Radiochemical Separation of $^{161}$Tb from Gd/Tb Matrix Using Ln Resin Column

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ABSTRACT

Terbium-$^{161}$ (161Tb) is a potential radiolanthanide due to its favorable properties for treatment small size of cancer. Preliminary study on radiochemical separation of $^{161}$Tb from Gd/Tb matrix using Ln resin column based on extraction chromatography method has been carried out. $^{161}$Tb radionuclide was produced by irradiation of natural Gd$_2$O$_3$ target through neutron thermal bombardment at G.A. Siwabessy Multipurpose Reactor. Fractions eluted from the column containing Gd/Tb matrix of irradiated natural Gd$_2$O$_3$ target were identified and quantified using a γ-rays spectrometer with HP-Ge detector coupled to a multichannel analyzer. The results show that the optimum condition on $^{161}$Tb separation from irradiated Gd$_2$O$_3$ target with radionuclide purity 99.27 ± 0.30% was obtained using HNO$_3$ solution with concentration of 0.8 and 3 N to separate gadolinium and terbium isotope, respectively. The yield of $^{161}$Tb obtained from the separation was 61.21 ± 2.05% and Gd recovered was 97.15 ± 2.23%. Based on this experiment, $^{161}$Tb has been separated from irradiated natural gadolinium oxide target with high radionuclide purity.

Keywords: radiolanthanide; terbium-161; carrier free; therapy; cancer

INTRODUCTION

Cancer is one of the leading causes of death worldwide [1-2]. World Health Organization (WHO) declared that cancer patients are increasing every year and two-thirds of them are come from developing countries, including Indonesia [3]. Endoradiotherapy or targeted radionuclide therapy is an evolving and promising modality of cancer treatment [4]. The killing of cancer cells is achieved using biological vectors and appropriate radionuclides [4-6]. Antibodies and antibody fragments as well as peptides are used as tracer molecules [5,7]. While, the radioisotopes are particle emitter that are able to deposit a high amount of energy in small volume via a high linear energy transfer (LET) [8,9]. Especially β-, α, and also Auger electron emitters are used or considered for therapeutic applications [9]. The radiolanthanides are particularly attractive and advantageous in the development of radiotherapeutic agents because they have chemical similarity, but they have various nuclear properties [10]. Various radiolanthanides are routinely applied for therapeutic purposes. Currently, $^{90}$Y and $^{177}$Lu radionuclides are commercially available for medical applications [11]. $^{90}$Y is a high energy β emitter suitable for treatment of large tumors. It provides no γ-rays for visualization by a gamma camera in nuclear medicine. On the contrary, $^{177}$Lu is a low energy β

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emitter \((E_\beta\text{ average} = 0.140\text{ MeV}, T_{1/2} = 6.7\text{ days})\) with a measureable γ-rays (11%). Because of the lower mean energy of the β' particles and therefore shorter range, it is preferred for therapy of small tumors. Recent successfully endoradiotherapy treatment with \(^{90}\text{Y}\) or \(^{177}\text{Lu}\)-labelled peptides and antibodies has renewed a strong interest in the potential of particle emitting radiolanthanides.

The dosimetric evaluation of therapeutic efficiency of electron emitting radiolanthanides shows that \(^{161}\text{Tb}\) provides better energy transfer in small tumor than \(^{177}\text{Lu}\) because of the high conversion and Auger electrons [12-13]. Accordingly, \(^{161}\text{Tb}\) may be useful as a complement to \(^{177}\text{Lu}\) due to its good tumor-to-normal-tissue mean absorbed dose ratios (TNDs) profile [11]. Certainly, in spite of promising clinical studies a further optimization of the treatment is necessary, so alternative radionuclides that can intensify therapeutic effect of radiopharmaceuticals is required [9]. The low energy β' emitter \(^{161}\text{Tb}\) (\(E_\beta\text{ average} = 0.150\text{ MeV}\)) with 6.9 days half-life emits only few low-energy photons which are useful for imaging purposes using a gamma camera [14]. Beside that, \(^{161}\text{Tb}\) also emits conversion and Auger electrons, so a better therapeutic effect can be expected in comparison to \(^{177}\text{Lu}\) as the currently used radionuclides [9,15]. Carrier free \(^{161}\text{Tb}\) can be produced by neutron irradiation of \(^{160}\text{Gd}\) (\(\sigma = 1.5\text{ barn}\)). It is accumulated from β' decay of the short-lived intermediate \(^{161}\text{Gd}\) via the \(^{160}\text{Gd}\) \((n,\gamma)\) \(^{161}\text{Gd}\) nuclear reaction (see reaction 1) and must be isolated from irradiated target chemically [9].

\[
^{160}\text{Gd} (n,\gamma)^{161}\text{Gd} \rightarrow^{161}\text{Tb} \rightarrow^{161}\text{Dy} \text{ (stable)} \quad (1)
\]

Beside that, when natural Gd is irradiated, other \((n,\gamma)\) nuclear reactions are also taking place leading to the formation of the other radiolanthanides as radionuclidic impurities (as seen in Table 1) and they have to be isolated from \(^{161}\text{Tb}\) chemically [7,16]. The separation of two neighboring lanthanides is, however, challenging because of their high chemical similarity. In the previous study reported that \(^{161}\text{Tb}\) can be separated from irradiated of enriched Gd target in nitrate form (Gd(NO\(_3\))\(_3\)) compound using 2 g of Ln resin and HNO\(_3\) eluen with concentration of 0.8 and 3 N to separate gadolinium and terbium, respectively [17]. The radionuclide purity of \(^{161}\text{Tb}\) obtained was greater than 99.99% [17].

The aim of the present study was to investigate the radiochemical separation of \(^{161}\text{Tb}\) from irradiated natural Gd target in oxide form (Gd\(_2\)O\(_3\)) compound. The separation based on extraction chromatography method which is a combination of column chromatography and solvent extraction using Ln (lanthanide) resin as a preliminary study on production of \(^{161}\text{Tb}\) radioisotope for cancer therapy. Radionuclide identification was ascertained from a γ-rays spectrometry with HP-Ge detector coupled with a multichannel analyzer.

**EXPERIMENTAL SECTION**

**Materials**

Natural abundance of \(^{160}\text{Gd}\) isotope target in oxide form (Gd\(_2\)O\(_3\)) was obtained from Aldrich. Ln resin (50–100 μm) was purchased from Eichrom Industries. Hydrochloric acid (p.a) and nitric acid (p.a) were ordered from E. Merck Germany. Sterile double-distilled water was obtained from IPHA Laboratory.

**Instrumentation**

G.A. Siwabessy Multipurpose Reactor was used in this experiment for irradiation of natural gadolinium oxide target in central irradiation position (CIP) at a thermal neutron flux of \(~10^{14}\text{ n.cm}^-2\text{.sec}^-1\). This nuclear reactor is located in Puspiptek Serpong, Indonesia. Dose calibrator (CRC-55TR) from Capintec was used for measurement the radioactivity of \(^{161}\text{Tb}\) solution that was obtained from dissolution of irradiated target. The measurement should be performed using nuclide button as well as calibration setting number of \(^{161}\text{Tb}\). Radionuclide identification as well as radioactivity measurement was ascertained by high resolution γ-ray spectrometer using a HP-Ge detector coupled to a multichannel analyzer system (Canberra). The energy calibration of the detector was performed regularly by a multielement γ-ray standard source covering the energy range from 59.5 keV (E\(_\gamma\) of \(^{241}\text{Am}\)) to 1332.5 (E\(_\gamma\) of \(^{60}\text{Co}\)). Samples were measured at a distance of 1 to 25 cm from the detector depending on the radioactivity of samples.

**Procedure**

**Irradiation of Gd\(_2\)O\(_3\) target**

A weighed amount (100 mg, \(n = 5\)) of natural abundance \(^{160}\text{Gd}\) isotope target in oxide form (Gd\(_2\)O\(_3\)) was sealed in a quartz ampoule under vacuum and welded into aluminum inner capsules. Sealed inner capsule was tested for leak tightness. After the leak test passes, aluminum inner capsules were inserted into aluminum outer capsule. The target material was irradiated for ± 4 days in central irradiation position (CIP) of G.A. Siwabessy Multipurpose Reactor at a thermal neutron flux of \(~10^{14}\text{ n.cm}^-2\text{.sec}^-1\). Samples were measured at a distance of 1 to 25 cm from the detector depending on the radioactivity of samples.

**Dissolution of irradiated target material Gd\(_2\)O\(_3\)**

Following irradiation (after cooling for 1 to 4 weeks), irradiated target material (\(^{161}\text{Gd}\(_2\)O\(_3\)) was dissolved in 5 mL of 2 N HCl solution by gentle...
warming inside the glove box facility. Dissolution of irradiated target material was done on the heater and magnetic stirrer plate until completely dissolved. The resultant solution was evaporated to near dryness and reconstituted with 1 to 2 mL of sterile double-distilled water.

**Preparation of extraction chromatography column**

A weighed amount (1 g) of Ln resin was inserted into a beaker and soaked in 0.1 N HNO₃ solution. Pretreated Ln resin was inserted carefully into the glass column that has been fitted glasswool support at the bottom of the column. Finally, on the top of Ln resin was also covered with glasswool. Ln resin was equilibrated with 0.1 N HNO₃ solution for 2 h. Irradiated target dissolved in 2 N HCl solution containing 3–5 mCi of ¹⁶¹Tb was loaded into the column. Radioactivity of this solution was measured using dose calibrator, previously. Radionuclide purity as well as radioactivity of this solution was ascertained by a γ-rays spectrometer using a HP-Ge detector coupled to a multichannel analyzer system. The column was kept submerged in 0.1 N HNO₃ solution over night.

**Radiochemical separation of ¹⁶¹Tb from irradiated target material**

Radiochemical separation of ¹⁶¹Tb from irradiated Gd₂O₃ target containing Gd/Tb matrix was performed using extraction chromatography method with Ln resin as a stationary phase and nitric acid solution as a mobile phase with different concentrations according to reported procedures previously [17-18]. Nitric acid (HNO₃) solution with a lower and higher concentration respectively has been used to separate gadolinium and terbium. However, in the previous study did not report the volume of eluent used on each separation of those isotopes. In this work, various combinations of HNO₃ concentrations were used to obtain the optimum condition on separation. The Ln column was eluted with each 50 mL of 0.1–3 N; 0.3–3.5 N; 0.8–3 N; 1.5–3 N; 2–3 N; and 2.5–3 N HNO₃ solution. Each 1 mL of fraction was collected. The purity of radionuclide as well as radioactivity in fractions eluted was ascertained by a γ-rays spectrometer using a HP-Ge detector coupled to a multichannel analyzer system.

**RESULT AND DISCUSSION**

**Activity of ¹⁶¹Tb from Irradiated Natural Gd₂O₃ Target**

Naturally occurring gadolinium (Gd) is composed of six stable isotopes i.e. ¹⁵⁴Gd, ¹⁵⁵Gd, ¹⁵⁶Gd, ¹⁵⁷Gd, ¹⁵⁸Gd, ¹⁵⁹Gd and one radioisotope ¹⁶²Gd with ¹⁵⁵Gd being the most abundant (24.87%) [16]. Their natural abundance, thermal neutron cross section and (n,γ) activation product are shown in Table 1.

The ¹⁶¹Tb containing Gd/Tb matrix has been produced from irradiated natural Gd₂O₃ target in central irradiation position (CIP) of RSG-G.A. Siwabessy at a thermal neutron flux of ~10¹⁴ n.cm⁻².sec⁻¹. The ¹⁶¹Tb activity during irradiation of natural Gd₂O₃ target is summarized in Table 2. The activity up to 105.93 mCi of ¹⁶¹Tb was produced for 4 days irradiation of 100 mg natural Gd₂O₃ targets at the end of irradiation (EOI). The activity of ¹⁶¹Tb formed from irradiation of 100 mg of natural Gd₂O₃ target for the same irradiation time were obtained different due to differences in neutron flux in the reactor during irradiation.

The scheme of (n,γ) nuclear reactions are taking place from irradiation of natural Gd target can be seen in Fig. 1. Carrier free ¹⁶¹Tb can be produced from activation of ¹⁵⁵Gd and ¹⁵⁷Gd isotopes present in natural Gd target. However, the activity of ¹⁶¹Tb produced is low because natural ¹⁵⁵Gd isotope only has a natural abundance of 21.90% and a thermal neutron cross section (σ) of 1.5 barn. Therefore, highly enriched target material is required to obtain ¹⁶¹Tb with high specific activity [9].

The presence of significant amounts of ¹⁵⁵Gd (14.73% natural abundance) and ¹⁵⁷Gd (15.68% natural abundance) in the target might result in self-shielding effects and a consequent decrease in the activation rate, due to the high cross-section of 61,000 barn and 254,000 barn, respectively [9].

**Table 1.** The natural isotopes of gadolinium and their (n,γ) activation product [7,16]

<table>
<thead>
<tr>
<th>Isotope</th>
<th>% Abundance</th>
<th>Thermal neutron cross section (barn)</th>
<th>Activation product</th>
</tr>
</thead>
<tbody>
<tr>
<td>¹⁵⁴Gd</td>
<td>0.20</td>
<td>10</td>
<td>¹⁵⁵Gd 241.6 d</td>
</tr>
<tr>
<td>¹⁵⁴Gd</td>
<td>2.15</td>
<td>80</td>
<td>Stable</td>
</tr>
<tr>
<td>¹⁵⁶Gd</td>
<td>14.73</td>
<td>61000</td>
<td>Stable</td>
</tr>
<tr>
<td>¹⁵⁷Gd</td>
<td>20.47</td>
<td>2</td>
<td>Stable</td>
</tr>
<tr>
<td>¹⁵⁸Gd</td>
<td>15.68</td>
<td>254000</td>
<td>Stable</td>
</tr>
<tr>
<td>¹⁵⁹Gd</td>
<td>24.87</td>
<td>2.3</td>
<td>¹⁵⁵Gd 18.6 h</td>
</tr>
<tr>
<td>¹⁶¹Gd</td>
<td>21.90</td>
<td>1.5</td>
<td>¹⁶¹Tb 3.7 m</td>
</tr>
<tr>
<td>¹⁶¹Tb</td>
<td>241.6</td>
<td>6.91</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2.** The activity of ¹⁶¹Tb formed during the irradiation of 100 mg of natural Gd₂O₃ target in central irradiation position (CIP) of RSG-G.A. Siwabessy at a thermal neutron flux of ~10¹⁴ n.cm⁻².sec⁻¹.

<table>
<thead>
<tr>
<th>No</th>
<th>Irradiation time (days)</th>
<th>Mass of target (mg)</th>
<th>Activity of ¹⁶¹Tb at EOI (mCi)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.1</td>
<td>100</td>
<td>57.56</td>
</tr>
<tr>
<td>2</td>
<td>4.1</td>
<td>100</td>
<td>83.50</td>
</tr>
<tr>
<td>3</td>
<td>4.5</td>
<td>100</td>
<td>105.26</td>
</tr>
<tr>
<td>4</td>
<td>4.5</td>
<td>100</td>
<td>75.49</td>
</tr>
<tr>
<td>5</td>
<td>4.5</td>
<td>100</td>
<td>105.93</td>
</tr>
</tbody>
</table>
Neutron activation of with a higher concentrations of \(^{158}\text{Gd}\) and hence as soon as post irradiation its activity will allow completing decay. A \(\gamma\)-rays spectrometry analysis of irradiated natural Gd target results in the accumulation of \(^{158}\text{Gd}\) (stable) in the target as impurity leading to the accumulation of \(^{158}\text{Tb}\) produced at the end of irradiation (EOI) via the \(^{158}\text{Gd}\) (n,\(\gamma\)) \(^{158}\text{Gd}\) nuclear reaction. It therefore decreases the specific activity of \(^{161}\text{Tb}\) technically achievable [9]. The presence of \(^{158}\text{Gd}\) in natural Gd target has to be taken into consideration since with a cross section 254,000 barn; this isotope is already transformed quantitatively into \(^{158}\text{Gd}\) at the start of irradiation. The original amount of \(^{158}\text{Gd}\) can be taken as sum of \(^{158}\text{Gd}\) and \(^{159}\text{Gd}\) [9]. \(^{159}\text{Gd}\) is a short-lived (\(T_{1/2} = 18.48\) h) and hence is not a major radionuclidic impurity in \(^{161}\text{Tb}\) due to \(\gamma\)-rays spectrometry analysis. Hence, 7 days cooling will allow the complete decay of \(^{159}\text{Gd}\) activity present in irradiated target.

The presence of \(^{158}\text{Gd}\) (stable) in the original target material as impurity leads to the accumulation of the relatively long-lived beta and photon emitter \(^{160}\text{Gd}\) (T\(_{1/2}\) = 72.3 d) via the \(^{158}\text{Gd}\) (n,\(\gamma\)) \(^{158}\text{Gd}\) reaction [9]. The accumulation of \(^{158}\text{Gd}\) additionally impacts on the content of \(^{160}\text{Gd}\) in the system. Nevertheless, the irradiation for 4 days at the \(10^{14}\) n\(\text{cm}^{-2}\) sec\(^{-1}\) neutron flux and target composition described above would result in only \(~0.02\) % of \(^{160}\text{Gd}\) activity in \(^{161}\text{Tb}\) as shown in Fig. 2. However, cooling time increases the ratio of \(^{160}\text{Gd}\) to \(^{161}\text{Tb}\) due to its significantly longer half-life.

Radiochemical Separation of \(^{161}\text{Tb}\) from Irradiated Natural Gd\(_2\)O\(_3\) Target

Radiochemical separation of \(^{161}\text{Tb}\) from irradiated Gd\(_2\)O\(_3\) target containing Gd/Tb matrix has been studied by extraction chromatography method using Ln resin and nitric acid solution with different concentrations according to reported procedures previously [17-18]. The Ln resin is comprised of a solution of di(2-ethylhexyl)orthophosphoric acid (HDEHP) (40% by weight) loaded onto the inert polymeric absorbent (60% by weight) Amberchrom™ CG-71 [17]. In this study, various combination of HNO\(_3\) concentrations of 0.1–3 N; 0.3–3.5 N; 0.8–3 N; 1.5–3 N; 2–3 N; and 2.5–3 N were used to obtain optimum condition on separation. Nitric acid (HNO\(_3\)) solution with a lower concentration was used to separate gadolinium isotope, whereas HNO\(_3\) solution with a higher concentration was used to separate terbium. The effect of HNO\(_3\) concentrations as eluent on \(^{161}\text{Tb}\) separation is shown in Fig. 3.

In the previous study reported that \(^{161}\text{Tb}\) can be separated from irradiated enriched Gd target in nitrate form (Gd(NO\(_3\))\(_3\)) using 2 g of Ln resin and HNO\(_3\) eluent with combination concentration of 0.8 and 3 N to

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**Radionuclide Purity of Irradiated Natural Gd\(_2\)O\(_3\) Target**

When natural Gd is irradiated, other (n,\(\gamma\)) nuclear reactions are also taking place leading to the formation of radionuclidic impurities such as \(^{152}\text{Gd}\), \(^{153}\text{Gd}\), and \(^{161}\text{Gd}\). The various nuclear reactions product are shown in Table 1 and Fig. 1. \(^{160}\text{Gd}\) is a parent radionuclide with a short-lived (T\(_{1/2}\) = 3.66 m) and hence as soon as post irradiation its activity will allow completing decay. A \(\gamma\)-rays spectrometry analysis of irradiated natural Gd\(_2\)O\(_3\) target after cooling for 1 to 4 weeks was obtained two radionuclides as impurities in \(^{161}\text{Gd}\) i.e. \(^{153}\text{Gd}\) and \(^{160}\text{Gd}\). The quantity of \(^{155}\text{Gd}\) and \(^{161}\text{Gd}\) produced at the end of irradiation (EOI) are shown in Fig. 2.

Percentage of \(^{155}\text{Gd}\), \(^{160}\text{Tb}\) and \(^{161}\text{Tb}\) radionuclide from five times of irradiation for 4 days at the \(10^{14}\) n\(\text{cm}^{-2}\) sec\(^{-1}\) neutron flux as shown in Fig. 2, were found to be 11.02 ± 1.48%, 0.02 ± 0.006% and 88.96 ± 1.49%, respectively. The results showed that \(^{153}\text{Gd}\) is a major impurity in irradiated natural Gd\(_2\)O\(_3\) target. \(^{155}\text{Gd}\) is produced from irradiated \(^{152}\text{Gd}\) present in the natural Gd\(_2\)O\(_3\) target material. The \(^{155}\text{Gd}\) has long-lived (T\(_{1/2}\) = 241.6 d) and becomes a prominent radionuclidic impurity in the final product [9].

The presence of \(^{158}\text{Gd}\) in natural Gd target has to be taken into consideration since with a cross section 254,000 barn; this isotope is already transformed quantitatively into \(^{158}\text{Gd}\) at the start of irradiation. The original amount of \(^{158}\text{Gd}\) can be taken as sum of \(^{158}\text{Gd}\) and \(^{159}\text{Gd}\) [9]. \(^{159}\text{Gd}\) is a short-lived (\(T_{1/2} = 18.48\) h) and hence is not a major radionuclidic impurity in \(^{161}\text{Tb}\) due to \(\gamma\)-rays spectrometry analysis. Hence, 7 days cooling will allow the complete decay of \(^{159}\text{Gd}\) activity present in irradiated target.

The presence of \(^{158}\text{Gd}\) (stable) in the original target material as impurity leads to the accumulation of the relatively long-lived beta and photon emitter \(^{160}\text{Gd}\) (T\(_{1/2}\) = 72.3 d) via the \(^{158}\text{Gd}\) (n,\(\gamma\)) \(^{158}\text{Gd}\) reaction [9]. The accumulation of \(^{158}\text{Gd}\) additionally impacts on the content of \(^{160}\text{Gd}\) in the system. Nevertheless, the irradiation for 4 days at the \(10^{14}\) n\(\text{cm}^{-2}\) sec\(^{-1}\) neutron flux and target composition described above would result in only \(~0.02\) % of \(^{160}\text{Gd}\) activity in \(^{161}\text{Tb}\) as shown in Fig. 2. However, cooling time increases the ratio of \(^{160}\text{Gd}\) to \(^{161}\text{Tb}\) due to its significantly longer half-life.
The effect of HNO$_3$ concentration as eluent on $^{161}$Tb separation

**Table 3.** The yield of $^{161}$Tb eluted from the column using various combination of HNO$_3$ concentration

<table>
<thead>
<tr>
<th>The combination of HNO$_3$ concentration (N)</th>
<th>Yield of $^{161}$Tb eluted (%)</th>
<th>Gd recovered (%)</th>
<th>Radionuclide purity of $^{161}$Tb (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1; 3.0</td>
<td>71.68 ± 1.69</td>
<td>57.99 ± 3.31</td>
<td>98.32 ± 0.40</td>
</tr>
<tr>
<td>0.3; 3.5</td>
<td>59.27 ± 4.18</td>
<td>70.49 ± 2.53</td>
<td>99.52 ± 0.12</td>
</tr>
<tr>
<td>0.8; 3.0</td>
<td>61.21 ± 2.05</td>
<td>97.15 ± 2.23</td>
<td>99.27 ± 0.30</td>
</tr>
<tr>
<td>1.5; 3.0</td>
<td>44.41 ± 1.15</td>
<td>21.97 ± 5.21</td>
<td>99.21 ± 0.10</td>
</tr>
<tr>
<td>2.0; 3.0</td>
<td>97.76 ± 1.02</td>
<td>17.37 ± 1.54</td>
<td>94.48 ± 0.64</td>
</tr>
<tr>
<td>2.5; 3.0</td>
<td>85.71 ± 5.34</td>
<td>9.32 ± 2.69</td>
<td>88.38 ± 1.45</td>
</tr>
</tbody>
</table>

separate gadolinium and terbium, respectively [17]. The radionuclide purity of $^{161}$Tb obtained was greater than 99.99% [17]. In this work as seen in Fig. 3, the separation of $^{161}$Tb with high radionuclide purity (greater than 99%) from irradiated natural Gd target in oxide form (Gd$_2$O$_3$) was also obtained using 1 g of Ln resin and HNO$_3$ eluent with combination concentrations of 0.8–3 N as well as for 0.3–3.5 N and 1.5–3 N. The radionuclide purities of $^{161}$Tb obtained from those combination concentrations were not different significantly and greater than 99%. The results showed that $^{161}$Tb can be separated from irradiated natural Gd$_2$O$_3$ target with high radionuclide purity using 1 g of Ln resin. Furthermore, radionuclide purity of $^{161}$Tb decreased by increasing concentration of HNO$_3$ solution that was used to separate gadolinium isotope.

The yields of $^{161}$Tb eluted and Gd recovery that were obtained from the separation with various combinations of HNO$_3$ concentrations are summarized in Table 3. The yields of $^{161}$Tb obtained were still low. In the previous study reported that $^{161}$Tb can be separated from irradiated of enriched Gd target in nitrate form (Gd(NO$_3$)$_3$) using 2 g of Ln resin and HNO$_3$ eluent with concentration of 0.8–3N with the yield of 100% and Gd recovered of 100% [17]. In this work, the separation of $^{161}$Tb from irradiated natural Gd target in oxide form (Gd$_2$O$_3$) using 1 g of Ln resin and HNO$_3$ eluent with concentration of 0.8 and 3 N was obtained by separation of $^{161}$Tb and Gd recovered of 61.21 ± 2.05% and 97.15 ± 2.23%, respectively. The yield of $^{161}$Tb obtained was low due to the different in amount of resin and type of target used. However, in this work as seen in Table 3, the highest of $^{161}$Tb eluted and Gd recovered were obtained using 0.8 and 3 N HNO$_3$ eluent respectively with radionuclide purity of $^{161}$Tb greater than 99%. In the previous study has also been conducted separation of $^{161}$Tb from Gd/Tb matrix using ion exchange resin; however Gd recovered was not obtained successfully [19]. Gadolinium isotope need to be considered in the recovery in this work due to the high cost of enriched gadolinium target if it used on production of $^{161}$Tb radioisotope. Furthermore, this system is expressed as optimum conditions on separation of $^{161}$Tb from irradiated natural gadolinium oxide target.

Elution profile on separation of $^{161}$Tb from irradiated natural Gd$_2$O$_3$ target containing Gd/Tb matrix using 0.8 and 3 N HNO$_3$ eluent are shown in Fig. 4. Radionuclide of $^{153}$Gd eluted after 4 mL of fractions. The main radioactivity of $^{153}$Gd was obtained in the fraction at 5 to 13 mL with the total volume of 9 mL. While, $^{161}$Tb eluted after 52 mL of fraction. The main radioactivity of $^{161}$Tb was obtained in the fraction at 53 to 58 with the total volume of 6 mL. The result showed that $^{161}$Tb obtained has a little volume, so a high radioactive concentration of $^{161}$Tb will be achieved.

**CONCLUSION**

The $^{161}$Tb has been separated from irradiated natural gadolinium oxide (Gd$_2$O$_3$) target by extraction...
chromatography method using Ln resin as a stationary phase and nitric acid solution as a mobile phase with concentration of 0.8 and 3 N to separate gadolinium and terbium isotope respectively. The separated $^{161}\text{Tb}$ radioisotope was obtained with radionuclide purity was 99.27 ± 0.30% and the yield of $^{161}\text{Tb}$ eluted was 61.21 ± 2.05%. While Gd recovered was obtained of 97.15 ± 2.23%. Therefore, to obtain highly specific activity, yield, as well as radionuclide purity of $^{161}\text{Tb}$, further research is needed using enriched Gd$_2$O$_3$ target with $^{160}\text{Gd}$ enrichment.

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