Measured Bremsstrahlung Photonuclear Production of ^{99}Mo ($^{99\text{m}}\text{Tc}$) with 34 MeV to 1.7 GeV Electrons

A.D. Roberts^{a*}, C.G.R. Geddes^b, N. Matlis^b, K. Nakamura^b, J.P. O'Neil^b, B.H. Shaw^b, S. Steinke^b, J. van Tilborg^b, W.P. Leemans^b

^aDepartment of Physics and Astronomy, Minnesota State University, Mankato, MN 56001, USA

^bLawrence Berkeley National Laboratory, 1 Cyclotron Road, Berkeley, CA 94720, USA

*Corresponding author: andrew.roberts@mnsu.edu

Abstract

^{99}Mo photonuclear yield was measured using high-energy electrons from Laser Plasma Accelerators and natural molybdenum. Spectroscopically resolved electron beams allow comparisons to Monte Carlo calculations using known $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ cross sections. Yields are consistent with published low-energy data, and higher energy data are well predicted from the calculations. The measured yield is $(15 \pm 2) \times 10^{-5}$ atoms/electron (0.92 ± 0.11 GBq/ μA) for 25 mm targets at 33.7 MeV, rising to $(1391 \pm 20) \times 10^{-5}$ atoms/electron (87 ± 2 GBq/ μA) for 54 mm/1.7 GeV, with peak power-normalized yield at 150 MeV.

Keywords

$^{99\text{m}}\text{Tc}$; ^{99}Mo ; Bremsstrahlung production

1. Introduction

The world's supply of technetium-99m ($^{99\text{m}}\text{Tc}$) is at risk, and alternate methods for production must be found to support the demands of diagnostic nuclear medicine. $^{99\text{m}}\text{Tc}$ is the most widely used medical radioisotope used today, accounting for approximately 80% of all nuclear imaging procedures (Sabel'nikov, 2006). $^{99\text{m}}\text{Tc}$ (6 hr) is most commonly supplied as the daughter product from beta decay of ^{99}Mo (66 hr), delivered in commercial generator systems. Over 90% of the world's supply of ^{99}Mo is produced at five nuclear reactors, each of which is over 45 years old. The short half life of the parent ^{99}Mo (66 hours) requires continuous resupply to meet the medical industry's needs. In 2007 the unanticipated closure of a single reactor facility in Canada decreased isotope stocks in North American hospitals by 80%, causing the cancellation of 50,000 medical procedures in a matter of weeks (Ruth, 2009). This was followed in 2008 by the unexpected failure of another major supplier reactor in the Netherlands. Smaller facilities in Belgium and France are scheduled to cease operation in the next few years, and the National

Research Universal (NRU) reactor in Chalk River, Ontario, is scheduled for shutdown in 2016 (Lougheed 2012, Bernard 2014). In recent years a great deal of international effort has therefore been made to evaluate alternate methods for ^{99}Mo and $^{99\text{m}}\text{Tc}$ production, summarized by the International Atomic Energy Agency (IAEA report, 2010).

Numerous approaches have been explored for alternate means of $^{99\text{m}}\text{Tc}$ production, either directly or as the daughter decay product of ^{99}Mo (Bernard 2014, TRIUMF report 2008, Wolterbeek 2014, Culter 2014, IAEA report 2013, Nagai 2014, Pillai 2012, Guerin 2010). Some promising methods are being adopted by commercial companies, including the use of low enrichment uranium (LEU), e.g. at SHINE Medical Technologies (SHINE, 2014), and photonuclear activation of molybdenum, e.g. at NorthStar Medical Radioisotopes (NorthStar, 2014). Any evaluation of the merits of a production strategy must include both evaluation of the available accelerator technology, and the subsequent techniques for efficient and high purity $^{99\text{m}}\text{Tc}$ extraction and conversion to labeled compounds of medical utility. Photonuclear production has been demonstrated as a viable option, with source photons from Bremsstrahlung (Avagyan 2014, Bennett 1999, Dzhilavyan 2011, Dikiy 2004, Dovbnya 2011, Sabel'nikov 2006, Starovoitova 2014) or Compton sources (Habs 2011). This method would provide a source of $^{99\text{m}}\text{Tc}$ (half life 6 hours, the primary decay product from ^{99}Mo) without the security concerns surrounding high enrichment uranium (HEU) targets, or the need for dedicated nuclear reactor facilities. However the method does suffer in that bulk amounts of molybdenum are required, and efficient separation of the $^{99\text{m}}\text{Tc}$ can be problematic (Dash 2013). Published yield data is scarce, and limited to low energies (below about 50 MeV). Potential for new developments in high energy electron accelerators, including laser plasma accelerators (Leemans 2006), raise the need for the experimental determination of yields at high energy.

The primary goal of this work is to investigate the feasibility and yield for producing ^{99}Mo using high energy electron beams using the laser plasma accelerator facility at the Lawrence Berkeley National Lab. While the use of the photonuclear reaction on molybdenum targets has been demonstrated at low energy, both with natural Mo and enriched ^{100}Mo , there is very little data on reaction yields at high energy (>50 MeV). Our experiment used gamma rays produced from stopping high energy electrons in a natural enrichment molybdenum metal target. The yield for ^{99}Mo produced was measured as a function of initial electron energy from 34 MeV to 1.7 GeV. In addition to the overall yield results, the depth distribution of the product radioisotopes was measured. This information can provide the basis for determining what energy and current of

accelerators are needed to provide sufficient ^{99}Mo to serve the need for $^{99\text{m}}\text{Tc}$, and what target material and geometry is required. The purpose of this experiment was not to define an idealized system for $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ production, but rather to provide experimental data which can be used to evaluate the photonuclear approach to production of this vital nuclear medicine radioisotope. The results obtained, over a broad energy range, provide an experimental basis for optimizing the activation energy, with calculations within the measured energy range presented. The work presented here outlines the methodology used, tests with activation of natural copper, and the molybdenum activation vs. energy.

2. Methods

High-energy electrons colliding with target material produce a broad spectrum of bremsstrahlung gamma rays, which then produce ^{99}Mo primarily by the $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ reaction over the giant dipole resonance energies from approximately 10-25 MeV. Other contributions to the ^{99}Mo yield from electron irradiation include $^{100}\text{Mo}(\gamma, p)^{99\text{g.m}}\text{Nb} - ^{99}\text{Mo}$, as well as secondary beam reactions in thick targets such as $^{98}\text{Mo}(n, \gamma)^{99}\text{Mo}$ (if ^{98}Mo present in the target). In this experiment the yield for ^{99}Mo is determined from the measured amount of $^{99\text{m}}\text{Tc}$ present in the irradiated samples, appropriately corrected for the time course of the parent-daughter isotope relationship. $^{99\text{m}}\text{Tc}$ can also be produced directly in the secondary beam reaction $^{100}\text{Mo}(p, 2n)^{99\text{m}}\text{Tc}$, and any direct production $^{99\text{m}}\text{Tc}$ is eliminated from the final $^{99\text{m}}\text{Tc}$ analysis for accurate ^{99}Mo yield.

Electrons covering a broad energy range beyond the giant dipole resonance were provided by laser plasma accelerators (LPA) at the Lawrence Berkeley National Lab (LBNL) LOASIS facility (Geddes 2004, Leemans 2006). These accelerators are primarily under development for high energy physics applications, but have the potential for future broader applications in radioisotope production (Leemans 2001, Reed 2007, Clarke 2013). High power, short pulse lasers interact with gas-sourced plasma targets, from either a gas jet, a preformed capillary plasma channel (Gonsalves, 2007) to guide the laser pulse and extend the accelerating length of the electrons, or a gas jet coupled to a capillary to control both the electron injection and laser guiding (Gonsalves 2011). The ^{99}Mo activation experiments were performed in parasitic mode to the ongoing accelerator development, and were used to determine yields at low average electron beam current vs. incident energy rather than optimizing for production. Typical operation provided electron pulses of 10's of pC charge at 1 Hz, sufficient for activation analysis but several orders of magnitude lower than desired to meet radioisotope production needs.

Development of LPAs towards operation at >10 kHz is in early development for high-energy physics (DOE report, 2013).

While the LBNL LOASIS/BELLA systems have demonstrated relatively narrow relative energy spread ($<10\%$) under optimized conditions, the activation experiments were intentionally performed under development conditions with a broad energy spread over the course of each experiment. Rather than restricting the LPA conditions to fix the energy, the beams were energy resolved using a downstream magnetic spectrometers (Nakamura, 2008). Figure 1 shows a schematic of the activation setup, shown for the high energy beam experiment. The dipole spectrometers used have been mapped for magnetic field and referenced to built in Hall probes to allow for day to day variations in field. At the spectrometer exit, the electrons pass through a 0.14 mm Lanex Fast Front scintillating screen (Kodak, Rochester, NY, USA) calibrated against known electron currents to give the absolute integrated charge (Nakamura 2011). The beam energy and angle are determined from the images at these exit screens. The location of the target past the magnet determines the energy window impacting the target material.

Figure 1

Two accelerator/magnet systems were used for these data. The high energy experiment (>1 GeV) performed on the BELLA beam line (Leemans, 2013) used electrons exiting at a nominal 8.5 degrees from the initial beam direction (see fig. 1). The beams passed through a Lanex screen and Lucite window at a shallow angle since the screen is oriented parallel to the initial beam direction. There was no further absorbing material, but the shallow incidence angle results in an effective 86 mm thick window. Beams from 30-300 MeV were produced on the TREX laser beamline (Toth, 2009, Leemans, 2006). On this line, the targets were placed to sample electrons emerging from the magnet at a nominal 10-15 degrees from the initial beam direction. The electrons passed through the Lanex screen normal to the initial beam direction, then through 12 mm Lucite vacuum window, 6 mm borosilicate glass imaging mirror and 6 mm aluminum mirror backing oriented at 45 degrees, and 6 mm aluminum assembly mount before reaching the target. The net effect of these upstream absorbers including incidence angles in

each accelerator system is included in subsequent model calculations, shifting the depth of the peak activation upstream in the targets with relatively little net effect on the total yield.

After activation the targets were removed to a separate counting facility for radioisotope analysis. The detector system used is a 2" Ge detector, with relative efficiency of 14.9%, and energy resolution of 616 eV at 122 keV, and 1.65 keV at 1.33 MeV (model GEM-10175-plus). Sources are placed along a shielded channel facing the detector. Prior to this experiment thorough tests of the apparatus were performed to establish the energy calibration, relative efficiency vs. energy, absolute activity correlation (for fixed source geometry), and stability. As an example, the absolute calibration for a source at 30 cm from the detector is 43 cpm/kBq at 141 keV (calibrated with a reference ^{152}Eu source, and checked against a known $^{99\text{m}}\text{Tc}$ source over more than two decades of decay from 370 kBq to 02 kBq). Reference peaks in the photon spectrum are corrected for background counts, and the absolute activity is corrected for geometric and self attenuation effects, appropriate for the gamma energy and target material in question.

Once total activity at the end of the activation run was determined, the yield is calculated according to the usual activation expression:

$$A = \left(\frac{\#electrons}{t} \right) Y (1 - e^{-t \ln 2 / t_{1/2}}) \quad \text{Eq. 1}$$

Where $A = N \ln 2 / t_{1/2}$ is the activity given N nuclei measured at the end of activation, Y is the yield in units of nuclei/electron, t the total activation time, and $t_{1/2}$ the isotope half life. The yield Y can then be compared to the results of Monte Carlo simulation using MCNP6 (Goorley 2012), using appropriate cross section data from the literature for the reaction.

The full experiment followed three steps. First, natural copper activation was performed to test both the absolute calibration of the charge measurement system against previous measurements (Nakamura 2011) and the energy response of the yield against Monte Carlo calculations. Next, natural molybdenum was activated at low energy (30-300 MeV) to confirm agreement with the expected yields based on published data (< 50 MeV) and to adjust simulation parameters if necessary in the MCNP6 code to reproduce the data. Finally, high

energy activation (1.5-2.0 GeV) was performed to test both the total yield and the activation vs. target depth.

3. Results

a. $^{65}\text{Cu}(\gamma,n)^{64}\text{Cu}$

In order to validate the methodology for determining the yield using the charge weighted mean energy impacting each target after the magnetic spectrometer, the yield of ^{64}Cu from irradiation of natural isotopic copper was measured. Natural copper blocks in a 1" cube (two 25.4mm square, 12.7mm thick blocks back to back) were irradiated to test both the absolute calibration of the charge measurement system against previous measurements and the energy response of the yield against Monte Carlo calculations. Data were compared to the yield calculated with MCNP6 (Goorley 2012) based on the giant dipole resonance cross section (Valamov 1995). Figure 2 shows the data with the calculation comparison. The ^{64}Cu signature was the 511 keV from positron decay, corrected for any residual short lived copper isotopes by half life analysis. The 1.35 MeV gamma in ^{64}Cu decay is <1%, compared to the 35% 511 keV signal, which coupled with the decreased detector efficiency at higher energy made the signal too weak to use. The self-attenuation through the thick copper targets (~50% depending on the geometry) is not negligible, and was accounted for in the analysis. The error bars include systematic uncertainties (12%) in the absolute 511 keV determination, as well as the counting statistics and the uncertainty in the electron charge from uncertainty in the target positioning relative to the magnetic spectrometer. The data are presented as a function of weighted mean energy on the target, weighed by the charge distribution measured at the Lanex phosphor screens during activation. All but two of the nine data points measured are well reproduced by the calculation within the uncertainties, with those two within 1.5 standard deviations. Previous measurements at our lab using a broad energy spread beam from ~30-250 MeV and a 25 mm thick copper target gave a measured production rate of $1.0 \pm 0.1 \times 10^{-3}$ atoms/electron (Nakamura, 2011), in reasonable agreement with our current results. This indicates the method used is well understood and valid.

Figure 2

b. $^{nat}\text{Mo}(\gamma, x)^{99}\text{Mo}$, $<300\text{MeV}$

Natural-enrichment molybdenum blocks were irradiated on the TREX system in the same way as the copper block activation. The targets consisted of back to back 12.7 mm, 25.4 mm square blocks. As before, the block positioning and dipole magnet field determined the energy distribution impacting the blocks.

The ^{99m}Tc decay activity is measured with the signature 141 keV gamma (89%). Neglecting the small amount of ^{99m}Tc present at the end of activation, the amount of ^{99}Mo activity is given by the usual parent/daughter decay relation (equation 2):

$$A_{Mo}^0 = A_{Tc}(t) \left(1 - \frac{t_{Tc}}{t_{Mo}} \right) (e^{-t \ln 2 / t_{Mo}} - e^{-t \ln 2 / t_{Tc}})^{-1} \quad \text{Eq. 2}$$

where A_{Mo}^0 is the activity of the ^{99}Mo at the end of activation, $A_{Tc}(t)$ the ^{99m}Tc activity measure at time t post activation, and t_{Tc} and t_{Mo} the half lives (6.01 hr and 65.94 hr respectively). The amount of ^{99m}Tc produced from ^{99}Mo decay during the short activation (typically 20 minutes) is less than a few percent and can be ignored. Most measurements were performed at least 18 hours after activation to allow the ^{99m}Tc to build up (peak activity at 23 hours).

Table 1 gives the summary of all measurements made for $^{nat}\text{Mo}(\gamma, x)^{100}\text{Mo}$. Figure 3 shows the results for the nine measurements below 300 MeV. The yield is given as atoms produced per incident electron. The error bars shown are the statistical uncertainties in the activity measurement added in quadrature with the uncertainty in the electron charge measurement. There is an estimated systematic uncertainty of 12% in the absolute activity measurement on the Ge detector, and the 1.7 GeV data point has an additional +12%/-35% systematic uncertainty. The lowest energy data are in reasonable agreement (<20%) with published calculations and measurements on similar targets (TRIUMF report 2008, Bennett 1999), although given the broad distribution of activity along the target full comparisons must account for the upstream converter material and precise target geometry. The solid line on fig. 3 shows the result of the Monte Carlo calculation with MCNP6. The calculation assumed a monoenergetic incident beam directed at the center of the target, rather than the broader energy

band directed non-uniformly across the surface. Nonetheless, using the published cross section for $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ from 9 MeV to 27 MeV (Beil 1974) did reproduce the measured results, albeit with lower yields. The cross sections were increased by 7% forming a better fit to the measured data. This value is consistent with the difference between the total photonuclear cross section on ^{100}Mo between the (γ, n) and $(\gamma, 2n)$ energy thresholds and the cross section for (γ, n) alone (IAEA 2000). Although this may suggest contributions to the yield from other reaction channels such as $^{100}\text{Mo}(\gamma, p)^{99g.m}\text{Nb} \rightarrow ^{99}\text{Mo}$, no distinction is made in this experiment and the adjustment falls within the range of systematic uncertainties in the method.

Figure 3

One difficulty with the measurement is the significant amount of self attenuation in the target for 141 keV gammas. The mass attenuation coefficient for 150 keV gammas in molybdenum is $0.42 \text{ cm}^2/\text{g}$, compared to $0.08 \text{ cm}^2/\text{g}$ for 500 keV gammas in copper (NIST, 2014). In order to account for this, the bulk samples were sampled at each target face and the integral activity is weighed by the attenuation as well as the relative depth dose activity predicted by MCNP6 simulations. This method was confirmed by the multiple measures of activity at each available depth, and verifying that the measured activity ratios matched calculations to within 10%. In a separate experiment, a stack of 1mm thick molybdenum disks was irradiated and individually measured to minimize the self attenuation effects. The integral yield for the stack of 25 disks irradiated at a mean 71 MeV is included in the summary plot (Fig. 3), showing the good agreement between the target types and measurement methods.

Table 1

c. $^{nat}\text{Mo}(\gamma, x)^{99}\text{Mo}$, 1.7GeV

In order to extend the energy range of measured yields as far as possible, an experiment was performed using the high energy electrons provided by the BELLA laser plasma accelerator (Leemans 2013). The scheme for the measurement was the same as for the previous measurements, although with a modified geometry. The beams passed through the dipole magnetic spectrometer, then through the Lanex screen and Lucite vacuum window at shallow incidence as described above. The target in this experiment consisted of a stack of 54 natural

molybdenum circular disks (>99.95% pure Mo), 1 mm thick, 70 mm diameter. The activation run consisted of 181 pC total charge in an energy window from 1.5 GeV to 2.0 GeV, with a mean energy of 1.7 GeV on target (weighed by the measured distribution, as with previous data).

Figure 4 shows the measured activity per mm vs. target depth. The error bars are counting statistics in the activity measurement only. There is an estimated +12%/-35% systematic uncertainty in the absolute activity measurement. The Monte Carlo calculations with MCNP6 were performed with the same parameters as the lower energy measurements, with the appropriate change in the upstream absorber material on the BELLA target system. The shaded area shows the calculations at the limits of 1.5 GeV and 2.0 GeV. The agreement with the parametrized calculation is within the uncertainty in the measured points. For comparison, the calculations for 1 and 2.5 GeV are also shown. The peak in the activity is 42 mm into the 54 mm target at 1.7 GeV, consistent with the measured data. The integrated yield over the full target gives $(1391 \pm 20) \times 10^{-5}$ atoms/electron, or 87 ± 2 GBq/ μ A at saturation activation. While the prospect of making such a massive target from high enrichment ^{100}Mo is daunting, we would expect this to translate to 900 GBq/ μ A for pure ^{100}Mo .

Figure 4

d. Contaminant radioisotopes

One issue of concern for using higher energy electrons is the potential for producing higher levels of contaminant radioisotopes (see e.g. Bennett 1999 for a summary). Published measurements on activated thick natural molybdenum targets up to 34 MeV suggest that ^{95}Nb (35 day half life) and $^{95\text{m}}\text{Nb}$ (3.5 day half life) are the dominant potential radioisotope contaminants (Dikiy, 2004b). Block samples from four experiments from 51 MeV to 107 MeV, as well as four disk samples at depths of 3, 23, 47, and 53 mm in the 1.7 GeV experiment were analyzed using high efficiency Ge detectors at the LBNL Low Background Facility (Thomas 2013). Measurements were taken 17-22 days after activation, allowing sufficient time for the $^{95\text{m}}\text{Nb}$ to decay to the ground state ^{95}Nb . The only potential contaminant radioisotope detected 17-22 days after activation was ^{95}Nb . The decay corrected percentage of activities was constant over all energies sampled (and depths in the 1.7 GeV experiment) at $3.2 \pm 0.7\%$. The ^{95}Nb presumably arises from $^{96}\text{Mo}(\gamma, p)^{95\text{g,m}}\text{Nb}$, so would be alleviated by using high enrichment ^{100}Mo targets, or can be chemically separated in subsequent $^{99\text{m}}\text{Tc}$ purification steps. The lower

detection limit for other radioisotopes was approximately a factor of 10 lower than the measured ^{95}Nb activity.

4. Discussion

Several pertinent conclusions can be drawn from the presented results. The copper activation confirms the methodological approach of using the magnetic spectrometer as an energy selector for the activation. The ^{64}Cu yields using the beam spread over the face of the target are comparable to our previous measurements using direct beam irradiation (Nakamura, 2011), albeit with a very different energy distribution. Using the same technique for the molybdenum irradiation gives yields comparable to published data for low energy beams (<50 MeV), and the MCNP6 simulation suggests >90% of the activation can be attributed to the $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ cross section over the giant dipole resonance alone (from 8.3 to 27 MeV). Finally, the high energy data suggest that much of the yield initially lost due to photons produced beyond the resonance energy was effectively recovered by capturing the ensuing photon cascade with thicker targets (or a series of thin targets). These measurements over a broad energy range allow us to use the simulations to further analyze the target system as an interpolation rather than as an extrapolation to unexplored energies.

Comparing the yield with initial electron beam energy is complicated by the difference in the activation distribution with target depth. The 1.7 GeV beam is a factor of 50 higher energy than 34 MeV, with a measured integral yield a factor of 94 higher for the specific targets tested, and this should increase further with a longer target. However this comes at a cost of significantly increased target material and all the associated challenges of extracting high purity $^{99\text{m}}\text{Tc}$. One comparison for different beam energies is to look only at the activation at the peak, keeping the total target geometry fixed. Figure 5 shows a comparison of the calculated yield per mm vs. target depth from 50 to 250 MeV, showing both the increase in the peak height and the characteristic shift of the peak deeper into the target. Figure 6 shows the calculation for the beam current normalized activation yield vs. energy for 1 mm or 10 mm targets centered at the peak of activation density. The yields have been converted to GBq/ μA at saturation, and assume 100% enriched ^{100}Mo targets. Even with the limited target thickness there are still significant gains in this parameter with increasing energy. However, a better comparison would be to normalize the activity produced to beam power, rather than beam current. Figure 7 shows the calculations from figure 6 normalized to beam power, in units of GBq/kW. Both the 1mm

and 10mm targets show a steep increase in production efficiency with a peak at approximately 150 MeV. While there is a decrease in the power normalized efficiency for ^{99}Mo production at higher energies, the decrease is only 21-23% at 2 GeV compared to 150 MeV.

It can be instructive to consider how the yields from these photonuclear systems might impact the isotope needs currently fulfilled by conventional reactor based methods. The Organisation for Economic Co-operation and Development (OECD) issued a report which documents the production capacities of current reactor facilities (NEA report, 2012). For instance, the NRU facility in Canada, providing approximately 30% of the world supply of ^{99}Mo , produces approximately 37,000 GBq (3000Ci) ^{99}Mo per day after processing (converting from 670 6-day Ci/day listed in the report). Matching this production with 200 MeV electrons and a 10 mm thick Mo target (figures 6 and 7) would require 13 mA (neglecting processing losses), for a total beam power of 2.6 MW. Rather than considering a single target system, a better model may be a distribution of multiple accelerators, analogous to the model proposed by Benard et al (Benard, 2014) for distributing multiple low energy proton cyclotron facilities for direct production of $^{99\text{m}}\text{Tc}$ via $^{100}\text{Mo}(p,2n)^{99\text{m}}\text{Tc}$. A 5 μA , 200 MeV electron beam would provide a reasonable yield for a small scale facility, with only 1kW total beam power on target. The heating issues in the photonuclear target model are further mitigated by the selection of only the peak activity region of the target, with much of the energy deposited in upstream electron beam to Bremsstrahlung photon converter material.

Extraction and purification of $^{99\text{m}}\text{Tc}$ from the bulk Mo is a problem beyond the scope of this work. The current supply chain was developed around methods using no-carrier added ^{99}Mo , so clearly the specific activity for the ^{99}Mo using activation of Mo targets is significantly lower. Other researchers have been developing the techniques for $^{99\text{m}}\text{Tc}$ separation from bulk Mo, including the recently published work of Bernard et al. (2014), and the unpublished work of NorthStar Medical Radioisotopes. A global summary of low specific activity $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ development is provided by Mushtaq, 2012, and references therein.

Future strategies for providing non-reactor based sources for $^{99\text{m}}\text{Tc}$ will necessarily rely on sound physics data as well as economic evaluation of existing technologies. This work adds experimental yield data for photonuclear production of ^{99}Mo to published results below 50 MeV, and provides new data using high energy electrons beyond previous reports. The current

normalized yield increases nearly linearly with energy from 100 MeV to 2 GeV for a fixed target length centered at the maximum yield per unit length, and power normalized yield shows a peak at 150 MeV, significantly higher than energies typically used for photonuclear activation systems. As new technologies for electron acceleration mature, higher energy beams may be more accessible, making photonuclear production methods for ^{99m}Tc more attractive.

Figure 5

Figure 6

Figure 7

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References

- Avagyan, R; Avetisyan, A; Kerobyan, I; Dallakyan, R, Photo-production of $^{99}\text{Mo}/^{99m}\text{Tc}$ with electron linear accelerator beam, *Nuc. Med. Biol.*, <http://dx.doi.org/10.1016/j.nucmedbio.2014.04.132> (2014)
- Beil, H; Bergere, R; Carlos, P; Lepretre, A; DeMiniac, A; Veyssiere, A, A study of the photoneutron contribution to the giant dipole resonance in doubly even Mo isotopes, *Nuclear Physics A* 227 (1974) 427, extracted from EXFOR, Experimental Nuclear Reaction Data Base, NNDC, Brookhaven National Laboratory (2014)
- Bennett, RG; Christian, JD; Petti, DA; Terry, WK; Grover, SB, A system of ^{99m}Tc production based on distributed electron accelerators and thermal separation, *Nuclear Technology* 126 (1999) 102-121
- Bernard, F; Buckley, KR, Ruth, TJ; Zeisler, SK; Klug, J; Hanemaayer, V; Vuckovic, M; Hou, X; Celler, A; Appiah, JP; Valliant, J; Kovacs, MS; Schaffer, P, Implementation of multi-Curie

- production of ^{99m}Tc by conventional medical cyclotrons, *J. Nucl. Med.*, April 10, 2014, doi: 10.2967/jnumed.113.133413 (2014)
- Clarke, R; Dorkings, S; Neely, D; Musgrave, I, The production of patient dose level ^{99m}Tc medical radioisotope using laser-driven proton beams, *Proc. of SPIE* 8779 (2013) 1-7
- Cutler, CS; Schwarz, SW, Diversification in the supply chain of ^{99}Mo ensures a future for ^{99m}Tc , *J. Nucl. Med.*, May 20, 2014, doi: 10.2967/jnumed.113.131953 (2014)
- Dash, A; Knapp Jr., FF; Pillai, MRA, $^{99}\text{Mo}/^{99m}\text{Tc}$ separation: An assessment of technology options, *Nucl. Med. Biol.* 40 (2013) 167-176
- Dikiy, NP; Dovbnya, AN, Uvarov, VL, The fundamentals of ^{99m}Tc production cycle at electron accelerator, *Problems of Atomic Science and Tech., Series Nucl. Physics Investigations* (42), No. 1 (2004 a) 168-171
- Dikiy, NP; Lyoshko, Yu.V; Uvarov, VL; Shlyakhov, Ecological aspects of $^{99}\text{Mo}/^{99m}\text{Tc}$ production at an electron accelerator, *Problems of Atomic Science and Tech., Series Nucl. Physics Investigations* (42), No. 1 (2004 b) 191-194
- DOE report, Workshop for Laser Technology for Accelerators, January 23-25 (2013)
<http://science.energy.gov/hep/research/accelerator-rd-stewardship/workshop-reports/>
- Dovbnya, AN; Mytrochenko, VV; Nikiforov, VI; Perezhogin, SA; Shevchenko, VA; Shramenko, BI; Tenishev, A.Eh.; Torgovkin, AV; Uvarov, VL, Two-channel mode of Mo-99 production at an electron accelerator, *Proc. IPAC2011*, San Sebastián, Spain (2011) 3627-3629
- Dzhilavyan, LZ; Karev, AI; Raevsky, VG, Possibilities for the production of radioisotopes for nuclear-medicine problems by means of photonuclear reactions, *Phys of Atomic Nuclei* 74 no.12 (2011) 1690-1696

- Geddes, CGR; Toth, Cs; van Tilborg, J; Esarey, E; Schroeder, CB; Bruhwiler, D; Nieter, C; Cary, J; Leemans, WP, High-quality electron beams from a laser wakefield accelerator using plasma-channel guiding, *Nature* 431 (2004) 538-541
- Gonsalves, AJ; Rowlands-Rees, TP; Broks, BHP; van der Mullen, JJAM; Hooker, SM, Transverse interferometry of a hydrogen-filled capillary discharge waveguide, *Phys. Rev. Lett.* 98, 25002 (2007) 1-4
- Gonsalves, AJ; Nakamura, K; Lin, C; Panasenkov, D; Shiraishi, S; Sokollik, T; Benedetti, C; Schroeder, CB; Geddes, CGR; van Tilborg, J; Osterhoff, J; Esarey, E; Toth, Cs; Leemans, WP, Tunable laser plasma accelerator based on longitudinal density tailoring,, *Nature Physics* 7 (2011) 862-866
- Goorley, T; James, M; Booth, T; Brown, F; Bull, J; Cox, LJ; Durkee, J; Elson, J; Fensin, M; Forster, RA; Hendricks, J; Hughes, HG; Johns, R; Kiedrowski, B; Martz, R; Mashnik, S; McKinney, G; Pelowitz, D; Prael, R; Sweezy, J; Waters, L; Wilcox, T; and Zukaitis, T, "Initial MCNP 6 Release Overview", LA-UR-11-07082, Los Alamos National Laboratory, also Nuclear Technology, 180, pg 298-315 (Dec 2012).
- Guérin, B; Tremblay, S; Rodrigue, S; Rousseau, JA; Dumulon-Perreault, V; Lecomte, R; van Lier, JE; Zyuzin, A; van Lier, EJ, Cyclotron production of ^{99m}Tc : An approach to the medical isotope crisis, *J Nucl Med* 51 no.4 (2010) 13N-16N
- Habs, D; Köster, U, Production of medical radioisotopes with high specific activity in photonuclear reactions with g-beams of high intensity and large brilliance, *Appl Phys B* 103 (2011) 501-519
- IAEA, Production and supply of Molybdenum-99, Nuclear Technology Review, annex (2010)
- IAEA, Non-HEU production technologies for Molybdenum-99 and Technetium-99m, *IAEA Nuclear Energy Series no. NF-T-5.4* (2013) 1-60
- IAEA, Handbook on photonuclear data for applications, Cross-sections and spectra, techdoc-1178 (2000)

Leemans, WP; Rodgers, D; Catravas, PE; Geddes, CGR; Fubioni, G; Esarey, E; Shadwick, BA; Donahue, R; Smith, A, Gamma-neutron activation experiments using laser wakefield accelerators, *Physics of Plasmas* 8 no.5 (2001) 2510-2516

Leemans, WP; Nagler, B; Gonsalves, AJ; Toth, Cs; Nakamura, K; Geddes, CGR; Esarey, E; Schroeder, CB; Hooker, SM, GeV electron beams from a centimeter-scale accelerator, *Nature Physics* 2 (2006) 696-699

Leemans, WP; Daniels, J; Deshmukh, A; Gonsalves, AJ; Magana, A; Mao, HS; Mittelberger, DE; Nakamura, K; Riley, JR; Syversrud, D; Toth, C; Ybarrolaza, N, Bella Laser and Operations, Proceedings of PAC 2013, Pasadena, CA USA (2013) 1097-1100

Lougheed, T; Resolving the market mysteries of medical isotopes, CMAJ October 2, 2012 vol. 184 no. 14 (2012) 1561-1562 First published August 27, 2012, doi: 10.1503/cmaj.109-4263

Mushtaq, A, Future of Low Specific Activity Molybdenum-99/Techneium-99m Generator, *Current Radiopharmaceuticals*, 5 (2012) 325-328

Nagai, Y, ^{99}Mo production via $^{100}\text{Mo}(n,2n)^{99}\text{Mo}$ using accelerator neutrons, *EPJ Web of Conferences* 66, 1007 (2014)

Nakamura, K; Gonsalves, AJ; Lin, C; Smith, A; Rodgers, D; Donahue, R; Byrne, W; Leemans, WP, Electron beam charge diagnostics for laser plasma accelerators, *Phys Rev ST Accel Beams* 14, 062801 (2011)1-11

Nakamura, K; Wan, W; Ybarrolaza, N; Syversrud, D; Wallig, J; Leemans, WP, Broadband single-shot electron spectrometer for GeV-class laser-plasma-based accelerators, *Rev. Sci. Inst.* 79, 053301 (2008) 1-5

NEA Report 7129, Westmacott, C; Cameron, R, Market Impacts of Converting to Low-Enrichment Uranium Targets for Medical Isotope Production, OECD Nuclear Energy Agency, Nuclear Development Division, ISBN 978-92-99197-2 (2012)

NIST data, <http://physics.nist.gov/PhysRefData/XrayMassCoef/tab3.html>, accessed 2014

NorthStar Medical Radioisotopes LLC, 5249 Femrite Drive, Madison, WI 53718, USA,
www.northstarnm.com (2014)

Pillai, MRA; Dash, A; Knapp Jr., FF, Sustained availability of ^{99m}Tc : Possible paths forward, *J Nucl. Med* 54 (2013) 313-323

Reed, SA; Chvykov, V; Kalintchenko, G; Matsuoka, T; Yanovsky, V; Vane, CR; Beene, JR; Stracener, D; Schultz, DR; Maksimchuk, A, Efficient initiation of photonuclear reactions using quasimonoenergetic electron beams from laser wakefield acceleration, *J Appl Phys* 102, 073103 (2007) 1-7

Ruth, T., Accelerating production of medical isotopes, *Nature* 457 (2009) 536-537

Sabel'nikov, AV; Maslov, OD; Molokanova, LG; Gustova, MV; Dmitriev, SN, Preparation of ^{99}Mo and ^{99m}Tc by $^{100}\text{Mo}(\gamma, n)$ photonuclear reaction on an electron accelerator, MT-25 Microtron, *Radiochemistry* 48 no.2 (2006) 191-194

Starovoitova, VN; Tchelidze, L; Wells, DP, Production of medical radioisotopes with linear accelerators, *Appl. Radiat. Isot.* 85 (2014) 39-44

SHINE Medical Technologies, 2555 Industrial Drive, Monona, WI 53713, USA, shinemed.com (2014)

Thomas, KJ; Smitch, AR; Chan, YD; Norman, EB; Wang, BS; Hurley, DL, Low Background Counting at the LBNL Low Background Facility, *AIP Conf. Proc.* 1549 (2013) 20-25

Toth, Cs; Albert, O; Canova, A; Gonsalves, AJ; Panasencko, D; Matlis, NH; Plateau, G; Leemans, WP, Contrast enhancement of the LOASIS CPA laser and effects on electron beam performance of LWFA, in Advanced Accelerator Concepts, *Amer. Inst. Of Phys. Conf. Proc.* 1086, ed. C.B. Schroeder, E. Esarey and W. Leemans (AIP Press, Melville, NY, 2009) 270-275

TRIUMF, Making medical isotopes: Final report of the task force on alternatives for medical-isotope production (2008)

Wolterbeek, B; Kloosterman, JL; Lathouwers, D; Rohde, M; Winkelman, A; Frima, L; Wols, F, What is wise in the production of ^{99}Mo ? A comparison of eight possible production routes, *J Radioanal Nucl Chem* doi 10.1007/s1067-014-3188-9 (2014)

Varlamov, VV; Efimkin, NG; Ishkhanov, BS; Sapunenko, VV; Stepanov ME, Evaluation of Cu-64,65(γ ,np) and Cu-63,65(γ ,p) reaction cross sections in the energy range of giant dipole resonance and isospin splitting of the gdr of Cu nuclei, *Izv. Rossiiskoi Akademii Nauk, Ser.Fiz.* 59, (1995) 222

Figure Captions

Figure 1: Schematic diagram of the experimental setup for the activation yield measurement (BELLA high energy system shown). Electrons produced in the laser plasma accelerator (LPA) enter from the right (a), are spatially separated by energy at the dipole magnetic spectrometer (b), allowing activation at narrow energy bands fixed by the target geometry and magnetic field. Incident charge vs. energy is measured at calibrated Lanex phosphor screens (c) (Nakamura 2011). The target shown (d) is a 54 mm long stack of 1 mm thick, 70 mm diameter disks.

Figure 2: $^{nat}\text{Cu}(\gamma, x)^{64}\text{Cu}$ yield measured for 25.4mm cube targets of natural copper (30.8% ^{65}Cu). The calculated yield generated with MCNP6 assumes only the cross section for $^{65}\text{Cu}(\gamma, n)^{64}\text{Cu}$ over the giant dipole resonance applies.

Figure 3: $^{nat}\text{Mo}(\gamma, x)^{99}\text{Mo}$ yield measured for 25.4mm cube targets (9.63% assumed ^{100}Mo), with one data point at 71 MeV for the stacked 1mm disk target. The calculated yield generated with MCNP6 assumes the cross section for $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ over the giant dipole resonance applies, scaled up 7% to account for possible alternate production channels.

Figure 4: $^{nat}\text{Mo}(\gamma, x)^{99}\text{Mo}$ yield measured for the 54 mm long, 70 mm diameter cylindrical target (9.63% ^{100}Mo). The ^{99}Mo activity was determined by the ^{99m}Tc measurements, and corrected for initial ^{99m}Tc from direct production during activation. The calculated yield generated with MCNP6 assumes the cross section for $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ over the giant dipole resonance applies, scaled up 7% as in Fig. 3.

Figure 5: Calculated $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ yield per mm target depth generated with MCNP6. The results assume 100% isotopic enrichment ^{100}Mo target.

Figure 6: Calculated $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ yield generated with MCNP6. The results assume 100% isotopic enrichment ^{100}Mo target. The yield is provided as GBq/ μA at saturation. The lower curve is for the peak 1mm of activation at each energy, and the upper is a 10mm target located at peak activation location $\pm 5\text{mm}$.

Figure 7: Calculated $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$ yield generated with MCNP6. The results assume 100% isotopic enrichment ^{100}Mo target. The yield is normalized to total beam power for each energy beam, listed in GBq/kW at saturation. The lower curve is for the peak 1mm of activation at each energy, and the upper is a 10mm target located at peak activation location $\pm 5\text{mm}$. The maximum energy normalized yield occurs near 150MeV in each case, with $<20\%$ reduction at 2GeV.

Table 1: Data for $^{nat}\text{Mo}(\gamma, x)^{100}\text{Mo}$ yields. The energy ranges listed were fixed by the target geometry and magnetic field. The data indicated by * were beyond the energy distribution of the beams produced. Yields are the integrated total over the full target used. Calculations were generated with MCNP6 as described in the text.

E(MeV)	target	energy range (MeV)	Measured yield (10^{-5} atoms/ electron)	+/- σ	Calculated yield
33.7	25mm cube	30 to 37	15	2	12
51	25mm cube	45 to 56	33	3	32
63.3	25mm cube	56 to 71	51	2	44
70.9	25x1mm disk	47 to 95	50	8	51
83	25mm cube	71 to 97	62	2	61
106.6	25mm cube	99 to 158*	84	4	77
186	25mm cube	164 to 202	150	60	117
232.5	25mm cube	203 to 258	160	60	135
303	25mm cube	258 to 354*	150	20	158
1700	54x1mm disk	1500 to 2000	1390	20	1380

Figure1

Figure2

Figure3

Figure4

Figure5

Figure

Figure