Cyclotron-based rhenium-186 production using proton beam of up to 50 MeV

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Abstract. Rhenium-186 (186Re) radioisotope has been suggested for palliative radiotherapy of bone metastatic cancer patients and radiosynovectomy in nuclear medicine. Currently 186Re has been mostly produced using neutron activation in nuclear reactors, whereas cyclotron-based production has not been well explored. In this paper, we theoretically propose cyclotron-based proton beams of up to 50 MeV for 186Re production. By Employing the TALYS 2017 codes, we calculated nuclear cross-section for (p,n) nuclear reaction and then built Matlab codes for the End-of-Bombardment (EOB) yield calculations of 186W(p,n)186Re nuclear reaction while the predicted impurities were calculated for (p,2n), (p,np), (p,α) and (p,d) nuclear reactions respectively. The TALYS calculated cross-sections indicated that the threshold energy for 186W(p,n)186Re nuclear reaction is 8 MeV. The maximum calculated EOB yield for 186W(p,n)186Re reaction at 50 MeV was 93.64 kBq/µAh which agreed with experimental data published elsewhere. The threshold energies for the (p,2n), (p,np), (p,α) and (p,d) were 7.58, 7.23, 2.0 and 4.99 MeV respectively. In addition, two radionuclides, i.e. 185W and 183mRe as well as two stable isotopes, i.e. 186Re and 184W were predicted to be the main impurities in the 186Re production. This study can be used as a reference for future 186Re production when proton beams of up to 50 MeV are employed.

1. Introduction

Radionuclides emitting particles such as α, β, and γ have been extensively used in nuclear medicine for imaging and therapy. The therapeutic radionuclides include 32P, 90Y, 211At, 153Sm, 186Re etc [1-3]. Previous reports radionuclides such as 153Sm and 186Re used for palliative therapy of bone metastatic patients with difference cancers such as prostate cancer, breast cancer and other malignancies [4-16]. Comparative studies of the effectiveness of 90Y and 186Re for radiosynovectomy in haemophilic synovitis of elbows and ankles have been recently conducted by Rodriguez-Merchan et al [17]. Meanwhile production of 188Re itself can be carried out using nuclear reactor [18] or cyclotron [19]. Cyclotrons and accelerators have been widely employed to produce radionuclides such as 18F, 99mTc [20,21] or for material studies [22-25].

Rhenium-186 is a β emitting radionuclide with a half life of 3.72 day which is suitable for radiotherapy application. Experimental production of 186Re has been discussed earlier by Solin and co-workers [26] by bombarding variable proton beam with energy of up to 16 MeV to produce 186Re from 186W(p,n)186Re nuclear reaction.

There has been very limited theoretical calculation found in the literature regarding cyclotron-based 186Re production. Experimental research on 186Re radioactivity yields available have also been mostly
for $^{186}$Re production using low or medium proton energy of up to 16 MeV [26]. Theoretical calculations are of paramount important as an early prediction of radioactivity yields as a result of proton and some other particle radiation. In this work, the End-of-Bombardment (EOB) yields are calculated for proton beams ranging from 5 to 50 MeV since they can be used as a reference for radioisotope radioactivity yields for future production.

2. Materials and Methods
Stopping and Range of Ions in Matters (SRIM 2013) code, which can be found on www.srim.org was employed to calculate the ranges of energetic proton in enriched $^{186}$W. The SRIM 2013 codes have been widely used to calculate target thickness for production of $^{18}$F [20], $^{99m}$Tc [27] and some other radionuclides [28-29]. The optimum optimum target thicknesses were then determined from the proton range while the energy loss or stopping power is used for the EOB yield calculations. Nuclear cross-sections for $^{186}$W(p,n)$^{186}$Re nuclear reaction was calculated using the TALYS 2017 codes where the TALYS-Evaluated Nuclear Data Library 2017 (TENDL 2017) could be downloaded online [30]. The TALYS codes have been previously employed to compute the cross-sections of several nuclear reactions as can be found elsewhere [31-33].

The end-of-bombardment (EOB) yields of $^{186}$W(p,n)$^{186}$Re nuclear reactions were calculated based on the yield formulae discussed elsewhere [27]. In this case Matlab codes were built to quickly compute the yields. The calculated results were then compared with available experimental data.

3. Results and Discussion
3.1 Nuclear cross-section
Nuclear reactions occurring when proton beams are bombarded to enriched $^{186}$W target. According to the TALYS 2017 calculated nuclear cross-sections (as can be seen in Figure 1) for several nuclear reactions, (p,2n) has the highest nuclear cross-sections (up to 857 mbarn) compared to the other ones such as (p,n), (p,np), (p,d) and (p,α). The highest nuclear cross-sections for (p,2n) reaction occurs at 16 MeV protons while the threshold energy is 7.58 MeV. For (p,n) reaction, the highest cross-section is 46.3 mbarn which happens when proton is directed at 9 MeV (see Figure 1, top inset). In addition, the threshold energy for (p,n) reaction is 1.43 MeV which is lower than that of (p,2n) reaction. The TALYS 2017 calculated results agree with the experimental results recently carried out by Solin et al [26] as seen in Figure 1, bottom inset.

![Figure 1. TALYS calculated nuclear cross-sections of (p,n), (p,np), (p,2n), (p,d) and (p,α) for 0-50 MeV protons bombarded to $^{186}$W (full blue lines) and experimental data by Solin et al (pentagram).](image-url)

Nuclear reaction (p,np) begins to take place when proton energy is bombarded at 7.23 MeV whereas the maximum cross-section is 154 mbarn for 55-MeV protons. Furthermore the maximum cross-sections
for (p,d) and (p,α) reactions are 23.2 and 17.1 mbarn which occurs at proton energy of 30 and 22 MeV respectively. The threshold energy for both (p,d) and (p,α) reactions are 4.99 and 7.65 MeV respectively.

3.2 Re-186 yield
The calculated $^{186}\text{Re}$ EOB yield of $^{186}\text{W}(p,n)^{186}\text{Re}$ nuclear reaction is shown in Figure 2, which indicates that the radioactivity yield increases with increasing incident proton energy. The yield starts at pretty low value (0.4 kBq/µAh) and the gradually increases to 76.1 kBq/µAh at 30-MeV proton. The EOB yield then saturates when proton energy employed in the bombardment is above 40 MeV. Experiment by Solin, et al indicated that the Re-186 yields for proton energy of 15.67 MeV and 16.5 MeV were 39.2 kBq/µAh and 41.2 kBq/µAh whereas in this calculation they are predicted to be 38.9 kBq/µAh and 41.5 kBq/µAh which agrees with the experimental data. It should be noted that, in general, the radioactivity yield increases with increasing proton energy.

![Figure 2. Calculated EOB yields of $^{186}\text{Re}$.](image)

The $^{186}\text{Re}$ 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 on EOB yield of $^{186}\text{W}(p,n)^{186}\text{Re}$ nuclear reaction is calculated for several widely available cyclotrons (accelerating 11, 18, 26 and 30 MeV protons) as depicted in Figure 3. As can be seen in Figure 3, the EOB yield increases linearly with increasing proton dose. For instance, at proton dose of 20 µAh and 11-MeV proton the EOB yield is 0.488 MBq, whereas the yield increases to 2.440 MBq for the same proton energy but higher proton dose of 100 µAh. Similar trend also occurs for the other higher proton energy.

![Figure 3. Dependence of proton dose on EOB yields of $^{186}\text{Re}$ for several proton energy.](image)
3.3 Predicted Impurities

Impurity identification in radionuclide production is of paramount importance in radionuclide production; thus understanding on nuclear reactions are required. Based on the nuclear cross-section calculations for (p,2n), (p,np), (p,α) and (p,d) reactions (Figure 1 and Figure 4), there are several impurities which may be produced in proton-produce $^{186}$Re radionuclide depending on the incident proton energy. The predicted impurities are summarised in Table 1, which indicates that there are two possible radionuclidic impurities such as $^{185}$W and $^{183m}$Re. $^{185}$W impurity which has quite long half life of 75.1 days can be generated from $^{186}$W(p,np)$^{185}$W or $^{186}$W(p,d)$^{185}$W nuclear reactions, whereas $^{183m}$Re impurity can be produced via $^{186}$W(p,α)$^{183m}$Re, though $^{183m}$Re would probably not complicate the chemical purity process since its half life is only 1.84 ms.

| Isotopes | Nuclear reaction | Threshold energy (MeV) | Decay mode | Half life |
|----------|------------------|------------------------|------------|-----------|
| $^{185}$W | $^{186}$W(p,np)$^{185}$W | 8.11 | β | 75.1 d |
| $^{185}$Re | $^{186}$W(p,2n)$^{185}$Re | 13.16 | - | stable |
| $^{183m}$Re | $^{186}$W(p,α)$^{183m}$Re | 13.49 | β⁺ | 1.84 ms |
| $^{185}$W | $^{186}$W(p,d)$^{185}$W | 13.49 | β | 75.1 d |
| $^{184}$W | $^{186}$W(p,t)$^{184}$W | 13.49 | - | stable |

The EOB yields for all impurities are shown in Figure 4, which indicates that the $^{185}$W occurred from $^{186}$W(p,np)$^{185}$W has the highest yield of up to EOB yield. Among the four impurities $^{185}$Re shows the highest yield of up to 223.98 kBq/µAh, whereas a small amount of $^{183m}$Re derived from $^{186}$W(p,α)$^{183m}$Re nuclear reaction 41.30 kBq/µAh. Since $^{185}$Re is very short half lived, it can be negligible during the chemical purity process. Thus, $^{185}$W is only the major impurities needs to be taken in to account. The EOB yield for $^{186}$W(p,t)$^{184}$W reaction was also calculated though it is insignificantly low and not shown in the figure.

![Figure 4](image_url)
4. Conclusion
Theoretical calculations of nuclear cross-section for (p,n) nuclear reaction has been performed to compute the End-of-Bombardment (EOB) yield of $^{186}$W(p,n)$^{186}$Re nuclear reaction, whereas predicted impurities were calculated for (p,2n), (p,np), (p,α) and (p,d) nuclear reactions respectively. Based on the TALYS 2017 calculated nuclear cross-sections, (p,2n) nuclear reaction has the highest nuclear cross-sections (up to 857 mbarn) compared to the others such as (p,n), (p,np), (p,d) and (p,α). The maximum calculated EOB yield for $^{186}$W(p,n)$^{186}$Re reaction is $93.64 \text{kBq/µAh}$ for incident proton of 50 MeV. Both nuclear cross-sections and EOB yields are in good agreement with previously reported experimental data. There are two radionuclides i.e. $^{185}$W and $^{183m}$Re as well as two stable isotopes, i.e. $^{185}$Re and $^{184}$W predicted in the calculation, though in the end only $^{185}$W is significant while the others has too short half life or too low yield. This work is expected to be used as a reference for future $^{186}$Re production when proton beams of up to 50 MeV are employed. Other calculations will be done for some other radionuclides relevant in nuclear medicine applications.

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