Radiochemical Synthesis and Characterization of Theranostic Radiopharmaceuticals

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INTRODUCTION

- Theranostics is described at the identification and treatment of a select lesion in the body via differing methods and techniques.
- "Radiotheranostics" is a term used in nuclear medicine to refer to the use of radioisotope (RI)-labeled agents to perform simultaneous imaging and therapy of a target lesion. This division of theranostics is unique in that it uses a targeting molecule that integrates either a therapeutic or diagnostic radionuclide (monoclonal antibody or small molecule).
- Commonly used terms for specific radiation therapy is Targeted Radionuclide Therapy or TRT
- Imaging data obtained from both Positron Emission Tomography or PET and Single-Photon Emission Computed Tomography or SPECT allow for analysis of absorbed radiation doses for targeted lesions.
  - Commonly used radionuclides include 64Cu and 89Zr for imaging and 90Y and 177Lu for therapy

Figure 1: Radiopharmaceutical Synthesis

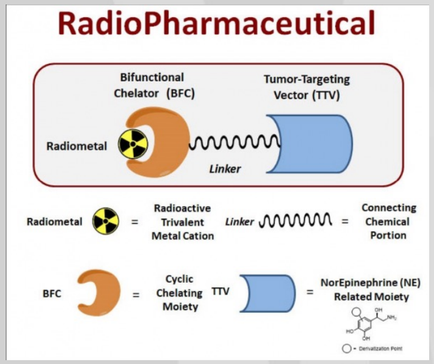


Figure 2: Table of radionuclide applications with targeted molecules

Radiopharmaceutical	Radionuclide	Targeted Molecule	Application
[^{177}Lu] Lu-PSMA-617	Lutetium-177	PSMA Prostate-Specific Membrane Antigen	TRT Metastatic Castration-Resistant Prostate Cancer
[^{177}Lu] Lu-NM600	Lutetium-177	NM600, tumor-targeting alkylphosphocholine	TRT Triple-Negative Breast Cancer
[^{90}Y] Y- NM600	Yttrium-90	NM600, tumor-targeting alkylphosphocholine	TRT T-Cell Non-Hodgkin's Lymphoma
[^{86}Y] Y- NM600	Yttrium-86	NM600, tumor-targeting alkylphosphocholine	PET Imaging T-Cell Non-Hodgkin's Lymphoma

METHODS

Radiochemical Synthesis of [^{177}Lu] Lu-NM600:

- From stock vial of Lutetium 177 the initial activity is measured
- Addition of buffer solution to radionuclide, this creates proper reaction conditions for pH
- Addition of Targeting Molecule (NM600)
- Incubation of radiochemical mixture at target conditions of 95°C with 400 RPM for 30 minutes. This causes a reaction that links the targeting molecule with the radionuclide.

Purification and Removal of Free Metals, Additional Impurities

- After incubation, draw H2O and radiochemical mixture into syringe
- Purify mixture through HLB SPE column to remove free radiometals and impurities from the mixture
- Measurements of both column and waste take to gauge initial impression of radiochemical purity, this will be tested later

Checkpoints	Activity
Starting ^{177}Lu Eppendorf	2.00 mCi
HLB SPE column after purification	1.547 mCi
Waste from column	88.7 µCi
Syringe + Needle used for mixture	122.2 µCi
Eppendorf after purification	196.5 µCi
Final product after resuspension	1.425 mCi

Figure 3: Radioactivity for significant checkpoints

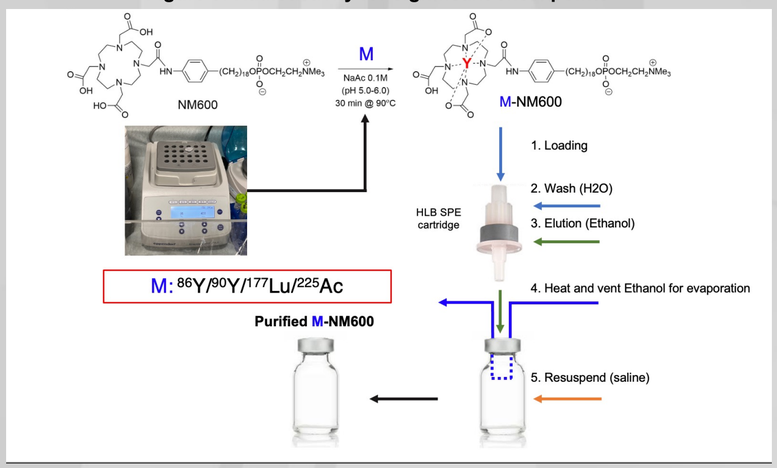


Figure 4: Radiolabeling steps flowchart

Radiochemical Purity Check

Use of HPLC Machine to read, identify, and determine purity of solution. Can also be used to conduct analysis of stability of final complex over set time period.

Preparation for Thin Layer Chromatography (TLC)

- Done **prior** to final preparation
- The purpose of this is a quality check and to examine the radiolabeling yield of our product and check the purity of the final complex
- Using an iTLC strip dotted with small amount of solution, we use Phosphor Imaging to display and conduct region of interest analysis
- Typically, in research > 90% purity is considered passable and > 95% in a clinical setting

Figure 5: TLC Profiles of ^{177}Lu

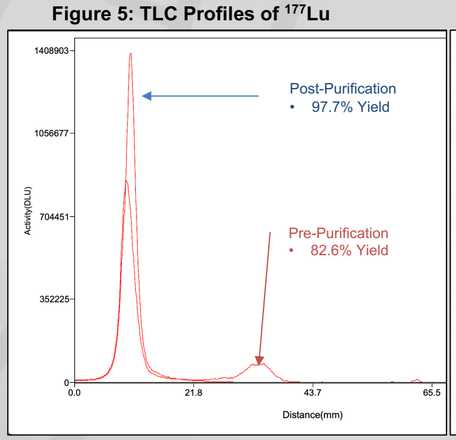
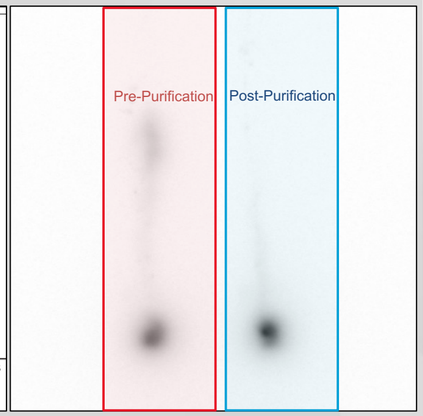


Figure 6: TLC Strip Images of ^{177}Lu



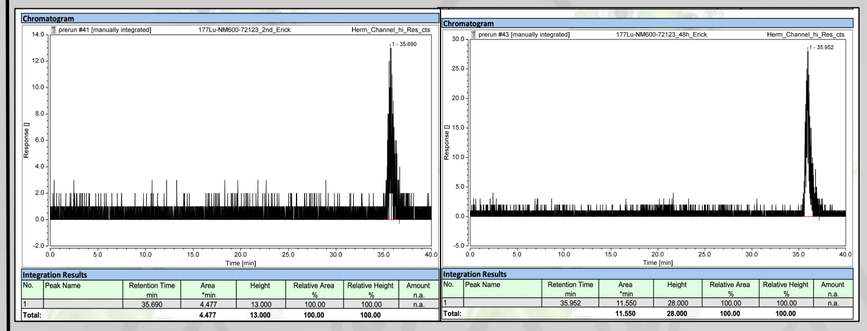


Figure 7: HPLC analysis

Final Solution Preparations

- Ethanol is pushed through the column to free the radiopharmaceutical
- Solution heated and vented to evaporate ethanol
- Addition of saline solution to the vial to dissolve and resuspend the product

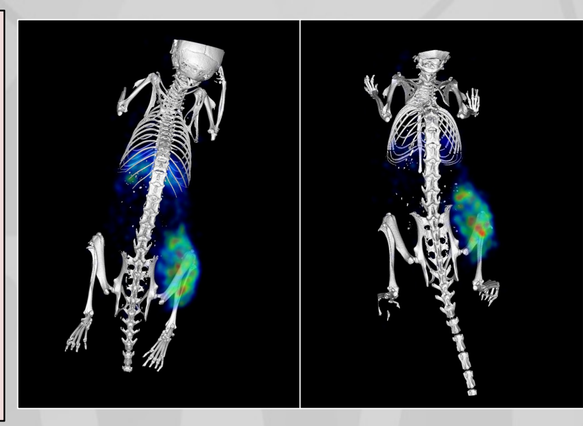


Figure 8: SPECT Imaging of mice with [^{177}Lu] Lu-NM600

CONCLUSIONS & FUTURE WORKS

- Based on data gathered from iTLC analysis during the radiolabeling of [^{177}Lu] Lu-NM600 a purity of 97.7% was obtained
- Before purifying of the complex, a purity of 82.6% was obtained, consistent with the assumption that free radiometals are still present in the mixture.
- Single peak obtained from HPLC supports very high purity of final product along with stability
- As referenced previously, this specific radiopharmaceutical can be for potential treatment of Triple-Negative Breast Cancer as TRT
- Work with[^{177}Lu] Lu-NM600 has show promise in tumor inhibition in mice with ability to deliver large doses of radiation to tumors
- This has shown increased tumor control and survivability of mice without incurring probative normal tissue toxicity

REFERENCES

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