^{47}Ca production for $^{47}\text{Ca}/^{47}\text{Sc}$ generator system using electron linacs

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Abstract

In this work we have studied the feasibility of photonuclear production of ^{47}Ca from ^{48}Ca for $^{47}\text{Ca}/^{47}\text{Sc}$ generators. Photon flux distribution for electron beams of different energies incident on a tungsten converter was calculated using the MCNPX radiation transport code. The ^{47}Ca production rate dependence on electron beam energy was found and $^{47}\text{Ca}/^{47}\text{Sc}$ yields were estimated for a 40 MeV electron beam. It was shown that irradiating enriched targets with a 40 MeV, 1 mA beam will result in tens of MBq g⁻¹ (few mCi g⁻¹) activity of ^{47}Sc . The results of the simulations were benchmarked by irradiating 22.5 g of CaCl₂ powder with a 39 MeV electron beam incident on a tungsten converter. Measured $^{47}\text{Ca}/^{47}\text{Sc}$ activities were found to be in very good agreement with the predictions.

Introduction

Only a limited number of radioisotopes for targeted radionuclide therapy are currently available. Several innovative, potentially useful α and β^- emitters have been recently proposed for new radiopharmaceutical development; however, many of them lack cheap reliable production methods. One such beta-emitter is ^{47}Sc with maximum β^- energy of 600 keV and half-life of 3.35 days. Being also a gamma-emitter with $E_\gamma = 159$ keV, ^{47}Sc could be an excellent alternative to ^{67}Cu or ^{177}Lu for targeted radionuclide therapy. ^{47}Sc was successfully produced at Brookhaven National Laboratory, and it was shown that classical chelating agents should efficiently bind ^{47}Sc for targeted radionuclide therapy (Kolsly et al., 1998). Currently, the availability of ^{47}Sc is limited despite the existence of several production methods including neutron capture on titanium and vanadium targets ($^{47}\text{Ti}(n,p)^{47}\text{Sc}$, $^{nat}\text{Ti}(n,x)^{47}\text{Sc}$, $^{nat}\text{V}(n,x)^{47}\text{Sc}$) (Mausner et al., 1993, DeLorme et al, 2014), high energy proton irradiation of Ti (Mausner et al., 1998, Srivastava and Dadachova, 2001), and photoproton production of ^{47}Sc via the $^{48}\text{Ti}(\gamma,p)^{47}\text{Sc}$ reaction (Yagi et al, 1977, Mamtimin et al., 2014).

Using $^{47}\text{Ca}/^{47}\text{Sc}$ generators is another alternative (Mausner et al., 1993) that was investigated. Unfortunately obtaining ^{47}Ca by neutron capture requires a highly enriched ^{46}Ca target which is currently only available at 30% enrichment level (Srivastava and Dadachova, 2001) and thus makes target cost prohibitive. In this work we investigated photoneutron production of ^{47}Ca from ^{48}Ca for the $^{47}\text{Ca}/^{47}\text{Sc}$ generator system.

Methods

The photonuclear reaction process is illustrated in Figure 1. During the irradiation, electrons from the accelerator impinge on a radiator, which converts a fraction of the high-energy electrons to bremsstrahlung γ -rays. The resulting high-energy bremsstrahlung beam is forward-directed and highly penetrating, making it ideally suited for isotope production with relatively thick dense targets. As the high-energy bremsstrahlung photons pass through the target, they induce photonuclear reactions in its constituent isotopes. Photonuclear reaction cross-sections strongly depend on photon energy. In the energy range of 10 to 30 MeV, the photon has the frequency comparable to the natural frequency of nucleus oscillations and comes into a resonance with the nucleus. This region, known as the giant dipole resonance (GDR) region, is characterized by a high photo-absorption cross-section. After the photon is absorbed and the nucleus becomes excited, the energy is released in the form of a photon, neutron, or a charged particle. While the (γ, n) and (γ, p) reactions are the primary reaction types in the GDR regime, other de-excitation channels such as $(\gamma, 2n)$, (γ, np) , and $(\gamma, 2p)$ are also possible. However, the threshold energies for such channels are much higher than those of (γ, n) and (γ, p) reactions, and the peak cross sections values are lower than those of single-nucleon emission reactions. It was shown earlier (Berman et al., 1975, IAEA TECDOC 1178, 2000, Starovoitova et al, 2014) that high Z elements photoneutron (γ, n) reactions typically result in higher radioisotope yield than photoproton (γ, p) ones.

Figure 1. Photonuclear reaction process.

The production rate of the isotope depends on a number of parameters, such as the threshold energy of the nuclear reaction E_{th} , the maximum energy of photons E_{max} , the photon flux density $\phi(E)$, and the cross-section of a photonuclear reaction $\sigma(E)$. The production rate per target nucleus can be found as:

(1)

If the target is significantly large so that the photon flux is not uniform throughout the target, the production rate R should be calculated as:

$$R = \int_{E_{th}}^{E_{max}} \int_V N(\vec{r}) \phi(E, \vec{r}) \cdot \sigma(E) dE d^3\vec{r}, \quad (2)$$

where $N(\vec{r})$ is the number of target nuclides per unit volume and $d^3\vec{r}$ is the volume element of the target.

To accurately predict the production rate we used MCNPX, a general purpose particle transport Monte Carlo code, developed by the Los Alamos National Laboratory (Pelowitz, 2008). MCNPX involves source characterization, target material and geometry specifications, physics process management, and output - tallies of the physical quantities of interest. The integral (2) was evaluated by simulating bremsstrahlung fluxes with F4 tallies (photon flux averaged over a cell) and multiplying them with ENDF/B-VII cross-sections (Chadwick et al, 2006) utilizing the FM tally multiplier card. The FM card is used in MCNPX to calculate any quantity of the form:

$$FM = C \int \phi(E) \cdot R(E) dE, \quad (3)$$

where $\phi(E)$ is the energy-dependent fluence (particle/cm²), $R(E)$ is an energy-dependent function, and C is a constant. In particular, if the cross-section $\sigma(E)$ of certain reactions is chosen to be the energy-dependent function R , and constant C is properly defined, the FM card allows calculating the production rate of the radioisotope.

The yield of the radioisotope produced in the sample after irradiation time t_{irr} can be found from the production rate as:

$$Y(t) = N_T \frac{dN}{dt} (1 - e^{-\lambda t_{irr}}), \quad (4)$$

where N_T is the number of target atoms in the sample and λ is the decay constant of the produced isotope.

The reaction under investigation here is $^{48}\text{Ca}(\gamma, n) ^{47}\text{Ca} \rightarrow ^{47}\text{Sc}$, where the “parent” radionuclide (^{47}Ca) decays into a radioactive “daughter” (^{47}Sc) isotope. For such a complex decay scheme, the number of the “daughter” atoms N_d during the irradiation can be expressed in terms of the number of the “parent” atoms N_p , “parent” decay constant λ_p , and “daughter” decay constant λ_d as (Segebade et al., 1988):

$$N_d = N_p \left(\frac{\lambda_p}{\lambda_d} \right) \frac{\left(1 - \frac{\lambda_d}{\lambda_d - \lambda_p} \right) e^{-\lambda_p t_{irr}} + \left(\frac{\lambda_p}{\lambda_d - \lambda_p} \right) e^{-\lambda_d t_{irr}}}{\left(1 - e^{-\lambda_p t_{irr}} \right)}, \quad (5)$$

and the yield of the “daughter” isotope Y_d by the end of irradiation as:

$$Y_d = Y_p \frac{\lambda_d}{\lambda_p} \frac{N_d}{N_p}. \quad (6)$$

After the irradiation, the “parent” activity decays following the standard exponential function. Since the production rate of the “daughter” equals the decay rate of the “parent”, the number of “daughter” nuclei as a function of decay time can be expressed as:

$$N_d(t) = N_p(t_{irr}) \frac{\lambda_p}{\lambda_d - \lambda_p} (e^{-\lambda_p(t-t_{irr})} - e^{-\lambda_d(t-t_{irr})}) + N_d(t_{irr}) e^{-\lambda_d(t-t_{irr})}. \quad (7)$$

Thus, “daughter” yield after irradiation can be found as:

$$Y_d(t) = Y_p(t_{irr}) \frac{\lambda_d}{\lambda_d - \lambda_p} (e^{-\lambda_p(t-t_{irr})} - e^{-\lambda_d(t-t_{irr})}) + Y_d(t_{irr}) e^{-\lambda_d(t-t_{irr})}. \quad (8)$$

Using the above Bateman equations, yields of both “parent” and “daughter” nuclides can be evaluated as a function of time for any given irradiation period. Optimum irradiation and elution times can also be found for each “parent-daughter” pair to maximize “daughter” yield.

Natural calcium consists of five stable isotopes (^{40}Ca , ^{42}Ca , ^{43}Ca , ^{44}Ca and ^{46}Ca) and radioactive ^{48}Ca - an isotope that is so long-lived that for all practical purposes it can be considered stable (see Table 1). Irradiating natural calcium will result in numerous byproduct isotopes with half-lives ranging from less than a second to hundred of thousands of years. In addition, ^{48}Ca abundance is very low (0.19%) and irradiating natural calcium target will result in extremely low specific activity of ^{47}Ca . Figure 2 shows the activity of different isotopes which will be produced if natural a calcium target is irradiated. A 40 MeV, 1 kW electron beam and 1 g of $^{\text{nat}}\text{Ca}$ target were assumed. Note that ^{39}Ca , an isotope with the highest yield, is extremely short-lived ($T_{1/2} < 1$ sec), so it will quickly decay into stable ^{39}K . ^{47}K also has a short half-life ($T_{1/2} = 17.5$ sec) and will decay quickly. Both ^{41}Ca and ^{45}Ca have yields several orders of magnitude lower than the isotope of interest, ^{47}Ca , and thus they do not pose a problem. However, ^{42}K , ^{43}K , and ^{45}K have yields comparable to ^{47}Ca and half-lives ranging from 17.4 min to 22.3 hours (see Table 1) and they will significantly contribute to the radioactivity of the sample. On the other hand, enriching target material in ^{48}Ca will result in only short-lived ($T_{1/2} < 2$ min) byproducts, such as ^{47}K , ^{46}K , and ^{46}Ar , even if higher order reactions are considered (see Table 2).

Table 1. Isotopic composition of calcium and possible products from (γ ,n) and (γ ,p) reactions. Reaction threshold energies are adopted from the IAEA TECDOC 1178.

Isotope	Natural abundance, %	Half-life	Reaction	Reaction threshold, MeV	Half-life of the produced isotope
^{40}Ca	96.94	Stable	$^{40}\text{Ca}(\gamma, n) ^{39}\text{Ca}$	15.64	0.86 sec
			$^{40}\text{Ca}(\gamma, p) ^{39}\text{K}$	8.33	Stable
^{42}Ca	0.65	Stable	$^{42}\text{Ca}(\gamma, n) ^{41}\text{Ca}$	11.48	1.0×10^5 years
			$^{42}\text{Ca}(\gamma, p) ^{41}\text{K}$	10.28	Stable
^{43}Ca	0.13	Stable	$^{43}\text{Ca}(\gamma, n) ^{42}\text{Ca}$	7.93	Stable
			$^{43}\text{Ca}(\gamma, p) ^{42}\text{K}$	10.68	12.4 h
^{44}Ca	2.09	Stable	$^{44}\text{Ca}(\gamma, n) ^{43}\text{Ca}$	11.13	Stable
			$^{44}\text{Ca}(\gamma, p) ^{43}\text{K}$	12.17	22.3 h
^{46}Ca	Trace	Stable	$^{46}\text{Ca}(\gamma, n) ^{45}\text{Ca}$	10.40	162.7 days
			$^{46}\text{Ca}(\gamma, p) ^{45}\text{K}$	13.82	17.4 min
^{48}Ca	0.19	4.3×10^{19} years	$^{48}\text{Ca}(\gamma, n) ^{47}\text{Ca}$	9.94	4.5 days
			$^{48}\text{Ca}(\gamma, p) ^{47}\text{K}$	15.81	17.5 sec

Table 2. Possible ^{47}Ca byproducts from enriched ^{48}Ca sample. Reaction threshold energies are adopted from the IAEA TECDOC 1178.

Reaction	Reaction Threshold Energy, MeV	Half-life of the produced isotope
$^{48}\text{Ca}(\gamma, n) ^{47}\text{Ca}$	9.94	4.5 days
$^{48}\text{Ca}(\gamma, p) ^{47}\text{K}$	15.81	17.5 sec
$^{48}\text{Ca}(\gamma, 2n) ^{46}\text{Ca}$	17.22	Stable
$^{48}\text{Ca}(\gamma, 2p) ^{46}\text{Ar}$	29.07	8.4 sec
$^{48}\text{Ca}(\gamma, np) ^{46}\text{K}$	24.16	105 sec

Figure 2. Activity of different isotopes which will be produced if 1 g of ^{nat}Ca target is irradiated with a 40 MeV, 1 kW electron beam.

It should be noted that photoproton reaction on ^{48}Ca will produce significant amounts of short-lived ^{47}K , which will in turn decay into ^{47}Ca . Thus, there are two routes of ^{47}Ca production from ^{48}Ca : one is the direct neutron knock-out $^{48}\text{Ca}(\gamma, n) ^{47}\text{Ca}$, and another one is proton knock-out, followed by the β^- decay $^{48}\text{Ca}(\gamma, p) ^{47}\text{K} \rightarrow ^{47}\text{Ca}$. Unfortunately, no reliable experimental cross-section data exist for the exclusive photoproton reaction cross-section for ^{48}Ca . To estimate the contribution of the two production channels of ^{47}Ca we used evaluated data (IAEA TECDOC 1178, 2000). According to this library, despite ^{48}Ca being a relatively low-mass nucleus, its proton production cross-section is about 100 times less than a corresponding neutron production cross-section. In addition, the threshold energy is higher for the (γ, p) reaction than for the (γ, n) reaction (15.81 MeV vs. 9.94 MeV). Using the above cross-section data we have estimated the contribution of ^{47}Ca coming from ^{47}K to be less than 2% of the amount of ^{47}Ca produced by a photoneutron route.

To verify the predicted yield values we have irradiated calcium chloride (CaCl_2) powder ($m = 22.5$ g) encapsulated in a cylindrical alumina crucible with an inner radius of 15 mm, and an inner height of 41 mm. A 48 MeV pulsed electron linac at the Idaho Accelerator Center was used for irradiation. A tungsten converter consisting of three plates served as a bremsstrahlung source. Each plate was 1.7 mm thick and separated by 2.3 mm thick channels for water-cooling. The average beam current was 12.5 μA , with the peak current of 90 mA and repetition rate of 15 Hz. The energy of the beam was 39 MeV, and the total time of irradiation was 5 hours. Gamma ray spectra of the irradiated sample 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 a few MeV.

Results and Discussion

Using MCNPX software we evaluated the ^{47}Ca production rate integral (1) for the $^{48}\text{Ca}(\gamma, n) ^{47}\text{Ca}$ reaction for different electron beam energies. Figure 3 shows the results of the calculations performed for a 3.2 cm x 4.2 cm cylindrical target (^{48}Ca target is assumed) and it is clear that as the energy of the electron beam increases, the ^{47}Ca yield grows rather quickly for energies below 40 MeV. Above 40 MeV the energy dependence of the yield begins to flatten out. To achieve an even higher yield of ^{47}Ca it might be easier to increase the beam current than pushing the beam energy above 40 MeV. The choice of the optimum beam energy also depends on the target enrichment in ^{48}Ca and the desired specific activity of ^{47}Ca . Irradiating natural targets with beam energy above 20 MeV will open new channels, such as $(\gamma, 2n)$ and (γ, np) and will further decrease the specific activity of ^{47}Ca . Irradiating a ^{48}Ca enriched target with 40 MeV (or higher) beam will not reduce the specific activity of ^{47}Ca as all the byproducts are short-lived. Thus we believe that the optimum ^{47}Ca production method will require a highly enriched ^{48}Ca target and a 40 MeV electron beam.

To evaluate ^{47}Sc yield and find the optimum time of irradiation and elution we constructed “parent”-“daughter” activity curves corresponding to a 40 MeV, 1 mA beam. For the first few days of irradiation ^{47}Ca activity grows almost linearly; after two weeks it gets close (90%) to its saturation value. ^{47}Sc activity keeps growing even after the irradiation is complete and reaches its peak value several days after irradiation (see Figure 4). The maximum ^{47}Sc activity time, or

optimum elution time, depends on the time of irradiation and can vary from five days to less than one day after ^{48}Ca irradiation is complete.

Figure 3. ^{47}Ca production rate as a function of the electron beam energy. One (1) mA beam current and one (1) hour of irradiation is assumed for the simulations.

Figure 4. ^{47}Ca (red) and ^{47}Sc (black) “parent-daughter” curves for one-day, three- day, and six- day irradiations. The peak activity of ^{47}Sc increases nearly linearly with the time of irradiation. A 40 MeV, 1 mA beam is assumed for the simulations. A 3.2 cm x 4.2 cm cylindrical sample of ^{48}Ca is used for modeling.

To benchmark the simulated values of ^{47}Ca and ^{47}Sc activities we irradiated calcium chloride (CaCl_2) powder as described above. The mass of ^{48}Ca in the sample was calculated using composition stoichiometry and found to be 18.2 mg. After the irradiation the sample was measured with gamma-spectroscopy and several spectra were obtained during the following week. One of these spectra is shown in Figure 5 revealing ^{47}Sc , ^{47}Ca , ^{42}K , and ^{43}K peaks. ^{47}Sc and ^{47}Ca activities were measured by calculating the number of counts under their gamma peaks (159 keV and 1297 keV correspondingly) and taking into account detector efficiency and transition branching ratio. Photon absorption and attenuation was also taken into account.

Figure 5. A gamma-spectrum of irradiated CaCl_2 sample showing ^{47}Sc , ^{47}Ca , ^{42}K , and ^{43}K peaks.

Measured ^{47}Sc and ^{47}Ca activities were compared to the predicted values, normalized to match the actual experimental conditions (electron beam current, time of irradiation, ^{48}Ca enrichment, etc.) Figure 6 shows the comparison of the measured activities of ^{47}Ca and ^{47}Sc and the results of the simulations. The spectra taken for the first few days had low signal-to-background ratio, especially in the Compton continuum region where the ^{47}Sc gamma-line is located (159 keV), which resulted in relatively high uncertainty (up to 20%). After about 100 hours the background count rate dropped significantly and the ^{47}Sc and ^{47}Ca peaks became more pronounced. ^{47}Sc activities were found to be consistently 15-20% higher than the predicted values, which can be explained by the uncertainty in the detector efficiency η . The $\eta(E)$ function reaches (0.000118 ± 0.00005) around 170 keV and has a steep slope at 159 keV. The actual detector efficiency in this energy region can vary significantly and relatively high uncertainty was expected.

Figure 6. Comparing predicted (dotted lines) and measured (circles) activities of ^{47}Sc (black) and ^{47}Ca (red). Both measurements and simulations were done for a five-hour irradiation of 22.5 g of CaCl_2 with a 39 MeV, 12.5 μA electron beam.

Conclusions

We have investigated the photonuclear production method of ^{47}Ca from ^{48}Ca for $^{47}\text{Ca}/^{47}\text{Sc}$ generators. MCNPX simulations were done to predict ^{47}Ca production rates for different electron beam energies and the optimum ^{47}Ca production method was found to require a highly enriched ^{48}Ca target and a 40 MeV electron beam. It was shown that irradiating a 3.2 cm x 4.2 cm cylindrical target with a 40 MeV, 1 mA beam will result in tens of MBq g^{-1} ($\sim \text{mCi g}^{-1}$) activity of ^{47}Sc . Spatial distribution of the bremsstrahlung photon flux density is not trivial (Howard, 2014). The photon flux intensity decreases inversely proportional to the square of the distance from the converter. At the same time, flux density drops off radially. Variations in photon flux density result in variations in ^{47}Sc activity distribution within the target – it is the highest in the small region on the electron beam axis close to the converter and drops off both radially and axially. Decreasing the size of the target will yield much higher average photon flux through the target and much higher specific activity of ^{47}Sc . The results of the simulations of ^{47}Sc activity were benchmarked by irradiating 22.5 g of CaCl_2 powder and found to be in good agreement with the predictions.

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