Estimations of fluorine-18 production yields from 13-MeV proton bombardment of enriched water target

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Abstract. Fluorine-18 (18F) is a positron emitter frequently used in Positron Emission Tomography (PET) to assist in the staging of primary tumors. Recent research suggests that the positron emitting radionuclide can also be applied for pneumonia imaging caused by Covid-19 infection. In this work, a 13-MeV proton beam was theoretically bombarded to 99.5% enriched water (H218O) target to produce 18F radionuclide via (p,n) nuclear reaction. The CalcuYield code was used in the predictions of the F-18 production yields. Using the CalcuYield code, the 18F radioactivity yields were calculated at the end of bombardment (EOB) at various proton beam currents, irradiation time and proton beam doses. Based on the CalcuYield calculated results, the maximum EOB yield of 18F at 13 MeV proton energy was 60.073 mCi/µAh. At a proton dose of 60 µAh, the EOB yield could be achieved as high as 3784.393 mCi, which could be used to diagnose more than 500 patients. The calculations also found that for the same proton dose, increasing proton beam current would result in greater 18F radioactivity yield than increasing irradiation time. In addition, radionuclide impurities which could predictably be present in the target were mostly due to nuclear reactions between proton beam and havar window. The predicted radionuclide impurities include 99Tc, 53Fe, 59Ni, 56Co, 52Mn, 186Re and 58Cu which were due to (p,n) nuclear reactions. The total radionuclide impurity yield was found to be 0.793 mCi/µAh. Among the other impurities, 58Cu was expected to have the highest radioactivity yield at all irradiation parameters. These predicted results could be used as a reference for future 18F radionuclide production should a 13-MeV proton beam is employed.

1. Introduction
Currently, Center for Accelerator Science and Technology, National Nuclear Energy Agency of Indonesia (BATAN) is developing a 13 MeV proton accelerating cyclotron in Yogyakarta, Indonesia. The ultimate goal of the cyclotron development is for fluorine-18 (18F) and other radionuclide productions applicable for cancer diagnosis in nuclear medicine. While there are 3 presently available cyclotrons in Indonesia, all of them are based in hospitals in Jakarta; thus, a new cyclotron is required to be developed in Yogyakarta to meet radionuclide demands in Central Java and the surrounding area. Since 18F is a short-lived radionuclide with a half-life of 109.7 minutes, it is recommended that the cyclotrons must be installed in hospitals or nearby area reasonably close to Positron Emission Tomography (PET) centers. Due to positron emitted by 18F radionuclide, it is therefore employed in nuclear medicine for diagnosis purposes. The most important application of 18F radionuclide is for cancer imaging [1-3]. Recent investigation highlighted the use of 18F radionuclide for pneumonia imaging of Covid-19 infection [4].
Fluorine-18 can be produced via $^{18}\text{O}(p,\alpha)^{18}\text{F}$ nuclear reaction with medium energy cyclotrons [5,6]. The high nuclear cross-sections (maximum 315 mbarn at 8 MeV protons) and low threshold energy of 2.66 MeV allow relatively easier production of $^{18}\text{F}$. Therefore, a 13 MeV cyclotron being built in Yogyakarta will expectedly cover optimum production of $^{18}\text{F}$ radionuclide.

Prior to radionuclide production, it is important to calculate all parameters theoretically to help researchers and practitioners to prepare the best target and optimum radioactivity yield. The CalcuYield code is a home-built software developed by researchers at the Center for Radioisotope and Radiopharmaceutical Technology, BATAN in Serpong, Indonesia [7]. The software is typical android based application in which it calculates radioactivity yields at the end of bombardment (EOB) of various important and emerging radionuclides used in PET scans. Previous experimental studies have demonstrated that the CalcuYield code is a powerful tool for predictions of $^{18}\text{F}$ radionuclide yields with relatively small deviations [7]. The code is based on the nuclear cross-section data extracted from the Talys Evaluated Nuclear Data Library 2017 (TENDL 2017) which have been discussed elsewhere [8-14] as well as the Stopping and Range of Ion in Matter 2013 (SRIM 2013) which can be found in literatures [15,16].

Since there has been no available data for $^{18}\text{F}$ production yields using a 13-MeV cyclotron in Indonesia and overseas, it is therefore of paramount importance to predict the yields at different irradiation parameters, including proton beam current, irradiation time and irradiation dose at variable beam currents and irradiation times. Furthermore, radionuclide impurities that might be generated during the $^{18}\text{F}$ production should also be predicted to assure the radiation workers and patients. The calculated data are expected to be used as a reference for future $^{18}\text{F}$ radionuclide production should the 13-MeV cyclotron is in operational.

2. Materials and Methods

In this present study, 99.5% enriched water ($\text{H}_2^{18}\text{O}$) target was simulated as the target of interest. The range of a 13-MeV proton was calculated by the Stopping and Range of Ion in Matter 2013 (SRIM 2013) [15,16] to obtain the optimum volume for the enriched water target. The SRIM 2013 has been largely used to predict the optimum target thickness for various radionuclide production elsewhere [17]. Based on the SRIM 2013 calculation, the range of a 13-MeV proton in 99.5% enriched water target is 2.13 mm. Since the proton beam diameter was 5 mm, the enriched water target volume should be 41.8 mL.

In the CalcuYield calculations of $^{18}\text{F}$ radionuclide yields, the proton beam was varied from 10 to 60 $\mu$A, whereas the irradiation time was varied from 10 to 60 minutes. The dependence of proton dose on the radioactivity yield was also studied by first keeping the proton beam current constant at variable irradiation time. Secondly, the irradiation time was kept constant while the proton beam currents were varied. The results for various proton dose calculations were then compared. The numerical calculations of the CalcuYield has been previously discussed by Wibowo, et al [7].

For radionuclide impurities prediction that might be present during the $^{18}\text{F}$ production, a havar foil consisting of 42.5% of cobalt, 20% of chromium, 18.1% of iron, 13% of nickel, 2.8% of tungsten, 2% of molybdenum and 1.6% of manganese was simulated as a window separating cyclotron vacuum chamber and the enriched target cavity. Each element contained in the havar window was studied from their possible nuclear reactions when a 13-MeV proton hit the window, particularly for $(p,n)$ nuclear reactions. The $(p,n)$ nuclear reactions was chosen in the impurity calculation since they have significantly higher nuclear cross-sections compared to the other nuclear reactions such as $(p,2n)$, $(p,2p)$ and $(p,\alpha)$ which require higher threshold energies to occur. The radioactivity yields of the possible radionuclide impurities were calculated as well.

3. Results and Discussion

3.1 Radioactivity Yields at Various Proton Doses

Based on the CalcuYield calculation, the maximum $^{18}\text{F}$ radioactivity yield at 13 MeV proton energy is 63.073 mCi/$\mu$Ah. The yields increase with increasing proton beam current and irradiation time as can
be seen in Figure 1. For example, at proton beam current of 20 µA and irradiation time of 10 minutes, the $^{18}$F radioactivity yield is 122.345 mCi. The yield then increases to 734.067 mCi when the beam current is increased to 60 µA. Similarly, at proton beam current of 50 µA and irradiation time of 10 minutes, the $^{18}$F radioactivity yield is 611.723 mCi, however the yield jumps to 3153.661 mCi when the irradiation time is increased to 60 minutes.

Surprisingly, for the same proton dose with fixed irradiation time and variable proton beam current, the $^{18}$F radioactivity yield appears to be different and vice versa as shown in Figure 2. The difference in the yield even greater for higher beam current and longer irradiation time. For example, when the irradiation time is fixed to 30 minutes, while the beam current is varied from 5 to 60 µA, the yield increases from 172.54 mCi to 2070.479 mCi. However, at the same proton dose, when the beam current is fixed to 30 µA, while the irradiation time is varied from 5 to 60 minutes, the yield increases from 186.407 mCi to 1892.197 mCi. This finding indicates that for the same proton dose, increasing proton beam current will result in greater $^{18}$F radioactivity yield than increasing irradiation time.

### Figure 1. Calculated $^{18}$F radioactivity yields at various proton beam currents and irradiation time.

### Figure 2. Calculated $^{18}$F radioactivity yields at various proton doses.

#### 3.2 Predicted Radionuclide Impurities

In this paper, radionuclide impurities are any other radionuclides than $^{18}$F radionuclide produced during proton bombardment of enriched water. In this case, the radioactive impurities may come from the havar window in front of the target. According to the TENDL 2017 and CalcuYield calculations, the most possible radionuclide impurities occur due to (p,n) nuclear reactions when a 13-MeV proton beam hit the havar window are $^{96}$Tc, $^{55}$Fe, $^{56}$Co, $^{52}$Mn, $^{184}$Re and $^{58}$Cu as listed in Table 1.

### Table 1. Various radionuclide impurities predicted during production of F-18 radionuclide production.

| Radionuclide | $T_{1/2}$ | Possible nuclear reaction | Threshold Energy (MeV) | Decay mode | Origin of impurities |
|--------------|----------|---------------------------|------------------------|------------|----------------------|
| $^{96}$Tc    | 4.28 days| $^{96}$Mo(p,n)$^{96}$Tc   | 3.79                   | $\beta^+$  | Havar                |
| $^{55}$Fe    | 2.74 years| $^{55}$Mn(p,n)$^{55}$Fe  | 1.02                   | $\beta^+$  | Havar                |
| $^{56}$Co    | 77.24 days| $^{56}$Fe(p,n)$^{56}$Co  | 5.44                   | $\beta^+$  | Havar                |
| $^{52}$Mn    | 5.59 days| $^{52}$Cr(p,n)$^{52}$Mn  | 5.60                   | $\beta^+$  | Havar                |
| $^{184}$Re   | 35.4 days| $^{184}$W(p,n)$^{184}$Re | 2.28                   | $\beta^+$  | Havar                |
| $^{58}$Cu    | 3.20 seconds| $^{58}$Ni(p,n)$^{58}$Cu | 9.51                   | $\beta^+$  | Havar                |

The most possible nuclear reaction between proton and individual havar foil atom is (p,n) nuclear reaction. Based on the CalcuYield calculated radioactivity yield of the individual havar foil atom, the highest yield is 0.476 mCi/µAh which is due to $^{58}$Ni(p,n)$^{58}$Cu nuclear reaction as shown in Table 2.
Since $^{58}\text{Cu}$ decay with a half life of 3.20 seconds, it will not be detected when the enriched water target is cooled for more than 1 hour. This hypothesis has been confirmed by previous experimental results with different proton energies \cite{18-22}. The total number of impurity yield is approximately 0.793 mCi/µAh, which is nearly 1.26% of the total radioactivity yield during the $^{18}\text{F}$ radionuclide production.

**Table 2.** Predicted radioactivity yields of radionuclide impurities.

| Radionuclide impurities | Radioactivity yield (mCi/µAh) |
|-------------------------|--------------------------------|
| $^{96}\text{Tc}$       | 0.189                          |
| $^{55}\text{Fe}$       | 0.0001                         |
| $^{56}\text{Co}$       | 0.035                          |
| $^{52}\text{Mn}$       | 0.09                           |
| $^{184}\text{Re}$      | 0.003                          |
| $^{58}\text{Cu}$       | 0.476                          |
| Total yield             | 0.793                          |

The type and the amount of radionuclide impurities greatly depend on the proton beam current and irradiation time. Based on the CalcuYield calculations, the radioactivity yields of all impurities increase with increasing irradiation time, except for $^{58}\text{Cu}$ which saturates at all time. For example, at proton beam current of 40 µA, the yield of $^{58}\text{Cu}$ radionuclide impurity remains at 19.036 mCi when the irradiation time increases from 10 minutes to 60 minutes, whereas the yield of $^{96}\text{Tc}$, $^{55}\text{Fe}$, $^{56}\text{Co}$, $^{52}\text{Mn}$ and $^{184}\text{Re}$ radionuclide impurities increase when the irradiation time increases from 10 minutes to 60 minutes as can be seen from Table 3.

**Table 3.** Calculated radionuclide yields of impurities at fixed proton beam current of 40 µA and variable irradiation time from 10 minutes to 60 minutes.

| Irradiation time (minute) | Yield (mCi) |
|---------------------------|-------------|
|                           | $^{96}\text{Tc}$ | $^{55}\text{Fe}$ | $^{56}\text{Co}$ | $^{52}\text{Mn}$ | $^{184}\text{Re}$ | $^{58}\text{Cu}$ |
| 10                        | 1.72        | 0             | 0.24          | 0.6           | 0.02            | 19.036            |
| 20                        | 3.2         | 0             | 0.48          | 1.2           | 0.036          | 19.036            |
| 30                        | 4.52        | 0.0036        | 0.72          | 1.8           | 0.056          | 19.036            |
| 40                        | 5.68        | 0.0038        | 0.92          | 2.4           | 0.072          | 19.036            |
| 50                        | 6.68        | 0.0044        | 1.16          | 3             | 0.092          | 19.036            |
| 60                        | 7.56        | 0.0042        | 1.4           | 3.6           | 0.112          | 19.036            |

4. **Conclusion**

Production yields of $^{18}\text{F}$ radionuclide have been calculated using the CalcuYield code from 13-MeV proton bombardment of enriched water (H$_2$18O) target. The maximum $^{18}\text{F}$ radioactivity yield at 13 MeV proton energy is 63.073 mCi/µAh. Several radionuclide impurities are predicted to be present in the enriched water target during the proton bombardment, including $^{96}\text{Tc}$, $^{55}\text{Fe}$, $^{56}\text{Co}$, $^{52}\text{Mn}$, $^{184}\text{Re}$ and $^{58}\text{Cu}$. Among the other impurities, $^{58}\text{Cu}$ yields the highest radioactivity, which is 0.476 mCi/µAh. The total number of impurity yield is approximately 0.793 mCi/µAh, which is nearly 1.26% of the total radioactivity yield during the $^{18}\text{F}$ radionuclide production. Based on the CalcuYield calculations, the radioactivity yields of all impurities increase with increasing irradiation time, except for $^{58}\text{Cu}$ which remains steady at all times.
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