

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

Azmairit Aziz^{1,*} and Widya Tania Artha²

¹Center for Nuclear Applied Science and Technology, National Nuclear Energy Agency
Jl. Tamansari 7, Bandung 40132, Indonesia

²Department of Chemistry, Faculty of Mathematics and Natural Sciences, Bandung Institute of Technology - ITB
Jl. Ganesha 10, Bandung 40132, Indonesia

Received January 28, 2016; Accepted May 12, 2016

ABSTRACT

Terbium-161 (^{161}Tb) 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_2O_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_2O_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_2O_3 target with radionuclide purity $99.27 \pm 0.30\%$ 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 $61.21 \pm 2.05\%$ and Gd recovered was $97.15 \pm 2.23\%$. 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

ABSTRAK

Terbium-161 (^{161}Tb) merupakan radiolantanida yang potensial untuk terapi kanker berukuran kecil. Studi awal pemisahan radiokimia ^{161}Tb dari matriks Gd/Tb telah dilakukan menggunakan kolom resin Ln berdasarkan metode kromatografi ekstraksi. Radionuklida ^{161}Tb dibuat melalui iradiasi bahan sasaran Gd_2O_3 alam dengan cara penembakan dengan neutron termal di Reaktor Serba Guna G.A. Siwabessy. Fraksi terelusi dari kolom yang mengandung matriks Gd/Tb hasil iradiasi bahan sasaran Gd_2O_3 alam diidentifikasi menggunakan alat spektrometry dengan detektor HP-Ge yang dilengkapi multichannel analyzer. Hasil ini menunjukkan bahwa kondisi optimum pemisahan ^{161}Tb dari hasil iradiasi bahan sasaran Gd_2O_3 alam diperoleh dengan kemurnian radionuklida sebesar $99,27 \pm 0,30\%$ menggunakan larutan HNO_3 dengan konsentrasi 0,8 dan 3 N masing-masing untuk memisahkan isotop gadolinium dan terbium. Hasil pemisahan diperoleh ^{161}Tb dengan yield sebesar $61,21 \pm 2,05\%$ dan Gd recovery sebesar $97,15 \pm 2,23\%$. Berdasarkan penelitian ini ^{161}Tb dapat dipisahkan dari hasil iradiasi bahan sasaran gadolinium oksida alam dengan kemurnian radionuklida yang tinggi.

Kata Kunci: radiolantanida; terbium-161; bebas pengemban; terapi; kanker

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

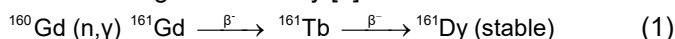
in small volume via a high linear energy transfer (LET) [8,9]. Especially β^- , α , and also Auger electron emitters are used or considered for therapeutic applications [9].

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^-

* Corresponding author. Tel : +62-81322068349
Email address : aaziz@batan.go.id

emitter ($E_{\beta^- \text{ average}} = 0.140$ MeV, $T_{1/2} = 6.7$ days) with a measurable 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}Y - or ^{177}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}Tb provides better energy transfer in small tumor than ^{177}Lu because of the high conversion and Auger electrons [12-13]. Accordingly, ^{161}Tb may be useful as a complement to ^{177}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}Tb ($E_{\beta^- \text{ average}} = 0.150$ 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}Tb also emits conversion and Auger electrons, so a better therapeutic effect can be expected in comparison to ^{177}Lu as the currently used radionuclides [9,15]. Carrier free ^{161}Tb can be produced by neutron irradiation of ^{160}Gd ($\sigma = 1.5$ barn). It is accumulated from β^- decay of the short-lived intermediate ^{161}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].



Beside that, when natural Gd is irradiated, other (n, γ) 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}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}Tb can be separated from irradiated of enriched Gd target in nitrate form ($\text{Gd}(\text{NO}_3)_3$ 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}Tb obtained was greater than 99.99% [17].

The aim of the present study was to investigate the radiochemical separation of ^{161}Tb from irradiated natural Gd target in oxide form (Gd_2O_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}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}Gd isotope target in oxide form (Gd_2O_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 $\sim 10^{14}$ n.cm⁻².sec⁻¹. This nuclear reactor is located in Puspitpek Serpong, Indonesia. Dose calibrator (CRC-55tR) from Capintec was used for measurement the radioactivity of ^{161}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}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_γ of ^{241}Am) to 1332.5 (E_γ of ^{60}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_2O_3 target

A weighed amount (100 mg, $n = 5$) of natural abundance ^{160}Gd isotope target in oxide form (Gd_2O_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 $\sim 10^{14}$ n.cm⁻².sec⁻¹.

Dissolution of irradiated target material Gd_2O_3

Following irradiation (after cooling for 1 to 4 weeks), irradiated target material ($^{161}\text{Gd}_2\text{O}_3$) 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. Pre-treated 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, ¹⁶⁰Gd and one radioisotope ¹⁵²Gd with ¹⁵⁸Gd being the most abundant (24.87%) [16]. Their natural abundance, thermal neutron cross section and (n,γ)

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

Isotope	% Abundance	Thermal neutron cross section (barn)	Activation product	Half-life
¹⁵² Gd	0.20	10	¹⁵³ Gd	241.6 d
¹⁵⁴ Gd	2.15	80	stable	-
¹⁵⁵ Gd	14.73	61000	stable	-
¹⁵⁶ Gd	20.47	2	stable	-
¹⁵⁷ Gd	15.68	254000	stable	-
¹⁵⁸ Gd	24.87	2.3	¹⁵⁹ Gd	18.6 h
¹⁶⁰ Gd	21.90	1.5	¹⁶¹ Gd	3.7 m
			¹⁶¹ Tb	6.91 d

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.

No	Irradiation time (days)	Mass of target (mg)	Activity of ¹⁶¹ Tb at EOI (mCi)
1	4.1	100	57.56
2	4.1	100	83.50
3	4.5	100	105.26
4	4.5	100	75.49
5	4.5	100	105.93

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 G.A. Siwabessy Multipurpose Reactor 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 ¹⁵⁸Gd and ¹⁶⁰Gd isotopes present in natural Gd target. However, the activity of ¹⁶¹Tb produced is low because natural ¹⁶⁰Gd 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]. The presence of the

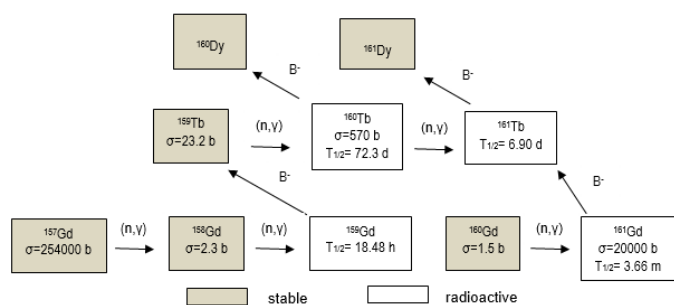


Fig 1. Neutron activation of ^{160}Gd target [9]

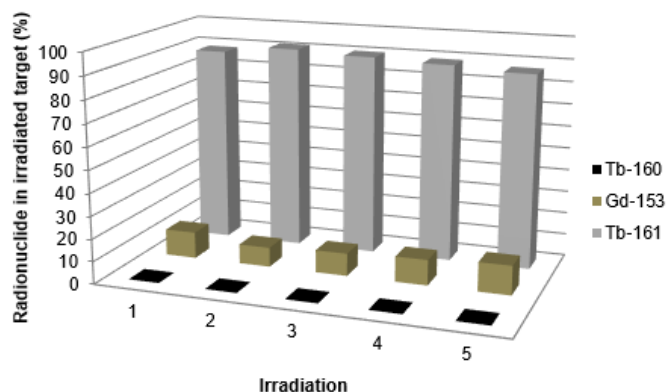


Fig 2. Percentage of radionuclide obtained from irradiated natural Gd_2O_3 target

stable isotope ^{158}Gd (24.87% natural abundance, $\sigma = 2.3$ barn) in the target results in the accumulation of stable ^{159}Tb during irradiation via the $^{158}\text{Gd} (n,\gamma) ^{159}\text{Gd}$ nuclear reaction. It therefore decreases the specific activity of ^{161}Tb technically achievable [9].

Radionuclide Purity of Irradiated Natural Gd_2O_3 Target

When natural Gd is irradiated, other (n,γ) nuclear reactions are also taking place leading to the formation of radionuclidic impurities such as ^{153}Gd , ^{159}Gd and ^{161}Gd . The various nuclear reactions product are shown in Table 1 and Fig. 1. ^{161}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 γ -rays spectrometry analysis of irradiated natural Gd_2O_3 target after cooling for 1 to 4 weeks was obtained two radionuclides as impurities in ^{161}Tb i.e. ^{153}Gd and ^{160}Tb . The quantity of ^{161}Tb and its radionuclide impurities (^{153}Gd and ^{160}Tb) produced at the end of irradiation (EOI) are shown in Fig. 2.

Percentage of ^{153}Gd , ^{160}Tb and ^{161}Tb radionuclide from five times of irradiation for 4 days at the 10^{14} $\text{n.cm}^{-2} \text{sec}^{-1}$ neutron flux as shown in Fig. 2, were found to be $11.02 \pm 1.48\%$, $0.02 \pm 0.006\%$ and $88.96 \pm 1.49\%$, respectively. The results showed that

^{153}Gd is a major impurity in irradiated natural Gd_2O_3 target. ^{153}Gd is produced from irradiated ^{152}Gd present in the natural Gd_2O_3 target material. The ^{153}Gd has long-lived ($T_{1/2} = 241.6$ d) and becomes a prominent radionuclidic impurity in the final product [9].

The presence of ^{157}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}Gd at the start of irradiation. The original amount of ^{158}Gd can be taken as sum of ^{157}Gd and ^{158}Gd [9]. ^{159}Gd is a short-lived ($T_{1/2} = 18.48$ h) and hence is not a major radionuclidic impurity in ^{161}Tb due to after 7 days post irradiation cooling period (~ 7 half-lives), there is no radioactivity was detected in a γ -rays spectrometry analysis. Hence, 7 days cooling will allow the complete decay of ^{159}Gd activity present in irradiated target.

The presence of ^{159}Tb (stable) in the original target material as impurity leads to the accumulation of the relatively long-lived beta and photon emitter ^{160}Tb ($T_{1/2} = 72.3$ d) via the $^{159}\text{Tb} (n,\gamma) ^{160}\text{Tb}$ reaction [9]. The accumulation of ^{159}Tb through activation of ^{158}Gd additionally impacts on the content of ^{160}Tb in the system. Nevertheless, the irradiation for 4 days at the 10^{14} $\text{n.cm}^{-2} \text{sec}^{-1}$ neutron flux and target composition described above would result in only $\sim 0.02\%$ of ^{160}Tb activity in ^{161}Tb as shown in Fig. 2. However, cooling time increases the ratio of ^{160}Tb to ^{161}Tb due to its significantly longer half-life.

Radiochemical Separation of ^{161}Tb from Irradiated Natural Gd_2O_3 Target

Radiochemical separation of ^{161}Tb from irradiated Gd_2O_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}Tb separation is shown in Fig. 3.

In the previous study reported that ^{161}Tb can be separated from irradiated of enriched Gd target in nitrate form ($\text{Gd}(\text{NO}_3)_3$) using 2 g of Ln resin and HNO_3 eluent with combination concentration of 0.8 and 3 N to

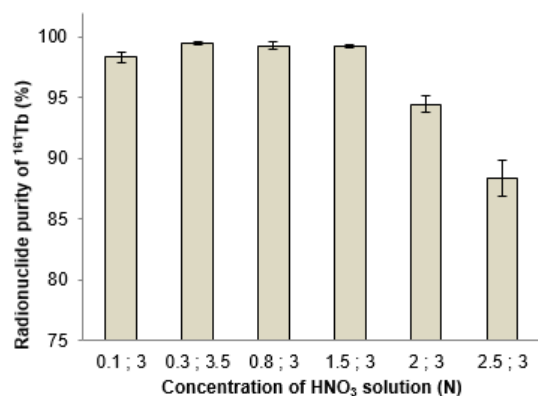


Fig 3. The effect of HNO₃ concentration as eluent on ¹⁶¹Tb separation

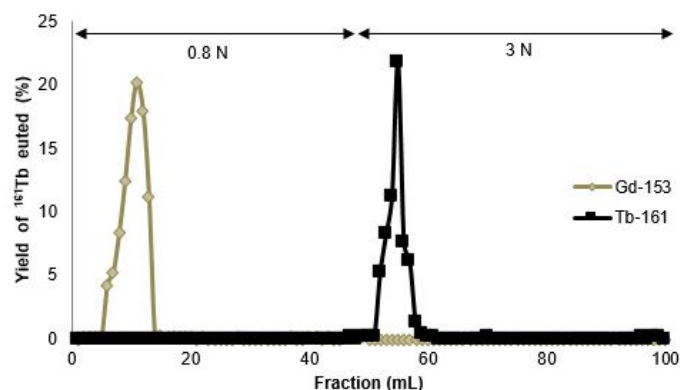


Fig 4. Elution profile on separation of ¹⁶¹Tb from irradiated Gd₂O₃ target using 0.8 and 3 N HNO₃

Table 3. The yield of ¹⁶¹Tb eluted from the column using various combination of HNO₃ concentration

The combination of HNO ₃ concentration (N)	Yield of ¹⁶¹ Tb eluted (%)	Gd recovered (%)	Radionuclide purity of ¹⁶¹ Tb (%)
0.1; 3.0	71.68 ± 1.69	57.99 ± 3.31	98.32 ± 0.40
0.3; 3.5	59.27 ± 4.18	70.49 ± 2.53	99.52 ± 0.12
0.8; 3.0	61.21 ± 2.05	97.15 ± 2.23	99.27 ± 0.30
1.5; 3.0	44.41 ± 1.15	21.97 ± 5.21	99.21 ± 0.10
2.0; 3.0	97.76 ± 1.02	17.37 ± 1.54	94.48 ± 0.64
2.5; 3.0	85.71 ± 5.34	9.32 ± 2.69	88.38 ± 1.45

separate gadolinium and terbium, respectively [17]. The radionuclide purity of ¹⁶¹Tb obtained was greater than 99.99% [17]. In this work as seen in Fig. 3, the separation of ¹⁶¹Tb with high radionuclide purity (greater than 99%) from irradiated natural Gd target in oxide form (Gd₂O₃) was also obtained using 1 g of Ln resin and HNO₃ 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 ¹⁶¹Tb obtained from those combination concentrations were not different significantly and greater than 99%. The results showed that ¹⁶¹Tb can be separated from irradiated natural Gd₂O₃ target with high radionuclide purity using 1 g of Ln resin. Furthermore, radionuclide purity of ¹⁶¹Tb decreased by increasing concentration of HNO₃ solution that was used to separate gadolinium isotope.

The yields of ¹⁶¹Tb eluted and Gd recovery that were obtained from the separation with various combinations of HNO₃ concentrations are summarized in Table 3. The yields of ¹⁶¹Tb obtained were still low. In the previous study reported that ¹⁶¹Tb can be separated from irradiated of enriched Gd target in nitrate form (Gd(NO₃)₃) using 2 g of Ln resin and HNO₃ eluent with concentration of 0.8–3N with the yield of 100% and Gd recovered of 100% [17]. In this work, the separation of ¹⁶¹Tb from irradiated natural Gd target in oxide form (Gd₂O₃) using 1 g of Ln resin and HNO₃ eluent with concentration of 0.8 and 3 N was obtained the yield of ¹⁶¹Tb and Gd recovered of 61.21 ± 2.05% and 97.15 ± 2.23%, respectively. The yield of ¹⁶¹Tb 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 ¹⁶¹Tb eluted and Gd recovered were obtained using 0.8 and 3 N HNO₃ eluent respectively with radionuclide purity of ¹⁶¹Tb greater than 99%. In the previous study has also been conducted separation of ¹⁶¹Tb 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 ¹⁶¹Tb radioisotope. Furthermore, this system is expressed as optimum conditions on separation of ¹⁶¹Tb from irradiated natural gadolinium oxide target.

Elution profile on separation of ¹⁶¹Tb from irradiated natural Gd₂O₃ target containing Gd/Tb matrix using 0.8 and 3 N HNO₃ eluent are shown in Fig. 4. Radionuclide of ¹⁵³Gd eluted after 4 mL of fractions. The main radioactivity of ¹⁵³Gd was obtained in the fraction at 5 to 13 mL with the total volume of 9 mL. While, ¹⁶¹Tb eluted after 52 mL of fraction. The main radioactivity of ¹⁶¹Tb was obtained in the fraction at 53 to 58 with the total volume of 6 mL. The result showed that ¹⁶¹Tb obtained has a little volume, so a high radioactive concentration of ¹⁶¹Tb will be achieved.

CONCLUSION

The ¹⁶¹Tb has been separated from irradiated natural gadolinium oxide (Gd₂O₃) 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}Tb radioisotope was obtained with radionuclide purity was $99.27 \pm 0.30\%$ and the yield of ^{161}Tb eluted was $61.21 \pm 2.05\%$. While Gd recovered was obtained of $97.15 \pm 2.23\%$. Therefore, to obtain highly specific activity, yield, as well as radionuclide purity of ^{161}Tb , further research is needed using enriched Gd_2O_3 target with ^{160}Gd enrichment.

ACKNOWLEDGEMENT

This research was supported financially by DIPA of Center for Nuclear Applied Science and Technology – National Nuclear Energy Agency of Indonesia No: 080.01.1.017283/2014. Thanks to Mr. Hotman Lubis and Mr. Abidin from Center for Radioisotopes and Radiopharmaceuticals Technology who help us in the preparation of target for irradiation in Nuclear Reactor of G.A. Siwabessy, Serpong.

REFERENCES

- Zhang, L., Chen, H., Wang, L., Liu, T., Yeh, J., Lu, G., Yang, L., and Mao, H., 2010, *Nanotechnol. Sci. Appl.*, 3, 159–170.
- Luo, T.Y., Tang, I.C., Wu, Y.L., Hsu, K.L., Liu, S.W., Kung, H.C., Lai, P.S., and Lin, W.J., 2009, *Nucl. Med. Biol.*, 36 (1), 81–88.
- YKI-Jakarta Race, 2012, Indonesian Cancer Foundation, <http://yayasankankerindonesia.org/2012/yki-jakarta-race/>, accessed on July 5, 2014.
- Ersahin, D., Doddamane, I., and Cheng, D., 2011, *Cancers*, 3 (4), 3838–3855.
- Sadeghi, M., Enferadi, M., and Shirazi, A., 2010, *J. Cancer Res. Ther.*, 6 (3), 239–248.
- Sisay, N., 2014, *Selection of Small Pretargeting Peptide with Affinity for Radiochelates and Separation and Purification of Radiolanthanides*, Dissertation, University of Missouri, USA, 1–122.
- Lehenberger, S., Barkhausen, C., Cohrs, S., Fischer, E., Grünberg, J., Hohn, A., Köster, U., Schibli, R., Türler, A., and Zhernosekov, K., 2011, *Nucl. Med. Biol.*, 38 (6), 917–924.
- Cutler, C.S., Hennkens, H.M., Sisay, N., Huclier-Markai, S., and Jurisson, S.S., 2013, *Chem. Rev.*, 113 (2), 858–883.
- Lehenberger, S.M., 2010, *Evaluation and Application of The Low Energy Electron Emitter ^{161}Tb* , Dissertation, Technische Universität München, Germany, 1–140.
- Rösch, F., 2007, *Radiochim. Acta.*, 95 (6), 303–311.
- Rösch, F., *Seventh International Conference on Nuclear and Radiochemistry*, Hungary, 24-29 August 2008.
- Uusijärvi, H., Bernhardt, P., Rösch, F., Maecke, H.R., and Forsell-Aronsson, E., 2006, *J. Nucl. Med.*, 47, 807–814.
- Grünberg, J., Lindenblatt, D., Dorrer, H., Cohrs, S., Zhernosekov, K., Köster, U., Türler, A., Fischer, E., and Schibli, R., 2014, *Eur. J. Nucl. Med. Mol. Imaging*, 41 (10), 1907–1915.
- Müller, C., Zhernosekov, K., Köster, U., Johnston, K., Dorrer, H., Hohn, A., van der Walt, N.T., Türler, A., and Schibli, R., 2012, *J. Nucl. Med.*, 53, 1951–1959.
- Müller, C., Reber, J., Haller, S., Dorrer, H., Bernhardt, P., Zhernosekov, K., Türler, A., and Schibli, R., 2014, *Eur. J. Nucl. Med. Mol. Imaging*, 41 (3), 476–485.
- Weast, R.C., 1987, *Handbook of Chemistry and Physics*, ed. Astle, M.J., and Beyer, W.H., 68th ed., CRC Press, Inc., Florida, USA, B-335.
- Guzman, F.M., Morales, J.A., 2010, *Radioisotope Production for Health Applications*, Eds. Mojica, G.D., Reyes, M.J., Guzman, F.M., Hernandez, S.R., and Guerrero, J.S., ININ, Mexico, 67–87.
- Ketring, A.R., Ehrhardt, G.J., Embree, M.F., Bailey, K.D., Tyler, T.T., Gawenis, J.A., Jurisson, S.S., Engelbrecht, H.P., Smith, C.J., and Cutler, C.S., 2003, *Alasbimn J.*, 5 (19), 1–6.
- Aziz, A., *Preliminary Study on Separation of Terbium-161 (^{161}Tb) Radioisotope from Gd/Tb Matrix Using Ion Exchange Resin*, Proceeding of National Conference on Nuclear Science and Technology, Bandung, 3 December 2015, 191–198.