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Photo-production of ^{99}Mo/^{99m}Tc with electron linear accelerator beam

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ABSTRACT

We report on the development of a relatively new method for the production of ^{99}Mo/^{99m}Tc. The method involves the irradiation of natural molybdenum using high-intensity bremsstrahlung photons from the electron beam of the LUE50 linear electron accelerator located at the Yerevan Physics Institute (YerPhi). The production method has been developed and shown to be successful. The linear electron accelerator at YerPhi was upgraded to allow for significant increases of the beam intensity and spatial density. The LUE50 was also instrumented by a remote control system for ease of operation. We have developed and tested the ^{99m}Tc extraction from the irradiation of natural MoO_3. This paper reports on the optimal conditions of our method of ^{99}Mo production. We show the success of this method with the production and separation of the first usable amounts of ^{99m}Tc.

1. Introduction

^{99m}Tc is the most widely used isotope in nuclear medicine today [1,2] with over 30 million diagnostic medical imaging scans every year around the world [3,4].

^{99m}Tc decays to the ground state ^{99g}Tc with a half-life of 6 hours by emitting a 140 keV photon that is detected by imaging detectors. With the short half-life of ^{99m}Tc it is important that the production takes place within close proximity of the hospitals or clinics in which they will be used.

Fortunately, ^{99}Mo decays predominantly to ^{99m}Tc with a half-life of 66 hours as shown in Fig. 1. Medical centers or commercial radiopharmaceutical distributors typically purchase ^{99}Mo/^{99m}Tc generators from which ^{99m}Tc (and as a by-product also ^{99g}Tc) can be extracted periodically in a simple chemical process as it accumulates from the decay of the ^{99}Mo parent. The ^{99m}Tc is then bound into the pharmaceuticals for use in the imaging procedure [4–7]. According to the Scientific Centre of Radiation Medicine and Burns at Armenian Ministry of Health, the need in Armenia for this ^{99m}Tc isotope is approximately 5,000 doses per year. Presently, Armenia gets this isotope from abroad with a frequency of 1 generator ^{99}Mo/^{99m}Tc every 1–1.5 months. This is sufficient for 40–50 patients per generator or about 500 patients per year. Thus there is an urgent need for a constant and reliable supply of this ^{99m}Tc isotope. This work will alleviate some of the gap between the need or demand and the supply of ^{99m}Tc isotope in Armenia.

In the spring of 2009, the National Research Universal (NRU) reactor in Chalk River was shut down for more than a year for repairs related to heavy water leaks. This caused an unprecedented shortage of medical isotopes, most importantly ^{99m}Tc and prompted investigations on alternative methods of isotope production. One of the considered options was photonuclear reactions [8–14]. Metastable ^{99m}Tc could be obtained in photonuclear reactions by the irradiation of ^{100}Mo by an intense photon beam (see Fig. 2).

At YerPhI, we have an electron accelerator, where the electron beam is converted to photons via bremsstrahlung. This method, while successful, does not provide a sufficient specific activity to be used for mass production and therefore it not used by standard Mo/Tc generators. It could, however, meet the demand for local and regional city clinics.

2. Electron beam

The linear electron accelerator (LUE50) at Yerphi was designed, built, and used for many years as an injector for the Yerevan ring synchrotron [13]. Several significant upgrades were needed to the machine in order to use it for ^{99m}Tc production. These included the electron gun and a new high intensity metallic cathode with slightly modified gun electrodes. The result was that the maximum beam production intensity was increased to 10 μA from an initial 3 μA. An electron beam of $E_e = 40$ MeV was produced using two of the three sections of the accelerator. The electron beam was transported to the target as a beam spot of 12 mm diameter (as measured by a vibrating wire scanner [16]). The beam pulse length was ~1.1 μsec with a repetition frequency of f = 50 Hz.

3. Experimental layout for irradiation

A special experimental setup [17] shown in Fig. 3 has been designed and mounted for material irradiation that provides remote

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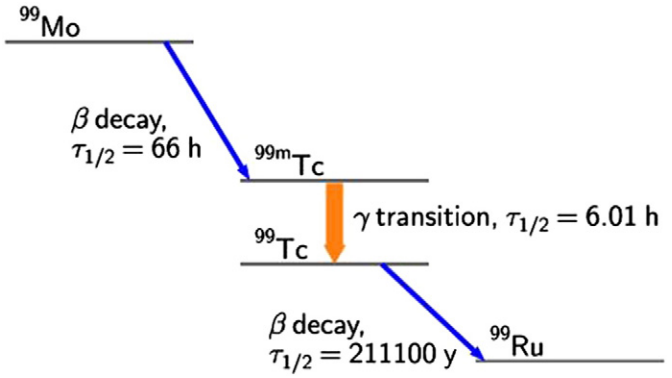

Fig. 1. The ^{99}Mo decay scheme showing the decay of ^{99m}Tc [7].

$$\gamma + {}^{100}\mathrm{Mo} \rightarrow {}^{99}\mathrm{Mo} + \mathrm{n} \quad \text{Threshold} = 9.1\ \mathrm{MeV}$$

$$\downarrow$$

$$T_{1/2} \sim 66\ \text{hours} \rightarrow {}^{99m}\mathrm{Tc}\ (T_{1/2} \sim 6\ \text{hours})$$

Fig. 2. ^{99m}Tc production by the photoexcitation of ^{100}Mo.

controlled motion of the target module across the beam direction adjusting the center of the target to the beam axis.

The target body module (Fig. 4) was made of copper. A thick tantalum plate has been installed on the entrance window to convert the electron beam to photons. A GEANT4 Monte-Carlo simulation of the optimal density of the converter has been performed. The resulting dependence of the photon yield on the converter thickness is presented in Fig. 5 which indicates that the optimum thickness of the tantalum radiator is about 2 mm (0.5 radiation length).

Beam intensity was measured by the Faraday cup (No. 1 on Fig. 3) [18]. In this case, the Faraday cup is a metal (conductive) cup designed to trap charged particles and consists of a 5 cm thick lead bottom and a magnet to repel secondary electrons. Intensity measurements were performed when the target module was remotely moved out of the beam position. During the irradiation, only a part of the secondary beam was captured by the Faraday cup, and therefore a more precise recalibration was required to get the experimental beam intensity.

At an electron beam energy of $E_e = 40$ MeV, and a beam current $I_e \sim 10$ μA, the total beam power is $P = 400$ W. The target module and Faraday cup were cooled by water and air. To avoid charge leakage from the Faraday cup, only pure distilled water (with high specific resistance 0.2 MOhm · cm) was used in the cooling system. The water temperature and beam current were displayed on a computer monitor. The data acquisition and visualization of these parameters were done via LabView [19].

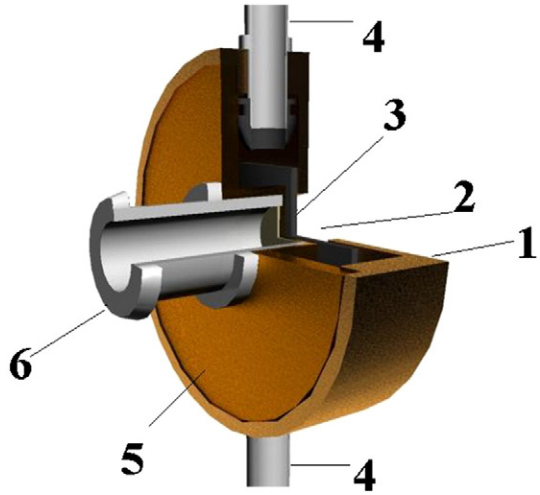

Fig. 4. The body of the target module with identified components: 1 is the framework, 2 is the beam entrance window, 3 indicates the tantalum plate, 4 is the water cooling pipe, 5 cap and 6 is the target capsule (shown in greater detail in Fig. 6).

4. Irradiation modes

The oxide of natural molybdenum, MoO_3, was used for the irradiation. The abundance of the stable isotope, ^{100}Mo/^{nat}Mo is 9.63%. The irradiated material was packed in a special aluminum capsule (Fig. 6). Two styles of target materials were used – a stack of pressed pellets (left) and full length pressed powder (right) covered by thin copper foil of 0.045 g/cm^2 areal density. The first type of target was used to measure the dependence of induced activity on the depth of target, and the second one was used for the trial production.

Gamma-spectra were measured by a 3 M3/3-X 905-4 type NaI(Tl) detector (producer - ORTEC) [20] and an HPGe (ORTEC) [21] detector.

5. Investigation of excited specific activity

One of the main parameters for the production of radioisotopes is the resulting specific activity normalized to the mass of the main isotope (^{100}Mo in our case), from the photonuclear reaction producing the final medical isotope, the beam current, and the duration of irradiation – Bq/mgμA h. The data available for the specific activity of ^{99}Mo published by different experimental groups have a very large variance (90 to 3200 Bq/mgμA h [9]).

The irradiation was done with a beam current of $I_e = 5.5$ μA for 5 hours. The energy spectrum from the irradiated material measured

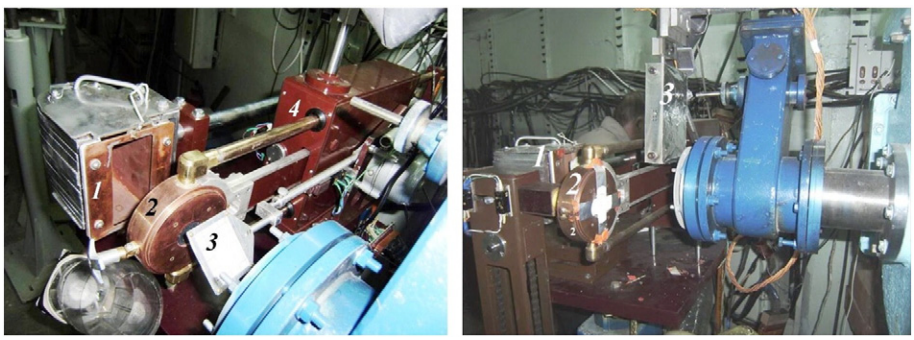

Fig. 3. Experimental setup with labels showing the various components as 1, 2, 3, and 4: 1 is the Faraday cup, 2 is the moveable target module, 3 is the luminofore for the beam spot size and position along with video TV control (left photograph) and vibrating wire scanner module (right photograph), and 4 is the target module moving system.

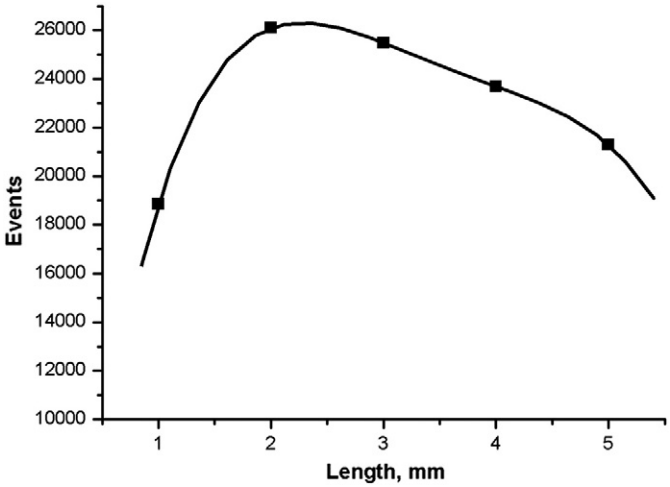

Fig. 5. Dependence of photon yield on the converter thickness.

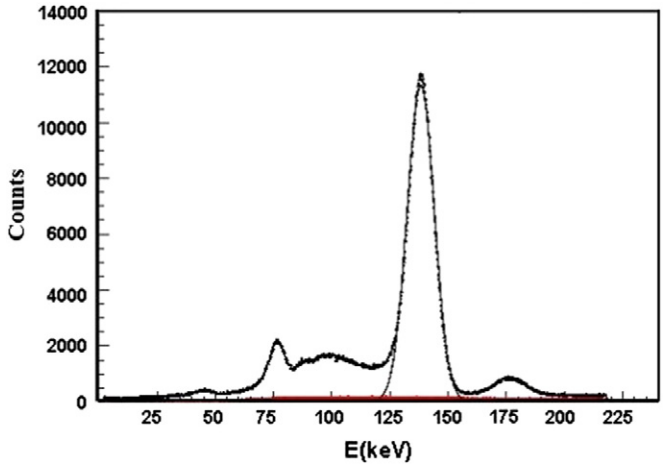

Fig. 7. The energy spectrum resulting from the irradiation of the MoO_3 measured with a NaI(Tl) detector.

by the NaI(Tl) detector is shown in Fig. 7. The spectrum was fit by a Gaussian, the mean value of the Gaussian function is Eγ ~ 140 keV. Two peaks are seen with energies E ~ 140 keV from ^{99m}Tc and E ~ 180 keV from ^{99}Mo.

The normalized specific activity calculated from the measurements reflected in this spectrum was A ≈ 3000 Bq/mgμ A h which is close to the maximum value of the published range of results [10].

6. Investigation of the depth dependence

To find the optimal thickness for the irradiated material inside the target capsule, we investigated the dependence of the excitation activity on the depth of the target material. A Monte-Carlo simulation (Fig. 8) using GEANT4 [22,23] was used to analyze the number of escaped photonuclear neutrons from the MoO_3 target.

To further test these simulation results a special experiment has been performed. A number of identical pellets, 2 g natural MoO_3 each, have been fabricated and then irradiated under electron beam with energy E_e = 40 MeV and beam current I_e ~ 8 μA for 2.5 hours. Then activity of each pellet was measured by a NaI(Tl) detector. Results of the measurements after 15.7 hours from the end of irradiation are presented in Fig. 9. Each point shows the counts in the gamma-ray peaks of interest. Also the sums of the activities resulting from these pellets are shown on Fig. 8 along with GEANT 4 Monte-Carlo calculations for comparison.

The data in Fig. 9 show that with increasing the thickness of the target, the activity of each pellet is reduced. Self-absorption of the photons limits the thickness of the target.

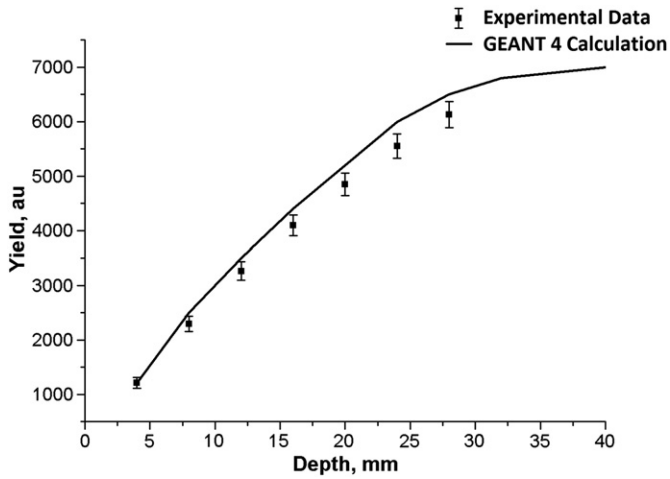

Fig. 8. The dependence of the activity on the depth of natural MoO_3 target. The solid line is the GEANT 4 Monte-Carlo calculation. The data points are the measured values and their associated uncertainties.

Thus, the determination of the optimum length for the target will provide economic benefits in the production of isotopes ^{99m}Tc. This is particularly important for the irradiation of enriched ^{100}Mo.

7. Trial production of ^{99m}Tc

For the low specific activity option the only reasonable option is the direct extraction of ^{99m}Tc from the irradiated material [15]. For

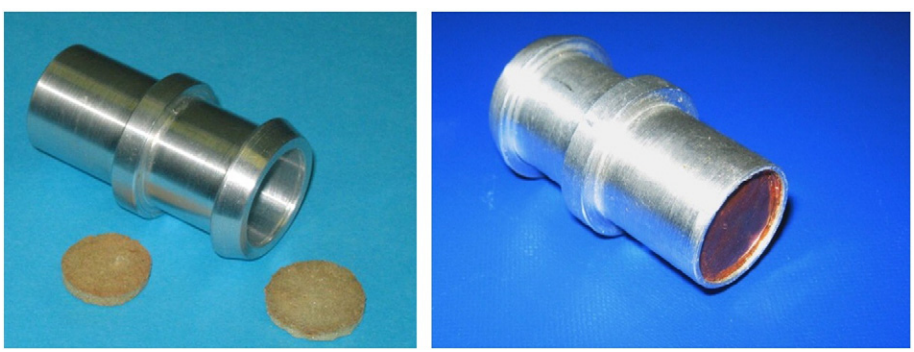

Fig. 6. The two modes of target preparation. The photograph on the left shows pressed pellets used in an aluminum tube whereas the photograph on the right reflects the same tube filled with the oxide powder with a copper film.

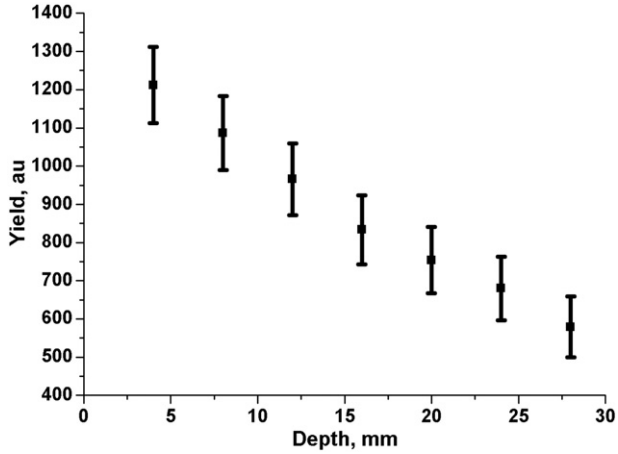

Fig. 9. The dependence of measured activity on depth of natural MoO_3 target.

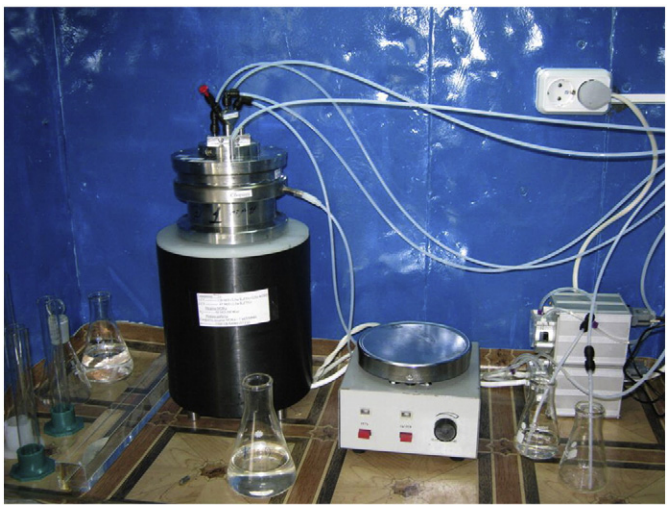

Fig. 10. The main part of the centrifuge extractor complex.

that, a centrifuge extractor based on methyl ethyl ketone (MEK) solvent technology was chosen. This technology has been successfully used for many years in Russia [24]. The irradiated MoO_3 is dissolved in KOH alkali, and then MEK liquid is added to that solution. The irradiated MoO_3 dissolves in KOH while ^{99m}Tc dissolves in MEK so that we have mixture of two solutions with very different densities. The centrifuge extractor was designed at the A.N. Frumkin Institute of Physical Chemistry and Electrochemistry in Moscow [25] and allows the separation of the two elements with high purity, followed by the separation of the ^{99m}Tc from MEK by evaporation. The complete automated system, developed by "Federal Center of Nuclear Medicine Projects Design and Development" of Federal Medical – Biological Agency of Russia (FMBA), was commissioned and installed in a "hot" cell shown in Fig. 10.

The natural MoO_3 is a powder with an absolute density 4.96 g/cm^3. After pressing, its volume density became ~2.4 g/cm^3. A natural MoO_3 target with a mass of 20 g and areal density 0.8 g/cm^2 has been irradiated under electron beam with energy $E_e = 40$ MeV and average current of $I_e \sim 9.5$ μA for a duration of T = 100 hours. The irradiated material was then processed by the centrifuge extractor and the first trial amount of ^{99m}Tc has been produced. The decay correction to the EOB (end of bombardment) yielded ~ 2.96 10^9 Bq (80 mCi).

On subsequent days a new allotment of ^{99m}Tc was produced from the ^{99}Mo decay and extracted daily for a period of 5–6 days with a value of extracted activity by coefficient k ~ 0.7 in comparison to the previous day.

The efficiency of extraction is >95%, according to the specification of the centrifuge.

The energy spectrum from the extracted ^{99m}Tc is shown on Fig. 11. The clean peak at energy of E ~ 140 keV from ^{99m}Tc is apparent. The peak around 180 keV from ^{99}Mo is clearly absent (Fig. 7). The left part of the spectrum is the edge of Compton scattering in the detector.

8. Conclusion

The theoretical and experimental investigations of the feasibility of ^{99m}Tc production by photonuclear reactions using an electron beam have been carried out. The optimal thickness for the target of MoO_3 to be irradiated has been found by theoretical simulations and compared with experimental measurements. The best thickness was ~30 mm. The extraction of the final product of ^{99m}Tc from the irradiated material has also been established. The required equipment was commissioned and installed. The full technology chain of ^{99m}Tc production has been implemented and tested; the first trial amount of ^{99m}Tc isotope was produced. One of the most important results is the normalized specific activity A ≈ 3000 Bq/mgμ A h which could allow production of ^{99m}Tc by the use of high intensity electron beams via photonuclear reactions. The next step would be to increase the beam intensity by repetition of the frequency and increasing the pulse length in order to enhance the intensity by a factor of 5–10. We aim to

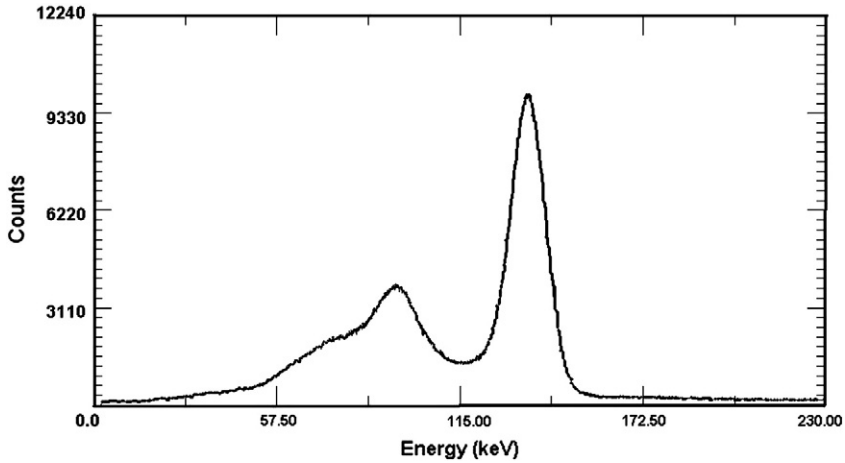

Fig. 11. The energy spectrum of the extracted ^{99m}Tc. The quality of the separation is excellent since there is no evidence of any ^{99}Mo gamma-rays at 180 keV.

increase the production yield to cover a significant part or the full demand for ^{99m}Tc in Armenian clinics.

The natural MoO_3 was chosen for this investigation since it is a low cost material and easy to work with. After the ^{99m}Tc extraction from the irradiated material, the MoO_3 could be recovered in its primary state for re-use in new irradiations. This is an important aspect when we use the very expensive, enriched $^{100}MoO_3$. As the procedure of recovery will be implemented with high efficiency, the use of enriched $^{100}MoO_3$ target material will or can become much more effective by commercial aspects. The use of enriched $^{100}MoO_3$ will increase the ^{99m}Tc activity more than 10 times. The approximate processing time from EOB to final ^{99m}Tc is 13 hours consisted of ~12 hours of target "cooling" (in case of natural MoO_3) and ~1 hour for the extraction procedure.

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