Calculated cyclotron-based scandium-47 production yields via $^{48}\text{Ca}(p, 2n)^{47}\text{Sc}$ nuclear reaction

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Abstract. Scandium-47 is a promising $\beta^-$ particle emitter that has been suggested as a candidate for radiotheranostics. Thus, better understanding of optimum irradiation parameters, radioactivity yields and possible impurities during its production is of paramount importance. The theoretical calculation of the end-of-bombardment (EOB) results is performed using Microsoft Excel following the calculation of the excitation function obtained from the TALYS software and the stopping power obtained from the SRIM software can be accessed for free. According to the TALYS code calculations, the threshold energy for $^{47}\text{Sc}$ production was 8.39 MeV, whereas the maximum cross-section (879 mbarn) occurred at proton incident energy of 17 MeV. The calculated EOB yield for $^{48}\text{Ca}(p,2n)^{47}\text{Sc}$ nuclear reaction at 60 MeV proton energy was found to be 449 MBq/μAh, which was suitable quality for typical radionuclide production. Besides, three radionuclides, i.e. $^{48}\text{Sc}$, $^{46}\text{Sc}$ and $^{47}\text{Ca}$ were predicted to be the main impurities in the $^{47}\text{Sc}$ production. However, in order to minimize the production of $^{48}\text{Sc}$, $^{46}\text{Sc}$ and $^{47}\text{Ca}$ impurities radionuclide the safest and optimum proton energy should be between 23 and 30 MeV, which can be achieved using the available 26 MeV cyclotron. This study can be used as a reference for future $^{47}\text{Sc}$ production when proton beams of up to 60 MeV are employed.

1. Introduction
Currently, nuclear medicine is increasingly being used for the treatment of cancers for both diagnostic and therapeutic purposes. In general, diagnostic and therapeutic are separate processes and use different radioisotopes. However, there are several radioisotope pairs that can be used for diagnostic and also therapeutic called radiotheranostics.

Radiotheranostics uses the same type of target material with the same molecule, and is then labeled diagnostic and therapeutic radionuclides which are of the same chemical element. [1]. Only a few pairs of radionuclides have been proposed for theranostics applications. These are iodine radioisotopes $^{123}\text{I}$ and $^{124}\text{I}$ for imaging, as well as $^{131}\text{I}$ for therapy. Other examples are $^{86}\text{Y}$, $^{61}\text{Cu}$ and $^{64}\text{Cu}$ for PET imaging and $\beta^-$ emitters $^{90}\text{Y}$ and $^{67}\text{Cu}$ for therapy. Recently, scandium radioisotopes were also proposed for theranostics application. Significant attention to $^{44}\text{Sc}$ and $^{43}\text{Sc}$ as tracers in positron emission tomography imaging has been observed [2]. While the production and application of $^{44}\text{Sc}$ were extensively studied, reports on optimum parameters of $^{47}\text{Sc}$ production are still limited.
In the previous study, several $^{47}\text{Sc}$ production methods have been discussed using both nuclear reactors [3] and cyclotron. The production of radioisotope using nuclear reactors has the disadvantage of being limited to the number of nuclear reactors making it unaffordable for hospitals far away from nuclear reactor locations. Therefore, one of the other alternatives that are more promising is by employing a cyclotron that can be installed in each hospital [4]. Moreover, the number of the cyclotron in the world has increased from year to year. Cyclotron based method has also appeared to be more attractive over nuclear reactor based methods in terms of a relatively low volume of radioactive waste, considerably lower ecological hazard, and its low cost and running expenses [5].

Previous research suggested that the production of $^{47}\text{Sc}$ could be performed by bombarding $^{48}\text{Ca}$ target using cyclotron-accelerated proton particles via $^{48}\text{Ca}(p,2n)^{47}\text{Sc}$ nuclear reaction. Due to low availability and high cost of $^{48}\text{Ca}$, Misiak and co-workers decided to irradiate $\text{CaCO}_3$ target with natural isotopic composition. Stacks of $\text{CaCO}_3$ target irradiated using proton incident energy ranging from 0 to 60 MeV. In their experimental results, they found that $^{47}\text{Sc}$ yield could reach up to 143.95 kBq/\mu A h with a proton dose of 30 nA for 5 hours. The radioactivity yield of $^{47}\text{Sc}$ was only 143.95 kBq/\mu A h which was considered very low to be used for medical purposes. The low yield was presumably due to the use of a very low proton dose and also due to the use of a natural calcium target that only contains 0.187% of $^{48}\text{Ca}$.

To provide another reference about cyclotron-based $^{47}\text{Sc}$ production, we propose $^{47}\text{Sc}$ theoretical production studies with different proton doses and a percentage of $^{48}\text{Ca}$ targets. To the best of our knowledge, there has been very limited theoretical calculation found in the literature regarding cyclotron-based $^{47}\text{Sc}$ production. The previous theoretical calculation for production $^{47}\text{Sc}$ has been performed by Mayir Mamtimin et al [6] by employing Monte Carlo for simulation of $^{47}\text{Sc}$ production from both natural and enriched titanium but by using electron linacs via $^{48}\text{Ti}(\gamma, p)^{47}\text{Sc}$ reaction mode. Theoretical calculations are of paramount importance as an early prediction of radioactivity yields as a result of proton and some other particle irradiations. In this study, such as stopping power, nuclear cross-section, end-of-bombardment (EOB) yield dependence of irradiation parameter, including proton beam energies and dose, as well as possible radionuclidic impurities are comprehensively discussed.

2. Method

In this study, the end-of-bombardment (EOB) yields of the $^{48}\text{Ca} (p, 2n)$ $^{47}\text{Sc}$ nuclear reaction was calculated using the yield calculation formula is previously discussed in some published work [7]. Though some changes to the irradiation parameters were performed due to different targets and radioisotopes produced in each published literature. SRIM (Stopping and Range of Ions in Matters) 2013 software [8], which can be found on www.srim.org was employed to calculate proton particles ranging from 0 to 60 MeV in the enriched $^{48}\text{Ca}$ target up to 69.2%.

The TALYS software calculations performed for the excitation function of $^{48}\text{Ca}(p,n)^{48}\text{Sc}$ and other nuclear reaction was the latest version of TALYS-Evaluated Nuclear Data Library (TENDL 2017) [9] which can be downloaded online [10]. In this work, Microsoft Excel was employed to quickly compute the end-of-bombardment (EOB) yield formula. The EOB yield ($Y$) is calculated as follows [11]:

$$ Y = \Phi \left(1 - e^{-\lambda t}\right) \frac{N_A}{M} \int_{E_1}^{E_2} \frac{\sigma(E)}{1 - \frac{d(E)}{M \Delta x}} dE, $$

(1)

Where $\Phi$ is the number of proton particles per unit of time, $\lambda$ is the decay constant of the resulting radioisotope, $t$ is the duration of irradiation, $N_A$ is the Avogadro number, $M$ is the atomic mass of the
target, $E_i$ is the initial energy of the incident particle, $E_{th}$ is the threshold energy, $\sigma(E)$ is cross-section for the nuclear reaction as proton energy function, $\rho$ is mass density and $d(E)/dx$ is the stopping power or energy loss of the incident proton.

Furthermore, the dependence of proton beam energy and proton dose on the produced radioactivity yield was simulated for proton beams energies ranging from 0 to 60 MeV and for proton dose starts from 0 to 100 $\mu$Ah that can be performed by widely available cyclotron in the world (accelerating 11, 18, 26, 30, 60 MeV protons).

In general, the sequence of procedures in this study can be shown in the following flowchart:

![Flowchart](image)

**Figure 1.** Research procedure

### 3. Results and Discussion

#### 3.1 SRIM-calculated Range and Stopping Power

Production of $^{47}$Sc requires knowledge of proton range in $^{48}$Ca target as a function of the incoming proton energy. According to the SRIM calculation result for a range of proton in $^{48}$Ca target, the proton range increases with increasing proton energy as shown in Figure 2, a 10-MeV proton can penetrate as deep as 1320 $\mu$m in a $^{48}$Ca target, whereas the range of a 60-MeV proton in the same target is approximately 31160 $\mu$m as shown in Figure 2.

Furthermore, when proton passes through a target, it is expected to lose some or all of its energy. The energy losses (stopping powers) of the proton particles are relatively large, i.e. $2.81 \times 10^{-2}$ and $7.02 \times 10^{-3}$ mg/cm$^2$ for 10-MeV and 60-MeV proton respectively.

For $^{47}$Sc radionuclide production, the recommended thickness of $^{48}$Ca target is listed in Table 1 for proton energies ranging from 10 to 60 MeV. The target thickness prepared for the irradiation should be made thicker with increasing proton energy. Increasing proton energy from 15 MeV to 55 MeV would consequently require increasing the $^{48}$Ca target thickness from nearly 2.69 mm to nearly 26.71 mm. Note that one could add up to 10% of the recommended thickness to account for the deviation of the proton range.
Figure 2. SRIM-calculated range of proton ($R_p$ - red line) and stopping power ($dE/dx$) of proton (blue line) in $^{48}$Ca targets for energy range of 1 – 60 MeV

Table 1. Recommended target thickness for $^{48}$Ca target for $^{47}$Sc production for several available cyclotrons

| Proton energy (MeV) | $^{48}$Ca target thickness (mm) |
|---------------------|--------------------------------|
| 11                  | 1.56                           |
| 18                  | 3.7                            |
| 26                  | 7.06                           |
| 30                  | 9.11                           |
| 60                  | 31.16                          |

3.2 Nuclear Cross-section

During irradiation, several nuclear reactions occurring when proton beams are bombarded to enriched $^{48}$Ca target. According to the TALYS 2017 calculated nuclear cross-sections (as can be seen in Figure 3) there are four reaction modes that have high cross-sections, the two highest ones are ($p_{,2n}$), ($p_{,n}$), then followed by ($p_{,3n}$) and ($p_{,np}$). Furthermore, the other two reaction modes, ($p_{,d}$) and ($p_{,\alpha}$), have a low cross-section (green line and yellow line). The highest nuclear cross-sections for ($p_{,2n}$) reaction is 879 mbarn that occurs at 17 MeV protons while the threshold energy is 8.39 MeV. At threshold energy, the cross-section increases dramatically with increasing energy, but then it goes down dramatically with increasing energy when the incoming particle is greater than 17 MeV. For ($p_{,n}$) reaction, the highest cross-section is 866 mbarn which happens when proton is directed at 9 MeV while threshold energy is 0.65 MeV. This is very similar to ($p_{,2n}$) reaction, in which at low proton energies, the cross-section increases dramatically with increasing energy, but then it goes down dramatically with increasing energy when the incoming particle is greater than 9 MeV. For ($p_{,3n}$) and ($p_{,np}$) reaction, the threshold energies for both are 19.8 MeV and 10.2 MeV respectively, while the maximum cross section are 426 mbarn and 179 mbarn which occurs at the same energy, e.g at 30 MeV. The same trend happens to ($p_{,2n}$) and ($p_{,n}$), for the ($p_{,3n}$) reaction, the cross-section increases and then goes down but not too dramatically as ($p_{,2n}$) and ($p_{,n}$) reaction. Different trends occur in ($p_{,np}$) reaction, the cross-section increases with increasing energy, and then it goes down slowly with increasing energy when the incoming particle is greater than 30 MeV.
Figure 3. TALYS calculated nuclear cross-sections of \((p,2n)\), \((p,n)\), \((p,3n)\), \((p,np)\), \((p,d)\) and \((p,\alpha)\) for 0-60 MeV protons bombarded to \(^{48}\text{Ca}\).

For the lowest level cross-sections \((p,d)\) and \((p,\alpha)\) reaction, the maximum cross-sections for \((p,d)\) reaction is 30.3 mbarn that occurs at 26 MeV, whereas for \((p,\alpha)\) reaction the maximum cross-sections is only 4.44 mbarn that occurs at 19 MeV. There is no peak and almost no cross-section level because the cross-section values are very low, but in more close (see Figure 3, top inset), the same event happens like other reactions, which are seen as an increase and decrease cross-section dependence proton energy.

3.3 Sc-47 EOB Yield dependence of proton beam energy and dose

The calculated \(^{47}\text{Sc}\) EOB yield of \(^{48}\text{Ca}(p,n)\) \(^{48}\text{Sc}\) nuclear reaction is shown in Figure 4 (a), which indicates that the radioactivity yield increases dramatically with increasing incident proton energy in the range of proton energy between 10 and 23 MeV. However the yield tends to flat out when the proton beam is increased further to greater than 23 MeV. At 60 MeV proton energy, the maximum \(^{47}\text{Sc}\) yield is 449 MBq/µAh, which is sufficient for theranostics purposes.

The \(^{47}\text{Sc}\) EOB yield can be increased by either increasing bombardment time or proton beam current or collectively called as proton dose. In this work, dependence of proton dose (0-100 µAh) on EOB yield of \(^{48}\text{Ca}(p,n)\) \(^{48}\text{Sc}\) nuclear reaction is calculated for several widely available cyclotrons (accelerating 11, 18, 26 and 30, 60 MeV protons) as depicted in Figure 4 (b). As can be seen in Figure 4 (b), the EOB yield increases linearly with increasing proton dose. For instance, at proton dose of 20 µAh and 18-MeV proton the EOB yield is 2.74 GBq, whereas the yield increases to 13.69 GBq for the same proton energy but higher proton dose of 100 µAh.
Similar trend also occurs in other higher proton energies of 60 MeV where maximum yields of up to 44.94 GBq which is good quality for typical radionuclide production. For 11 MeV proton energy, the maximum yield only 0.98 GBq (see Figure 4 (b), top inset), the yield are considered low for typical radinuclide production. The condition occurs because the energy of the proton incident is too close to the reaction threshold \((p, 2n)\) that is 8.9 MeV where the value of the cross section that causes a nuclear reaction is still very low up to 11 MeV proton energy. Therefore, the 11 MeV cyclotron is not recommended for \(^{47}\text{Sc}\) radionuclide production.

### 3.4 Predicted Impurities

Other nuclear reactions could possibly occur during proton beam irradiation of the enriched \(^{48}\text{Ca}\) target. Thus, in the \(^{47}\text{Sc}\) production radionuclide impurities can be generated. Impurity identification in radionuclide production is of paramount importance in radionuclide production. Radionuclide impurities can be predicted from their excitation functions which can be seen in Figure 5. Based on the excitation functions, there are three biggest possibilities of nuclear reactions involving the incoming proton beams, namely \((p, n)\), \((p, 3n)\) and \((p, np)\) reactions which may produce high activity radionuclide impurities in proton-produce \(^{47}\text{Sc}\) radionuclide depending on the incident proton energy.
The predicted impurities are summarised in Table 2, which indicates that there are three possible radionuclidic impurities such as $^{48}$Sc, $^{46}$Sc, and $^{47}$Ca. $^{48}$Sc impurity which has a shorter half-life than $^{47}$Sc that is 43.67 hours can be generated from $^{48}$Ca(p,n)$^{48}$Sc. $^{46}$Sc impurity which has quite long half-life of 83.79 days can be generated from $^{48}$Ca(p,3n)$^{46}$Sc nuclear reactions. $^{47}$Ca impurity can be produced from $^{48}$Ca(p,np)$^{47}$Ca nuclear reaction which has half-life of 4.54 days which decays through β⁻ particle emission and eventually generates additional $^{47}$Sc activity. Due to longer half-life of $^{47}$Ca than half of $^{47}$Sc, $^{47}$Ca removal must go through chemical separation.

| Isotopes | Nuclear reaction | Threshold energy (MeV) | Decay mode | Half-life | Product |
|----------|-----------------|------------------------|------------|-----------|---------|
| $^{48}$Sc | $^{48}$Ca(p,n)$^{48}$Sc | 0.65 | β⁻ | 43.67 h | $^{48}$Ti |
| $^{46}$Sc | $^{48}$Ca(p,3n)$^{46}$Sc | 19.8 | β⁻ | 83.79 d | $^{46}$Ti |
| $^{47}$Ca | $^{48}$Ca(p,np)$^{47}$Ca | 10.2 | β⁻ | 4.54 d | $^{47}$Sc |

The EOB yields for calculated impurities are shown in Figure 5, which indicates that $^{48}$Sc occurring from $^{48}$Ca(p,n)$^{48}$Sc has the highest EOB yield. Among the three impurities $^{48}$Sc shows the highest yield of up to 249 MBq/µAh. Since $^{48}$Sc have shorter half-life than $^{47}$Sc, it can be removed by waiting for decay. Furthermore the EOB yield for $^{47}$Ca derived from $^{48}$Ca(p,np)$^{47}$Ca nuclear reaction increases linearly with increasing proton dose from 19 MeV, whereas the maximum yield of 217 MBq/µAh occurs at 60 MeV. Although $^{47}$Ca can decay into $^{47}$Sc, but because the half-life of $^{47}$Ca is greater than $^{47}$Sc so to eliminate $^{47}$Ca the possible way is through chemical separation.

**Figure 5.** EOB yields of various impurities predicted during the production of $^{47}$Sc radionuclide production
A small amount of $^{46}$Sc derived from $^{48}$Ca(p,3n)$^{46}$Sc nuclear reaction with maximum yield only 12 MBq/µAh at 60 MeV proton energy. Since the long half-life of $^{46}$Sc then it needs to be taken into account. Based on Figure 5, to minimize the production of $^{46}$Sc it can be done using the energy of protons below 30 MeV where the yield for $^{46}$Sc and also $^{47}$Ca is still been very low. However, considering $^{47}$Sc yield, based on Figure 4 (a) where the most significant increase of yield $^{47}$Sc at 23 MeV proton energy, then the safest and optimum proton energy for $^{47}$Sc production should be ranging from 23-30 MeV that available for 26 MeV cyclotron.

4. Conclusion
Theoretical calculation of $^{47}$Sc radioisotope production using proton beams accelerated in cyclotron have been discussed in this paper. Based on the TALYS 2017 calculated nuclear cross-sections, (p,2n) nuclear reaction has the highest nuclear cross-sections (up to 879 mbarn) compared to the others such as (p,n), (p,3n), (p,np), (p,d) and (p,α). The maximum calculated EOB yield for $^{48}$Ca(p,2n)$^{47}$Sc reaction by 60 MeV proton beams energy is 449 MBq/µAh. Based on the excitation functions or nuclear cross-sections, there are three possible biggest radionuclide impurities produced during $^{47}$Sc production process i.e $^{48}$Sc, $^{46}$Sc and $^{47}$Ca that are also calculated in this paper. Based on calculation results, $^{48}$Sc has the highest yield of up to 249 MBq/µAh, followed by $^{47}$Ca up to 217 MBq/µAh and for lowest yield is $^{46}$Sc which is only at 12 MBq/µAh. It should be noted that $^{48}$Sc radionuclide impurities have a high yield, but due to the shorter half-life of $^{46}$Sc then $^{47}$Sc. $^{48}$Sc can be removed by waiting for decay. For $^{47}$Ca impurities radionuclides, due to its longer half-life, it is suitable to use chemical separation to eliminate $^{47}$Ca. However, in order to minimize the production of $^{48}$Sc, $^{46}$Sc and $^{47}$Ca radionuclide impurities the safest and optimum proton energy should be between 23 and 30 MeV that is available for 26 MeV cyclotron. Based on the results obtained from this study, $^{47}$Sc has the potential to be produced by employing a cyclotron accelerating proton above 23 MeV which is suitable for clinical applications. However, the study of economic aspects needs to be conducted further due to the high cost of enriched calcium targets.

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