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A Simulation of Irradiation Calculations on Lutetium-177 Production in RSG-GAS Using U_3Si_2-Al and U_9Mo-Al Fuels

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A B S T R A C T

This research is a simulation of irradiation calculations on the production of the radioisotope Lutetium-177 (^{177}Lu) in the G.A Siwabessy Reactor (RSG-GAS). This study aims to analyze the comparative calculation of ^{177}Lu activity and its purity. One of the production methods of ^{177}Lu in RSG-GAS is carried out by irradiating Lu_2O_3 targets. This Lu_2O_3 target irradiation produced the radioisotope ^{177}Lu along with ^{177m}Lu as an impurity. For Medical treatment using radioisotopes, the minimum activity for ^{177}Lu is 20 GBq/mg, and the impurity should not exceed 0.1%. Calculations were carried out with thermal neutron flux input at 15 MWt operational power for the RSG-GAS core with U_3Si_2-Al fuel (density 2.96 gU/cc and 3.55 gU/cc) and U_9Mo-Al fuel (density 3.55 gU/cc). Calculations were carried out by simulating 8 days of irradiation using ORIGEN2.1. The results showed that the ^{177}Lu activity resulting from irradiation of Lu_2O_3 targets at various CIP positions in the U_9Mo-Al reactor core was larger than that of the U_3Si_2-Al core. Until the 30th day, the ^{177}Lu product resulting from irradiation on the U_3Si_2-Al and U_9Mo-Al cores still meets the minimum value of 20 GBq/mg for treatment needs in nuclear medicine, with the activity value of ^{177}Lu resulting from irradiation on the U_3Si_2-Al core ranging from 241-403 GBq/mg, while the activity of irradiated ^{177}Lu in the U_9Mo-Al core ranges from 335-561 GBq/mg. In addition, until the 30th day of decay, ^{177}Lu has a percentage value of ^{177m}Lu irradiated in the U_9Mo-Al and U_3Si_2-Al cores of 0.0346% and 0.0344%, respectively. The results are still below the maximum impurity value of 0.1% and thus safe to use as a therapeutic agent.

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1. INTRODUCTION

Lutetium-177 (^{177}Lu) is a radioisotope being developed and tested for treating various types of cancer in clinical trials around the world. The radioisotope ^{177}Lu is used in nuclear medicine for radiotherapy because of its favorable decay characteristics, such as low beta decay energy of 497 keV (78.6%) and relatively short half-life of 6.71 days. This radioisotope also emits gamma rays with energies of 113 keV (6.4%) and 208 keV (11%), making it suitable for in-vivo local imaging with a gamma camera [1].

In the last decade, related publications on ^{177}Lu have tripled, and demand for them is expected to grow significantly in the coming years. The availability of ^{177}Lu is entirely dependent on the availability of nuclear reactors. This may put this ^{177}Lu radioisotope at risk of shortage in the future.

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The increasing demand for ^{177}Lu is in line with its increasing application in several radionuclide therapies, especially for neuroendocrine tumors and PSMA ligand prostate cancer [2]. Given the challenges associated with producing the radioisotope ^{177}Lu, this raises concerns that the availability of ^{177}Lu as a medical isotope may need to be expanded in the long term. For this reason, it is necessary to develop research related to the production of this ^{177}Lu radioisotope as one of the factors supporting the availability of ^{177}Lu in the future.

^{177}Lu is becoming increasingly popular as a treatment option and is labeled as intensive therapy by major pharmaceuticals. Demand for the ^{177}Lu is expected to be close to 500,000 Curies by 2025[3]. Currently, ^{177}Lu production is being developed in Indonesia, one of which is at RSG-GAS. To support the global market demand, a high neutron flux is required to produce this radioisotope (>1×10^{14} n.cm^{-2}.s^{-1}). Irradiating a Lu_2O_3 target with a low neutron flux will result in a low specific activity (a low ratio of ^{177}Lu is a useful fraction of all lutetium isotopes). This could be a limit to the probability of success in therapeutic applications [4].

The G.A Siwabessy (RSG-GAS) reactor is one of the research reactors in Indonesia which is developing the production of the radioisotope ^{177}Lu. One of the studies related to the production of ^{177}Lu, carried out by Rohadi (2015) was regarding the type of radioactivity and purity of ^{177}Lu production in RSG-GAS by irradiation carried out in a pneumatic rabbit system (PRS) with a net flux 5×10^{13} n.s^{-1}.cm^{-2} and in Central Irradiation Position (CIP) with a net flux 1.4×10^{14} n.s^{-1}.cm^{-2}. The results indicate that the production of ^{177}Lu irradiated for 12 days contained impurity radionuclides ^{177m}Lu, which was less than 0.1% at the end of irradiation, then increased rapidly after irradiation was stopped until it reached 0.1% after 24 days of decay [5].

Radioisomer ^{177m}Lu ($T_{1/2}$: 160.5 days) was experimentally confirmed as the only relevant long-lived radionuclide impurity found in ^{177}Lu generated by target activation of enriched ^{176}Lu. Radioisomers ^{177m}Lu are inseparable as it has a much longer half-life than ^{177}Lu. The longer the storage of ^{177}Lu, the greater level of contamination ^{177m}Lu in it [6]. The maximum value of radionuclide impurities in treatment using a ^{177}Lu radioisotope is 0.1% [5].

In its production in the reactor core, the activity of ^{177}Lu is influenced by several factors, namely the type of target used in the form of natural or enriched lutetium, the neutron flux, and the duration of irradiation. The neutron flux is influenced by several factors, including the position of the target irradiation and the type of fuel used [7]. Thus, in this study, an analysis of the activity of ^{177}Lu and its purity was carried out when natural lutetium targets were irradiated in the CIP reactor core with the fuel currently used in RSG-GAS and other fuels that have the potential to be used in the future. The fuel currently used in RSG-GAS is uranium silicide (U_3Si_2-Al) with a density of 2.96 gU/cc, while other fuels that have the potential to be used in the future are U_3Si_2-Al with a density of 3.55 gU/cc and U_9Mo-Al with a density 3.55 gU/cc. Radioactivity analysis was carried out using the ORIGEN2.1 program, and it is expected that from the research, it will be known which fuel is adequate to be used in the production of ^{177}Lu.

2. THEORY

a. ^{177}Lu Radioisotope

^{177}Lu radioisotope can be produced directly by irradiating natural lutetium targets (Lu_2O_3) in the reactor core [8]. Lu_2O_3 (lutetium oxide) contains Lu isotopes ^{175}Lu and ^{176}Lu. ^{175}Lu, when irradiated, will produce ^{176}Lu, which in turn will produce activation products in the form of ^{177}Lu when irradiated, as shown in Table 1 [9].

Table 1. Composition of natural Lutetium to form isotopes ^{177}Lu

Mass number	Abundance (%)	Core reaction	Radio isotope	Half-life	Cross section (σ)
^{175}Lu	**97,4%**	^{175}Lu(n,γ) ^{176m}Lu	^{176m}Lu	3,96 hour	16,7 barn
		^{175}Lu(n,γ) ^{176}Lu	^{176}Lu	3,38×10^{10} year	6,6 barn
^{176}Lu	**2,6%**	^{176}Lu(n,γ) ^{177m}Lu	^{177m}Lu	160 days	2,8 barn
		^{176}Lu(n,γ) ^{177}Lu	^{177}Lu	6,65 days	2020 barn

At the time of neutron irradiation in the reactor, the activity equation is expressed by the following equation [10]:

$$A = N_t \emptyset \sigma \left(1 - e^{-\lambda t}\right) \qquad (1)$$

where A is the resulting activity (Bq), N_t is the number of target atoms at the t (atoms), $\emptyset$ is the flux of neutrons (n.s^{-1}cm^{-2}), σ is the cross-section of the nuclear reaction (barn = 10^{-24} cm^2), λ is the radioisotope decay constant, and t is the irradiation time duration (s).

The radioisotope decay activity equation of ^{177}Lu and its impurities at post-irradiation is expressed by the following equation [9] :

$$A_t = A_0 e^{-\lambda t} \quad (2)$$

where A_t is the decay activity of the radioisotope at time t (bq) and A_0 is the initial radioisotope activity (bq).

b. ORIGEN2.1

ORIGEN2.1 (Oak Ridge Isotope Generation and Depletion Code Version 2.1) is a widely used computer code for calculating radioactive materials' buildup, decay, and processing. The basis for calculating the inventory of radionuclides formed in the irradiation process in reactors through the ORIGEN2 program based on the first-order linear differential equation for the depletion group and radioactive decay as follows [11] :

$$\frac{dX_i}{dt} = \sum_{j=1}^{N} l_{i,j}\lambda_j X_j - \emptyset.\sum_{j=1}^{N} f_{i,j}\sigma_k X_k - (\lambda_i + \emptyset\sigma_i + r_i).X_i + F_i \quad ; i\ 1,2,\dots,N \quad (3)$$

Eq. 3 describes the rate of change in the number of nuclides i to the change in Time $\left(\frac{dX_i}{dt}\right)$, which is the calculation of the decay term $(\sum_{j=1}^{N} l_{i,j}\lambda_j X_j)$ minus the absorption rate with average flux $(\emptyset.\sum_{j=1}^{N} f_{i,j}\sigma_k X_k)$ and the radionuclide displacement term $((\lambda_i + \emptyset\sigma_i + r_i).X_i)$ and the feed (F_i) which will become a particular radionuclide. X_i is the atomic density of the radionuclide i, N is the number of radionuclides, l_{ij} is the fraction of radioactive decay by other nuclides j leading to species formation i, λ_j is the radioactive decay constant, $\emptyset$ is the mean neutron flux of position and energy, $f_{i,j}$ is the fraction of the absorption of neutrons by other nuclides leading to species formation i, j.

3. METHODOLOGY

The research includes four stages, namely, the calculation of the target mass, the creation of ORIGEN2.1 input, the process of running ORIGEN2.1, and data analysis.

a. Calculation of the mass of the target composition

Calculation of the mass of the target composition wass carried out before assembling the ORIGEN2.1 input. Only the target mass and its enrichment were known from the target data used, as shown in Table 2, while the ORIGEN2.1 input data requires mass details of the target composition used. To calculate the mass of Lu, the following equation is used:

$$\text{massa}_{\text{Lu}} = \frac{\text{Ar}_{\text{Lu}}}{\text{Mr}_{\text{Lu2O3}}} \text{x massa}_{\text{Lu2O3}} \quad (4)$$

Table 2. Lu target data Lu_2O_3

Mass of Lu_2O_3	0.3 mg
Enrichment	74% Lu-176

Based on Eq. 4, the mass of lutetium is 2.6 mg. After that, the masses of ^{175}Lu and ^{176}Lu can be determined by entering their respective abundances according to Table 2. Then, the masses of ^{175}Lu and ^{176}Lu were obtained at 0.06 mg and 0.2 mg, respectively. Meanwhile, the O element was obtained from the mass of Lu_2O_3 minus the result of calculating the mass of Lu, which is equal to 0.04 mg.

b. Writing program input on ORIGEN2.1

The input data needed to run the ORIGEN2.1 program include the composition and target mass of Lu_2O_3, thermal neutron flux at the CIP position, and the length of irradiation time. The duration of irradiation to be used is eight days. The input data for the flux value of the CIP irradiation position on the reactor core was differentiated into U_3Si_2-Al (density 2.96 gU/cc) and U_9Mo-Al (density 3.55 gU/cc), operated at a power of 15 MWt (shown in Table 3) [12,13]. The input data will then be entered into the listing of ORIGEN2.1 for each fuel.

Table 3. Thermal neutron flux data in different fuel cores

Fuel	Density (gU/cc)	Position in CIP (X 10^{14} n.cm^{-2}.s^{-1})			
		D6	D7	E6	E7
U_3Si_2-Al	2.96	1.75	1.75	1.56	1.56
U_9Mo-Al	3.55	2.42	2.42	2.43	2.43

c. Process of the running program

At this stage, confirm that the input file extensions are all.INP, also make sure that all input files from the ORIGEN2.1 program contain Filespecs.dat, Origen2.exe, and Photon.Lib, Runorg.Bat, and Thermal. Lib are also complete. After all inputs and ORIGEN2.1 program packages were complete, code running was done by entering the name of the input file in RUNORG by editing and saving the name of the input file using notepad. Then open the RUNORG file; the ORIGEN2.1 program will download the running input file that has been saved and then an output file with the extension file.OUT will appear, which can be opened using notepad. These steps were performed on all input files in turn.

d. Data analysis

Data analysis was performed using Microsoft Excel. From the ORIGEN2.1 output file, radioactivity data of ^{177}Lu and ^{177m}Lu were taken.

From the output data, a decay graph of the activity comparison of ^{177}Lu and ^{177m}Lu was made. Then an analysis of the effect of variations in the neutron flux in the reactor core produced by each fuel at activity ^{177}Lu and ^{177m}Lu was carried out.

4. RESULTS AND DISCUSSION

The results of ^{177}Lu activity calculations on variations of the reactor core at the end of irradiation using ORIGEN2.1 are shown in Fig. 1. The graph shows the resulting ^{177}Lu activity from Lu_2O_3 irradiation targets at various CIP positions on the U_9Mo-Al and U_3Si_2-Al reactor cores. From irradiation carried out for eight days, it was found that the activity of ^{177}Lu irradiated on the reactor core with U_9Mo-Al fuel is in the range of 560-562 GBq/mg, while the activity of ^{177}Lu irradiated on the reactor core with U_3Si_2Al fuel is in the range of 383-424 GBq/mg. The irradiation results for the two types of fuel showed that the production of ^{177}Lu in both cores met the minimum activity value of ^{177}Lu for medical purposes, namely 20 GBq/mg. The activity of ^{177}Lu irradiated on the reactor core with U_9Mo-Al fuel has a more excellent value than the target irradiated on the reactor core with U_3Si_2-Al fuel. This is related to the thermal neutron flux in the reactor core with respective fuels. Although the density of the fuel used by the two fuels is almost the same, the neutron flux in the reactor core with U_9Mo-Al fuel is larger than that of U_3Si_2-Al.

Fig. 2 shows the activity ^{177}Lu calculated from the average flux of each reactor core from post-irradiation to 30 days of decay time. From this figure, it can be seen that activity ^{177}Lu is decaying as time passes. Until the 30th day of decay, the activity of ^{177}Lu irradiated in the U_9Mo-Al core is larger than U_3Si_2Al. This is related to the value of the thermal neutron flux in each core of the two fuels.

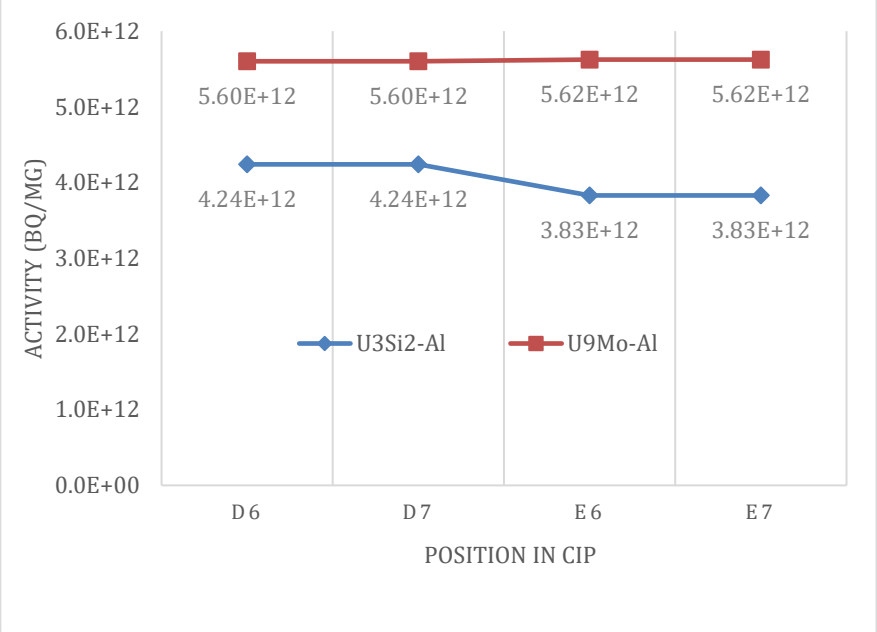

Fig. 1. Activity ^{177}Lu at the end of irradiation

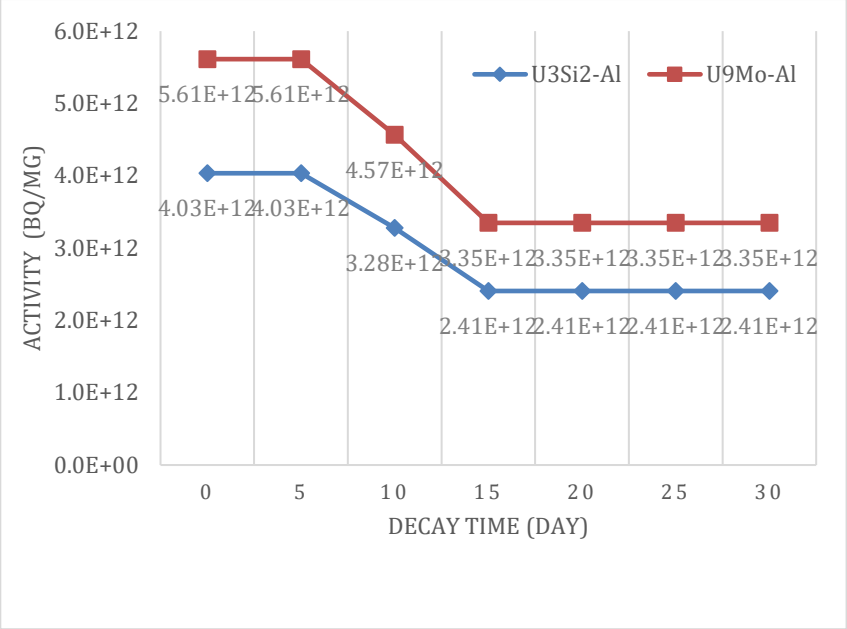

Fig. 2. Activity ^{177}Lu in decay Time

Fig. 2 shows that the activity ^{177}Lu irradiated in the reactor core of U_9Mo-Al until the 30th day of decay is around 335 GBq/mg, while for U_3Si_2-Al is 241 GBq/mg. This means that up to the 30th day of decay, the ^{177}Lu product resulting from irradiation in the reactor core with these fuels still meets the requirements for medical needs in nuclear medicine.

As is well known, the production of the radioisotope ^{177}Lu is accompanied by the formation of ^{177m}Lu, which is a radioisotope impurity. One of the conditions for a safe radioisotope to be used for medical purposes is that the impurity composition must not exceed 0.1% of the activity of the radioisotope. The results of calculating the activity comparison of ^{177}Lu and ^{177m}Lu after irradiation are shown in Fig. 3.

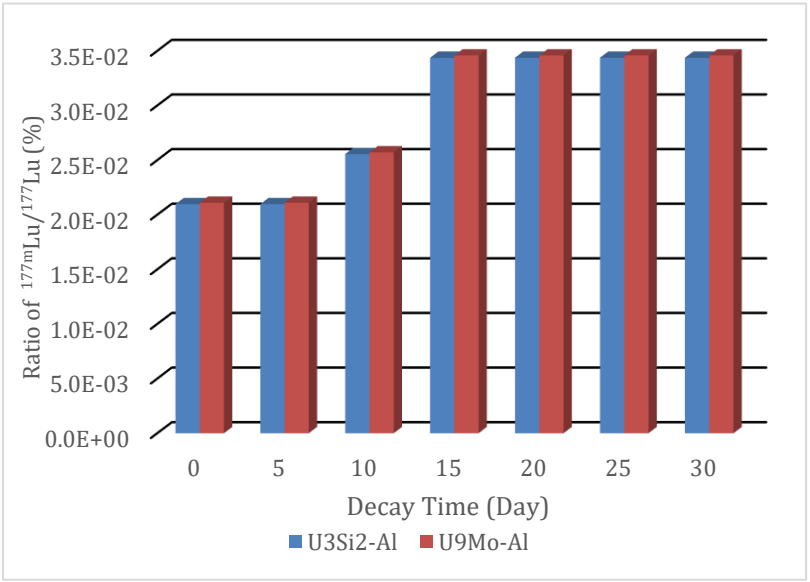

Fig. 3. The ratio of ^{177}Lu and its impurity

Fig. 3 shows that, in general, the percentage of activity of ^{177m}Lu as an impurity of ^{177}Lu resulting from irradiation in the reactor core with U_9Mo-Al fuel is slightly more significant than the results of irradiation in the reactor with U_3Si_2-Al fuel. At the end of the irradiation, the ratio of ^{177}Lu and ^{177m}Lu of the target irradiated results on the reactor core with U_9Mo-Al fuel was 0.0211%, while in the U_3Si_2-Al

reactor core, it was 0.021%. These results indicate that the result of irradiation in the reactor core with these two fuels, the composition of ^{177m}Lu, is still below the maximum value of impurities.

After the irradiation was stopped, the percentage of impurities increased. This is influenced by the decay rate of ^{177}Lu and ^{177m}Lu. ^{177}Lu has a shorter half-life than ^{177m}Lu. This causes ^{177}Lu to decay faster, so the longer the decay time, the higher the percentage of ^{177m}Lu produced. Until the 30th day of decay, the percentage of ^{177m}Lu irradiated in the reactor core with U_9Mo-Al and U_3Si_2-Al fuel was 0.0346% and 0.0344%, respectively. These values are still below the maximum limit for the percentage of impurities of 0.1%. This means that this ^{177}Lu product is safe to use as a therapeutic agent until the decay time of 30 days.

5. CONCLUSION

The activity of ^{177}Lu resulting from irradiation of Lu_2O_3 targets at various CIP positions on the U_9Mo-Al reactor core is higher than that of irradiation on the U_3Si_2-Al core. Until the 30th day, the radioisotope product ^{177}Lu resulting from irradiation on the U_3Si_2-Al and U_9Mo-Al cores still meets the requirements for medical needs in nuclear medicine. At the end of the irradiation until the 30th day of decay, the activity of ^{177}Lu irradiated in the reactor core with U_3Si_2-Al fuel was around 241-403 GBq/mg, while the activity of ^{177}Lu irradiated in the reactor core with U_9Mo-Al fuel was around 335-561GBq/mg. In addition, until the 30th day of decay, the ^{177}Lu products irradiated in the reactor core with these fuels are safe to use as therapeutic agent, with a percentage of ^{177m}Lu of 0.0346% and 0.0344% for U_9Mo-Al and U_3Si_2-Al, respectively. Taking into account the activity of the ^{177}Lu produced and the percentage of impurities, the irradiation results in the reactor core with U_9Mo-Al fuel are better since they produce more significant ^{177}Lu activity. Meanwhile, the resulting impurity is similar to the irradiation results in the U_3Si_2-Al reactor core.

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AUTHOR CONTRIBUTION

Lena Rosmayani calculated the percentage of ^{177}Lu production activity with impurities in U_3Si_2-Al and U_9Mo-Al fuel using the ORIGEN2.1 code. Anis Rohanda and R Farzand Abdullatif participated together as reviewers and performed data analysis. Lena Rosmayani, Anis Rohanda, and R Farzand Abdullatifi equally contributed as the main contributors to this paper. All authors read and approved the final version of the manuscript.

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