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Optimized chromatographic production of high-purity 177Lu radionuclide at IRT-T research reactor for nuclear medicine applications

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ABSTRACT

Indirect method produces Beta Particles (50%) and Gamma (6.7%) of energies 0.497 MeV and 0.11 MeV respectively which makes the produced 177Lu suitable for bone pain palliation studies, targeted therapy of cancer and metastasis, medium and small joint synovectomy. Chromatographic method completely separates Ytterbium and Lutetium with the degree of separation of 1.34, indicating 99 % yield of 177Lu and 177Yb, implying minimal radiation safety and waste disposal concerns. Furthermore, this method produces 177Lu with a longer lifespan, approximately 2 weeks which makes it successful in endoradiotherapy, brachytherapy and treatment of malignancies. In this method Neutron flow has no effect on specific activity and 177Lu integral yield depends on numbers of irradiation cycles and on the amount of Lutetium present in the target material. Therefore, the method yields the greatest specific activity of 177Lu (1181.9 GBq) which has the ability to deliver 177Lu with the greatest radionuclide purity (99%) conceivable and suitable for treatment of radionuclide therapy such as thyroid cancer, bone metastases and lymphomas. Indirect method provides acceptable radiolabeling results with insignificant amount of impurities, making it best method for production of Radiolabelled Nuclides for treatment of cancer.

Keywords: Yb-176, Lu-177, Chromatographic, Nuclear Medicine, Radionuclide Production, Resins, Dowex 50-WX8

INTRODUCTION

A number of procedures can be employed for the purpose of producing different radioisotopes. The interactions between neutrons and particles are different in these pathways. The most common technique of synthesis is direct activation of the material by neutron capture and gamma emission. When the target material is isotopically and chemically very pure and has a very high neutron absorption cross-section, the radioactive technique works well [53, 12]. For this direct mode of production, the highest degree of flux that can be achieved is desirable in order to convert as much of the target material into the intended product as possible before a significant percentage of the product decays. This technique delivers lower specific activity materials because the product isotope belongs to the same chemical family as the target [53]. In today's environment, irradiating bone tumors and internal organs using radiopharmaceuticals based on the nuclide ^{177}Lu is a well-known approach of treating them [29]. This method is distinct from others in that it has a low toxicological impact on the body of the patient (maximum energy of beta radiation is 497.1 keV for 79.3 %, gamma radiation is 113.1 keV and 208.1 keV with

intensities of 6.4 % and 11 % respectively [12]. The use of the N.C.A. nuclide ^{177}Lu in radiopharmaceutical synthesis can result in less toxicological effect [12]. The nuclide ^{177}Lu is created by bombarding Ytterbium with neutrons in an active core nuclear reactor [8].

$$^{176}Yb(n,\gamma)\text{->}\ ^{177}Yb(\beta^-)\text{->}\ ^{177}Lu\ (\beta^-)\text{->}\ ^{177}Hf \quad [1]$$

Both classical and non-classical separation methods, such as extraction [42], cementation [19], separation using an ion-exchange resin [21], and non-classical methods, such as thermal methods [37] or methods operating under the action of an external periodic symmetric electric field [8,54], can be utilized to separate Lutetium from the Ytterbium target in the future. The major purpose of this research is to find the Optimized Chromatographic Production of High-Purity ^{177}Lu Radionuclide at IRT-T Research Reactor for Nuclear Medicine Applications.

Reactions

Lutetium-177 desintergrates in 76.1 % of events with maximum energy of 0.50 MeV to the stable forming ^{177}Hf which has a half-life of 6.70 days [33]. And in 9.70 % of events Maximum energy of 0.38 MeV and intensity of 13.0 % of the time maximum energy of 0.18 MeV to an excited state and form ^{177}Hf that is between the energies of 0.25 MeV and 0.32 MeV above the ground state. [33,17]. It loses energy and form ^{177}Lu and produce particles with maximum energies of 497.1 keV and intensity of 78.6 %, 384.0 keV and intensity of 9.11 % , and 176.1 keV and intensity of 12.21%. It also forms low-energy gamma rays of energies 113.1 keV and intensity 6.60 %, 208.1 keV and intensity of 11.10 %, during these times of radioactive decay [33]. Figure 1.1 shows a simple decay scenario for ^{177}Lu.

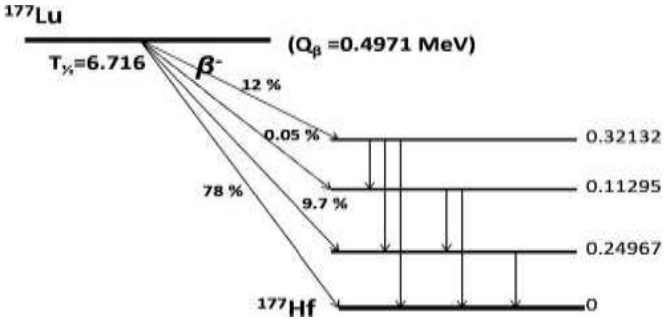

Figure 1. Shows a simplified ^{177}Lu decay strategy [33].

Both direct and indirect reactors can generate ^{177}Lu. The Products of neutron activation of natural Lutetium and Ytterbium targets, as well as the nuclear disintegration parameters of the radionuclides that occur, are listed in Table 1. It is crucial to note that while some of the mentioned nuclear reactions are substantial, others might be overlooked due to their modest reaction cross sections, short decay times, or low initial target content [23].

Benefits of Indirect Production

This method yields the greatest specific activity of ^{177}Lu: >2.960 Tera Becquerel (80.1 Curies per milligrams) vs. theoretical 4.071 Tera Becquerel (110.1 Curies per milligrams) and It has the ability to deliver ^{177}Lu with the greatest radionuclide purity conceivable. The existence of long-lived radioactive contaminants (e.g., ^{177m}Lu, 10–5%) is prohibited (below the detection limit), implying minimal radiation safety and waste disposal concerns [22]. In most cases Neutron flow has no effect on specific activity as a result it provides acceptable radiolabeling results. Because there is no discernible decline in particular activity, this method produces ^{177}Lu with such a longer lifespan, approximately 2 weeks [33].

Setbacks of Indirect Production

There is low yields attributed to ^{176}Yb's (2.50 barn) low heat neutrons decomposition cross section contrasted to 2090.0 barns for "direct" ^{176}Lu synthesis [17] and not only is it too hard to separate micro amounts of ^{177}Lu from macro amounts of the irradiated Yb target, but it also needs a sophisticated radiochemical separation and purification

procedure [17]. Indirect method produces large volumes of radioactive waste. This technique of manufacture is by far the most expensive way to acquire ^{177}Lu with the required purity. It is not only necessary to have a ^{176}Yb target that has been enriched, but also to recover and recycle it [17].

Despite its disadvantages, the application of N.C.A. ^{177}Lu has a lot of potential. As a result, numerous Universities are pursuing this manufacturing option vigorously [17]. Because Yb follows the same coordination chemistry as the chelating agents used to prepare Lu-based radiopharmaceuticals, the implementation of an appropriate technique for efficiently separating pure ^{177}Lu from cumbersome masses of the neutron bombarded Yb target, as well as the restoration of the Yb target for reuse, is critical to the success of this manufacturing process [17].

Table1: The Products of neutron activation of natural Lutetium and Ytterbium targets, as well as the nuclear disintegration parameters of the radionuclides that occur [17]

Element	Target isotope	%Natural Abundance	Cross section σ(barn)	Activation product	Decay mode	$T_{\frac{1}{2}}$	Decay product
Lu	^{175}Lu	97.41	16.7 6.6	^{176m}Lu ^{176}Lu	ß$^-$, γ ß$^-$, γ	3.66 h 4×10^{10} y	^{176}Hf ^{176}Hf
	^{176}Lu	2.59	2.8 2090	^{177m}Lu ^{177}Lu	ß$^-$, γ & IT ß$^-$, γ	160.4 d 6.65 d	^{177}Hf(78.6 %) ^{177}Hf (21.4 %) ^{177}Hf
Yb	^{168} Yb	0.13	2300	^{169} Yb	EC	32.02 d	^{169}Tm
	^{170} Yb	3.04	9.9	^{171} Yb	Stable		
	^{171} Yb	14.28	58.3	^{172} Yb	Stable		
	^{172} Yb	21.83	1.3	^{173} Yb	Stable		
	^{173} Yb	16.13	15.5	^{174} Yb	Stable		
	^{174} Yb	31.83	63	^{175}Yb	ß$^-$, γ	4.18 d	^{175}Lu
	^{176} Yb	12.76	2.85	^{177} Yb	ß$^-$, γ	1.9 h	^{177}Lu

Resin (Dowex 50-WX8)

Lutetium-177 can be separated from Ytterbium (III) oxide and Lutetium (III) oxide of purity greater than 99 % using resins called Dowex-50X8, which are in the H^+ form (Goeckeler et al, 1986) [18]. Some research has reported successful separation of ^{177}Lu with a 68 % yield, purity more than 99 %, and a 4 hour separation time (Balasubramanian, 1994). While on the other hand, the Board of Radiation and Isotope Technology (1994) separated Lutetium-177 using Dowex-50-WX8, with bead size of 200 to 400 mesh resins and which are in Zn^{2+} with a 70 % yield and with a radionuclidic purity more than 99 %, 0.04M-hydroxyisobutyric acid was used to elute carrier-free Lutetium-177 at pH 4.62 and temperature 26/1 degrees Celsius [4]. Dowex 50-WX8 resin has shown a potential method in separation and purification of radionuclides for nuclear medicine. This study used Dowex-50-WX8 resin which are in the H^+ form to separate Lutetium 177 [4]. Below is a summary table comparing merits and demerits of different separation techniques.

Table 2. Advantages and disadvantages of different separation methods [13, 17]

Method	Advantages	Disadvantages
Precipitation	• Simple process • Cost-effective • Selective with proper chemical agents	• High consumption of chemical reagents • Generation of solid waste • Limited control and co-precipitation • Complex scalability
Solvent Extraction	• High selectivity • Scalable • Established method in the industry	• High consumption of organic solvents • Generation of organic wastes • Significant cost of solvents • High energy consumption
Ion Exchange	• High selectivity • Low energy consumption • Reusable resins	• Fouling of the resin • Operational complexity to prevent breakthrough • Chemical agents required for resins regeneration • High cost of resin
Electrodialysis	• Selective ion removal • Energy efficient • Low consumption of chemical • Scalable	• Fouling of membrane • High initial cost • Limited to ionic species • Dependency on electrical energy

LITERATURE REVIEW

Ion Exchange Resins

Generally, there are many chromatographic methods which can be used to separate Lutetium-177 from adjacent rare earth elements. In this literature we will only review two chromatographic methods and these are:

- Extraction Chromatographic resins abbreviated as EXC which is based on the use of Organophoshorus Extractants LN and LN2 Resins from mineral acids (nitric acid and Hydrochloric acid) [13].
- Cation exchange resin (Dowex-50-WX8) for strong acids (Dash et al, 2015) [13].

LN and LN2 Resins

In a patented "method for manufacturing high specific activity ^{177}Lu," Mirzadeh and Knapp, (2005) employed LN Resin [15]. By elution with increasing concentrations of HCL (Fig 2), the N.C.A. ^{177}Lu was quantitatively extracted from 10 mg of Ytterbium in a one-step Chromatographic method. The authors claimed that the ^{177}Lu produced would have a specific activity of at least 100 Ci/mg Lu (i.e. 91 % of the theoretical one). Unfortunately, the yield and purity of the separation were not disclosed. Lu/Yb could not be eluted from LN Resin with HNO_3 concentrations up to 2 M [15], as suggested by the manufacturer, according to (Knapp et al, 2007) [23]. On the other hand, a researcher used LN Resin which is comprised of acid called di(2-ethylhexyl) orthophosphoric and in a one-step

Chromatographic process, the N.C.A. ^{177}Lu was quantitatively separated from 10 mg of Ytterbium by elution with increasing concentrations of HCL [23]. It has been observed that the aforementioned researchers did not use various concentrations of hydrochloric acid for successive elution of ^{170}Tm ^{176}Yb and ^{177}Lu, which might have improved efficiency for statistical separation of ^{177}Lu from 10.0 mg of non - radioactive Ytterbium carrier [23]. Furthermore, there have been excellent results report by Knapp et al (1995) who tried to use LN to extract ^{177}Lu from Ytterbium which was washed with varying amounts of hydrochloric acid (fig 2). The elution process consisted of an initial elution with 2 M HCL, followed by 3.1 M HCl, and finally 6.01 M HCL [37]. However, the research did not consider how the period of enrichment of natural Lutetium and Ytterbium affected the percentage yield of Lutetium 177 [37].

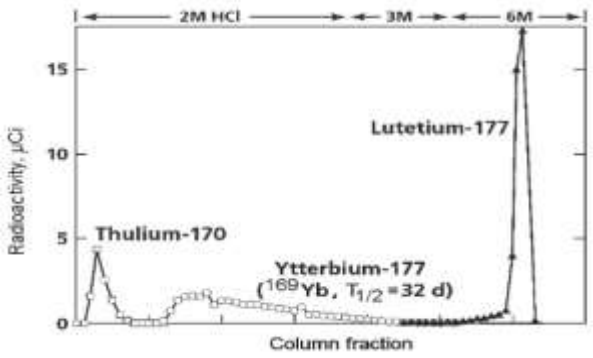

Figure 2: LN used to extract ^{177}Lu from Ytterbium was washed with varying amounts of hydrochloric acid.

In addition, some researchers criticized use of LN resins in extraction Chromatographic separation of Lutetium-177, they argued that LN resin could not be used to separate heavier rare earths such as Dysprosium, Lutetium, Ytterbium and Scandium (McAlister & Horwitz., 2007) [41].They suggested that as these metallic ions could be achieved from LN2 resin by using more different dilute acids as compared to LN resin [41]. LN2 resin has successfully given positive results for example Horwitz et al., (2005a), used LN2 resin with functional capacity <5% and recovered more than 99 % Lutetium and 50 % Ytterbium (E. P. Horwitz , 1975 & 1976) [21]. However, the researcher did not consider the activity of ^{177}Lu as a function of time of irradiation for different values of thermal neutron flux density and how it affected the purity of the extracted ^{177}Lu [21]. The researchers paid less attention to the percentage purity of the separated Lutetium-177 which is very essential for any radiopharmaceutical used in nuclear medicine for treatment of cancer [21]. This article employs a new technique which reduces sample volume, acidity and improves purification from chemical impurities.

There is a growing body of research on techniques that may improve purity of Lutetium-177 and reduce acidity for example some have suggested use of DGA resins together with LN2 resins in the separation scheme in order to remove traces of nitrate ions in the eluate so that the Lutetium is obtained in 0.05 M HCL [22] (fig 4). This concentration of HCL acid may be dangerous to introduce in the human body since HCL acid is a strong acid it may cause severe tissue damage and burns.

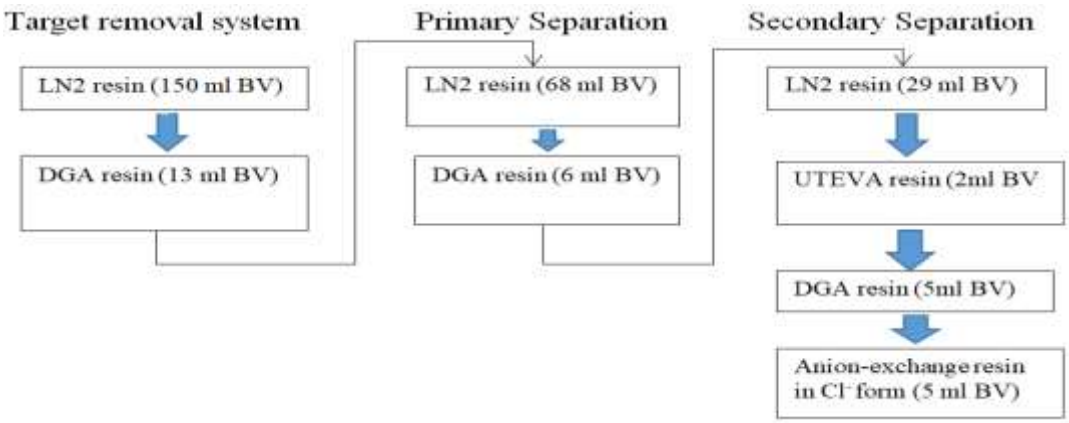

Figure 3: Horwitz presented a separation strategy for separating N.C.A. 177Lu from an irradiation Ytterbium target. BV stands for bed volume [22].

This process of separation of Lutetium-177 has many disadvantages which cannot be ignored for instance it is expensive, LN2 Resin can only be used once and the DGA Resin can only be used three times owing to extractant leaching and radiolytic deterioration [23].

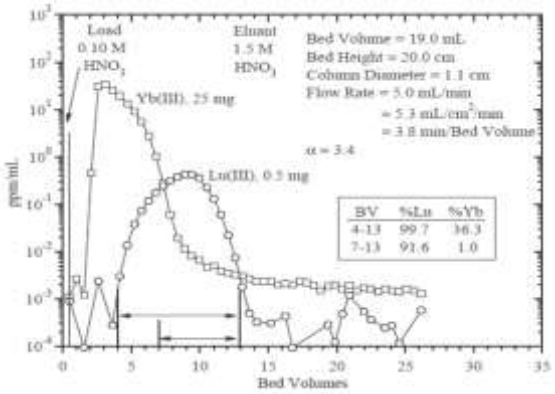

Figure 4: Using 1.5 M HNO_3 and 4.8 % of the total column capacity, N.C.A. ^{177}Lu was separated from a 25 mg Ytterbium target on LN2 Resin (19 mL BV). [22]

Dowex 50-WX8 Resin

Dowex-50X8 resin is a strong acidic cation exchanger which can also be used in separation of Lutetium-177. This research discusses only two (2) types of Dowex-50-WX8 resin namely H^+ form and Zn^{2+} form [18]. Balasubramanian (2005) reported that ^{177}Lu can be separated from Ytterbium of mass 10.35 mg by using Dowex 50-WX8, with mesh size of 200 to 400 cation exchanger which are in Zn^{2+} form and 0.04 M-HIB at pH 4.6 for elution with 68 % yield, purity more than 99 %, and a 4 hour separation time [4, 20]. This technique sacrifices more than 30% of the Lutetium that was contaminated with Ytterbium and the isolated Lutetium was extremely diluted in huge amounts of eluent, and it was contaminated by the barrier-ion Zn^{2+} [4]. Therefore, a different technique of separation of Lutetium is needed that would improve yield of Lutetium and cannot be contaminated by barrier ions.

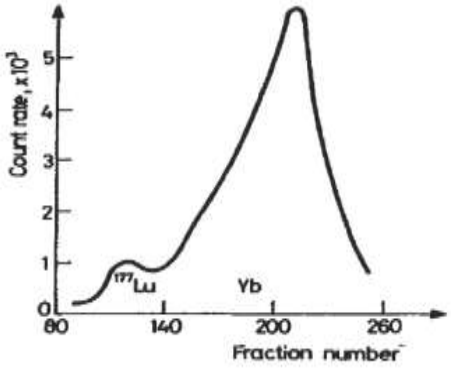

Figure 5: Using Zn^{2+} as the barrier-ion, an elution profile for the Lutetium and Ytterbium pair was absorbed on a Dowex 50-WX8, with bead size of 200 to 400 meshes, dimension 33 cm and 0.7 cm cation exchange column. At pH 4.6, the eluent was 0.04 M-HIB. Each fraction was equal to 1 mL of eluent. [4]

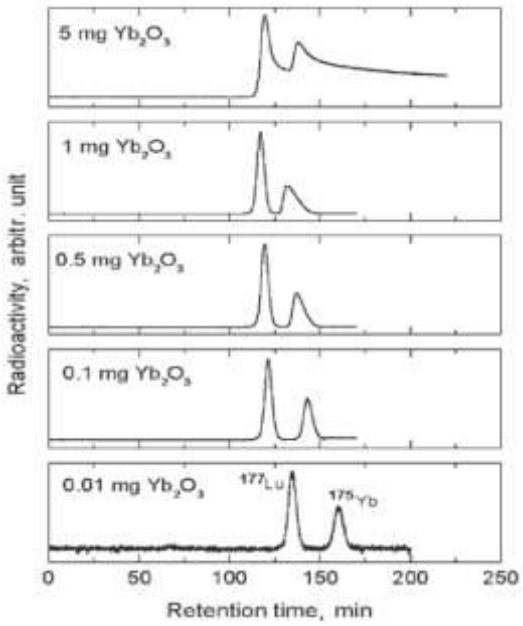

Figure 6: The amount of Yb_2O_3 used had an effect on the efficiency of separation of the Lu/Yb pair. 0.8 centimeter x 30 cm column eluent: 0.25M-HIB/0.1M1 octanesulfonate; flow rate: 2ml/min; resolve C18Radial-Pak [20]

Researchers have suggested that Radioactive Ytterbium (III) oxide targets could be used to separate non carrier added ^{177}Lu [20]. The activity was put onto a Resolve C18 column and eluted using a 0.25 M -HIB integration of chelating agent and 0.1M 1-octanesulfonate charge carrier agent [20, 22]. Complete separation was only obtained when the quantity of Ytterbium was less than 1 mg, as shown in Fig.6. The Ytterbium peak shifted toward the Lutetium peak as the quantity of Yb_2O_3 was raised from 0.01 to 5 mg, reducing separation efficiency [20]. As a result, this approach is ineffective for producing ^{177}Lu for nuclear medicine. Therefore, this research aims at improving separation efficiency and establish an approach which is effective for production of radiopharmaceutical for nuclear medicine [20]. Below is a summary table comparing advantages and disadvantages of different types of resins.

Table 3. Advantages and disadvantages of different types of resins [20, 22, 58]

Types of Resin	Advantages	Disadvantages
Dowex-50-WX8	• High Capacity • Strong Acidic Nature • Particle Size Control • Clean and Predictable Separations • Durability • pH Tolerance	• Eye and Skin Irritation • Respiratory Issues • Handling Precautions • Thermal Sensitivity
LN	• Good reproducibility • Established technology • Organic solvent-free method	• High temperature process • High energy input, • Complex equipment required
LN2	• Smaller particle size • Higher density • Better conversion factor	• Possible metal Contamination • Higher density may affect some applications

Dowex-50-WX8 is a dependable option for use in radiopharmaceutical and fine chemical separations as well as other analytical procedures because of these characteristics [20]. It has shown a potential method in separation and purification of individual radionuclides.

Resistance of Dowex-50-WX8 Resins to Radiation Effects

When metallic Dowex-50-WX8, with mesh size of 50 to 100 mesh of about 10 Milliequivalents/sample in distilled water is exposed to 6.1×10^7 rad dose the absorbed ions when irradiating causes loss capacity of the strong-acid of the resin (Chikawa & Hagiwara, 1973) [56]. Chikawa & Hagiwara (1973)

suggested that Dowex-50-WX8 resins saturated with H^+, Na^+, K^+, NH_4^+, Ca^{2+}, Mg^{2+}, and Mn^{2+} lose roughly 7% of their initial strong-acid capacity, but resins saturated with Cu^{2+} , Fe^{3+}, or $U0_2^{2+}$ lose less than 0.7 %, and all three metallic forms can be decreased to some amount [56]. Kunin & Mayer (1950) suggested that when irradiating, the $Cu^{2+}R_2$ type yields Cu^+ R due to a reaction with Cu^{2+}, and the decreasing species produced as a result of irradiation and the Cu^+ generated in the resin causes disproportion in Cu^{2+} and metallic copper [37]. Additionally, continued irradiation of Fe^{3+}R3 yielded Fe^{3+}, whereas that of UO_2^{2+}R2 produces U^{4+} (or UO^{2+}) and UO_4, hence forming the latter peroxide [37], as shown by the equation below:

$$UO_2^{2+}+H_2O_2+2H_2O \rightarrow UO_4 2H_2O+2H^+. \quad [2]$$

The interaction of H atoms synthesized by the resin during irradiation is suspected to cause the majority of the resin degradation [44]. The amount of ions absorbed in the resin phase after irradiation is decreased, which lowers the resin's degradation [44]. The reduction of strong-acid capacity, creation of sulfate, de-crosslinking, and development of weak-acid capacity are all caused by exposing the resin to –radiation [44]. The degradation to the resin is worsened when the entire dose is increased, although the use of reducible ionic forms of resin can aid to mitigate the damage [44, 52]. When poor resin is irradiated, it loses its strong-acid capability rather quickly, implying that resin fragments made up of lower molecular species created by irradiation rapidly liberate themselves from the resin matrix (Ichikawa & Hagiwara , 1973) [37].

Ionizing radiation doses in the range of the powers of tens (≈10^5 Gy), often these synthetic organic ion exchangers' characteristics are significantly changed. Exchange ability, selection, and exchange kinetics are all affected by the increase received doses [52]. Other physical and chemical characteristics also change [49]. In general, anion exchangers suffer more radiation damage than cation exchangers [49]. Based on the resin's constitution, radiolytic impacts affecting ion exchangers can occur: chemical makeup, ionic form, and water holding capacity, swelling properties, and degree of cross-linkage in the molecular structures are all factors to consider [52]. Strong-acid cation exchange resins are much more resistant to radiation than strong-base anion exchange resins, while polyvinylpyridine resins are much more resistant than polystyrene resins [32, 37, 58]. Cross-linkage, salt form, moisture content, and the surrounding medium all affect the radiation stability of a specific exchanger [37]. Inorganic exchangers usually, but not always, exhibit high radiation resistance. Liquid ion exchangers, which have been used so extensively in nuclear processing applications, also are included (Pillay, 1980) [49].

Exchange Capacity of Ion Exchange Resin

Lee T.A (2005) suggested that exchanging sodium ion (Na^+) for hydrogen form (H^+) previously bound to the resin can be used to determine exchange capability [59]. After that, a normal sodium hydroxide solution can be used to titrate the hydrogen ion [39]. The following is a representation of the exchange reaction:

$$2R\text{-}H^+ + 2Na^+_{(aq)} + SO_4^{-2}{}_{(aq)} \Leftrightarrow 2R\text{-}Na^+ + 2H^+_{(aq)} + SO_4^{-2}{}_{(aq)} \quad [3]$$

The ion exchange resin is represented by R in the formula. The interaction is an equilibrium process (shown by the dual arrow,) that may be accelerated by employing a "concentrated" sodium sulfate solution. For this experiment, you will need to have the following solutions: 0.50 Molarity sodium sulfate 0.10 Molarity sodium hydroxide standardized (Lee T.A .2005) [39].

Procedure for Preparation of Ion Exchange Resins

- In a 150.0 or 250.0 mL beaker, pour 1 gram of cation exchange resin. Place the beaker in your equipment locker overnight, covered with a watch glass (Huang, 2001) [28].
- Load the chromatographic column with deionized water to about 2/3 volume. By carefully hitting the column's surfaces with a glass stirring

rod, unwanted air may be eliminated [28].

- Put a 0.9-1.0 gram sample of air dried resin to a 50 mililitres volumetric flask [28].
- Pour the resin mixture to the column after adding approximately 20-25 mL deionized water to the resin. To thoroughly transfer all resin to the column, use a wash bottle of deionized water [28, 39].
- If appropriate, a strip of tubing could be connected to the injection tip, and intermittent stress exerted to the tube causes the level of water inside the column to gradually rise and fall, allowing air bubbles to escape. (Obviously, you will need to control the pressure in order to function properly) [28, 39].
- After the column has indeed been prepared, raise the level of water to 1cm over the top of the resin bed. (Make sure the water level does not dip below the top of the resin bed.) (Lee T.A .2005) [39].
- Make a 300.0 mL sodium sulfate (Na_2SO_4) solution using 21.30 g sodium sulfate (Na_2SO_4) and 280.0 mL deionized water by dissolving 21.30 g sodium sulfate (Na_2SO_4) in 280 mL deionized water [28].
- Fill the column with 5 mL sodium sulfate solution and set the nozzle such that the solution flows through to the column at a velocity of 2-3 mL /minute [28].
- Add 5 mL amounts of new sodium sulfate solution to the column as necessary to keep the liquid level from dropping underneath the resin's surface [28, 39].
- Fill a 500.0 mL volumetric flask with the effluent (liquid flowing out from column's bottom). Feed 50.0 mL deionized water through into the column once all 300.0 mL sodium sulfate has indeed been transferred, collecting the deionized in the very same flask as the effluent. (Lee T.A .2005) [39].

Titration

Titrate the whole contents of the 500-mL Volumetric flask to the phenolphthalein endpoint (Dardel.2021), using a standardized 0.1000 M sodium hydroxide solution [35]. (NOTE: You only get one chance to do this titration, so be cautious!)

- The formula for calculating the exchange capacity in milliequivalents per gram of resin is:

$$\text{Capacity} = \frac{\text{mL(NaOH)}\times\text{M(NaOH)}}{\text{Mass(resin)}} \qquad [4]$$

Preparation and Standardization of Sodium Hydroxide Solution.

- Dry 2 grams of pure potassium hydrogen phthalate (KHP) inside the oven for 2 hours around 110 degrees Celsius. Transfer the cookies again from oven and place them in a centrifuge tube [47].
- 1L of 0.1N sodium hydroxide can be made simply filling a sterile 1L small container halfway with deionized water, 4.0 milligrams (5.31 mL) 8.0 grams (5.31 mL) sodium hydroxide (NaOH) solution or powdered sodium hydroxide (NaOH) [11, 47].
- After thoroughly combining the components, fill the container with deionized water and stir until the sodium hydroxide (NaOH) is completely dissolved. To blend the ingredients, shake the bottle [11].
- Distribute three 0.5 gram samples of potassium hydrogen phthalate into separate beakers or flasks using an analytical balance. Ensure that the mass of potassium hydrogen phthalate used is recorded to four decimal places. To each sample, add around 25 mL of water. The potassium hydrogen phthalate should dissolve fully [11, 14].
- Add 2 to 3 drops of phenolphthalein solution to each KHP sample.
- Using the sodium hydroxide solution, titrate each KHP sample to the very

first, light pink endpoint that is stable over a period of ten (10) seconds. The whole components of the beaker/flask should be light pink, with the lightest endpoint possible being the most ideal. Keep track of how much sodium hydroxide solution you used (Dardel. 2021) [11, 14].

- The concentration of sodium hydroxide is calculated using the following equation:

$$N(NaOH) = \frac{\frac{Grams(KHP)}{MW(KHP)}}{mL(NaOH)} \quad [5]$$

The milliliters of sodium hydroxide required to attain the phenolphthalein endpoint are denoted by mL (NaOH). Potassium hydrogen phthalate ($KHC_8H_4O_4$) has a molecular mass of 204.2 g/mole. The mean concentrations from triple titrations should be labeled onto your sodium hydroxide solution. (Lee T.A, 2005) [39].

According to Huang (2001), acid–base titration can be used to measure IEC [Meq g^{-1}(mL)]. To transform H^+ form resin to Na^+ form, it is first neutralized with sufficient aqueous NaOH. The excess NaOH is then detected by adjusting the pH to 7 with a weak hydrochloric solution [40]. As a result, ion exchange capacity (IEC) is computed as follows:

$$IEC = [\frac{MV(NaOH) - MV(HCL)}{M(resin)}] \times 1000[(Meq\ g^{-1}(mL)] \quad [6]$$

M and V are the molar concentration and volume of the solutions, respectively, while m_{resin} is the weight of the products (H^+ type).

Dardel (2021)_also suggested that the total capacity of a resin sample is measured by titration and expressed in eq/L. The procedure involves a volume measurement and must be carried out under strict conditions [11]. As the volume changes according to the ionic form of the resin, some ions have a higher mass and their volume is different from others, the ionic form of measurement must always be reported [3, 11].

The total capacity must also be reported as dry weight capacity after drying of the resin sample. The dry weight capacity measures the number of active groups per kg of dry resin, i.e. without the moisture content [3]. It is expressed in eq/kg. Mention of the ionic form is critical here as well, as different ions have different masses [3].

Dry weight capacity is important for two different purposes:

- For new resins, it gives information about the efficiency of the activation process: for instance, if every aromatic ring has been sulphonated in a strongly acidic resin, the theoretical maximum total dry weight capacity is about 5.5 eq/kg in H^+ form [59].
- For used resins, it gives information about a possible fouling: a fouled resin sample contains foreign matter, which increases the dry weight, and as a consequence the dry weight capacity (number of active groups per kg of dry matter) decreases, even if no functional group has been lost (Dardel, 2021) [54].

Application of Lutetium -177 in Nuclear Medicine

Characteristics of Lutetium 177 Which Makes it Suitable for Medical Application

The physical half-life of Lutetium-177 is 6.65 days [14]. In soft tissue, Lutetium-177 produces βeta-particles with a small range (average 0.231 mm, maximum 1.71 mm). The Lu-176(n,) Lu-177 reaction produces the radionuclide [26]. Lutetium-177 has the atomic number 71 and is a rare earth element (Hosono .et.al, 2018) [58]. Lutetium-177 accumulates in tissue and organs, according to Hosono et al. (2018) (60.0 % in bone, 2.0 % in the liver, and 0.5 % in the kidneys) [26]. Furthermore, Lutetium-177 has a biological half-life of 3500.0 days in bone and liver, and 10.0 days in the kidneys [14]. As a result, the majority of the Lutetium-177 absorbed by the

body ends up in bone, where it accumulates over time. According to Howe, D B, et al. (2008), Lutetium-177 has a maximum beta energy of 498.1 keV (78.61 %), 208.1 keV (11.0 %) gamma, and 113.1 keV (6.41 %) gamma, in addition to a half-life of 6.75 days [32]. The beta tissue penetration reaches a maximum of 1.71 mm; with an average of 0.230 mm. Lutetium-177 is efficient in destroying specific tumor cells while having a little effect on nearby normal cells due to these exceptional properties [32].

In addition to that Lutetium-177 (^{177}Lu) oxodotreotide has a high affinity for subtype 2 somatostatin receptors, according to Calopedos.et.al. (2017) [8]. It attaches itself to cancer cells that have an overabundance of sst2 receptors [8]. Lutetium-177 (^{177}Lu) is an emitting radionuclide with a maximum penetration range of 2.2 mm (mean penetration range of 0.67 mm) in tissue, which is adequate to kill targeted tumor cells while having a little effect on nearby normal cells [8]. The peptide oxodotreotide has no clinically meaningful pharmacodynamic impact at the concentration utilized (about 10.0 grams/mililitre in total, both for unlabeled and radiolabeled versions) (Calopedos.et.al. 2017) [8].

Uses of Lu-177 in Nuclear Medicine

Lutetium -177 dotatate is a radioactive medication that attaches to a specific portion of tumor cells, allowing radiation to penetrate and kill them [8, 53]. Certain malignancies of the digestive system, for example the stomach, pancreas, and intestines, are treated with Lutetium-177 dotatate [53]. In individuals with carcinoma of the prostate that really has progressed and is resistant to treatment, Prostate-specific membrane antigen tagged with Lutetium-177, simply written as PSMA-617, is being employed as a novel treatment agent (mCRPC). Prostate-specific membrane antigen, abbreviated as PSMA, is a protein that is found in the prostate [44]. For individuals with mCRPC, targeted radionuclide therapy using (PSMA)-617 (Lu-PSMA) binding, having a strong affinity for PSMA is a viable treatment option [8]. In nations with limited access to positron emission tomography abbreviated as PET, ^{177}Lu-PSMA might be employed as a pre-therapeutic imaging agent in addition to treatment (Ahmadzadehfar.et.al. 2015) [53].

Prostate specific membrane antigen Lutetium-177 (PSMA) therapy is a cutting-edge molecular therapy for carcinoma of the prostate, commonly described as carcinoma of the prostate that really has advanced across the body (PSMA) is a one-of-a-kind receptor that may be identified on the surface of many prostate cancer cells (tumor cells) [21]. Prostate specific membrane antigen Lutetium-177 (PSMA) will be identified in other sections of the body if Prostate cancer can spread to other organs or locations [21]. Lutetium-177 is used to precisely target these receptors in PSMA treatment (a radioactive substance). Lutetium-177 is put into the circulation and goes to parts of the body where Prostate-specific membrane antigen Lutetium-177 (PSMA) is present, emitting radiation that kills cancer cells. PSMA treatment minimizes the harm to surrounding healthy cells by providing a high, targeted radiation dosage to cancer cells (Bodei et. al .2013) [21]. According to Zaknun et al. (2013), Lutetium-177 is being utilized to treat patients with gastro-entero-pancreatic neuroendocrine tumors in the United States with the FDA-approved radiopharmaceutical Lutathera, which is manufactured by Advanced Accelerator Applications [10].

Lutetium (Lu 177-dotatate) is meant to treat gastroenteropancreatic and neuroendocrine tumors, according to Bednarczuk.et.al. (2017) [42]. It is used in individuals with somatostatin receptor positive malignancy. Lutetium Lu 177-dotatate is also being investigated for use in curing various cancers. Somatostatin receptor positive gastroenteropancreatic and neuroendocrine tumors that are unresectable or metastatic tumors (GEP-NETs) that are advancing and extremely differentiated are treated with Lutathera (G1 and G2) (von Eyben FE, et. al.2018) [2]. Lutetium is also employed in scientific studies. The oxide is employed in optical lenses, and its compounds are utilized as hosts for scintillators and X-ray phosphors. It acts like a normal rare earth, generating a sequence of oxidation state +3 compounds

such Lutetium Sesquioxide, Sulfate, and Chloride (Kos-Kuda.et.al. 2017) [47].

The efficacy of Lu-177 has been noticed in recent years; for example, in the current literature, the proportion of men who have a >50 % drop in serum PSA (prostate specific antigen) levels ranges from 30 % to 70 %, which is comparable to the PSA response rates observed with chemotherapeutic drugs used in mCRPC (Cabazitaxel and Docetaxel) [22]. The percentage of guys with a progressive condition who do not react to PSMA treatment with ^{177}Lu ranges from 10 % to 32 %. In one of the larger trials, 80 percent of the men recruited had a PSA response to treatment (Emmett.el.at. 2017) [22].

Dangers and Side Effects of Lu-177 Dotatate

Lutetium -177 dotatate, according to Mutum (2021), might damage an unborn baby or cause birth problems if the mother or father is taking it. As a result, avoid becoming pregnant or breastfeeding while using Lutetium-177 dotatate [28]. While receiving Lutetium-177 dotatate and for at least 4 months following your last dosage, do not breast-feed. Other cancers, such as leukemia, may be caused by Lutetium-177 dotatate [28]. It has the ability to cause infertility in both males and females in some situations. To avoid negative effects, it's best to take birth control while using Lutetium-177 dotatate. The most common ^{177}Lu-PSMA-related adverse effects, according to Rahbar et al (2016), impact the dose-limiting organs, such as the bone marrow, glands of saliva and tears, and kidneys [9].

The most frequent adverse effects of Lutetium -177, according to NHS Foundation Trust (2021), are a little dry mouth, lack of appetite, nausea (feeling ill), and exhaustion (extreme tiredness) [1]. In the first few weeks after starting Lutetium-177 PSMA treatment, some patients experience a modest drop in their blood count as a side effect. All of these adverse effects are often transient and will go away without further treatment [1]. The therapy's radiation may cause some harm to healthy cells. This damage has the potential to turn into cancer in the future. The potential benefit of the treatment, however, exceeds the radiation danger (NHS Foundation Trust, 2021) [1].

Safety Protocols for Medical Personnel

Radioactive pollutants from medical sources should be kept and disposed in "disposal facilities (storage and disposal)," according to Hosono.et.al (2019) [58]. In a hospital or other medical establishment, waste collecting facilities explains how to manage or handle a diaper or urine collection bag soiled with human excreta or blood of patients who have been administered a Radiopharmaceutical [44].

Use necessary safety precautions when handling Lu-177, such as waterproof gloves and good radiation shielding, inorder to reduce radiation exposure [44]. Lutetium-177 should only be used or controlled by physicians who have received specific trainings and experience in the safe use and handling of radiopharmaceuticals, and whose experience and trainings have been given approval by the appropriate governmental agency responsible for radiopharmaceutical licensing. Prior to starting Lu-177 treatment, medical staff should confirm that females of reproductive capacity are not pregnant (Alexandraki & Kaltsas. 2012) [29].

3.0. METHODOLOGY

3.1. Theoretical Calculations

3.1.2. Determination of the Activity of Lutetium-177

Sample calculation

Data given

- m_1 =10 mg, m_2 = 100 mg, m_3 = 1000 mg
- Mass of target (M) = 176 g/mol
- Abundance (ɵ) = 99.5 % = 0.995
- Activation total time (t) = 1000 hours (Note that time interval of 100 hours)
- Cross section of thermal neutron of the target nuclide:

(σ) = 3200 mbarn = $3.2 \times 10^{-24} cm^{-2}$

(1 barn ≈ 1×10^{-24}cm^{-2})

- $Halflife = T_{\frac{1}{2}} = 6.7\ days = 160.8\ hours$

- Thermal neutron flux rate (ϕ)

$$\phi_1 = 1.10\times10^{12}\ \text{n/cm}^2/\text{s}$$

$$\phi_2 = 1.10\times10^{13}\ \text{n/cm}^2/\text{s}$$

$$\phi_3 = 1.10\times10^{14}\ \text{n/cm}^2/\text{s}$$

- Avogadro's' constant (N_a) = 6.02×10^{23} atoms /mole
- Decay constant (Λ)

$$\Lambda = \frac{In2}{T_{\frac{1}{2}}} = \frac{In2}{160.8} = 0.004310616\ hour^{-1}$$

Ascertain that all quantities are translated to the appropriate units. It is important to note that you need to convert thermal neutron cross section values to square centimeters and time to hours.

Calculate specific activity (GBq/g):

$$S\left[\frac{Bq}{g}\right] = \left[\frac{N_a * \sigma * \phi}{M}\right](1 - e^{-\Lambda t}) \qquad [7]$$

Where:

- $S\left[\frac{Bq}{g}\right]$: specific activity
- (ϕ) : flux density
- ɵ : barns
- Λ : decay constant

Calculate activity (GBq):

$$A = S \times m \times \theta \qquad [8]$$

When mass (m) = 1000 mg (1g) and

Flux (ϕ) = 1.10 ×10 ^{12} (n/cm^2/s), t = 0 hours

$$S\left[\frac{Bq}{g}\right] = \left[\frac{6.02\times10^{23}\times3.2\times10^{-24}\times1.10\times10^{12}}{176}\right](1 - e^{-(0.004310616\times0)})$$

$$S\left[\frac{Bq}{g}\right] = [1.204\times10^{10}](1-1) = 0\ \text{GBq/g}$$

We define activity as: $A = S \times m \times \theta = \frac{0Bq}{g} \times 1g \times 0.995 = 0\ GBq$

When mass (m) = 1000 mg and Flux (ϕ) = 1.10 ×10 ^{12} (n/cm^2/s), t = 100 hours

$$S\left[\frac{Bq}{g}\right] = \left[\frac{6.02\times10^{23}\times3.2\times10^{-24}\times1.10\times10^{12}}{176}\right](1 - e^{-(0.004310616\times100)})$$

$$S\left[\frac{Bq}{g}\right] = [1.204\times10^{10}](0.350181119) = 4.216\times10^{9}\text{Bq/g} = 4.216\ \text{GBq/g}$$

We define activity as: $A = S \times m \times \theta = \frac{4.216GBq}{g} \times 1g \times 0.995 = 4.19\ GBq$

Specific activity and activity of Lu-177 were determined over 1000 hours at thermal neutron fluxes density of 1.10×10^{12} n/cm^2/s, 1.10×10^{13} n/cm^2/s and 1.10×10^{14} n/cm^2/s and different masses of the target: 10 mg, 100 mg and 1000 mg. However, table 4 and figure 7 show results obtained at thermal neutron flux density of 1.10×10^{12} n/cm^2/s and mass of the target of 1000 mg. The results obtained could be achieved by following the steps outlined above [2]. To investigate the influence of mass and flux on the sample's activity of Lu-177, a graph of activity as a function of time of irradiation for different values of thermal neutron flux density (ϕ) was plotted as shown in fig. (7).

Table 4: Specific activity and activity of Lu-177, target mass of 1000 mg for different values of thermal neutron flux density

Time (t) hours	Specific activity (GBq/g)	Activity(GBq)
0	0.000	0.00
100	4.216	4.19
200	6.956	6.92
300	8.736	8.69
400	9.893	9.84
500	10.645	10.60
600	11.133	11.10
700	11.451	11.40
800	11.657	11.60
900	11.791	11.70
1000	11.878	11.80

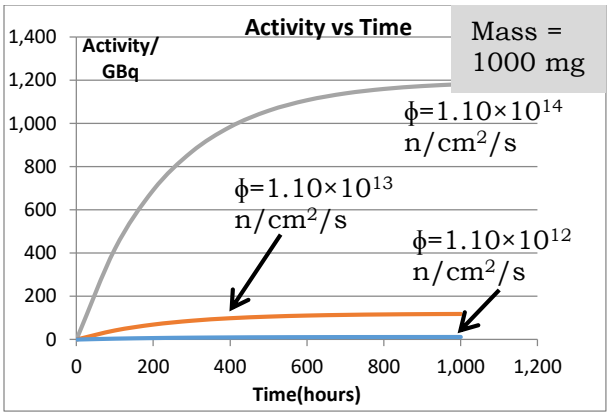

Figure 7: Activity of 177Lu as a function of time of irradiation for different values of thermal neutron flux densities (ϕ)

Fig. (7). shows ^{177}Lu activity as a function of the duration of irradiation with different thermal neutron flux densities. From table 4 and fig (7) we can deduce that ^{177}Lu integral yield depends on numbers of irradiation cycles and on the amount of Lutetium (table 5) in the target material [2].

Table 5: Maximum specific activity and activity of Lu-177 with target masses of 10 mg, 100mg and 1000 mg for different values of thermal neutron flux densities.

Thermal Neutron Flux Density, (n.cm^{-2} s^{-1})	Max. Time (hours)	Mass (mg)	Max. Specific Activity(GBq/g)	Max. Activity (GBq)
1.10×10^{12}	1000	10	11.88	0.118
		100	11.88	1.182
		1000	11.88	11.800
1.10×10^{13}		10	118.78	1.1819
		100	118.78	11.819
		1000	118.78	118.190
1.10×10^{14}		10	1187.84	11.819
		100	1187.84	118.190
		1000	1187.84	1181.900

3.1.2. Dose Rate as a Function of Radius [$D_{(r)}$]

Lutetium-177 has a half-life of 6.75 days with a maximum beta energy of 498.1 keV (78.61 %), 208.1 keV (11.0 %) gamma, and 113.1 keV (6.41 %) gamma [58].

Sample calculations

Data given

Activity (A) = 1.182 GBq
E_{y1}= 208.1 keV ≈ 0.21 MeV
Intensity (I_1) = 11.0% = 0.11
Gamma constant(Γ_1) =11.1 aSv*m²/ (s.Bq)
E_{y2} (gamma energy) = 113.1 KeV ≈ 0.11 MeV
Intensity (I_2) = 6.41% = 0.0641
Gamma constant (Γ_2) =6.25 aSv*m²/ (s.Bq)
Radius of column =10 mm

We define dose rate as:

$$G = G1 + G2 = \frac{A \times I_1 \times \Gamma_1}{r^2} + \frac{A \times I_2 \times \Gamma_2}{r^2} \qquad [9]$$

When radius (r) = 0.5 mm = 0.5 ×10 $^{-3}$

$$G = \frac{1.181 \times 10^9 \times 0.11 \times 11.1 \times 10^{-18}}{(0.5 \times 10^{-3})^2} + \frac{1.181 \times 10^9 \times 0.0641 \times 6.25 \times 10^{-18}}{(0.5 \times 10^{-3})^2}$$

$$G = 0.004\ \frac{Sv}{s} + 1.892552 \times 10^{-3}\ \frac{Sv}{s} = 5.892552 \times 10^{-3}\ Sv/s$$

Converting dose into (Sv/hr)

$$1\text{second} = \frac{1}{3600}\ hours = 2.778 \times 10^{-4}\ hours$$

$$G = \frac{5.892552 \times 10^{-3}\ Sv/s}{2.778 \times 10^{-4}\ hrs/s} = 21.21149208\ \frac{Sv}{hr} = 24.811\ Sv/hr$$

When radius (r) = 1.0 mm = 1.0 ×10 $^{-3}$

$$G = \frac{1.181 \times 10^{9} \times 0.11 \times 11.1 \times 10^{-18}}{(1.0 \times 10^{-3})^2} + \frac{1.181 \times 10^{9} \times 0.0641 \times 6.25 \times 10^{-18}}{(1.0 \times 10^{-3})^2}$$

$$G = 1 \times 10^{-3}\ \frac{Sv}{s} + 4.71381 \times 10^{-4}\ \frac{Sv}{s} = 1.471381 \times 10^{-3}\ Sv/s$$

$$G = \frac{1.471381 \times 10^{-3}\ Sv/s}{2.778 \times 10^{-4}\ hrs/s} = 5.296547876\ \frac{Sv}{hr} = 5.297 Sv/hr$$

The dose rates were calculated at various lengths along the column's radius, i.e. r =0.5 mm, 1.0 mm, 1.5 mm...5 mm. The column's overall radius length was 5 mm. The findings were recorded into the tables below, and graphs were drawn to show how the dose rates varied with column radii.

Table 6: Dose distribution along the radius of the column at thermal neutron flux density of 1.10×10^{12} n/cm^2/s and target mass of 1000 mg.

Radius (mm)	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	4.5	5.0
Dose rate (Sv/hr)	259.18	64.79	28.80	16.20	10.37	7.20	5.29	4.05	3.20	2.59

Table 6 shows dose rate at thermal neutron flux density of 1.10×10^{12} n/cm^2/s and target mass of 1000 mg. The steps were repeated to obtain dose rates at thermal neutron flux densities of 1.10×10^{12} n/cm^2/s, 1.10×10^{13} n/cm^2/s and 1.10×10^{14} n/cm^2/s with different target masses of 10 mg, 100 mg and 1000 mg (Table. 7). Dose rate significantly decreased with increase in radius (fig.8) and this assessment is important as it can help to determine the necessary radiation shielding material in the separation of Lu/Yb nuclides [2].

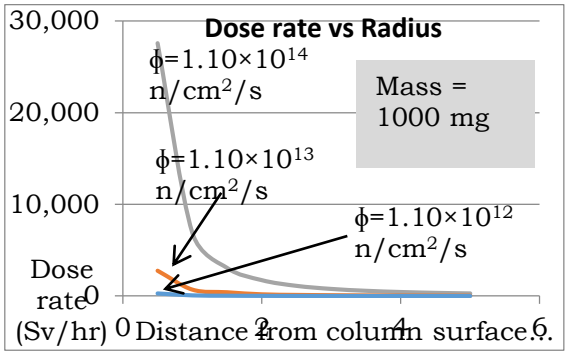

Figure 8: Dose rate of 177Lu as a function of radius for different values of thermal neutron flux densities (ϕ)

Table 7: Maximum and minimum dose rate of Lu-177 with target masses of 10 mg, 100 mg and 1000 mg for different values of thermal neutron flux densities.

Thermal Neutron Flux Density, (n.cm^{-2} s^{-1})	Activity (GBq)	Mass (mg)	Min.Dose Rate (Sv/hr)	Max.Dose Rate (Sv/hr)

1.10×10^{12}	0.12	10	0.028	2.76
	1.18	100	0.212	24.81
	11.80	1000	2.590	259.18
1.10×10^{13}	1.18	10	0.212	24.81
	11.82	100	2.590	259.18
	118.19	1000	27.50	2750.18
1.10×10^{14}	11.82	10	2.590	259.18
	118.19	100	27.500	2750.18
	1181.90	1000	275.880	27588.19

Dose Rate as a Function of Length of Column [$D_{(X)}$]

The dose was calculated as a function of column length. The estimated values were used to determine whether or not the resins had been damaged. It is important to note that a high dose rate has an impact on resin exchange capacity [30].The dose rate was calculated at different positions along the length of the column, which was divided into 30 mm intervals. Finally, a graph of dose rate against length was plotted (fig 10).

Data given

Activity (A)=1.0592GBq
Radius (r) = 30 mm = 3.0×10^{-2} m
E_{y1}= 208.1 keV ≈ 0.21 MeV
Intensity (I_1) = 11.0% = 0.11
Gamma constantΓ_1)=11.1 aSv*m²/ (s.Bq)
E_{y2} = 113.1 KeV ≈ 0.11 MeV
Intensity (I_2) = 6.41% = 0.0641
Gamma constant (Γ_2)=6.25 aSv*m² / (s.Bq)
Length of column =30 cm

$$G = G1 + G2 = \frac{A \times I_1 \times \mathbb{\Gamma}_1}{x^2} + \frac{A \times I_2 \times \mathbb{\Gamma}_2}{x^2} - -a4$$

$$= \frac{1.0592 \times 10^9 \times 0.11 \times 11.1 \times 10^{-18}}{(3.0 \times 10^{-2})^2} + \frac{1.0592 \times 10^9 \times 0.0641 \times 6.25 \times 10^{-18}}{(3.0 \times 10^{-2})^2}$$

$$G = 1.582 \times 10^6\ Sv/s$$

Converting dose into (mSv/hr)

$$1\text{second} = \frac{1}{3600}\ hours = 2.778 \times 10^{-4}\ hours$$

$$G = \frac{1.582 \times 10^6\ Sv/s}{2.778 \times 10^{-4}\ hrs/s} = 0.005696912\ \frac{Sv}{hr} = 5.697\ mSv/hr$$

The dose rates for various masses at various fluxes and activities were calculated and the findings were recorded in the tables below. The link between dose rate and column length was shown using the graph (fig 9). It is worth noting that the activity used in each computation was the activity obtained when time (t)=500 hours.

Table 8: Dose distribution as function of length of the column at thermal neutron flux density of 1.10×10^{12} n/cm²/s and target mass of 1000 mg

Length Mm	30	60	90	120	150	180	210	240	270	300
Dose rate (mSv/h)	5.697	1.000	0.444	0.250	0.160	0.111	0.082	0.063	0.049	0.004

Table 9: Maximum and minimum dose rate of Lu-177 with target masses of 10 mg, 100 mg and 1000 mg for different values of thermal neutron flux densities

Thermal Neutron Flux Density, (n.cm^{-2} s^{-1})	Activity (GBq)	Mass (mg)	Min.Dose Rate (Sv/hr)	Max.Dose Rate (Sv/hr)
1.10×10^{12}	0.11	10	0.007	0.69
	1.06	100	0.004	5.70
	10.60	1000	0.640	64.00
1.10×10^{13}	1.06	10	0.004	5.70
	10.59	100	0.640	64.00
	105.92	1000	6.840	685.68
1.10×10^{14}	10.59	10	0.640	64.00
	105.92	100	6.840	685.68
	1059.20	1000	68.395	6856.82

The dose rate for a target mass of 1000 mg and a thermal neutron flux density of 1.10×10^{12} n/cm^2/s is shown in Table 9. The procedures were repeated to get dose rates for target masses of 10 mg, 100 mg, and 1000 mg, at thermal neutron flux densities of 1.10×10^{12} n/cm^2/s, 1.10×10^{13} n/cm^2/s, and 1.10×10^{14} n/cm^2/s (Table. 9). The dose rate decreased as the length of column increased (fig. 10) [30].

Experimental procedure

Preparation of Lu-177 and Yb-176 Tracers

Materials and Equipment

Two beaker, two Petri dishes, four thongs, Two Detectors, Ventilator, Heater (oven), Pipette and Tips, Aluminum foils.

Reagents

- HCL (6M) , Distilled water, Tracers, Yb_2O_3 and Lu_2O_3 powders

The irradiation procedure involved natural Yb_2O_3 (mass=19.0 mg) of high chemical purity (99.999%) and Lu_2O_3 (mass =11.6 mg). Irradiation was carried out for approximately 30 minutes at the neutron flux (1.10×10^{12} n/cm^2/s, 1.10×10^{13} n/cm^2/s and 1.10×10^{14} n/cm^2/s) [38].

Procedure

- First, the beta detector was used to measure the activity of the irradiated target, which was found to be 35 mSv/hr.
- The irradiated samples of Yb_2O_3 and Lu_2O_3 targets were removed from aluminum foil and put in a petri dish, using the thongs [do not handle radioactive samples with bare hands].
- Two dry beakers with transparent labels were filled with irradiated powders.
- About 2 µl HCL was added to each beaker, and the solution was gently stirred.
- More HCL was then added to the solution.
- Beakers holding the solutions were then placed on a (heater/oven) set to 100 ^{o}C, while ensuring that the solution did not boil and that only a semi-solid mixture was left in the beaker.
- Once the solution had dried to a semi-solid state, a little amount of distilled water was added, and the process was repeated until a PH of 6 or 7 was reached.
- 1ml of HCL was added to the semi-solid sample after it had been heated [use a pipette to administer hydrochloric acid]
- Gently shook the mixture to thoroughly mix the acid and the sample.
- After that Ytterbium was transferred to a bottle.

- Rinsed the beaker with acid to verify that everything was fully transferred [rinsing is necessary to avoid losing any sample, and it also raises the percentage yield of the required Ytterbium].
- The process was continued until the dose rate was as low as it could possibly be.
- Rinsing was stopped as soon as the dose rate was as low as possible.

Precautions

- When dealing with powder, turn off the ventilator to prevent air from blowing into the powder.
- Check the activity of the solutions as well as the working surface area using the gamma/beta detector.
- Check any activity on your hands with the (hand detectors), then wash your hands completely with soap and water and rinse your mouth with clean water.

Preparation of Ion Exchange Resin Before Use

The purpose of this section is to highlight the steps involved in preparation of Ion Exchange Resins before use.

Apparatus and material

Three conical flasks, filter paper, petri dish, beaker, filtering flask, measuring cylinder, electronic balance, mixer, vacuum pump, stirring rod, sodium hydroxide and distilled water.

Procedure

- First, attach a funnel to the conical flask.
- Then, to remove air molecules, connect the conical flask to a vacuum pump.
- After that, place a filter paper inside the funnel and use distilled water to keep it at the bottom.
- Put Ion exchange resins directly on the filter paper in the funnel, and wash the resins using distilled water.
- Then spread the resins over the filter paper with a stirring rod and wait a few minutes in order to allow water to filter from the resin and collect at the bottom of the conical flask as filtrates.
- Switch off a vacuum pump, and remove the filter paper containing ion exchange.
- Transfer the resins in a petri dish.
- Wait for 1 hour for the resins to dry completely.
- Using an electronic scale, weigh about 1.009 gram of ion exchange resins. Then transfer the resins into a dry, empty beaker.
- Pour 100 mL of 0.1 M sodium hydroxide solution into the beaker containing the resins and then stir.
- Place the beaker on top of the mixer and wait for 30 minutes.
- Turn off the mixer after 30 minutes and titrate the resulting solution with HCL acid.

Titration

- Fill the column with hydrochloric acid. Column capacity of 25 ml.
- Pipette and pour10 mL, 0.1 M of resulting solution into three separate conical flasks.
- Measure 50 mL of distilled water and then add to the resulting solution. Shake gently to thoroughly mix the solution.
- Add five (5) drops of phenolphthalein to the resulting solutions in the conical flasks. Shake until a homogenous pink solution is observed.
- Titrate the resulting solution until the solution turned colorless, with 0.1M hydrochloric acid.
- Record the volume of Hydrochloric acid in each case that is needed for titration of the solution to reach end point.
- Determine the average volume and record the values.

Caution: Note that liquid level in the column should always be approximately above the resin surface.

Standardization of sodium hydroxide

- Weigh approximately 20 grams of sodium hydroxide pellets and transfer to a clean dry beaker.
- Then add 500 mL distilled water to sodium hydroxide pellets in small portions.

- Note that this process maybe dangerous, so it should be carried out under shielding materials to avoid any possible accidents.
- Store the obtained solution in a clear labelled flat bottomed flask.

Preparation of phenolphthalein

- First, weigh 100 milligrams of phenolphthalein powder and transfer into a clean conical flask.
- Then, add 50% of ethanol to phenolphthalein powder.
- Finally store the resulting solution in a clear labelled flask.

Preparation of ion exchange column

- Place the resins into the column and rinse the beaker with distilled water.
- Pour distilled water into the column.
- Using distilled water, wash the resin until it reaches a PH of 5 or 6.
- Then gradually add drops of ammonium chloride (NH_4Cl) to the water until the PH reaches 0 or 1.
- Finally, rewash the resins with distilled water until there are neutral.

Determination of the Effect of Dose Rate on Ion Exchange Resins

Ion exchange resins can be damaged by high dose rates. Partition the column into tiny parts to assess the effect of dose on ion exchange resins. The dose rate can then be calculated for each segment of the column along its full length. Keep changing the position of the source, and determine the dose distribution at various locations along the column [30]. Then plot a graph of dose rate as a function of column length and determine dose distribution. Below are the sample calculations:

Dose rate is defined by means of an equation as:

$$H = H_1 + H_2 \qquad [10]$$

$$H_1 = \frac{A.\Gamma_1}{r^2}e^{-b} \qquad [11]$$

$$H_2 = \frac{A.\Gamma_2}{r^2}e^{-b} \qquad [12]$$

Where $b = \mu d$ [13]

'd' is the thickness of defense and 'μ' is attenuation factor.

Substituting equation [11], [12] and [13] into [10] we have:

$$H = \frac{A.\Gamma_1}{r^2}e^{-b} + \frac{A.\Gamma_2}{r^2}e^{-b} = \frac{A}{r^2}\left[I_1 \times \mathbb{\Gamma}_1 \times e^{-\mu_1 d} + I_2 \times \mathbb{\Gamma}_2 \times e^{-\mu_2 d}\right] \qquad [14]$$

Data Given

$\Gamma_1 =$ $6.81\ aGy.m^2/\text{s.Bq}$	$\mu_2 = 0.0297\ cm^{-1}$
$\Gamma_2 =$ $2.96\ aGy.m^2/\text{s.Bq}$	L = 1 cm = 0.01 m
$A = 1181.9\ GBq$	d = 1 cm (distance from the source)
$\phi = 1.10 \times$ $\text{n/cm}^2/\text{s}$	Intensity (I_1) = 11.0% = 0.11
$\mu_1 = 0.0254\ cm^{-1}$	Intensity (I_2) = 6.41% = 0.0641

$$H = \frac{1181.9\times10^9}{(0.01)^2}\left[0.11 \times 6.81 \times 10^{-18} \times e^{-(0.0254\times1)} + 0.0641 \times 2.96 \times 10^{-18} \times e^{-(0.0297\times1)}\right]$$

$$H = 0.0108\frac{Gy}{s} = \frac{0.0108\ Gy/s}{2.778 \times 10^{-4} hours/s} = 38.9\frac{Gy}{hour} = 3.99 \times 10^{01} = 3.99E+01$$

The dose rate was calculated at several distances from the source and then data was recorded in the tables as shown below. The source was placed on top of the resin, and then placed at the middle point of the whole length of the column containing the resin and so on. The results were recorded in table 10.

Figures 10 and 11 depict dose distribution per minuscule part along the column's full length. Figure 10 demonstrates how dose decreases as distance from the source increases while figure 11 shows how the dose reduced equally when it was positioned in the center of the column, in the reverse way of the source. It is important to know that comparable graphs may be created simply shifting the source around along the column [56]. The ion exchange resin was not damaged, and the exchange capacity might not have been affected, because the average absorbed dose was less than the theoretical value.

Table 10: Dose distribution per unit length of column

Length(L)m	Dose rate Gy/hour	Length(L)m	Dose rate Gy/hour
0.00	3.99E+03	0.13	2.36E-01
0.01	3.99E+01	0.12	2.77E-01
0.02	9.99E+00	0.11	3.30E-01
0.03	4.44E+00	0.10	3.99E-01
0.04	2.50E+00	0.09	4.93E-01
0.05	1.60E+00	0.08	6.24E-01
0.06	1.11E+00	0.07	8.15E-01
0.07	8.15E-01	0.06	1.11E+00
0.08	6.24E-01	0.05	1.60E+00
0.09	4.93E-01	0.04	2.50E+00
0.10	3.99E-01	0.03	4.44E+00
0.11	3.30E-01	0.02	9.99E+00
0.12	2.77E-01	0.01	3.99E+01
0.13	2.36E-01	0.00	3.99E+03
0.14	2.04E-01	0.01	3.99E+01
0.15	1.77E-01	0.02	9.99E+00
0.16	1.56E-01	0.03	4.44E+00
0.17	1.38E-01	0.04	2.50E+00
0.18	1.23E-01	0.05	1.60E+00
0.19	1.11E-01	0.06	1.11E+00
0.20	9.98E-02	0.07	8.15E-01
0.21	9.05E-02	0.08	6.24E-01
0.22	8.24E-02	0.09	4.93E-01
0.23	7.54E-02	0.10	3.99E-01
0.24	6.93E-02	0.11	3.30E-01
0.25	6.38E-02	0.12	2.77E-01
0.26	5.90E-02	0.13	2.36E-01
0.27	5.47E-02	0.14	2.04E-01
0.28	5.09E-02	0.15	1.77E-01
0.29	4.74E-02	0.16	1.56E-01
0.30	4.43E-02	0.17	1.38E-01

The column had a total length of 30 cm, and elution took about 20 hours, therefore the elute velocity was 0.667 hours/cm. The total estimated absorbed dose was determined using the figures 9 and 10 as well as other data not included in this research. [Note: the remaining graphs may be obtained by repeating the steps above].

Table 10 shows the computed dose rate and absorbed dose, which was used to assess the influence of the absorbed dose on the ion exchange resin's capacity. When all activity (1181.9 GBq) passed through the column, the average absorbed dose was 2.74 kGy.

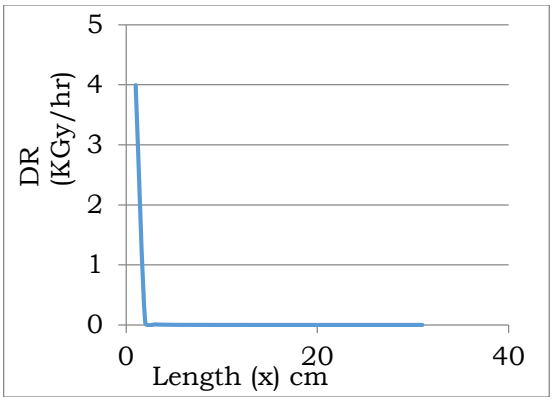

Figure 9: Dose rate as a function of length of column, Activity at top part of column

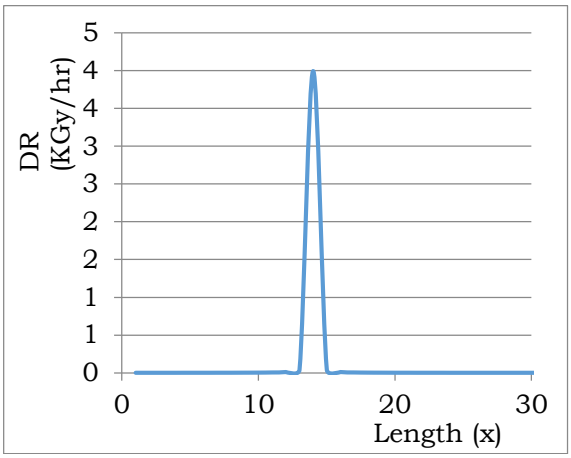

Figure 10: Dose rate as a function of length of column, Activity at middle part of column.

Table 11: Total absorbed dose

Length (m)	Time (hours)	Total Dose Rate (Gy/Hr)	Total Absorbed Dose (Gy)
0.00	0.00	4059.0	2706.0
0.05	3.34	4117.2	2744.8
0.10	6.67	4120.2	2746.8
0.15	10.01	4120.8	2747.2
0.20	13.34	4120.2	2746.8
0.25	16.68	4117.2	2744.8
0.30	20.00	4059.0	2706.0

If the adsorbed dose is 1 MGy or above, major changes in resin characteristics would have occurred [38].

Summary of Experimental Procedure

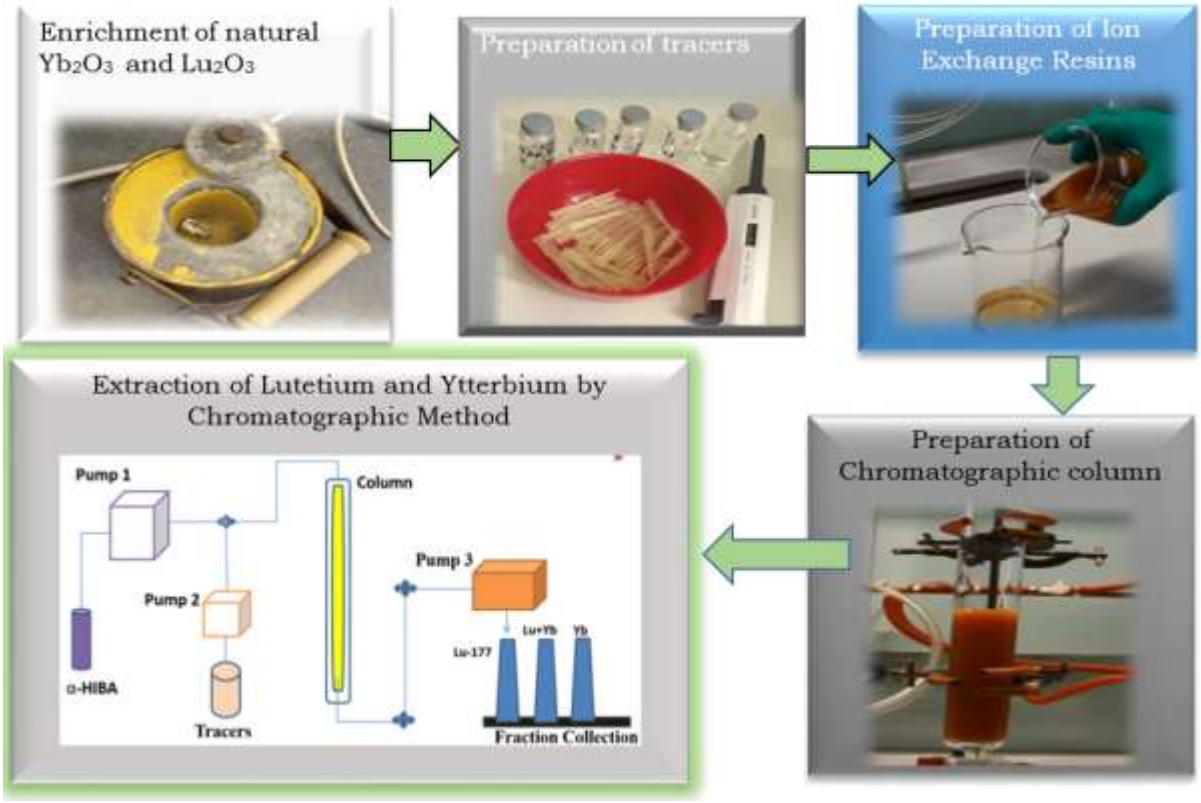

Figure 11. Flowchart summarizing experimental procedure

Safety Protocols for Handling Radioactive Materials [5, 30]

- Wear personal protective clothing when working with an open radioactive source.
- Do not eat or drink in any room labeled with a Caution: Radioactive Materials sign on the door.
- Be mindful of your distance from sources of radiation.
- Use proper shielding for the type of radiation.
- Isolate or contain harmful radioactive materials properly.
- Armor yourself with appropriate protective clothing and dosimeters.
- Acquire adequate training to better understand the nature of radiation hazards.
- Reduce handling time of radioactive materials and equipment.
- Use fume hoods and biosafety cabinets.
- Follow good laboratory practices.

FINDINGS

Sample Calculations of Concentration of Lu_2O_3 and Yb_2O_3

- **Ytterbium-176**

Chemical Reaction

$$Yb_2O_3 + HCL \rightarrow YbCl_3 + H_2O$$

Mass of Ytterbium obtained from the sample (Yb_2O_3).

Molar mass of Yb_2O_3 = (2×176) + (3×16) = 400 g/mol

Mass of Ytterbium in 1 mole of the sample **(**Yb_2O_3) = (2×176) =352 g

Then mass of Ytterbium in 19.0 mg Yb_2O_3 sample will be:

$$\text{Number of moles} = \frac{\text{mass}}{\text{molar mass}}$$

$$n = \frac{19\text{ mg}}{400\text{ g/mol}} = \frac{19\times10^{-3}\text{g}}{400\text{ g/mol}} = 0.0000475\text{ moles} = 4.75\times10^{-5}\text{ moles}$$

In 1 mole of Yb_2O_3 there is 352 grams of ytterbium

In 4.75×10^{-5} moles of Yb_2O_3 (19 mg) irradiated sample the mass of ytterbium will be:

Mass of ytterbium = Mass of ytterbium in 1 mole Yb_2O_3 × number of moles of irradiated sample Yb_2O_3

Mass of ytterbium = 352 g/mol × 4.75×10^{-5} moles = 0.01672 grams = 16.7 mg

Calculating concentration of Ytterbium obtained from irradiation of (Yb_2O_3).

Data obtained

Mass of ytterbium obtained = 16.7 mg

Volume of acid added = 10 ml

We define concentration as:

$$\text{concentration} = \frac{\text{mass}}{\text{volume}} = \frac{16.7\text{ mg}}{10\text{ ml}} = 1.67\text{ mg/ml}$$

- **Lutetium-177**

Chemical reaction

$$Lu_2O_3 + HCl -> LuCl_3 + H_2O$$

Mass of Lutetium obtained from the sample (Lu_2O_3).

Molar mass of Lu_2O_3 = (2×177) + (3×16) = 402 g/mol

Mass of Lutetium in 1 mole of the sample (Lu_2O_3) = (2×177) =354g

Then mass of Lutetium in 11.6 mg Lu_2O_3 sample will be:

$$\text{Number of moles} = \frac{\text{mass}}{\text{molar mass}}$$

$$n = \frac{11.6\text{ mg}}{402\text{ g/mol}} = \frac{11.6\times10^{-3}\text{g}}{402\text{ g/mol}} = 0.000028855\text{ moles} = 2.89\times10^{-5}\text{ moles}$$

In 1 mole of Lu_2O_3 there is 354 grams of Lutetium

In 2.89×10^{-5} moles of Lu_2O_3 (11.6 mg) irradiated sample the mass of Lutetium will be:

Mass of Lutetium = Mass of Lutetium in 1 mole Lu_2O_3 × number of moles of irradiated sample Lu_2O_3

Mass of Lutetium = 354 g/mol × 2.89×10^{-5} moles = 0.0102306 grams =10.2 mg

Calculating concentration of Lutetium obtained from irradiation of (Lu_2O_3).

Data obtained

Mass of Lutetium obtained = 10.2 mg

Volume of acid added = 10 mL

We define concentration as:

$$\text{concentration} = \frac{\text{mass}}{\text{volume}} = \frac{10.2\text{ mg}}{10\text{ mL}} = 1.02\text{ mg/ml}$$

Preparation of Natural Samples

Concentration of Ytterbium in 19.0 mg Yb_2O_3 = 1.67 mg/ml, implying that there are 1.67 mg of Ytterbium per unit volume. If volume is reduced to 100 µl then the equivalent mass would be 0.167 mg Yb as shown below:

1 ml → 1.67 mg

100 µl → x

X = 0.167 mg (100 µl = 0.167 mg)

Concentration of Lutetium in 11.6 mg Lu_2O_3 = 1.02 mg/ml, implying that there are 1.02 mg of Lutetium per unit volume.

If volume is reduced to 100 µl then the equivalent mass would be 0.102 mg Lutetium as shown below:

1 ml → 1.02 mg

100 µl → x

X = 0.102 mg (100 µl = 0.102 mg and 10 µl = 0.0102 mg)

Therefore, 1 ml → 1.67 mg (Yb) + 98.33 mg (Lu). (Note that the ratio of Lutetium to Ytterbium should be 1:10)

If the mass of Ytterbium in the sample is 0.833 mg then the mass of Yb_2O_3 should be 0.95 mg. See calculations below:

0.833 mg (Yb) → 352 (Yb) g

X → 400 (Yb_2O_3) g

$$X = 0.95\ mg\ (Yb_2O_3)$$

Total mass of Ytterbium

Measured the mass of natural sample (Yb_2O_3) on an electronic beam balance and it was 0.81 mg.

Mass of ytterbium in 0.81 mg natural sample (Yb_2O_3):

$$0.81mg\ (Yb_2O_3) \times 0.833mg\ (Yb) = 0.675\ mg\ (Yb)$$

The summation of the weight of Lutetium in an irradiated sample (Yb_2O_3) and the weight of Lutetium in a natural sample should equal the combined weight of Lutetium (Yb_2O_3).

$$Mass(Yb)_{total} = 0.67\ mg + 0.167\ mg = 0.842\ mg$$

Volume of Lutetium (tracer) to be added

Volume of Lutetium equivalent to 0.0842 mg will be:

10 µl → 0.0102 mg (Lu)

X → 0.0842 mg (Lu)

X = 82.549 µl = 83 µl (Lu-Tracer)

Measure Capacity of Ion Exchange Resins

To evaluate and compare ion exchange capacity, two types of resins were used: one that was not irradiated and the other that was irradiated. For one week, the resin was exposed to gamma radiation. Capacity of ion exchange resins was determined using the equation below:

$$Capacity = \frac{NaOH(Inital) - NaOH(final)}{m_{resin}} \quad [15]$$

$$Capacity = \frac{V*C(NaOH) - \frac{V}{v}*V(HCl)*C(HCl)}{m_{resin}} \left[\frac{Meq}{g}\right] \quad [16]$$

The findings obtained and the values of the quantities used to determine the capacity of ion exchange resins are listed in Table 8.

Sample Calculations

Un-irradiated resins

$$\text{Capacity} = \frac{(100 \times 0.085) - \frac{100}{10}(6.1 \times 0.1)}{1.008}$$

$$= 2.38\ \text{Meq/g}$$

Irradiated resins

$$\text{Capacity} = \frac{(100 \times 0.085) - \frac{100}{10}(6.0 \times 0.1)}{1.081}$$

$$= 2.31 \frac{\text{Meq}}{\text{g}}$$

Table 12: Capacity of irradiated and un-irradiated ion exchange resins

V(HCL) ml	V(NaOH) Ml	V(NaOH) Ml	IEC Meq/g(mL	Resin
6.1	10	100	2.38	un-irradiated
6.0			2.31	Irradiated

Table 12, shows that the difference in capacity between irradiated and non-irradiated ion exchange resins is insignificant, indicating that gamma radiation may have had little or no effect on irradiated resins.

Feasibility or Superiority of Chromatographic Method

According to theory, un-irradiated ion exchange resins usually have a larger capacity because the ion exchange sites are whole and operational. Strong base anion resins can have a capacity of 1.0 to 3.5 Meq/mL, while strong acid cation resins can have a capacity of 1.5 to 5 Meq/mL [28, 39]. Conversely, ion exchange resins exposed to radiation may see a decrease in capacity as a result of the radiation-induced disintegration of ion

exchange sites. Depending on the radiation dose and kind, a capacity decline of 10–30% is typical, though the exact amount can vary [39].

In this article, the experimental measure capacity for Un-irradiated and irradiated Ion Exchange Resins were found to be 2.38 Meq/g(mL) and 2.31 Meq/g(mL) respectively , which is within the given range of theoretical results since Dowex 50WX8 Resins used was strong acid cation resins. This clearly indicates that the Resins used were well prepared and did not loss hydrophobicity during the process of preparation could successfully separate Lutetium and Ytterbium by Chromatographic method [3]. The Resins lost 2.9% of its original strong-acid capacity when exposed to dose of $2.74 \times 10^3 Gray$ while on the other hand, theoretically, resins lose 7 % of its original strong-acid capacity when exposed to dose of 6.1×10^7 rad or range of 10^5 Gy [3, 11]. Hence proving the superiority of this method since dose of Enriched natural Lu_2O_3 and Yb_2O_3 is low and has little effect on Dowex 50WX8 Resins and possess less danger on researcher carrying out this separation technique [11]. High dose rates of Enriched natural Lu_2O_3 and Yb_2O_3 may result in strong acid cation resin having small measure capacity and limited ability to exchange ions. This can lead to reduced efficiency and you need to regenerate the Resin more frequently, which can increase operational costs and downtime [47].

DISCUSSION

Degree of Separation

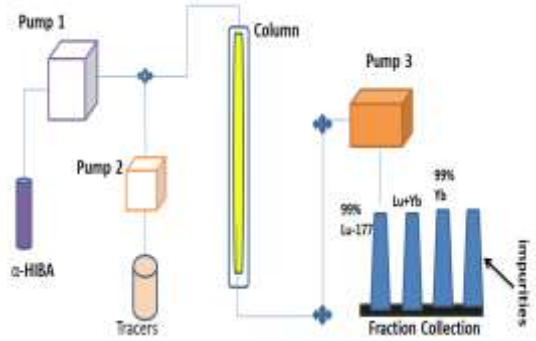

Figure 12: Schematic separation process

Pump 1 delivers alpha hydroxybutyric acid (α-HIBA) to the column while pump 2 pump tracers to the column at a speed of 0.5 mL/min. Tracers comprises of Ytterbium and Lutetium radioactive which were obtained after irradiation of natural enriched Ytterbium (III) oxide and Lutetium (III) oxide. Use 100 mg of natural Lutetium (III) oxide and Ytterbium (III) oxide together with tracers to obtain pure Lutetium and Ytterbium. Elution takes place in the column. Pump 3 supplies the eloquent to the right-hand test tubes. Impurities collect in a separate test tube and 99 % of ^{177}Lu and ^{177}Yb is obtained. The eloquent obtained in several test tubes can be analyzed using the **germanium detector**. Plot a graph of Lutetium and Ytterbium counts against number of test tubes in order to obtain Lutetium and Ytterbium peaks as shown in (figure 13). Then initial counts of Lutetium and Ytterbium were found to be 49688 and 88115 respectively.

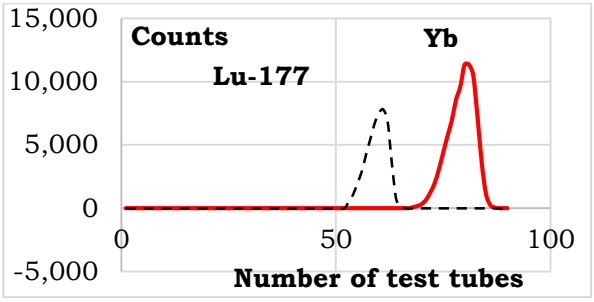

Figure 13: Yb and Lu peaks after separation

The degree of separation between any two peaks, A and B, can be expressed as the resolution of the peaks. This is defined as the difference between the two retention times divided by their average peak width.

$$R_S = \frac{X_{max\_peak2} - X_{max\_peak1}}{FWHM_{peak1} + FWHM_{peak2}} = \frac{19.5}{14.5} = 1.34$$

As, you can see Rs>1 therefore the two peaks were completely separated.

Separation Efficiencies using Different methods

Here is a table comparing the separation efficiency of Lutetium-177 (Lu-177) using chromatographic and other methods.

***Table 11**. Comparison table of separation efficiencies using different methods*

Method	Separation Efficiency (%)	Degree of Separation (Rs)
Chromatography (Ion Exchange)	95-99	High (1 - 4.9)
Solvent Extraction	85-90	Moderate
Electrochemical Separation	90-95	Moderate
Precipitation	80-85	Low

For Lu-177, the above table gives a brief summary of how various techniques compare in terms of separation efficiency. For this research, the separation efficiency and degree of separation of Lu-177 were 99 % and 1.34 respectively. Therefore, Chromatographic method can completely separate Lu-177 and achieve high purity and specific activity, making it suitable for medical applications.

Scalability of Chromatographic Method of Production of Lu-177

One important factor in the commercial use of chromatographic method for producing Lutetium-177 (^{177}Lu) is their scalability [56]. Today reactor neutrons are now used to irradiate isotopically enriched ^{176}Lu or ^{176}Yb, and the irradiated targets are then processed radiochemically to produce ^{177}Lu [38].
Here are some of the key points to consider for scalability of this technique:

- **Reactor and Radiochemical Processes**: For large-scale manufacturing, new facilities must be built or existing ones must be upgraded. Reactor and radiochemical processes both need to be significantly improved [10].
- **Quality Control:** It is crucial to set control criteria and guarantee product quality. The essential quality control inspection methodology has been created and validated [10].
- **Market Demand:** The market for radiopharmaceuticals based on ^{177}Lu is expanding, particularly for the treatment of neuroendocrine and prostate cancers. It needs scalable and effective production techniques to meet this demand [10].

Impact of Gamma Radiation on Resin Performance

Gamma radiation can have a big impact on resin performance, usually in a positive way. Here are a few significant effects:

- **Crosslinking**: Resins can undergo crosslinking when exposed to gamma radiation, which increases their chemical resistance, mechanical strength, and thermal stability [59].
- **Degradation**: Excessive amounts of gamma radiation can break down the resin, reducing its mechanical qualities and perhaps making it brittle [3].
- **Surface Modification:** The surface characteristics of resins can be changed by gamma radiation, which enhances printability, wettability, and adherence [11].
- **Thermal Conductivity**: The ability of gamma radiation to affect resin composites' thermal conductivity is significant for applications that call for effective heat dissipation [3, 11].

Because of these effects, gamma radiation can be used to customize resin characteristics for high-performance uses in the automotive, aerospace, and nuclear medicine.

CONCLUSION AND RECOMENDATIONS

The main goal of this article was to analyze optimized chromatographic production of high-purity ^{177}Lu radionuclide at IRT-T research reactor for Nuclear Medicine applications. The separation efficiency and degree of separation of Lu-177 were 99 % and

1.34 respectively, clearly demonstrating the ability of Chromatographic method to completely separate Lu-177 and achieve high purity and specific activity, making it suitable for medical applications such as treatment of prostate cancer and neuroendocrine tumors. Lu-177's purity is crucial to guaranteeing safe, reliable, and successful cancer treatment results.

Using this technique, resins (Dowex-50-WX8) lost approximately 2.9% of its original strong-acid capacity when exposed to dose of $2.74 \times 10^3 Gray$.This lead to increased efficiency and reduced operational costs and downtime. The average absorbed dose due to gamma radiation was found to be 2.74 kGy when activity was 1181.9 GBq, making this technique less dangerous to the researcher who may wish to carry out this separation technique in a Nuclear Reactor.

In the future, it will be important to account for the effects of beta radiations on ion exchange resins, as well as conducting a separation technique using cementation method with a high sample activity. In addition, researchers may consider testing other Resins such as OASIS-HDEHP and Diglycolamide (DGA) and compare purity and activity of obtained Lu-177. Furthermore, others may address radioactive waste disposal challenges.

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