Applied Radiation and Isotopes 122 (2017) 211–214

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

A simple thick target for production of ^{89}Zr using an 11 MeV cyclotron

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ARTICLE INFO

Keywords:
^{89}Zr production
11 MeV production
Target
Experimental yields
RDS Eclipse

ABSTRACT

The growing interest but limited availability of ^{89}Zr for PET led us to test targets for the ^{89}Y(p,n) reaction. The goal was an easily constructed target for an 11 MeV Siemens cyclotron. Yttrium foils were tested at different thicknesses, angles and currents. A 90° foil tolerated 41 µA without damage and produced ~800 MBq/h, > 20 mCi, an amount adequate for radiochemistry research and human doses in a widely available accelerator. This method should translate to higher energy cyclotrons.

1. Introduction

Zirconium-89 is a positron emitting radionuclide with a half-life of 78.4 h. We first produced ^{89}Zr on a biomedical cyclotron and described its potential as a useful radionuclide for PET antibody imaging at the 3rd International Symposium on Radiopharmaceutical Chemistry in Boston (Link, 1986). In recent years, the use of ^{89}Zr has increased significantly, particularly as a radiolabel for antibodies where a several-day half-life is required (Link et al., 1986; DeJesus and Nickles, 1990; Fischer et al., 2013; Holland et al., 2009; Meijs et al., 1992, 1997; Borjesson et al., 2006; Zhang et al., 2011; Bhattacharyya et al., 2013). The most common method for production of ^{89}Zr uses a cyclotron and the ^{89}Y(p,n) ^{89}Zr reaction (Sadeghi et al., 2012) and the cross sections for this production have been reported by many investigators including Levkovskii (1991); Wenrong et al. (1992); Uddin et al. (2005); Omara et al. (2009); Sadeghi et al. (2012); Kakavand and Taghilo (2013); and for the ^{89}Y(d,2 n) ^{89}Zr reaction by Zweit et al. (1991). Despite the increasing use of this radionuclide, production has been limited to a few centers that have specialized targets for cyclotrons of ≥15 MeV. The purpose of the work presented here was to develop and evaluate alternative targets for production of ^{89}Zr with the goal of a target that was easily made and could withstand reasonably high beam currents using natural yttrium targets to obtain multi-millicurie yields of ^{89}Zr.

2. Methods

Yttrium metal foils with thicknesses of 0.1, 0.25, 0.50 and 1.0 mm, and 99.9% purity were obtained commercially (Sigma-Aldrich, Alfa Aesar, Fluka and ESPI) and used as provided. Yttrium oxide was obtained from Sigma-Aldrich. Helium gas was research grade. The cyclotron used was a Siemens Eclipse with 11 MeV proton beam.

A 4-position Siemens Eclipse target holder or "carousel" was used for holding the Zr-targets that were tested. A 25 µm thick aluminum window separates targets mounted in the carousel from the cyclotron vacuum tank. The proton beam on target after passing through the aluminum window was nominally 10.7 MeV based on stopping power calculations (Ziegler and Littmark, 1980).

All targets were machined from 6061-T6 aluminum rod that was milled to fit into a Siemens Eclipse cyclotron modified Faraday cup "paper burn" unit. The Siemens paper burn unit consists of two parts. The outside of the unit is a hollow cylinder, essentially a Faraday cup, that is water-cooled on the outside (Fig. 1). A smaller cylinder, 2.05 cm diameter by 7.6 cm long, with a paper attached to the front, inserts tightly into the hollow cavity of the paper burn unit and is irradiated at low current to qualitatively assessing beam shape. We also irradiated nickel instead of paper to make radioactive copper. We imaged the irradiated material using a BioRad phosphor imager to obtain quantitative images of the beam profile (Fig. 2). The beam is approximately 3 mm X 3 mm beam and gaussian.

New aluminum inserts for the hollow cylinder part of the paper burn unit were made to hold yttrium foils or yttrium oxide and the inserts were the same diameter, 2.05 cm, as the paper burn insert for at least part of the length of the insert. The inserts that were tested ranged from 6.5 to 7.5 cm in length with a flat section ~ 5 mm wide milled off the top of the insert to allow helium gas to escape. Four target insert designs were tested to make ^{89}Zr (Fig. 1). One was a target with a 12°

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http://dx.doi.org/10.1016/j.apradiso.2017.01.037
Received 26 October 2016; Received in revised form 29 January 2017; Accepted 29 January 2017
Available online 30 January 2017

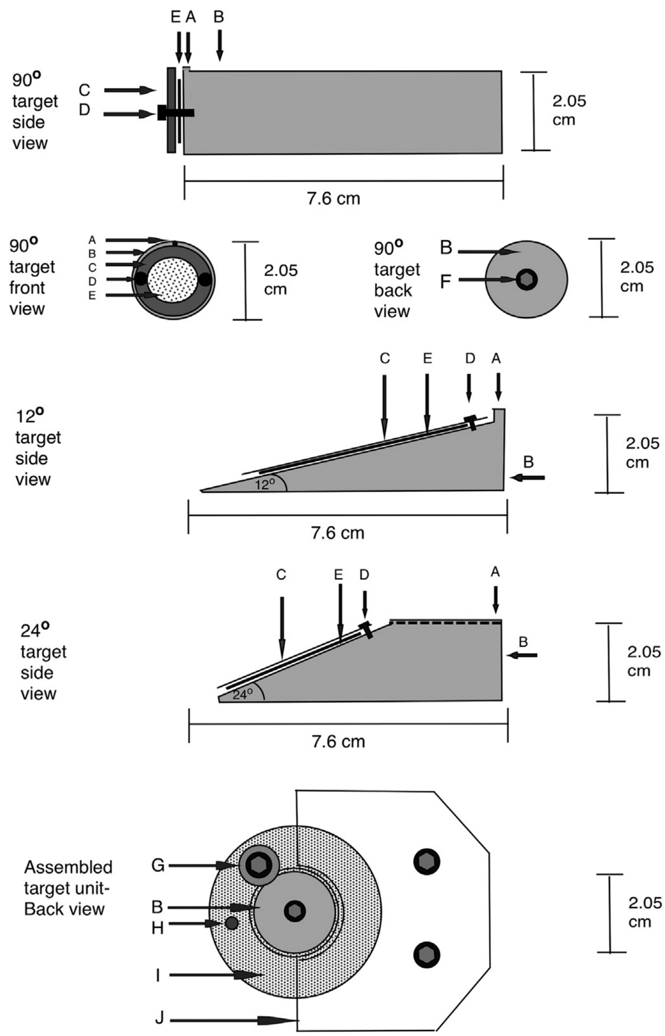

Fig. 1. Scale diagrams of the three target inserts tested for production of ^{89}Zr using 0.5 or 0.25 mm thick Y foils. Top panel shows side, front and back views of the 90° target insert with the best performance. Middle panel shows the 12° target. The bottom panel shows side view of the 24° target. The back view for all targets were similar. The target components are labeled the same in all views. A is the position for helium gas entry into the target foil, B is the aluminum target body, C is the aluminum or steel washer or flange that held the yttrium foil against the aluminum target back. D denotes screws to tighten the flange against the aluminum back. There were two #2 screws used for the 90° target. E denotes the yttrium foil. The insert fit tightly into a water-cooled sleeve in the Eclipse target changer. Each insert had a screw mounted in the back (F) so that the insert could be pulled from the target changer quickly into a lead pig for transport. The bottom drawing shows the back of the entire mounting of the hollow cylinder with the target insert from the back. G denotes a washer and screw that is used to hold the insert (B) in place within the hollow cylinder so that the helium cooling gas does not push the insert out. H denotes the 1/8" line for helium cooling inserted in the hollow cylinder (I) that is part of the paper beam unit. The hollow cylinder is kept in place by the plate (J), this is a normal part of the clamping on the Siemen's target carousel.

angle to the incident proton beam with a rectangular aluminum carrier having sides 2 mm high to hold yttrium oxide powder that was pressed by hand. The powder was covered by a foil of 0.17 mil Arnavar® foil to prevent powder loss. Aluminum inserts (targets) for irradiating solid yttrium metal foils had 12°, 24°, or 90° angles to the beam to test the value of spreading the beam area to reduce current density (watts.cm-^{2}) on the yttrium metal (Fig. 1). For each target, helium gas was passed through a 1/8" line fitted into the side of the main hollow cylinder piece and used for cooling of the yttrium target insert. The yttrium target inserts were cooled using helium passed over the foils at a rate of 300–500 $cm^3\,min^{-1}$. Irradiations on the yttrium targets used times ranging between 15 and 60 min with varying beam currents on target.

After irradiation we typically waited at least 20 min before removing the target from the hollow cylinder. The irradiated yttrium was measured using calibrated ion chambers (Capintec, Ramsey, NJ) until measurements of the half-life showed that only ^{89}Zr remained. Low level counting using a Cobra II counter (Packard) with a 3" detector and MCA detection was used to search for other radionuclides by studying photopeaks or counting over sufficient time to evaluate decay curves for more than one component.

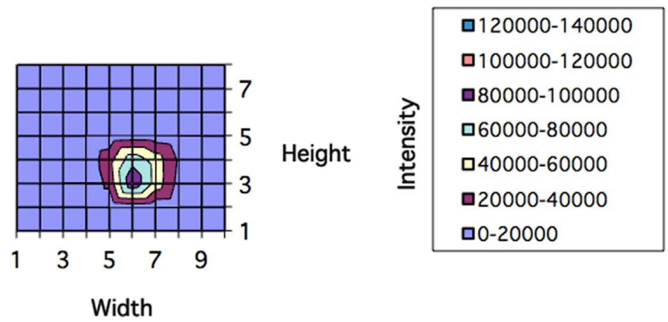

Fig. 2. Image of quantitative beam current position and density measured by Phosphor imaging of an irradiated foil from a paper burn target. The left image shows a typical beam profile for our Siemen's Eclipse cyclotron. The picture is oriented with the height on the Y-axis and the width on the X-axis. Each square is 1 mm on a side. The right scale gives linear scale of signal intensity.

The Siemen's Eclipse tunes the beam for each run at low current on target. In order to determine the total amount of current that was put on the yttrium target, current was logged every second from the start of low current beam tuning on target and through the total irradiation irradiation. Total integrated beam was the sum of this logged current. Average beam on target was calculated as the total current divided by time irradiated. Typical tuning time was 2 min at 10 μA.

We measured the fraction of the beam lost to the aluminum clamps holding the yttrium material in each target by comparing the yield in mCi/ uA h at end of bombardment (EOB) from a direct 90° irradiation on a thick-to-beam unclamped piece of Y metal in the paper burn position with the yield on targets with clamps that intercepted some of the beam. Beam current for these tests was between 10 ot 20 μA on the Y foil to avoid any warping or loss from the foils. The fraction of beam current that was estimated by this method to actually reach the Y foil compared with the aluminum clamps on the clamped targets and the losses to the back of the target from thin to beam foils is called effective current for the remainder of this manuscript.

The difference in yield for one 0.25 mm foil compared with thick to beam 2 × 0.25 mm Y foils was also measured.

3. Results

The yttrium target irradiations produced trace amounts of ^{13}N from oxygen on the surface of the yttrium, along with ^{89m}Zr (T1/2 4.16 min) and the desired ^{89}Zr. No other radionuclides were detected out to 6 half-lives of the ^{89}Zr.

The Y_2O_3 target did not transfer heat well and showed melting in the center with only 12 μA on target and, as expected, had lower measured yields 12.2 MBq/μA h (0.33 mCi/μA h) at end of bombardment (EOB) compared with yttrium metal. We did not perform further evaluation of Y_2O_3 targets.

Multiple yttrium foil thicknesses were tested. For a 10.7 MeV beam directly hitting natural ^{89}Y foils we calculated that 0.47 mm thick of yttrium foil would reduce the energy of the proton beam to 4.0 MeV, reducing the cross section from 700 to 850 mb at 10.7 MeV to < 20 mb (Zeigler and Littmark, 1980; Sadeghi et al., 2012). Stacks of 0.1 mm foils totaling 0.5 mm were tested but the foils did not transfer heat well enough to the next foil, even with compression to improve contact and the foils were vaporized through the center. This was anticipated due to lack of convective gas cooling in the middle layers and the poor