Simulation Study on Medical Isotope Production Using Electron Accelerator Photoneutron Source

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Abstract

Photonuclear reactions and compact neutron sources are emerging tools for medical isotope production. East China University of Technology (ECUT) is constructing an electron accelerator-driven photoneutron source (ECANS) for research on medical isotope production. This paper establishes a radionuclide production model comprising a neutron energy moderator layer and a neutron reflector layer based on the analysis of neutron yield and 99Mo production from a W- 100Mo photoneutron source, performs radionuclide production simulations and by-product analysis for various natural oxide materials (MoO3, Lu2O3, Y2O3), and investigates the feasibility of producing medical isotopes using photonuclear reaction neutron sources. The results demonstrate that the production yield of 99Mo isotope in highly enriched 100Mo targets reaches 54.1 Ci/day, while in oxide targets the yields are 17.4 Ci/day for 99Mo, 18.2 Ci/day for 177Lu, and 57.0 Ci/day for 90Y. Furthermore, the content of radioactive impurities in natural oxides under irradiation conditions is analyzed, providing data references for subsequent separation and purification processes.

Full Text

Preamble

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Simulation Study of Medical Isotope Production Using Electron Accelerator-Driven Photoneutron Source

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Abstract

[**Background**]: Photonuclear reactions and compact neutron sources have emerged as promising tools for the production of medical isotopes, providing alternatives to conventional reactor-based high-enriched uranium methods. East China University of Technology (ECUT) is currently constructing an electron accelerator-driven photoneutron source (ECANS) for medical isotope production research. [**Purpose**]: Investigate the photonuclear reaction with 100Mo isotope and utilize the generated neutrons for isotopic production. [**Methods**]: The study involves analyzing the photonuclear reactions of 100Mo and investigating the neutron spectrum and activation yield of 99Mo within a high purity 100Mo target. Based on this photonuclear source, a new model to produce medical isotopes is established, comprising neutron energy modulation layer and neutron reflection layer. The study calculates the production yields of 99Mo, 177Lu, and 90Y in various natural oxides and assesses the feasibility of using photonuclear sources for medical isotope production. [**Results**]: The research results demonstrate that photo-nuclear reactions can effectively produce medical isotopes such as 99Mo, 177Lu, and 90Y, with respective activities of 17.4/day, 18.2 Ci/day, and 57.0 Ci/day. In the high purity 100Mo target, the daily output of 99Mo reaches 54.1 Ci/day. [**Conclusions**]: The study demonstrates the feasibility of using the photodisintegration reaction of 100Mo as a neutron source for secondary production of medical isotopes. This approach offers the potential to enhance the economic viability of isotope production. The study analyzed the content of radioactive impurities in natural oxides under irradiation conditions, providing preliminary insights for subsequent separation and purification processes. Therefore, this research has certain reference value for the development of tools for radioactive isotope production.

Keywords: Photonuclear reaction, Neutron source, Electron linear accelerator, Medical isotopes

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Nuclear medicine represents a crucial branch of modern medicine, where radioactive isotopes enable effective diagnosis and treatment of complex diseases, particularly tumors and cancers [1]. 99Mo, 177Lu, and 90Y are three commonly used radioisotopes with extensive applications in radiopharmaceuticals. 99mTc, the decay daughter of 99Mo, emits 140 keV gamma rays and is routinely employed in SPECT (Single Photon Emission Computed Tomography) for various

cancer diagnoses, making it one of the most in-demand medical isotopes today [2]. 177Lu is utilized for tumor and cancer therapy, featuring a 6.7-day half-life and emitting 497 keV beta particles [3]. 90Y serves in radioimmunotherapy as an in vivo cancer treatment modality, with a 64.1-hour half-life and emission of 2.28 MeV beta particles [4].

Traditionally, medical radioisotopes have been produced primarily through reactor irradiation of highly enriched uranium. However, with reactor decommissioning and nuclear non-proliferation restrictions, countries are actively seeking alternative strategies for medical isotope production. High-flux neutron irradiation facilities are critical for current and future production of novel medical radioisotopes. Compact neutron sources, in particular, can provide high neutron flux while offering advantages of miniaturization and low spatial footprint, potentially substituting for or complementing reactor-based production [5]. Swami et al. [6] employed a 14 MeV D-T neutron generator to study daily production yields of MoO3 and Lu2O3 in a neutron radiation field, obtaining 1.14 Ci of 99Mo and 0.3 Ci of 177Lu. Masayuki et al. [7] utilized a D-Li high-flux fusion neutron source to investigate activation of natural MoO3 under low-energy neutron irradiation, achieving 27 TBq of 99Mo after two days of irradiation—sufficient to meet 95% of Japan's current demand. Additionally, producing 99Mo through high-flux photonuclear reactions with 100Mo has become a research focus. Tkac et al. [8] used a 40 MeV electron accelerator to irradiate highly enriched 100Mo for 0.5 hours, yielding 1.49 Ci of 99Mo. Moreover, high-flux photon-driven photoneutron sources can achieve a balance between neutron yield, operational time, spatial footprint, and cost-effectiveness. Yang Yigang et al. [9] proposed a neutron source system based on an electron linear accelerator, using a 50 MeV/50 kW electron beam to bombard a tungsten target, obtaining a neutron flux of 8.125$\times$10^{13}$ n/s at the neutron channel exit.

Currently, photoneutron conversion targets typically use tungsten/uranium, whose reaction products are difficult to utilize, reducing cost-effectiveness. However, when 100Mo serves as the photonuclear reaction conversion target, the reaction product 99Mo can be directly applied in medicine with high radionuclide purity, enhancing target material recycling benefits and offering significant research value.

This study first investigates neutron emission and 99Mo production from highly enriched 100Mo targets under photonuclear reactions. Subsequently, a photoneutron irradiation model comprising a neutron energy modulation layer and neutron reflection layer is established. Based on this model, production yields and byproduct analyses are simulated for various natural oxide materials (MoO3, Lu2O3, Y2O3), exploring the feasibility of using photonuclear reaction neutron sources for medical isotope production.

1. Nuclear Reaction Cross-Sections

The photonuclear reaction of 100Mo isotope involves two steps for neutron production. First, electrons are converted to photons using high-Z materials such as tungsten or tantalum. [Figure 1: see original paper] shows the high-energy bremsstrahlung photon spectra obtained from 1 mm thick tungsten targets bombarded by electron beams of different energies, achieving a photon conversion efficiency of 1.817 at 35 MeV electron beam energy. Second, photons are converted to neutrons, with efficiency governed by interactions between photons and atoms. [Figure 2: see original paper] presents the 100Mo(γ,n)99Mo reaction cross-section and the total photonuclear reaction cross-section of 100Mo [10], from which preliminary estimates indicate a maximum photoneutron reaction yield of less than 4%.

The 100Mo(γ,n)99Mo reaction cross-section peaks at 14.5 MeV incident photon energy, after which it decreases with increasing photon energy. Since photon energy distribution depends on incident electron energy, increasing electron energy can effectively ensure high-energy photon yield. Given the relatively small photoneutron cross-sections, neutron yield can be effectively enhanced by increasing electron beam current intensity when electron-photon conversion efficiency is high.

In the thermal neutron energy range, cross-sections can exceed 10 barns. [Figure 3: see original paper] shows the reaction cross-sections for these reactions, with data sourced from TENDL.

This study selected natural oxides MoO3, Lu2O3, and Y2O3 as neutron irradiation target materials. 98Mo is the most abundant natural molybdenum isotope with a relative abundance of 24.13%; other molybdenum isotopes include 100Mo (9.63%), 97Mo (9.55%), 96Mo (16.68%), 95Mo (15.92%), 94Mo (9.63%), and 92Mo (14.84%). In natural lutetium, 176Lu has a low relative abundance of 2.59%, while 175Lu has 97.41%. In natural yttrium, 90Y has a relative abundance of 100% [14].

2. Preliminary Design of Photoneutron Source and Irradiation Model

Production Pathways and Target Materials for Neutron Irradiation

Under neutron irradiation conditions, 99Mo can be produced through two nuclear reactions: the neutron capture reaction 98Mo(n,γ)99Mo and the neutron multiplication reaction 100Mo(n,2n)99Mo [11]. Notably, the neutron multiplication reaction requires an energy threshold, with neutron energies above 8 MeV. The neutron capture reaction exhibits cross-sections below 100 mb in neutron energy regions above 1 MeV, but shows higher cross-sections in the 1 keV–100 keV range and thermal neutron energy range, enabling effective 99Mo production. 177Lu can be obtained through the 176Lu(n,γ)177Lu neutron capture reaction [12], which has cross-sections exceeding 10,000 barns in the thermal

neutron region. Using effective moderators in neutron source devices to adjust neutron energy spectra can significantly enhance 177Lu yield. 90Y can also be obtained through neutron capture reactions via 89Y(n,γ)90Y [13], with reaction cross-sections below 100 mb for incident neutron energies above 1 MeV, similar to the 98Mo neutron capture cross-section.

2.1. 99Mo Production and Neutron Yield from Photoneutron Source

Using the FLUKA program [15], a photoneutron source model was established as shown in [Figure 4: see original paper], where a highly enriched 100Mo cylindrical target is placed in a tungsten container with 1 mm wall thickness, filled with helium gas for heat dissipation.

Electron beam parameters were selected from the ECUT linac data: electron energy of 35 MeV and beam current of 2 mA. The irradiation target consists of highly enriched 100Mo with the following nuclide composition: 100Mo at 97.39%, 98Mo at 2.59%, Fe at 540 ppm, Cr at 64 ppm, W at 75.1 ppm, Ni at 39.4 ppm, Cu at 14.9 ppm, Ge at 11.4 ppm, and Mn at 5.7 ppm.

[Figure 5: see original paper] shows the neutron yield from 100Mo targets under electron beam irradiation. As the irradiation target volume increases, the detected neutron count also increases. However, photonuclear reactions have low utilization efficiency of 100Mo, requiring target recycling to ensure production economics [16]. Therefore, the target should not be designed too large to improve recycling efficiency.

To obtain the production distribution of 99Mo in the target, a large-sized 100Mo target was studied. [Figure 6: see original paper] presents the 99Mo nuclide yield distribution after 8 hours of electron irradiation and 1 hour of cooling decay for a 100Mo target with 2 cm diameter and 3 cm height (Y-axis averaged). Results show that 99Mo nuclides are primarily distributed along the axial direction. Regions with higher 99Mo yield (specific activity $>$ 1.7 Ci/g) exhibit a truncated oblate elliptical shape, related to the forward distribution of bremsstrahlung photons. The core region can achieve 99Mo specific activity yields up to 4.5 Ci/g.

To balance 99Mo production and neutron yield, the highly enriched 100Mo target geometry was set as a cylinder with 0.3 cm radius and 1.4 cm height, as shown by the box in [Figure 6: see original paper]. Under this design, the neutron count detected on the tungsten shell surface reaches 6.67$\times$10^{13}$ n/s. After 24 hours of irradiation, a total of 54.1 Ci of 99Mo is obtained with a specific activity of 13.4 Ci/g. [Figure 7: see original paper] shows the neutron energy spectrum on the tungsten shell surface under 35 MeV, 2 mA electron beam irradiation, with a neutron energy peak slightly below 1 MeV. Compared to the 14 MeV neutron peak of D-T neutron sources [17], this spectrum is more conducive to neutron moderation design and implementation.

After determining target geometry, [Figure 8: see original paper] demonstrates

that as electron beam irradiation time increases, the radioactive isotope 99Mo yield in highly enriched 100Mo gradually approaches saturation, with production and decay reaching equilibrium. Therefore, the maximum target replacement cycle for the photoneutron source using highly enriched 100Mo should not exceed 10 days.

2.2. Establishment of Photoneutron Irradiation Model

A neutron irradiation model was established as shown in [Figure 9: see original paper], with an energy modulation layer surrounding the neutron source, consisting of a neutron multiplication layer and a moderation layer to adjust the neutron energy spectrum. Beryllium was selected as the neutron multiplication layer, as just 2 cm thickness can significantly enhance neutron multiplication effects [18]. Outside the multiplication layer, polyethylene material was placed to moderate intermediate and fast neutrons, thereby increasing medical isotope yield. Additionally, a sufficiently thick graphite layer outside the oxide target reflects neutrons to improve utilization efficiency. The neutron irradiation target material was placed between the energy modulation layer and graphite layer, shaped as a cylinder with 10 cm radius and 25 cm height, with a cylindrical section of 5 cm radius and 17 cm height removed from the left side.

[Figure 10: see original paper] presents the radioactivity yields of natural oxides under different polyethylene moderation layer thicknesses. The 99Mo yield fluctuates around 7 Ci, showing a slight decreasing trend. This occurs because the 98Mo(n,γ)99Mo reaction cross-section has similar values in both fast and thermal neutron regions, so neutron energy reduction has minimal impact on total yield. Conversely, as polyethylene thickness increases, inevitable neutron loss leads to a slight decrease in 99Mo yield.

In contrast, for 177Lu and 90Y production, reaction cross-sections differ significantly between thermal and fast neutron regions. Comparing cases with 2 cm multiplication layer plus moderation layer versus no energy modulation layer, the former increases yields by 408.55% and 428.69% respectively.

[Figure 11: see original paper] shows the neutron energy spectrum entering the oxide surface. The figure reveals a very significant increase in neutron flux in the thermal neutron region, indicating that the established neutron energy modulation layer possesses excellent neutron energy adjustment capability, meeting the requirements for isotope production. Notably, due to different natural abundances of 176Lu (approximately 2.59%) and 89Y (nearly 100%), higher 90Y production is obtained from Y2O3 after irradiation.

3.1. Isotope Production at Different Irradiation Times

In Sections 2.1 and 2.2, a photoneutron source model with neutron yield of 6.67$×10^{13}$ n/s was obtained using 35 MeV, 2 mA electron beam irradiation of highly enriched 100Mo targets. The simulation structure also demonstrated effective production of medical isotopes. However, electron accelerators

cannot operate at full power for extended periods like reactors [19], and this neutron source is based on photonuclear reactions of highly enriched 100Mo. As irradiation time progresses, the enrichment of 100Mo decreases, potentially reducing neutron flux and even irradiation efficiency. Therefore, determining reasonable irradiation duration is crucial for production economics and safe accelerator operation.

The neutron irradiation production model was used to calculate medical isotope production in three natural oxides (MoO_3 - 4.69 g/cm^3, Lu_2O_3 - 9.42 g/cm^3, Y_2O_3 - 5.03 g/cm^3) under irradiation times ranging from 8 hours to 15 days. [Figure 12: see original paper] shows isotope activities after irradiation and 1 hour of cooling decay. Results indicate that after 8 hours of irradiation, 6.22 Ci of 177Lu, 6.51 Ci of 99Mo, and 17.78 Ci of 90Y can be obtained. After 1 day, yields reach 17.43 Ci of 99Mo, 18.02 Ci of 177Lu, and 57.03 Ci of 90Y. After 15 days, production increases to 145.95 Ci of 177Lu, 78.92 Ci of 99Mo, and 259.46 Ci of 90Y.

Due to the short half-lives of required medical isotopes, as total radioisotope inventory accumulates, production and decay gradually reach equilibrium, weakening the growth trend. During the initial irradiation stage (8 hours–2 days), production exhibits linear growth. Therefore, actual production must consider local radioisotope demand and accelerator operational status comprehensively. The optimal irradiation duration should be less than 2 days, with maximum irradiation time not exceeding 7 days. Beyond 7 days, the production growth rate becomes minimal and economically unfavorable.

[Figure 13: see original paper] shows the activity decay of 177Lu, 99Mo, and 90Y radioisotopes after 8 hours, 1 day, and 2 days of irradiation. Since radioactivity decays exponentially, nuclide separation should be performed promptly after irradiation.

3.2. Byproduct Analysis in Natural Oxides

Irradiating natural oxides with photoneutrons from highly enriched 100Mo can effectively produce medical radioisotopes 99Mo, 177Lu, and 90Y. However, due to the presence of multiple isotopes of Mo, Lu, and Y in natural oxides, some radioactive byproducts unsuitable for nuclear medicine are generated. Investigating these byproduct contents during simulation is therefore important for subsequent separation and purification processes.

, , and list the detected byproduct contents in natural MoO_3, Lu_2O_3, and Y_2O_3 after 24 hours of irradiation and 1 hour of cooling decay.

In MoO_3, primary byproducts include 93mMo, 91Mo, 90Mo, 97Nb, 96Nb, 95Nb, 91mNb, and 90Nb. Isotopes such as 97Nb, 91Mo, and 101Mo have short half-lives and require no complex processing. However, longer half-life isotopes like 95,96Nb require additional measures, such as co-precipitation with ferric iron to remove Zr and Nb nuclides [20]. As shown in , isotopes like 95mNb and

91Nb, despite relatively low yields, still require removal due to their long half-lives, as they may accumulate during subsequent chemical processing and reduce radiochemical purity.

In Lu_2O_3, main byproducts include 174Lu, 173Lu, 174mLu, and 176mLu isotopes. These isotopes have similar chemical properties to 177Lu and relatively long half-lives, requiring high-performance liquid chromatography or other separation techniques to isolate them from dissolved targets and ensure high radiochemical purity of the final product [21].

In Y_2O_3, due to the natural relative abundance of 89Y approaching 100%, fewer radioactive byproduct species are detected, primarily 88Y, 87Y, 87mY, and 87mSr. In processing, ion exchange resins or other appropriate separation methods can effectively separate these impurity nuclides from 90Y [22] to ensure the final product meets medical standards for radioactive purity.

4. Conclusion

Based on the W-100Mo photoneutron source, a radioisotope production model for photoneutron irradiation was established to investigate the feasibility of medical isotope production using photoneutron sources. Under 35 MeV, 2 mA electron beam irradiation conditions, the photoneutron source achieves a neutron yield of 6.67$\times$10^{13}$ n/s, yielding 17.43 Ci/day of 99Mo, 18.21 Ci/day of 177Lu, and 57.02 Ci/day of 90Y in natural oxide target materials. This demonstrates that photoneutron sources based on 100Mo photonuclear reactions can effectively produce medical isotopes by irradiating natural oxides of Mo, Lu, and Y.

The study analyzed byproducts generated in natural oxide materials under irradiation conditions, providing recommendations for subsequent separation and purification. This research offers reference value for ECANS facility implementation and presents a new option for radioactive isotope production.

Author Contributions: Zhang Zixiong proposed and designed the research, established simulation models, performed calculations, and drafted and revised the manuscript. Li Kaixuan and Zhang Qintuo collected and organized data and validated models. Wei Qianglin provided computational guidance and research design. Liu Yibao revised the final version, supervised the project, and managed administration.

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Note: Figure translations are in progress. See original paper for figures.