Sc-47 production from titanium targets using electron linacs

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Abstract

In this work we have studied the feasibility of photonuclear production of ⁴⁷Sc from ⁴⁸Ti via ⁴⁸Ti(γ,p)⁴⁷Sc reaction. Photon flux distribution for electron beams of different energies incident on tungsten converter was calculated using MCNPX radiation transport code. ⁴⁷Sc production rate dependence on electron beam energy was found and ⁴⁷Sc yields were estimated. It was shown that irradiating a natural Ti target results in numerous scandium isotopes which can reduce the specific activity of ⁴⁷Sc. Irradiating enriched ⁴⁸Ti targets with a 22 MeV 1 mA beam will result in hundreds of MBq/g activity of ⁴⁷Sc and no other isotopes of scandium. Decreasing the size of the target will result in much higher average photon flux through the target and tens of GBq/g levels of specific activity of ⁴⁷Sc. Increasing the beam energy will also result in higher yields, but as soon as the electron energy exceeds the ⁴⁸Ti(γ,np)⁴⁶Sc reaction threshold, ⁴⁶Sc starts being produced and its fraction in total scandium atoms grows as beam energy increases. The results of the simulations were benchmarked by irradiating natural titanium foil with 22 MeV electron beam incident on the tungsten converter. Measured ⁴⁷Sc activities were found to be in very good agreement with the predictions.

1. Introduction

Scandium-47 is a promising β⁻ emitter for the preparation of radiolabeled antibodies due to its favorable energy (average β⁻ energy is 162 keV) and convenient half-life (T_{1/2} = 3.35 days). ⁴⁷Sc therapeutic beta-emissions are accompanied by 159.4 keV gamma (68.3% branching ratio) which allows in vivo imaging to assess tumor targeting, to document disease status, and to predict therapeutic efficacy.

Currently its clinical application is inhibited by the lack of regular availability of sufficient quantities. Possible production methods include neutron capture on titanium and vanadium targets (⁴⁷Ti(n,p)⁴⁷Sc, ^{nat}Ti(n,x)⁴⁷Sc, ^{nat}V(n,x)⁴⁷Sc) (Mausner et al., 1993, DeLorme et al, 2014). Another production route involves (p,2p) reaction on ⁴⁸Ti and requires high energy protons (Mausner et al., 1998, Srivastava and Dadachova, 2001). Using ⁴⁷Ca/⁴⁷Sc generators is yet another alternative (Mausner et al., 1993) which unfortunately requires highly enriched ⁴⁶Ca targets to produce ⁴⁷Ca and thus makes the target cost prohibitive.

To provide a reliable supply of ⁴⁷Sc we propose a photonuclear production method which has proven to be a robust means of isotope production. This technique has also appeared to be more attractive over nuclear reactor based methods in view of a relatively low volume of radioactive waste, considerably lower ecological hazard, and its low cost and running expenses. Electron accelerators have been proven to have feasibility for significant quantities of other valuable

radioisotopes, including ^{67}Cu and ^{225}Ac (Maslov et al., 2006, Danon et al., 2008, Starovoitova et al., 2014).

2. Methods

An essential component of photonuclear production of radioisotopes with electron linacs is a bremsstrahlung converter, which transforms electrons' energy into photons. Conventional converters are made of solid high Z metals with a high melting point, such as W or Ta, however liquid metal converters capable of dissipating tens of kilowatts of beam power can be used for high power accelerators. Bremsstrahlung photons form a forward cone and are incident on the sample with is typically placed right after the converter. The most suitable photon energy for photonuclear production of radioisotopes is 10-40 MeV – the region where the photo-absorption cross-section is the greatest.

The activity A of the produced isotope depends on a number of parameters, such as the number of target nuclides that are irradiated N_T , the threshold energy of the nuclear reaction E_{th} , the maximum energy of photons E_{max} , the photon flux density $\phi(E)$, the cross-section of a photonuclear reaction $\sigma(E)$, decay constant of the produced radioisotope λ and irradiation and cooling time t_i and t_c (Eq. 1):

$$A(t_i) = N_T \cdot \int_{E_{th}}^{E_{max}} \phi(E) \cdot \sigma(E) dE \cdot (1 - e^{-\lambda \cdot t_i}) \cdot e^{-\lambda \cdot t_c} \quad (1)$$

Scandium (Z=21) is a mononuclidic element composed of ^{45}Sc , so the only way to obtain ^{47}Sc from natural scandium is by neutron capture. Titanium (Z=22), on the other hand, consists of five stable isotopes (see Table 1), including the most abundant ^{48}Ti which can be used to produce ^{47}Sc via $^{48}\text{Ti}(\gamma, p)^{47}\text{Sc}$ reaction. Using the $^{49}\text{Ti}(\gamma, np)^{47}\text{Sc}$ channel is also an option for ^{47}Sc production from titanium, however the yield of ^{47}Sc in this case is much lower due to a lower cross-section and low ^{49}Ti abundance. An advantage of producing ^{47}Sc from titanium is that it can be chemically separated from the target material relatively easily; such methods have already been developed and published elsewhere (Kolsky et al, 1998).

Table 1. Isotopic composition of natural titanium.

Isotope	Relative abundance
^{46}Ti	8.0%
^{47}Ti	7.3%
^{48}Ti	73.8%
^{49}Ti	5.5%
^{50}Ti	5.4%

To accurately predict the yield it is necessary to know all the parameters mentioned in Eq.1. Most of them are straightforward, however the integral of the product of the $^{48}\text{Ti}(\gamma, p)^{47}\text{Sc}$ cross-section and photon flux is usually challenging to evaluate. We used MCNPX, a general purpose particle transport Monte Carlo code, developed by the Los Alamos National Laboratory (Pelowitz, 2008). In MCNPX, the integral values in Eqn.(1) were obtained by using flux (F4) tally. The flux values were further multiplied by the ENDF/B-VII cross-sections (Chadwick et al, 2006) using FM cards.

To verify the predicted yield values we have irradiated natural titanium targets (0.05 mm x 2 cm x 2 cm) using the 25 MeV pulsed electron linac at the Idaho Accelerator Center. The gamma ray spectra of the irradiated samples were obtained with a spectroscopic setup, which consisted of a high-energy resolution high purity germanium detector, ORTEC 672-type amplifier, analog-to-digital converter, and a fast list-mode multichannel analyzer. The MPA3 software was used for data processing. The efficiency of the detector was determined with a set of standard gamma ray calibration sources covering energy range from tens of keV to few MeV.

3. Results and Discussion

$^{nat}\text{Ti}(\gamma,p)^{47}\text{Sc}$

A number of simulations were performed to find the optimum energy of the electron beam for photonuclear production of ^{47}Sc via $^{48}\text{Ti}(\gamma,p)^{47}\text{Sc}$ reaction. A thin titanium target (0.05 mm x 2 cm x 2 cm) was assumed for all the simulations. The reaction's cross-section threshold energy is 11.5 MeV; it peaks at 20.1 MeV and significantly drops by about 30-35 MeV (see Figure 1, left). As the electron energy increases the yield of ^{47}Sc initially grows quickly, eventually saturating (Figure 1, right). If maximizing ^{47}Sc yield is the only goal, the energy of the beam should be as high as possible; however exceeding 25 MeV might not be economically feasible.

Figure 1. Left: $^{48}\text{Ti}(\gamma,p)^{47}\text{Sc}$ cross-section (red) and photon flux corresponding to different electron beam energies (black). Thin titanium target was used for the simulations. Right: ^{47}Sc production rate (from $^{48}\text{Ti}(\gamma,p)^{47}\text{Sc}$ reaction) as a function of electron beam energy. 1 μA current was assumed.

However, if a natural titanium target is used a lot of other scandium isotopes are generated through (γ,p) and (γ,np) channels (see Table 2) from ^{46}Ti , ^{47}Ti , ^{49}Ti , and ^{50}Ti . We have ignored neutron capture reactions, which can potentially result in some scandium isotopes, for example $^{46}\text{Ti}(n,p)^{46}\text{Sc}$ since their contribution is insignificant. To estimate the yield of all possible isotopes using different electron beam energies, we have performed a number of MCNPX simulations as described above. The time of irradiation was chosen to be ten days, which corresponds to about three half-lives of ^{47}Sc and thus is optimum for its production. The results of the simulations are summarized in Table 3.

Table 2. Photonuclear reactions in natural titanium resulting in scandium isotopes.

Product	Reaction	Threshold energy, MeV	Product half-life, hours
^{44}Sc	$^{46}\text{Ti}(\gamma, np)^{44}\text{Sc}$	21.7	4
^{46}Sc	$^{47}\text{Ti}(\gamma, p)^{46}\text{Sc}$	10.5	2,013
	$^{48}\text{Ti}(\gamma, np)^{46}\text{Sc}$	22.1	2,013
^{47}Sc	$^{48}\text{Ti}(\gamma, p)^{47}\text{Sc}$	11.5	82
	$^{49}\text{Ti}(\gamma, np)^{47}\text{Sc}$	19.6	82
^{48}Sc	$^{49}\text{Ti}(\gamma, p)^{48}\text{Sc}$	11.4	44
	$^{50}\text{Ti}(\gamma, np)^{48}\text{Sc}$	22.3	44
^{49}Sc	$^{50}\text{Ti}(\gamma, p)^{49}\text{Sc}$	12.2	1

Table 3. Scandium isotope yields using natural titanium target. Ten days irradiation with 1 μA beam is assumed. A thin titanium target was used for the simulations.

Isotope	Isotope yield, MBq/g			
	20 MeV	30 MeV	40 MeV	50 MeV
^{44}Sc	0.00	0.01	0.05	0.10
^{46}Sc	0.05	0.43	0.89	1.27
^{47}Sc	0.26	2.65	5.36	7.66
^{48}Sc	0.25	2.58	5.24	7.43
^{49}Sc	0.05	0.57	1.36	2.24

$^{48}\text{Ti}(\gamma, p)^{47}\text{Sc}$

Even though ^{48}Ti is the most abundant isotope in natural titanium, many other scandium isotopes can be produced if natural titanium is irradiated which significantly reduces specific activity of the final product. Enriching the target in ^{48}Ti can decrease the amount of unwanted scandium isotopes and increase the specific activity of ^{47}Sc . Enriched ^{48}Ti typically comes in the form of dioxide (TiO_2). For example, ISOFLEX USA provides 96.2% enriched ^{48}Ti with small quantities of ^{46}Ti (0.86%), ^{47}Ti (1%), ^{49}Ti (0.81%), and ^{50}Ti (1.13%). Due to their low concentrations, these impurities do not produce significant amount of activation products. Therefore only ^{46}Sc and ^{47}Sc production from ^{48}Ti are considered in this work.

Irradiating ^{48}Ti will result in only two scandium isotopes, ^{47}Sc and ^{46}Sc . Notably, the threshold energy for $^{48}\text{Ti}(\gamma, np)^{46}\text{Sc}$ is significantly higher than the threshold energy for $^{47}\text{Ti}(\gamma, p)^{46}\text{Sc}$ and thus an optimum irradiation energy can be found depending on the desired specific activity of the final product. In addition, ^{46}Sc half-life significantly exceeds half-life of ^{47}Sc and thus irradiation time might be shortened to maximize the ratio of ^{47}Sc to ^{46}Sc . To find the optimum time of irradiation we have performed a number of MCNPX simulations to estimate the ratio of the yields of ^{47}Sc to ^{46}Sc as a function of time of irradiation for 30 MeV, 40 MeV, and 50 MeV.

Figure 2 (left) shows the results of such simulations for a 30 MeV electron beam. Black curves represent ^{46}Sc and ^{47}Sc activities as a function of time. While ^{47}Sc activity starts saturating after about 240 hours (10 days), the yield of much longer-lived ^{46}Sc keeps growing. The red dashed curve shows the ratio of activities of ^{47}Sc to ^{46}Sc . The ratio of ^{47}Sc to ^{46}Sc was found to be about 31,000 after 1 hour of irradiation dropping by about 50% after 10 days of irradiation. Although the optimum production time of ^{47}Sc is about 240 hours (~ 3 half-lives), shorter irradiation time is beneficial for irradiations with energies above 22.1 MeV to minimize the build-up of the longer-lived ^{46}Sc (Figure 2, left). For higher energies (40 MeV and 50 MeV) the ratio of $^{47}\text{Sc}/^{46}\text{Sc}$ activities is lower, but the overall shape of the curve remains similar (see Figure 2, right). The results confirm that to maximize the specific activity of ^{47}Sc , the enriched ^{48}Ti target should be used and the energy of the electron beam should be kept right below 22.1 MeV, the $^{48}\text{Ti}(\gamma, \text{np})^{46}\text{Sc}$ reaction threshold. As electron beam energy exceeds the threshold, ^{46}Sc starts being produced, and its fraction in the total number of scandium atoms grows as beam energy increases.

The expensive ^{48}Ti (or $^{48}\text{TiO}_2$) enriched target recycling should not be an issue as a simple but efficient recovery procedure has been developed (Kolsky et al., 1998). Titanium may be easily recovered and reused since no radioactive Ti isotopes will be produced as a result of photonuclear reactions. In case of using natural titanium, the only radioactive Ti isotope will be ^{45}Ti with the half-life of about 3 hour produced via $^{46}\text{Ti}(\gamma, \text{n})^{45}\text{Ti}$ reaction. If the energy of the beam exceeds 22 MeV, relatively long-lived ^{44}Ti ($T_{1/2} = 60$ years) will be produced via $^{46}\text{Ti}(\gamma, 2\text{n})^{44}\text{Ti}$ reaction and will be accumulating in the target material.

Figure 2. Left: Activities of ^{46}Sc and ^{47}Sc as a function of time of irradiation for 30 MeV beam. Also, the ratio of the two activities is shown (red dotted curve). Right: Ratio of activities of ^{47}Sc to ^{46}Sc is shown for 30 MeV, 40 MeV, and 50 MeV electron beam as a function of time of irradiation.

Benchmarking the simulations

To verify the yield predicted using MCNPX code we have irradiated natural Ti foil (0.05 mm x 2 cm x 2 cm) for one hour using a 22 MeV electron beam. The average current was 4.5 μA . After

irradiation the gamma-spectra were obtained (see Figure 3) and activity of three scandium isotopes (^{46}Sc , ^{47}Sc , and ^{48}Sc) was measured. ^{44}Sc and ^{49}Sc isotopes were not observed due to their short half-life. The results of the experiment are in good agreement with the theoretical predictions of the activities (see Table 4).

Table 4. Comparison of MCNPX simulations and experimental results of scandium isotopes yield. One hour of irradiation with 22 MeV 4.5 μA electron beam was used for simulations to match the experimental conditions.

Product	Yield of scandium isotopes, kBq/g ($\mu\text{Ci/g}$)	
	MCNPX simulations	Experimental results
^{46}Sc	1.11 (0.035)	0.74 ± 0.37 (0.02 ± 0.01)
^{47}Sc	22.6 (0.61)	19 ± 7.4 (0.5 ± 0.2)
^{48}Sc	5.92 (0.16)	3.33 ± 1.48 (0.09 ± 0.04)

Figure 3. Gamma-spectrum of the irradiated natural titanium foil. Several peaks representing ^{46}Sc , ^{47}Sc , and ^{48}Sc isotopes can be clearly seen.

4. Conclusions

We have performed Monte-Carlo simulations for ^{47}Sc production from both natural and enriched titanium and estimated the specific activity as a function of the electron beam energy and time of irradiation. The results confirm that to maximize the specific activity of ^{47}Sc , the enriched ^{48}Ti target should be used and the energy of the electron beam should be kept right below 22.1 MeV, the $^{48}\text{Ti}(\gamma, np)^{46}\text{Sc}$ reaction threshold. It was shown that using a 20 MeV 1 mA electron beam ^{47}Sc activity reaches hundreds of MBq/g. Decreasing the size of the target, one can easily reach a level of tens of GBq/g. Increasing the beam energy will also result in higher yields, but as soon

1 as electron energy exceeds the $^{48}\text{Ti}(\gamma, np)^{46}\text{Sc}$ reaction threshold, ^{46}Sc starts being produced and its fraction in total scandium atoms grows as beam energy increases.

3 Using natural titanium results in a large number of byproduct scandium isotopes and reduces the specific activity of ^{47}Sc . In addition, if electron beam with $E > 22$ MeV is used for natural titanium target irradiation, a long-lived titanium isotope will be formed, namely ^{44}Ti ($T_{1/2} = 60$ years), which will hinder recovery and reuse of the titanium target.

7 We also benchmarked the calculated ^{47}Sc activity with experimental data, which were found to be in good agreement with the predictions. The specific activity of ^{47}Sc produced via $^{48}\text{Ti}(\gamma, p)^{47}\text{Sc}$ reaction using electron linac is comparable to ones obtained with the $^{47}\text{Ti}(n, p)^{47}\text{Sc}$ method (100 GBq/g). We also compared our simulations with experimental results of ^{47}Sc yields from $^{48}\text{Ti}(\gamma, p)^{47}\text{Sc}$ reaction using 30-60 MeV energy electron beams (Yagi and Kondo, 1977) and found them to be good agreement. It was shown in their work that irradiating enriched ^{48}Ti (99.13%) with 30 and 40 MeV beams where resulted in only trace amounts of scandium isotopes other than ^{47}Sc . Their results also confirm that in order to increase specific activity of ^{47}Sc , electron beam energy should be kept right blow 22.1 MeV. Taking into account advantages of using low energy electron linacs in comparison to reactor systems or high energy proton accelerators, we believe that the photoproton production of ^{47}Sc using 22 MeV electron beam is highly viable.

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