ACCELERATOR BASED TECHNOLOGIES OF ISOTOPES PRODUCTION IN ARMENIA – CURRENT STATUS AND FUTURE PLANS

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Abstract. Since 2008 A.Alikhanyan National Science Laboratory (the Yerevan Physics Institute) started an activity in the area of development of accelerator based medicine intended isotopes production technologies. The first step has been carried out by use of linear electron accelerator LUE50. Under financial support of ISTC an experimental layout has been mounted and theoretical and experimental investigation of ^{99}Mo/^{99m}Tc and ^{123}I trial production via photonuclear reaction has been carried out under electron beam with energy Ee=40 MeV. The full cycle of extraction from irradiated material was chosen, purchased, built and executed. The next steps are planned to do under proton beam from C18 cyclotron which will be mounted and commissioned close to end of 2013. Technology of irradiation, cooling, target preparation, isotope extraction and target material recovery are targets of our investigation for next year.

1. Introduction

A.Alikhanyan National Science Laboratory (the Yerevan Physics Institute) was founded in 1943 for an activity in an area of high energy particles and cosmic ray investigation. On the first stage it was based on a high altitude cosmic ray stations (~2000 and 3000 m s.l.a.). Since 1967 the ring synchrotron with 4.5 GeV energy of electrons has been commissioned. Till 2000 a lot of fundamental investigation in the area of photoproduction and electroproduction has been done using that accelerator. Besides ring accelerator a few small linear accelerator are working for applied research, technology development and other areas. In particular the injector of ring accelerator is enough powerful linac with energy up to E_e=75 MeV (see Fig.1)[1].. It was used as a source of intensive electron beam for ^{99}Mo/^{99m}Tc and ^{123}I production technology development.

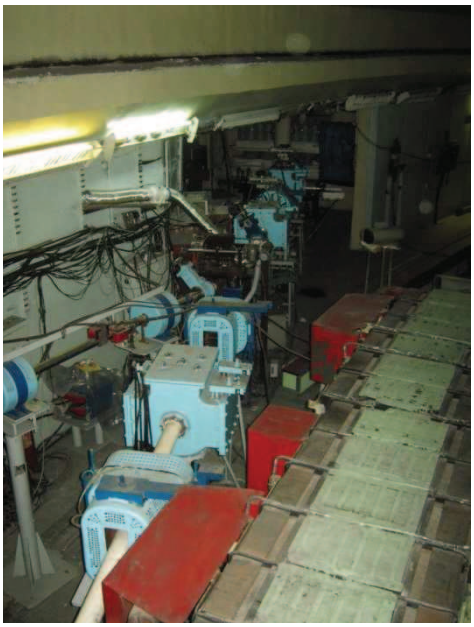

Fig.1. Ring accelerator tunnel and experimental layout on the end of linac beampipe.

2. ^{99}Mo/^{99m}Tc production

2.1. Production option

The ^{99m}Tc is derived as a daughter isotope from ^{99}Mo decay (see Fig. 2)

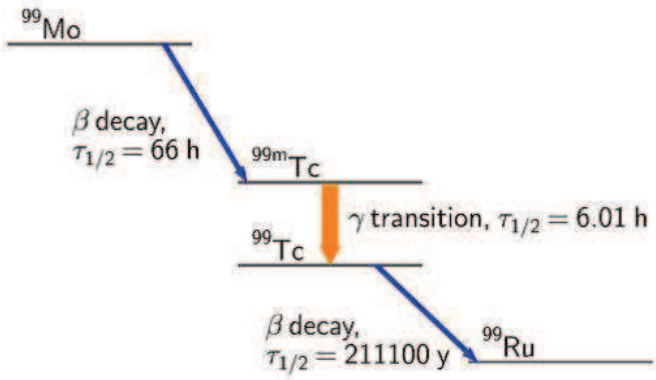

Fig.2.^{99}Mo decay chain.

One of considered options of alternative methods of^{99m}Tc production was a photonuclear reaction [2-6].Metastable ^{99m}Tc could be obtained in the photonuclear reaction by irradiation of ^{100}Mo under intensive photon beam (see Fig. 3.).

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

$$\downarrow$$

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

Fig. 3.^{99m}Tc production chain under photo beam.

For this option the electron beam should be converted to a photon beam via bremsstrahlung. This method cannot provide high specific activity and therefore does not permit the use of standard Mo/Tc generators but could cover the demand for regional and city clinics.

To use its electron beam for photon-induced reactions the electron gun had to be upgraded. A new high intensity metallic cathode was installed with slightly modified gun electrodes so that the maximum intensity was increased from 3 μA to ~10 μA. From 3 accelerator sections 2 were in use providing E_e= 40 MeV electron energy. The electron beam was transported to the target magnetic optics in a way that the beam spot diameter on the target was 12 mm, measured by luminofore frame or vibrating wire scanner [7]. The beam pulse length was ~1.1 μsec, repetition frequency f=50 Hz.

2.2. Experimental layout for irradiation

A special experimental setup [8] (see Fig. 4) has been designed and mounted for material irradiation that provides remote controlled motion of the target module across the beam direction adjusting the center of the target to the beam axis.

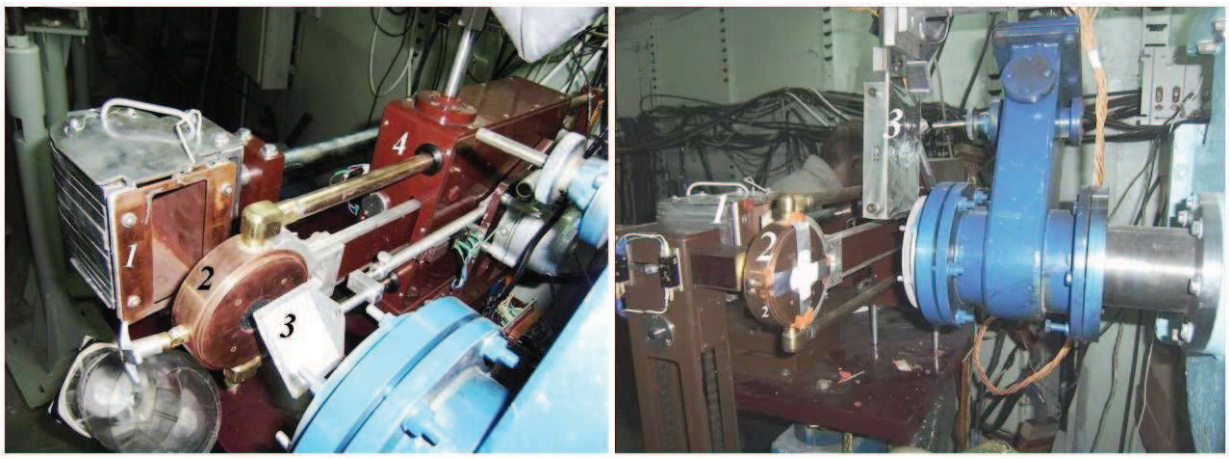

Fig. 4.Experimental setup with labels showing the various components as labeled 1, 2, 3, and 4: 1 is the Faraday cup, 2 is the moveable target module and 3 is the luminofore for the beam spot size and position along with video TV control (left photo), and 3 is vibrating wire scanner module (right photo).

The target body module (Fig. 5) was fabricated of copper. A thick tantalum plate has been installed on the entrance window to convert the electron beam to photons. A Monte-Carlo simulation of an optimal thickness of the converter has been performed. The optimum thickness of the tantalum radiator is about 2 mm (0.5 r.l.).

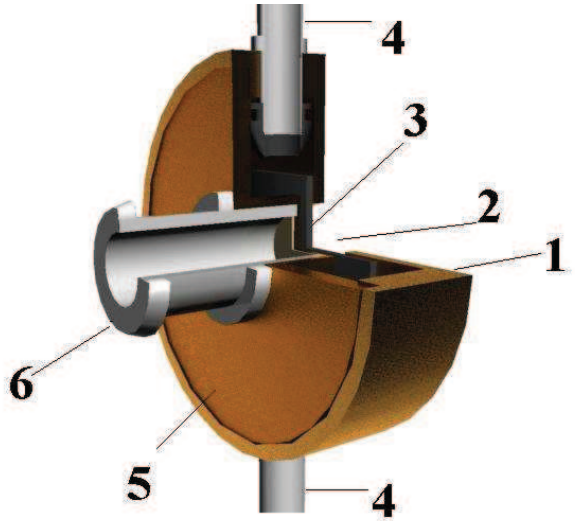

Fig. 5. The body of the target module with identified components: 1 is the framework, 2 is the beam entrance window, 3 indicates the tantalum plate, 4 is the water cooling pipe, 5 is the Faraday cup, and 6 is the target capsule (shown in greater detail in Fig. 6).

For direct measurement of the beam intensity, the Faraday cup (1 on Fig. 4) has been used.

At an electron beam energy of Ee =40 MeV, and a beam intensity I_e ~10 μA, the total power of the beam 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 displayed by LabView software.

2.3. 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 with 0.045 g/cm^{2}areal density. First one was used to measure the dependence of excitation energy on the depth of target, and the second one was used for the trial production.

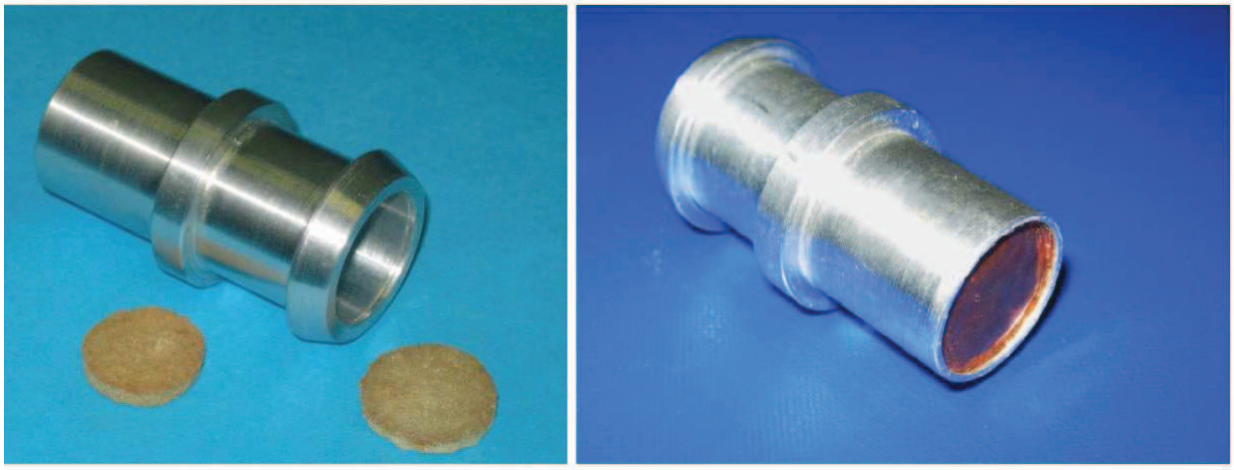

Fig. 6. Target capsule for different tasks with pellets (left) and full amount (18 g) pressed powder of MoO_3 (right).

The energy spectra from the irradiated materials were measured by a 3M3/3-X 905-4 typeNaI(Tl) detector (producer- ORTEC) and an HPGe(ORTEC) detector.

2.4. 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 irradiated material, the beam current, and the duration of irradiation – Bq/mg·μA·h. The data on the specific activity of ^{99}Mo published by different experimental groups has a very large variance (from 90 to 3200 Bq/mg·μA·h [4]).

The irradiation has been performed with a beam intensity of Ie = 5.5 μA for 5 hours. The energy spectrum from the irradiated material measured by the NaI(Tl) detector is shown in Fig. 7. The spectrum was fit by a Gaussian function; parameters of the fit are presented on the right top corner of the histogram. The mean value of the Gaussian function is Eγ~140 keV. Two peaks are seen in the spectrum with energies E ~ 140 keV from ^{99m}Tc and E ~ 180 keV from ^{99}Mo.

The normalized specific activity calculated from this spectrum is A≈3000 Bq/mg·μA·h which is close to the maximum value of the published range of results.

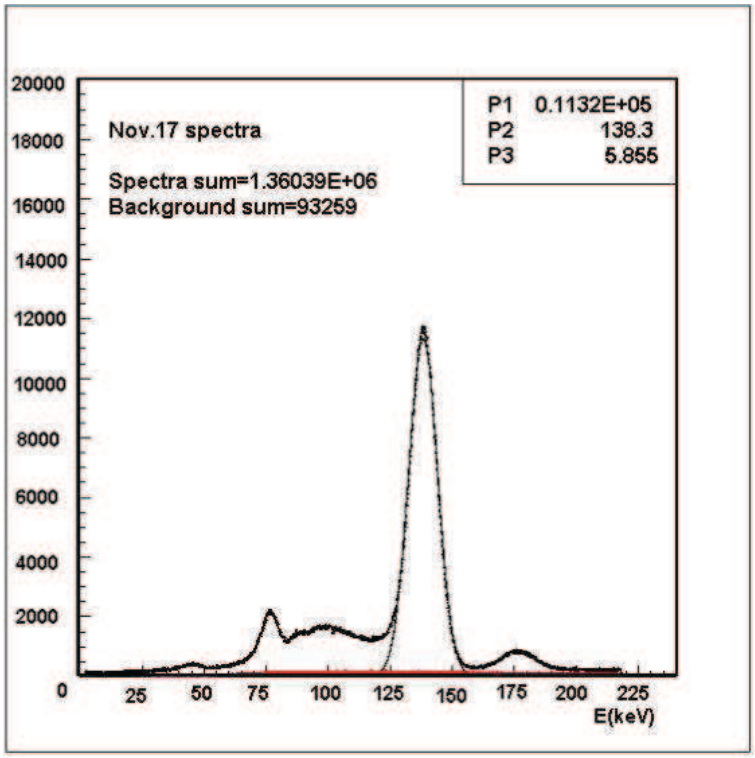

Fig. 7.The energy spectrum from the irradiation of the MoO_3 measured with a NaI(Tl) detector.

2.5. Investigation of the depth dependence

To find an 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 GEANT-4 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 done. A number of identical pellets, 2 g natural MoO_3 each, have been fabricated and then irradiated under electron beam with energy Ee=40 MeV and beam intensity Ie~8μA for 2.5 hours. Then activity of each pellet was measured by NaI(Tl) detector once per day for 4 days. Results of the measurements after 15.7, 37.8, 62.7 and 84.3 hours are presented in Fig. 9. Each point shows the number of gamma-quanta under photo peak in the respective energy spectra from the irradiated material.

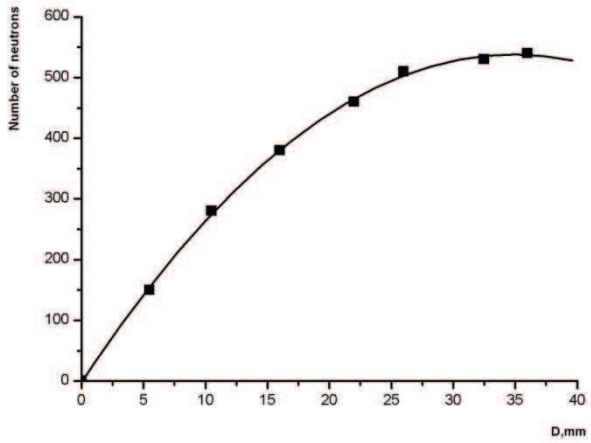

Fig. 8. The dependence of the activity on the depth of natural MoO_3 target

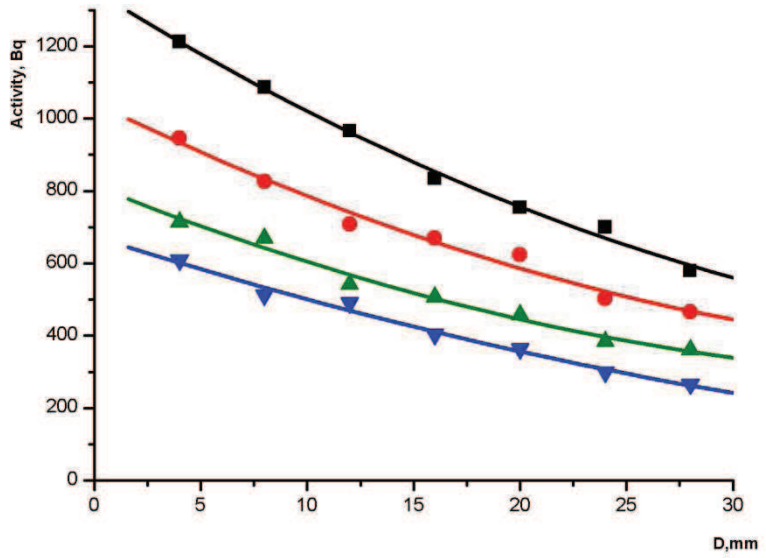

Fig. 9. The dependence of measured activity on depth of natural MoO_3 target after EOB: ■ – 15.7 hours, ● - 37.8 hours, ▲- 62.7 hours, ▼- 84.3 hours.

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.

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.

2.6. Trial production of ^{99m}Tc

For the low specific activity option only direct extraction of ^{99m}Tc from the irradiated material is a reasonable option. For that, a centrifuge extractor with Methyl Ethyl Ketone (MEK) solvent technology was chosen. This technology has been successfully used for many years in Russia [9]. 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 [10] 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 semi-automated system commissioned from the Moscow "Federal center of nuclear medicine projects design and development" and developed by FMBA (Russian company) was installed in a "hot" cell shown in Fig. 10.

Fig.10. "Hot" cell (left) and centrifuge extractor(right).

The natural MoO_3 is a powder with a density 4.96 g/cm^3. After pressing, its density became ~2.4 g/cm^3. The natural MoO_3 target of 20 g mass and areal density 0.8 g/cm^{2}has been irradiated under electron beam with energy Ee = 40 MeV and average intensity Ie ~ 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 ~ 80 mCi.

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

3. ^{123}I production

^{131}I-containing preparations are widely used in order to examine thyroid glands and kidneys. The long lifetime of ^{131}I (8 days) and accompanying β-decay has made the use of ^{131}I dangerous for life. Recently, other iodine isotopes such as ^{123}I were produced in several countries. It is short-lived and radiates only via γ-rays and X-rays, which decrease the absorbed dosage of radiation patients by approximately 100 times. Production of ^{123}I isotope now are based on hundreds MeV proton accelerators and tens of MeV cyclotron beams of protons, deuterons, ^{3}He, and ^{4}He. In both cases, together with ^{123}I, there are undesirable isotopes produced with activities exceeding that of ^{123}I a thousand times. This requires having a remote control system for target handling, very thick biological shielding, and a special system for removing radioactive waste. The operations costs for accelerators or cyclotrons as mentioned above and their associated systems for radioactivity handling/management is significantly higher in comparison to the operations costs of electron accelerators.

The most pure isotope of ^{123}I is produced in the following reaction:

$$\gamma + {}^{124}\mathrm{Xe} \rightarrow {}^{123}\mathrm{Xe} + n \qquad \text{threshold of reaction} - 8.3\ \text{MeV}$$

$$\downarrow$$

$$T_{1/2} = 2.2\ \text{hours} \qquad {}^{123}\mathrm{Xe} \rightarrow {}^{123}\mathrm{I}\ (T_{1/2} = 13.3\ \text{hours})$$

The effective cross-section for this reaction is rather high; for photons of approximately 15 MeV the cross section is 450 mbarn. The width of the excitation curve is about 5 MeV. So the effective energy of electrons should be 25-35 MeV. For the higher energy, the number of hard photons increases as well as the number of undesired nuclear reactions. The yield of ^{123}I could exceed 200 μCi/μA*h*g of ^{124}Xe. Experiments performed at JINR (Dubna, Russia) on a 10 g target of pure xenon ^{124}Xe irradiated

in the course of 8 hours by an electron beam of 25 MeV and current of 20 μA, yield 200 mCi activity of ^{123}I [11].

The stainless still target cell for Xe irradiation has been prepared (Fig. 11, left) and installed in the experimental layout under electron beam (Fig. 11, right). The cell has been filled by natural Xe using cryogenic condensation method till 230 bar of pressure on room temperature. Just after filling the tendency of pressure in the target cell was the increasing due to the equalization of temperature in the target body volume. To avoid the overpressure the remaining part of gas was transferred to the gasholder. The weighting of target cell shows that accumulated amount of Xe is about 40 grams. The control weighting during one week didn't show any leakage. Simultaneously the pressure control shows a divergence to both sides repeating the daily fluctuation of the room air temperature.

The Xe target has been irradiated under electron beam. The following parameters have been achieved:

- Amount of natural Xe gas - ~40 gram
- Xe pressure in the stainless still cylinder - ~200 bar
- Beam energy – 40 MeV
- Beam current - ~9 μA
- Duration of irradiation – 12 hours.
- Target pressure was increased during irradiation – up to 250 bars.

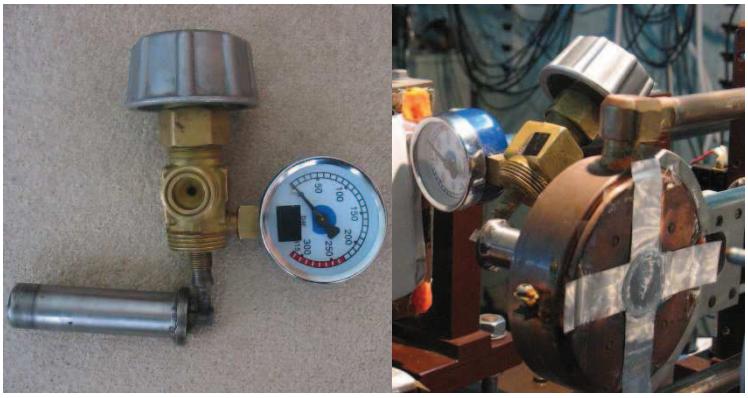

Fig. 11. The stainless steel target sell (left) installed in a target module (right).

The Xe target has been removed from beam position a day after irradiation finished. Then all chemical procedures of ^{123}I extraction have been done.

The activity for EOB was

$$A_{tot} = 7*10^5 Bq \sim 20\ mcCi$$

The main often use parameter of yield of irradiation is the total activity after irradiation normalized to the amount of target material (for pure ^{124}Xe), beam current and exposition time - duration of irradiation. Taking into account that concentration of ^{124}Xe in the natural Xe is only 0.96% and the mass of irradiated gas was only 40 gram – the real mass of irradiated ^{124}Xe was only 40 mg, therefore this parameter for the current irradiation was

$$Y = 143 Bq/mg*\mu A*h$$

4. Future plans

The development of commercially feasible accelerator based production of medical isotopes in nearest future will be possible by use of proton cyclotron C18 (see Fig. 12) (producer – IBA, Belgium) to be installed nearby AANL (YerPhI) in fall of 2013. The main task of that cyclotron is

short life isotopes production such as ^{18}F for PET. In addition the 18 MeV protons will be used to investigate accelerator-based schemes for the direct production of ^{99m}Tc [12-21].

We propose the ^{99m}Tc direct production method (avoiding ^{99}Mo stage) using proton beams from that C18 cyclotron. That is in a coincidence with the goals of Coordinated Research Project (CRP) sponsored by the IAEA.

4.1. Proposed activity

The theory and technology of ^{99m}Tc direct production method (avoiding ^{99}Mo stage) using metallic ^{100}Mo target is well known and published in many articles. Monte- Carlo simulation should be done to tune irradiation parameters and estimate final product yield. On the first step we will use a standard solid target module [22] to irradiate different target materials such as metallic Mo and powder of MoO_3. For that we are in a close contact with experts from IBA Molecular and use their consulting. Then may be a special target module with higher level of cooling should be designed and constructed because the IBA standard module could utilize no more than 500 W. The thin foils of enriched ^{100}Mo have been used in above mentioned articles. We are going to investigate an opportunity of $^{100}MoO_3$ suitability for that production too. The reason is that a present technology of extraction is based on use of MoO_3. The problem is that even pressed powder of MoO_3 cannot provide necessary high temperature conductivity; therefore much more intensive cooling should be applied.

All other technology components for ^{99m}Tc production are ready from the previous irradiation experiments with the electron beam. An existent facility of ^{99m}Tc extraction from the irradiated material, specialized building with "hot" rooms and radiochemical purity testing system by use of HPGe detector will be used in the proposed project. Some investment will be required for radiology and chemical purities testing, packing, and certifying. The efficiency of ^{99m}Tc production under proton beam from cyclotron expected to be as minimum 10 times larger than that under electron beam due to much higher beam intensity from cyclotron; duration of irradiation will be only 2-3 hours instead of 100 hours for electron beam. The estimated produced activity of ^{99m}Tc is expected to be ~1-2 Ci per day (1 irradiation per day with max. 2-3 hours of duration) which is even more than current daily demand of Armenian clinics.

Concerning this method authors of published results always note the short life time of ^{99m}Tc as a disadvantage; thus the transportation to a long distance is impossible. That is drawback for production and distribution of isotopes to many remote clinics and for export to abroad. If the task is to fulfill a local demand of a few clinics but in the one and the same city – this way could be reasonable especially taking into account that medicine intended cyclotrons are currently in wide use. This technology could be the best solution for Armenia where only 2-3 clinics use ^{99m}Tc and all of them are in a car driving short distance, and this technology could cover whole demand with much lower price.

The new method using $^{100}Mo_2C$ targets [23] published in the last volume of Nuclear Medicine and Biology is seen as very perspective option, and we will try to master that method too.

4.2.Detailed plan of activity

- Theoretical calculation and Monte-Carlo simulation of nuclear processes in different target materials under proton beam from C18 cyclotron.
- Calculation of excitation function under different energies of protons for $^{nat}Mo0_3$, enriched $^{100}MoO_3$, metallic ^{nat}Mo and enriched ^{100}M for following reactions
  $^{100}MoO_3(p,2n)^{99m}Tc$, $^{100}Mo(p,2n)^{99m}Tc$,
  $^{100}MoO_3(p,pn)^{99}Mo\rightarrow^{99m}Tc$, $^{100}Mo(p,pn)^{99}Mo\rightarrow^{99m}Tc$,
  $^{100}MoO_3(p,2p)^{99}Nb\rightarrow^{99}Mo\rightarrow^{99m}Tc$, $^{100}Mo(p,2p)^{99}Nb\rightarrow^{99}Mo\rightarrow^{99m}Tc$
- R&D of Mo and MoO_3 targets, construction, test under real proton beam from C18 cyclotron.

- ^{99m}Tc real yield measurement depending of protons energy, beam intensity and duration of irradiation
- Comparison of our experimental results with published theory and experimental results
- Further development of ^{99m}Tc extraction technology from irradiated material
- Further development of target material Mo recovery for multiple uses.
- Test of chemical and radionuclide impurities of final ^{99m}Tc product.
- Creation of trial production covering full of a part of demand of Armenian clinics.
- Test of chemical and radionuclide impurities of final ^{99m}Tc product.

The part of above mentioned points is already in progress. The real work with proton beam will start on spring 2014.

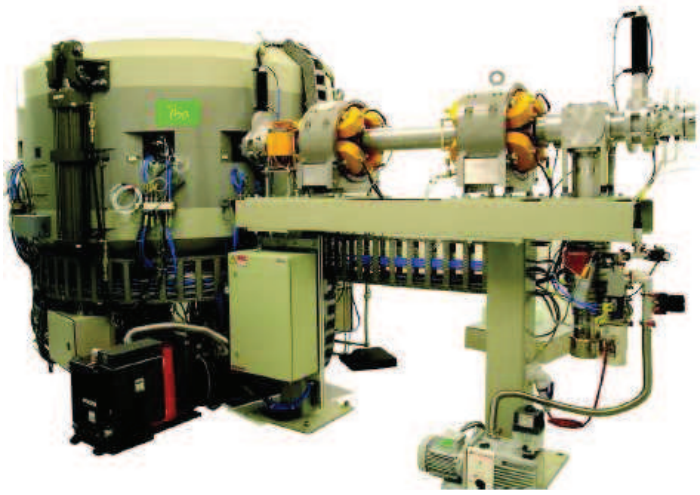

Fig. 12. C18/18 cyclotron with estracted beam line

One of the proposed way to prepare a pillet from powder style material (e.g. Mo or MoO_3) is the use of some compaund to “glue” microparticles of materail. That compaund should be with high adhesive and thermoconductivity propertise. On the first step we use 10% of silber powder (see Fig. 13).

Fig. 13. Mo pillet with 10% of silberpowder compaund, pressed under 1000 kg force.

The investigations of their physical and chemical properties are in progress.

Another point is remote controlled devices for technology processes such as transportation of irradiated material from contayner to hot cell. The design of that machine is completed, mounting is started (see fig. 14).

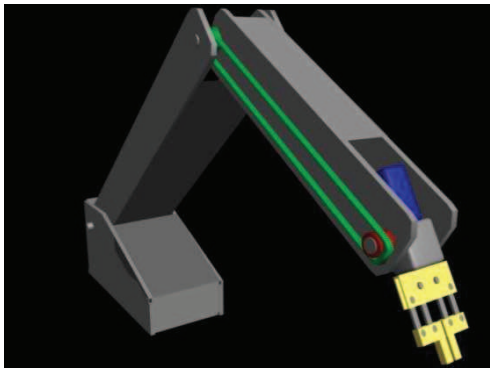

Fig. 14. Remote controlled device for target transportation from container to "hot" cell.

Conclusion

The Yerevan team has enough good expirience in the area of photonuclear method of isotopes production and it is absolute beginner of cyclotron based area. In general we repeat and master all the expirience is accumulated by the community of experts in that are – using in particular the infrastructure from previous activity , and will do some owner investigationas soon. In general they will be in the area of technology development, implementation of results to a trial and real producttion scheme to cover a demand of Armenian clinics.

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