10, 2017, P. e2698-e2699
2. Yang, Xue & Fogal, Thomas & Xiao, Shanjie & Kruger, Jens & Jevremovic, Tatjana. 2010. Visualization as a bridge between chemical and nuclear engineering simulations. AIChE Annual Meeting, Conference Proceedings.