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Opportunity to Produce Radioisotopes Astatine-211 (^{211}At) using DECY-13 Conceptual Design with Computational Approach

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Abstract: *To catch up research gap with developed countries, Indonesia going to build a cyclotron-type accelerator with the code name DECY-13. Detailed design and conceptual design of DECY-13 were published. Further, to accelerate applied research of DECY-13, it is necessary to hold a preliminary study even before the cyclotron is commissioned. Astatine-211 (^{211}At) is an alpha-rays that emit a radioisotope that is easy to direct label for targeted alpha therapy. Targeted alpha therapy (TAT) is the selectively delivered therapy that uses alpha-ray base radioisotopes produced using a cyclotron like DECY-13. DECY-13 was designed to accelerate a proton to 13 MeV. However, it does not rule out the possibility of accelerating alpha particles. A computational approach will be used to simulate the possibility of DECT-13 to accelerate alpha particles to produce ^{211}At from natural Bismuth. The theoretical calculation predicted that the alpha particle (helium nucleus) could be accelerated in DECY-13. The energy decreased increasingly after hitting the niobium layer twice and the helium cooling layer at 4.06 MeV. The 0.924 grams of natural bismuth were irradiated for 8 hours and 4 hours of cooling. At EOB was not found radioisotopes, radioactivity, and dose were emitted. The inability to produce ^{211}At is because the energy of the accelerated alpha particles has not been able to penetrate the bismuth nucleus. The continuation simulation successfully predicts if the niobium layer thinned to 125 mm can obtain ^{211}At with low impurity. On the other hand, if the energy of DECY-13 would be increased until 28 MeV, ^{211}At could be produced, but the impurity was increased. Furthermore, DECY-13 Cyclotron is not able to produce ^{211}At from ^{209}Bi. To obtain ^{211}At from ^{209}Bi, it is necessary to create another engineering design of cyclotron or use another proton-base reaction.*

INTRODUCTION

Indonesia has cyclotrons that accelerate a negative ion modified from a positive ion cyclotron of the CS-30 type, but it doesn't work well [1]. Therefore, Indonesia wants to build a new cyclotron with 13 MeV energy, which is located in Yogyakarta, with code name DECY-13. The Detail design and conceptual design of DECY-13 was published [2]. Thus, to accelerate the catch-up research gap with developed countries, it is necessary to conduct preliminary studies on radioisotope production even before the cyclotron is commissioned.

Astatine-211 (^{211}At) is a radioisotope that emits alpha rays that used for Targeted alpha therapy (TAT). TAT is the therapy that uses alpha-ray base radioisotopes labeled with carrier drugs to treat the specific organ [3]. ^{211}At is easily labeled as radiopharmaceuticals which is ^{211}At can be tagged directly to the target molecules without chelators, linkers, and spacers [4][5]. The ^{211}At has a half-life of 7.21 hours that is produced by irradiating natural bismuth (^{nat}Bi) that contains 100% bismuth-209 (^{209}Bi) isotopes with accelerated alpha particles (helium nucleus) [6]. The reaction occurs in 3 schemes that the percent of yields according to reaction cross sections in figure 1.

$$^{209}_{83}Bi + {}^{4}_{2}\alpha \longrightarrow {}^{211}_{85}At + 2\,{}^{1}_{0}n$$
$$^{209}_{83}Bi + {}^{4}_{2}\alpha \longrightarrow {}^{210}_{85}At + 3\,{}^{1}_{0}n$$
$$^{209}_{83}Bi + {}^{4}_{2}\alpha \longrightarrow {}^{210}_{85}At + x$$

On the one hand, ^{211}At emitted alpha rays with a higher absolute intensity of 41.81% with an energy of 5.87 MeV that will be decayed to Bismuth-207 (^{207}Bi)[8]. On the other, with electron capture schemes ^{211}At will be decayed to

Polonium-211 (^{211}Po) with an absolute conversion electron intensity of 57.93% that will emit alpha with an intensity of 100% and energy of 7.45 MeV. Astatine-210 (^{210}At) is an unwanted side reaction because ^{210}At will be decayed into Polonium-210 (^{210}Po) which is toxic to the body [9].

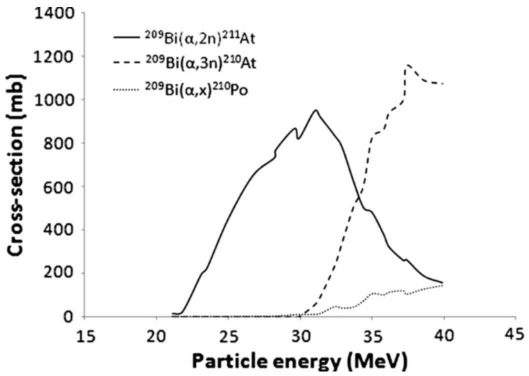

Figure 1. Cross sections of ^{209}Bi + alpha reaction [7].

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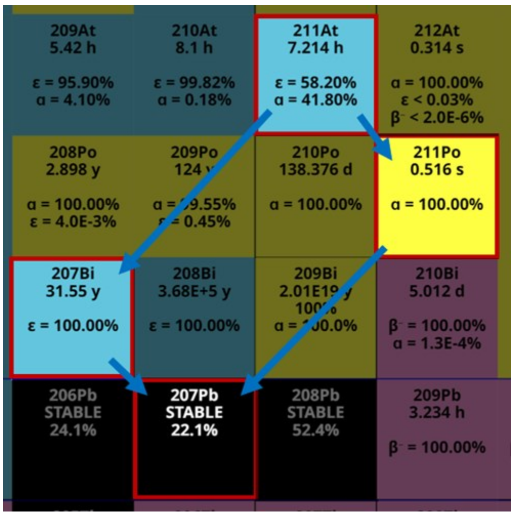

Figure 2. Decay chain of Astatine-211

According to the design, DECY-13 initially accelerated the proton to 13 MeV. However, it is possible to accelerate alpha particles [10]. Theoretical calculations is needed to predict the energy conversion from an accelerated proton to an accelerated alpha particle. The resulting energy will then be calculated computationally using the Monte Carlo method to simulate the interaction between the alpha particle projectile and the target. The result of the interaction is then further processed to determine the radioisotopes formed, the radioactivity, dose-rate and heat that are emitted during the irradiation process.

METHODOLOGY

The Irradiation Target

The irradiation target is natural bismuth that is 100% ^{209}Bi isotope abundance [11]. The metal Bismuth powder density is 9.80 g/cm^3 with rhombohedral crystals forms [12]. The 0.924 grams of bismuth metal is placed in the target chamber with a diameter of ϕ = 2 cm [2].

The Irradiation Energy

The cyclotron can accelerate the proton until 13 MeV, yet in this simulation, the cyclotron will accelerate the alpha particle. The energy of accelerated alpha particle can be determined using formula below:

$$E_{kinetic} = \frac{1}{2}mv^2 \qquad (1)$$

Where $E_{kinetic}$ is kinetic energy of particles in Joule, m is mass of Particle in kg, and v is velocity of particle in m/s.

In the Cyclotron, centripetal force is equal to accelerated force from electromagnetic force:

$$F_{Centripetal} = F_{Electromagnetic}$$
$$\frac{mv^2}{r} = \mathrm{q}.v.B$$
$$v = \frac{\mathrm{q}.B.r}{m} \qquad (2)$$

where $F_{Centripetal}$ is centripetal force of particle in cyclotron in Neutons (N), $F_{Electromagnetic}$ is electromagnetic/lorentz force of particle in cyclotron in Neutons (N), q is charge of particle in Coulomb, B is Magnetic Field in tesla (T), and r is Radius of dees in meters(m).

Formula 2 can be split with formula 1 to determine the energy of the alpha particle:

$$E_{kinetic} = \frac{(\mathrm{q}.B.r)^2}{2m} \qquad (3)$$

The alpha particle will go through the niobium foil twice with 30 µm thickness and 5 mm helium as a cooling medium before hitting the target. The projectile energy will decrease so that real energies can be calculated using formula 4:

$$E_{Final} = E_{Initial} - (E_{1st\ Foil\ out} + E_{Helium\ out} + E_{2nd\ Foil\ out}) \quad (4)$$

$$E_{out} = E_{in} - \left[\left(\frac{dE}{\rho.dx}\right) x\ \rho\ x\ d\right] \quad (5)$$

Where E is accelerated particle energy in MeV, $\left(\frac{dE}{\rho.dx}\right)$ is stoping power in MeV.cm^2.g^{-1}, ρ is Material density g.cm^{-3}, and d is material thickness in cm.

The stopping power values for all materials are calculated using the SRIM program [13]. The real alpha particle energy will be used for irradiation simulation.

Monte Carlo Simulation

Monte Carlo simulation is due using PHITS ver. 3.28 software [14]. The simulation using number of particles of 10,000 and number of iterations of 1,000 [15]. The target was irradiated computationally for 8 hours plus 4 hours of cooling time. The output of the simulation was processed using the D-CHAIN algorithm that includes in PHITS packages[16]. The D-CHAIN simulation was used to determine the radioisotopes, radioactivity, and dose rate generated during the irradiation process.

RESULTS AND DISCUSSION

The research result was divided into three sections; Energy of irradiation, irradiation result and improvement in the irradiation process.

The Irradiation Energy

The conversion of accelerated proton energy to alpha particle was calculated using formula 3. A proton (^1_1p) have electric charge q = e = 1.602×10^{-19} coulombs and mass m = m_p = 1.673×10^{-27} kg. For an alpha particle ($^4_2\alpha$), q =2.e and mass $m_\propto = 4.m_p$. The energy of accelerated alpha particle was :

$$\frac{E_{kinetic\ of\ proton} = \frac{(q.B.r)^2}{2m} = \frac{(e.B.r)^2}{2.m_p}}{E_{kinetic\ of\ alpha} = \frac{(q.B.r)^2}{2m} = \frac{(2.e.B.r)^2}{2.4.m_p}}$$

$$E_{kinetic\ of\ proton}: E_{kinetic\ of\ alpha} = 1:1$$

The theoretical calculation predicted that the alpha particle (helium nucleus) could be accelerated in DECY-13 with energy equal to the accelerated proton projectile.

The real energy was determined to depend on the stopping power value. The stopping power was the repulsive energy that came from the difference in molecular charge

Using formula 4 and 5, the real energy of alpha particle was:

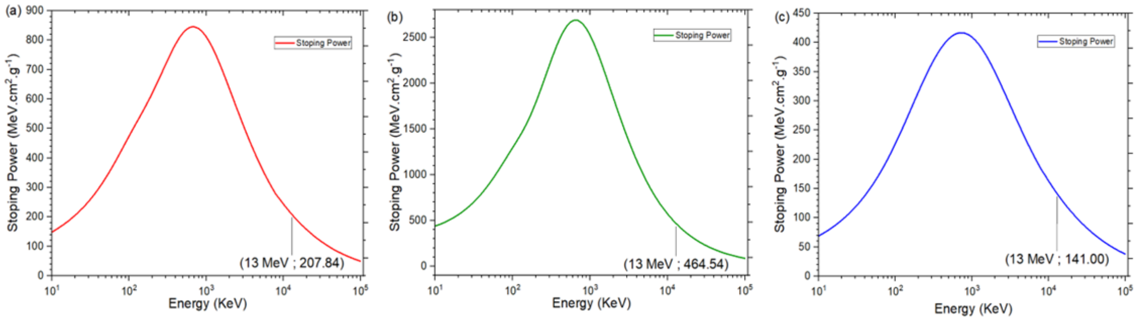

Figure 3. Alpha particle stopping power on: (a) Niobium, (b) Helium gas, (c) Bismuth metal

Table 1. Real accelerated alpha energy after interaction with the target chamber parts

Materials	Stopping power (MeV.cm^{-2}.g^{-1})	Density (g.cm^{-3})	Thickness (cm)	Proton Energy (MeV)	
				in	out
1st Niobium Foil	207.84	8.57	2.50x10^{-3}	13	8.55
Helium	464.54	1.66x 10^{-4}	0.5	8.55	8.51
2nd Niobium Foil	207.84	8.57	2.50x10^{-3}	8.51	4.06
Bismuth Metals	141.00	4.91	0.03	4.06	~0

The real energy of the alpha particle that hit the bismuth target was 4.06 MeV. Energy from the alpha particle was reduced more than a proton (8.51 MeV). This action happens because the charge of the alpha is more than the proton, which causes the repulsion force from the Ni layer and He cooler that was passed to be higher [17]. The energy will be used as Monte Carlo input and the result will be presented in the following subchapter.

Irradiation Result

Monte Carlo simulation was done for 23 minutes 3 seconds long using a 36 Core processor. The time parameter of irradiation was 8 hours plus 4 hours of cooling. The profile of the irradiation process was shown in figure 4.

According to figure 4, during the irradiation and cooling process was found a few values of total radioactivity amount of 3.26×10^{-5} Bq and activated atom amount 2.82×10^{22} atoms.cm^{-3} that was stagnant until the end of the process. Similarly, the emitted heat from alpha was stagnant during processing at 1.64×10^{-17} watts. On the other hand, the heat emitted from beta, gamma and ɣ-ray dose-rate were not found or had zero value during the process. This phenomenon is caused by the strength of the accelerated alpha particles being 4.06 MeV. It cannot oppose the repulsion force from the Bismuth nucleus, so the projectile cannot trigger by the nuclei reaction[18].

Radioisotope ^{209}Bi emits alpha-ray with has longest half-life of approximately 2.01×10^{19} years [19]. It can be concluded that the radioactivity, alpha-ray heat emitted, and activated atoms found during the process came from the ^{209}Bi target. On the other side, during the irradiation process, no radioisotopes were found instead of ^{209}Bi, which reinforces that there was no nuclear reaction from bismuth irradiation.

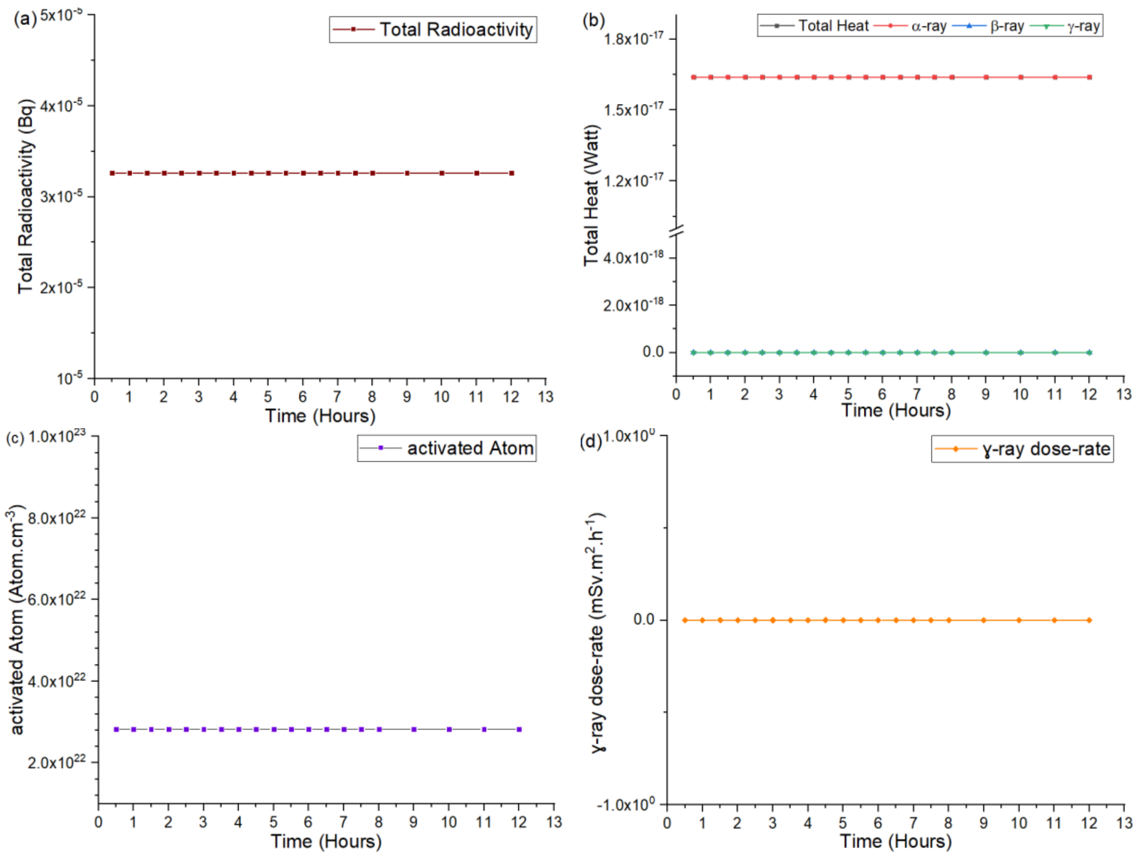

Figure 4. Irradiation profile graph of: (a) Total radioactivity; (b) Total Heat; (c) Activated Atom; and (d) ɣ-ray dose-rate.

Table 2. Real energy interacted with the target chamber parts after thickness reduction

Materials	Stopping power ($MeV.cm^{-2}.g^{-1}$)	Density ($g.cm^{-3}$)	Thickness (cm)	Proton Energy (MeV)	
				in	out
1st Niobium Foil	207.84	8.57	$1.25x10^{-3}$	13	10.77
Helium	464.54	$1.66x\ 10^{-4}$	0.5	10.77	10.73
2nd Niobium Foil	207.84	8.57	$1.25x10^{-3}$	10.73	8.51
Bismuth Metals	141.00	4.91	0.03	8.51	~0

The radioactivity profile during the irradiation process was shown in figure 5:

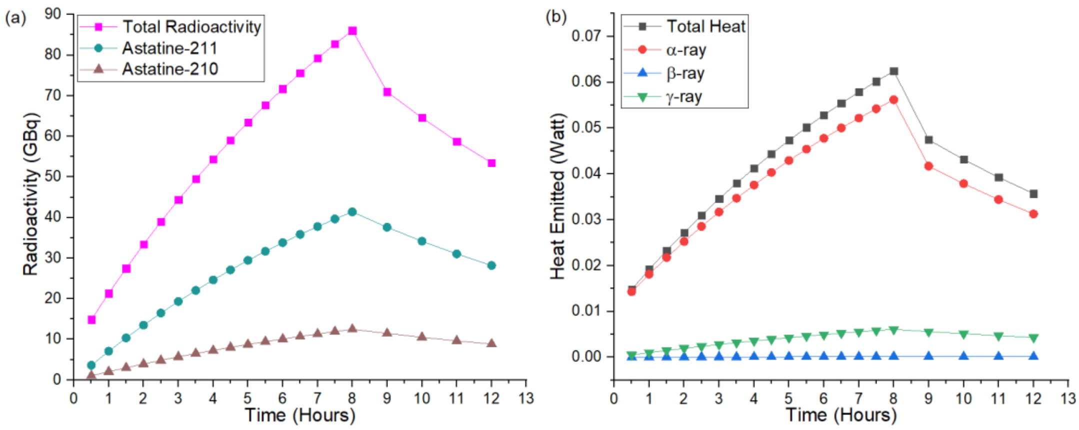

Figure 5. Irradiation profile graph of: (a) Radioactivity; and (b) Heat.

Improvement in irradiation process

The three rough improvements on the process were made to see if there is an opportunity of producing ^{211}At from DECY-13. The improvements will be simulated in Monte Carlo, and the interesting result will be discussed.

Reduce thickness of twin niobium layer

The initial thickness of the twin niobium layer was $2.50x10^{-3}$ cm, which a manufacturer found selling niobium as thick as $1.25x10^{-3}$ cm. using the thickness adjustment obtained alpha-energy

At the end of the bombardment (EOB), the total radioactivity of 86.08 GBq was reduced to 53.49 GBq after 2 hours of cooling. At EOB, the radioactivity of ^{211}At was 41.41 GBq and ^{210}At its toxic behaviors were 12.47 GBq. The radioactivity of ^{211}At was lower than the product from another accelerator. However, the radioactivity of ^{210}At was close to ^{211}At feared to cause toxic effects when used for therapy. The Improvement of twin niobium thickness reduction is possible because it does not change the basic design, but further studies must do on the impact of the reduction on the existing chamber design.

Increases energy to 28 MeV

The production was done with the increase of a real accelerated proton energy of 28 MeV, which was the most optimal energy to obtain maximum ^{211}At radioactivity and minimize the side product of ^{210}At [9]. The used target was 0.2 cm thick and weighed 6.16 grams preventing the projectile from the target chamber. The radioactivity obtained can be seen in the figure 6.

At the end of bombardment (EOB), total radioactivity was obtained $3.86x10^{12}$ Bq which was reduced to $1.43x10^{12}$ Bq after 2 hours of cooling. At EOB, the radioactivity result of ^{211}At was $1.67x10^{11}$ Bq and ^{210}At was $9.07x10^{1}$ Bq. The bit radioactivity found from ^{210}At during the process was suitable for use as a targeted alpha therapy.

Even though this improvement produces good results after simulation, it is difficult to do. It is because the improvement will change the conceptual design of DECY 13, especially the DEE size, cyclotron radius and charge.

Increases energy to 39 MeV

The higher energy used is usually equal to the number of radioactivity yields. However, other factorswere influence such as cross-section [20]. Cross section of ^{211}At and ^{210}At can be seen in figure 5.

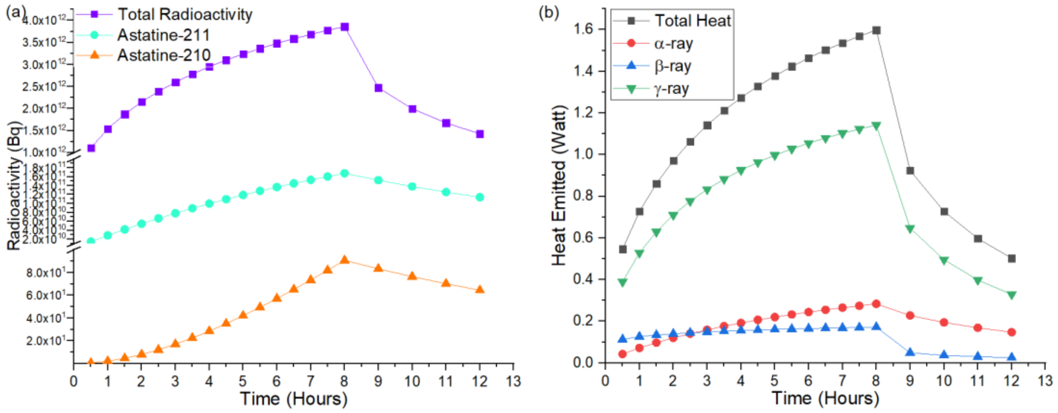

Figure 6. Irradiation profile graph of: (a) Radioactivity; and (b) Heat.

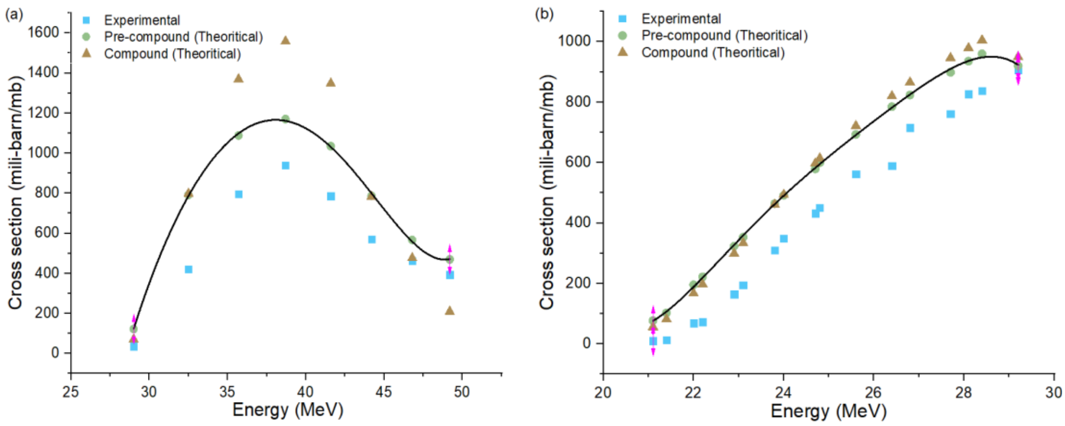

Figure 7. Cross Section (mb) of : (a) ^{209}Bi(α,3n)^{210}At; and (b) ^{209}Bi(α,2n)^{211}At [18].

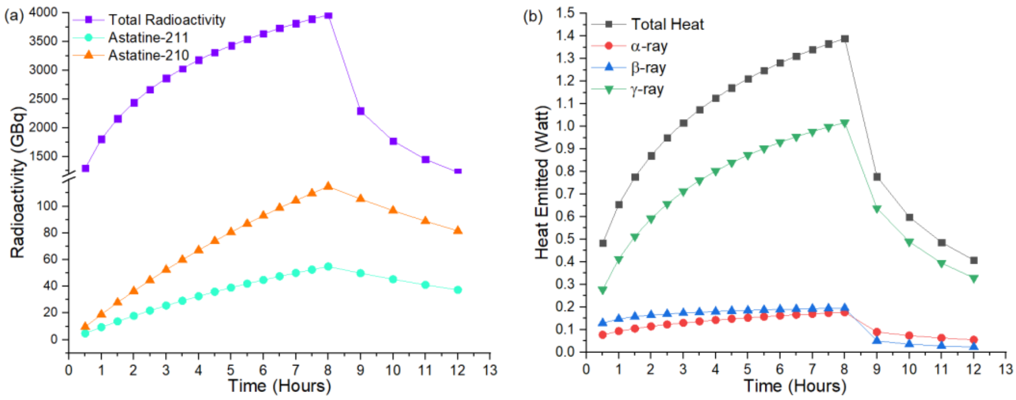

Figure 8. Irradiation of 39 MeV profile graph of: (a) Radioactivity; and (b) Heat.

The result of 39 MeV irradiation simulation was shown in figure 8:

At the end of bombardment (EOB), total radioactivity was obtained 3966.60 GBq, which was decreased to 1223.50 GBq after 2 hours of cooling. At EOB, radioactivity from ^{211}At was 54.89 GBq and ^{210}At was 114.88 GBq. The Radioactivity of ^{210}At was found to be twice that ^{211}At. It is because the cross-section was dependent on energy. In 39 MeV cross-section of ^{210}At reaction was maximum. However, a cross-section of ^{211}At was the minimum that the radioactivity found equivalent to the cross–section value [21]. From the third improvement, suggestions can be given if the researcher wants to make or upgrade a cyclotron, especially to produce ^{211}At. It is better not to have as much energy as 39 MeV because the impurities obtained will be high.

CONCLUSION

Monte Carlo simulation using DECY-13 design could not produce ^{211}At from ^{nat}Bi/^{209}Bi. The inability is because the energy of the accelerated alpha particles has not been able to penetrate the bismuth nucleus. The continuation simulation successfully predicts if the niobium layer thinned from 2.5 mm to 125 mm can be obtained ^{211}At with radioactivity 41.41 GBq with low toxic impurity ^{210}At at EOB. On the other side, increasing the energy of DECY-13 to 28 MeV can be produced ^{211}At but the impurity ^{210}At was found more. Furthermore, the result of this paper might be considered if Indonesia will produce ^{211}At in the future.

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