Development of medicine-intended isotopes production technology at Yerevan Physics Institute

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- **AANL experience based on photonuclear reactions – status, problems, results.**
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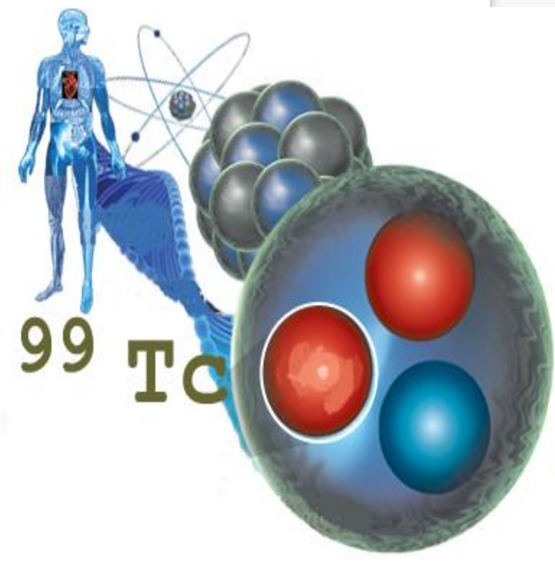

After Alikhanyan National Laboratory (AANL) experience – status, problems, perspectives

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Yerevan Physics Institute

Short introduction to history

* **Was founded in 1943 for an activity in an area of high energy particles physics and cosmic ray investigation.**
* **First stage - high altitude cosmic ray stations (~2000 and 3200 m s.l.a.)**
* **Since 1967 - electron ring synchrotron with 4.5 GeV energy of electrons.**

ANSL experience – status, problems, perspectives

Yerevan Physics Institute

Short introduction to history (continue)

* Fundamental investigation in the area of photoproduction, electroproduction and cosmic ray physics.
* Theoretical physics, accelerator physics and technique, applied physics.

How we started

The ISTC project titled "Development of medicine intended isotopes production methods on the basis of accelerator facility of Yerevan Physics Institute" has started on 2009.

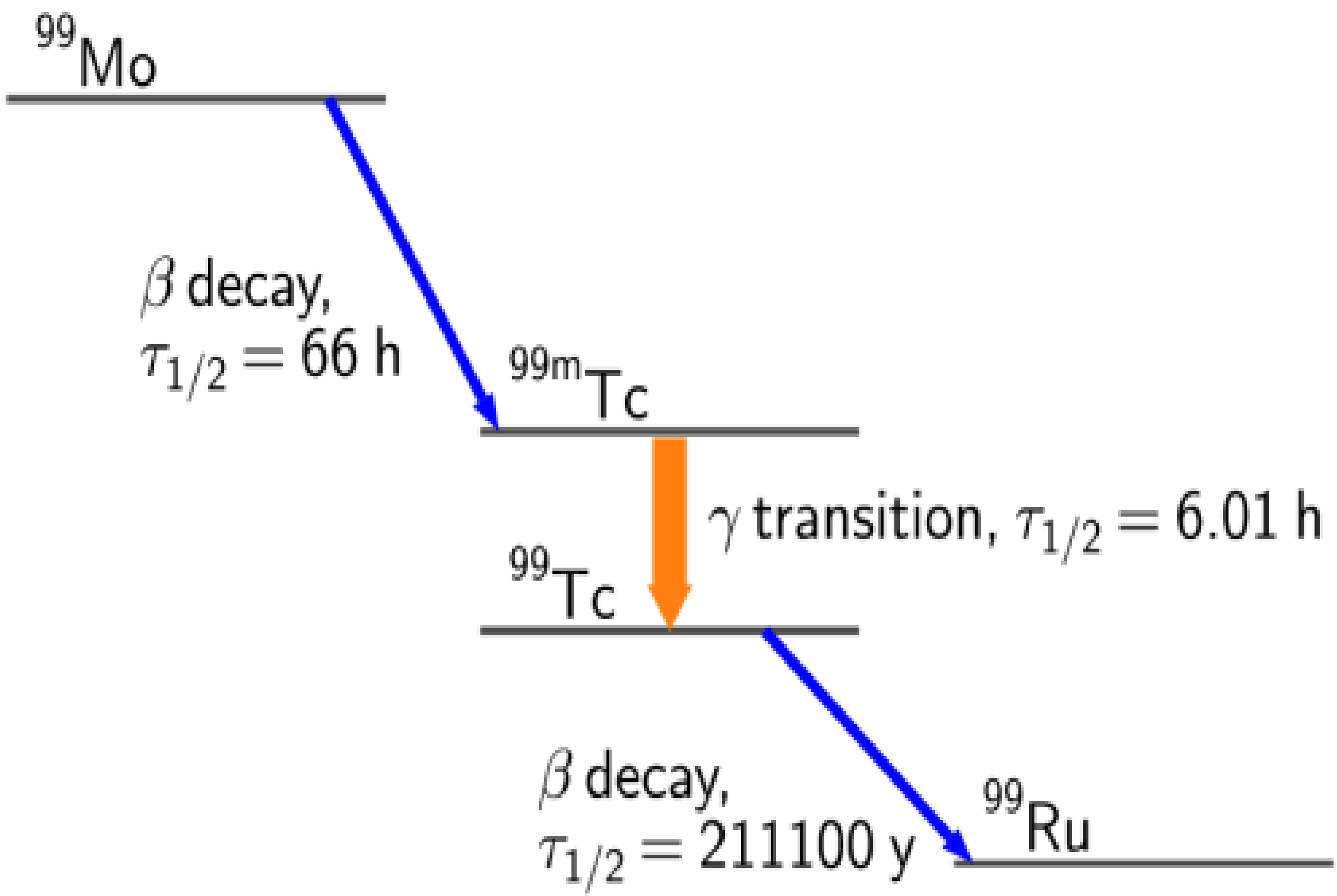
How we started (continue)

And partner project from CNCP "Production of Medical Intended Isotopes Using Electron Accelerator Facilities" started on April 2010 supporting commercial aspects of this program.

How we started (continue)

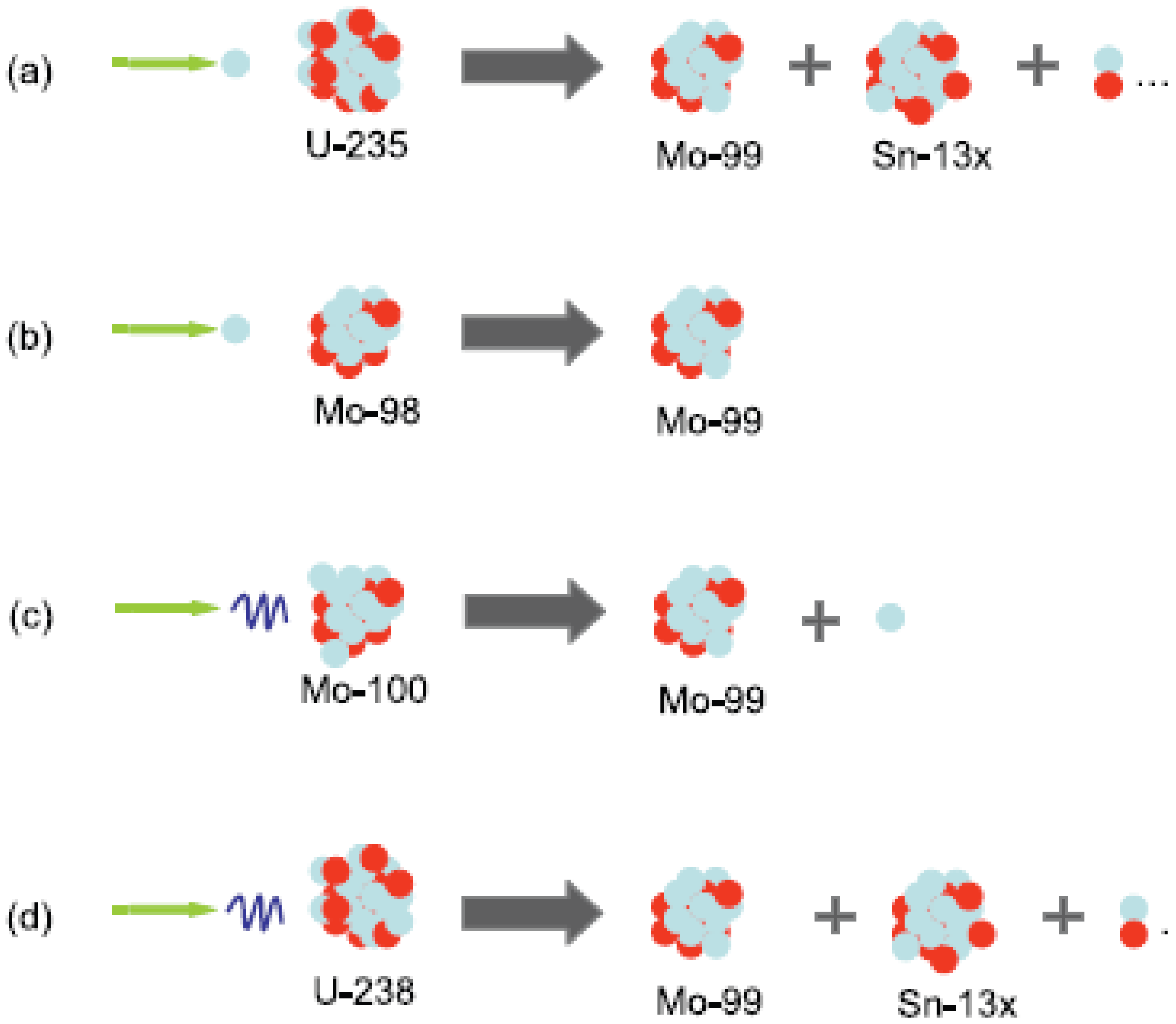
Investigations of an opportunity of Technetium-99m and Iodine-123 production using present accelerator facility on the Yerevan Physics Institute have been carried out under support of these two projects.

Technetium-99m **^{99m}Tc** ($T_{1/2}$= 6h; $E\gamma$~140 keV) is known to be the most useful radioisotope in diagnostic radiopharmaceuticals. More than 80% of all diagnostic procedures done worldwide in nuclear medicine centers are with ^{99m}Tc.



99Mo
β decay,
τ1/2 = 66 h
99mTc
γ transition, τ1/2 = 6.01 h
99Tc
β decay,
τ1/2 = 211100 y
99Ru

Main methods of 99mTc production



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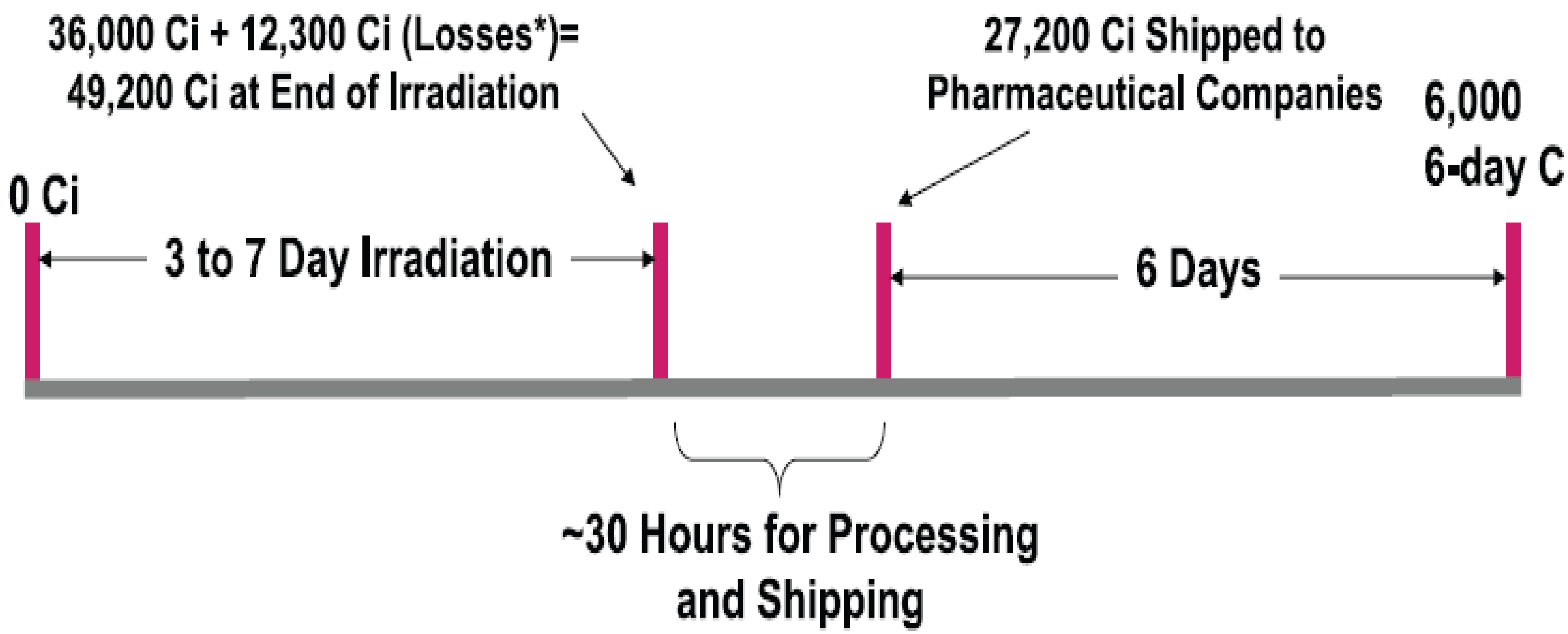
Estimated 2009 U.S. Mo-99 Demand
at least 6,000 6-day Curies/Week



*Assumes 75% Mo-99 Recovery During Processing

Current situation

The present world demand for ^{99}Mo is about 450000 GBq/week, and the annual demand for ^{99}Mo is considered to have an 8 – 12% growth over the next decade. Currently, most ^{99}Mo is produced by using five nuclear research reactors in Canada, Belgium, France, Netherlands, and South Africa.

The situation is hazardous: first, routine shipments of ^{99}Mo could be stopped for any reasons, such as planned maintenance of or an unscheduled shutdown of a reactor, or due to any problems related to the transportation of ^{99}Mo, etc

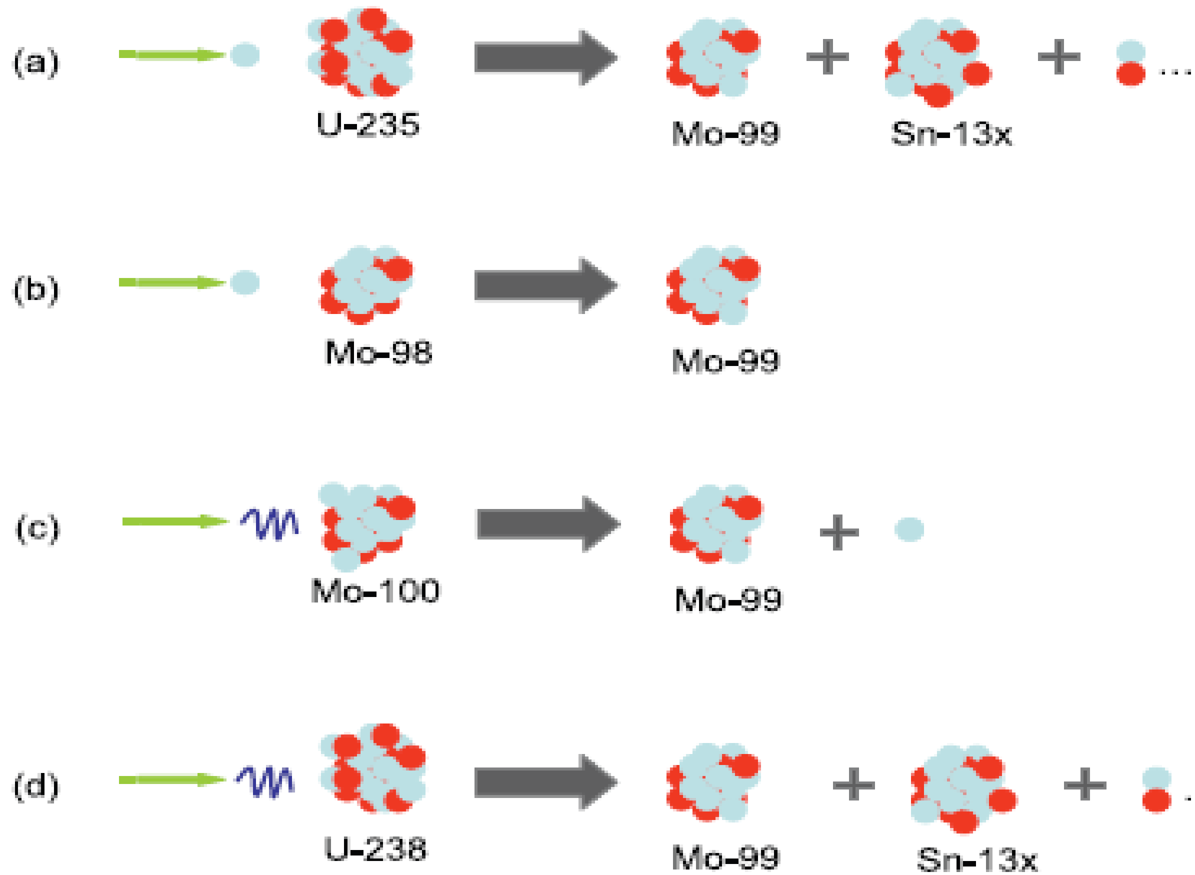
Second, these reactors use highly enriched ^{235}U (HEU), which is a direct use material for nuclear weapons.

In 2007 about 50 kg of HEU was used by the reactors mentioned above, and the quantity is considered to be sufficient for the construction of the two nuclear bombs.

In fact, about a five week unscheduled shutdown of a reactor in Canada, which happened in 2007, reinforced concerns about a reliable long-term supply of ^{99}Mo.

Note that the reactors mentioned above range in age from 42 and 51 year, and it is considered to be quite difficult nowadays to get approval to build a new reactor.

Alternative (nonreactor based) methods of 99mTc production



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Accelerator based method of ^{99m}Tc production

Metastable ^{99m}Tc could be received in

the **photonuclear reaction** by irradiation

of ^{100}Mo under intensive photon beam

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

$\downarrow$

T1/2 ~ 67 hours $\rightarrow {}^{99m}Tc$ (T1/2 ~6 hours)

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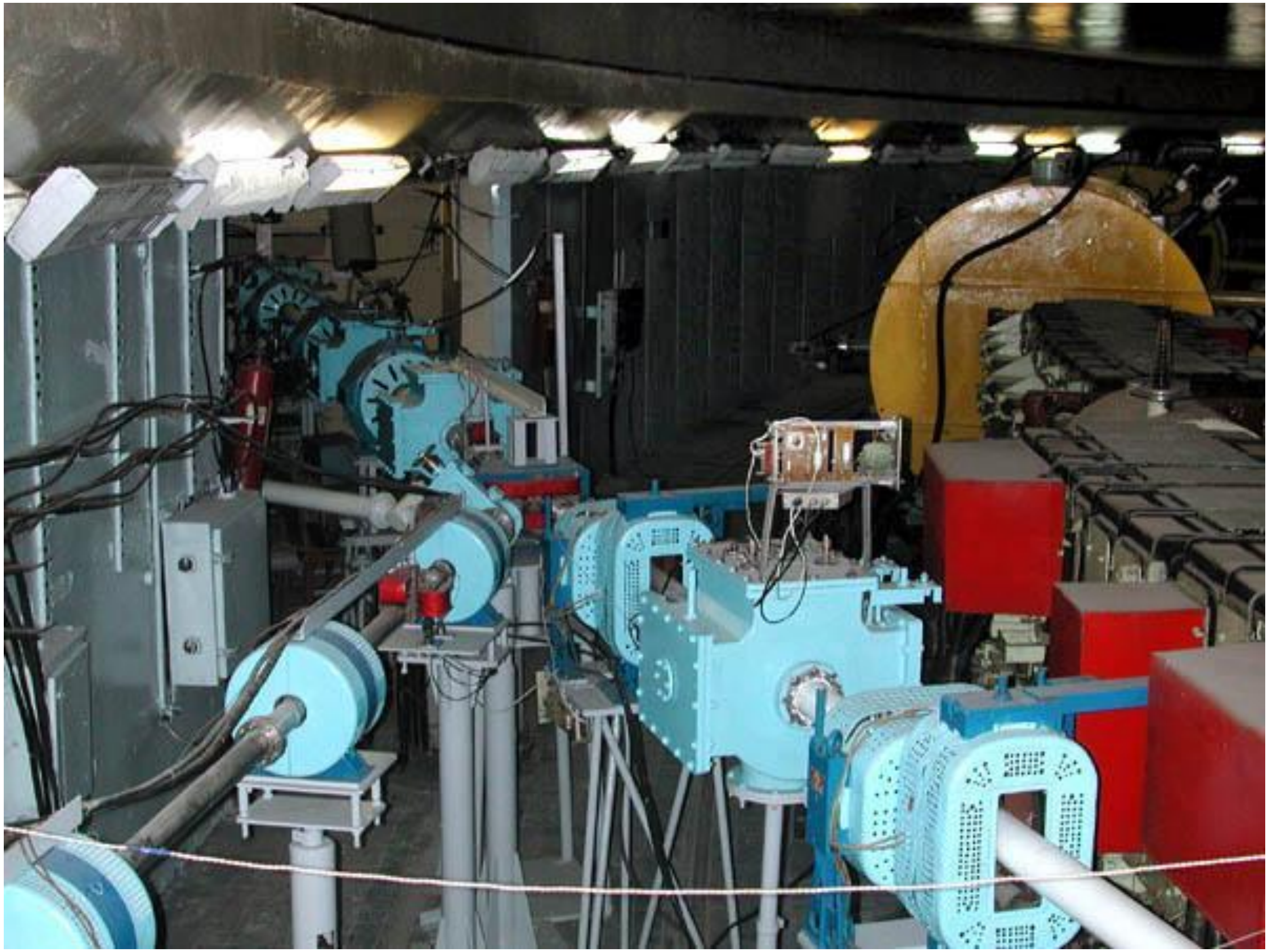
LUE50 LINEAR ELECTRON ACCELERATOR



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NEW HIGH EMISSION CATHODE IN A GUN

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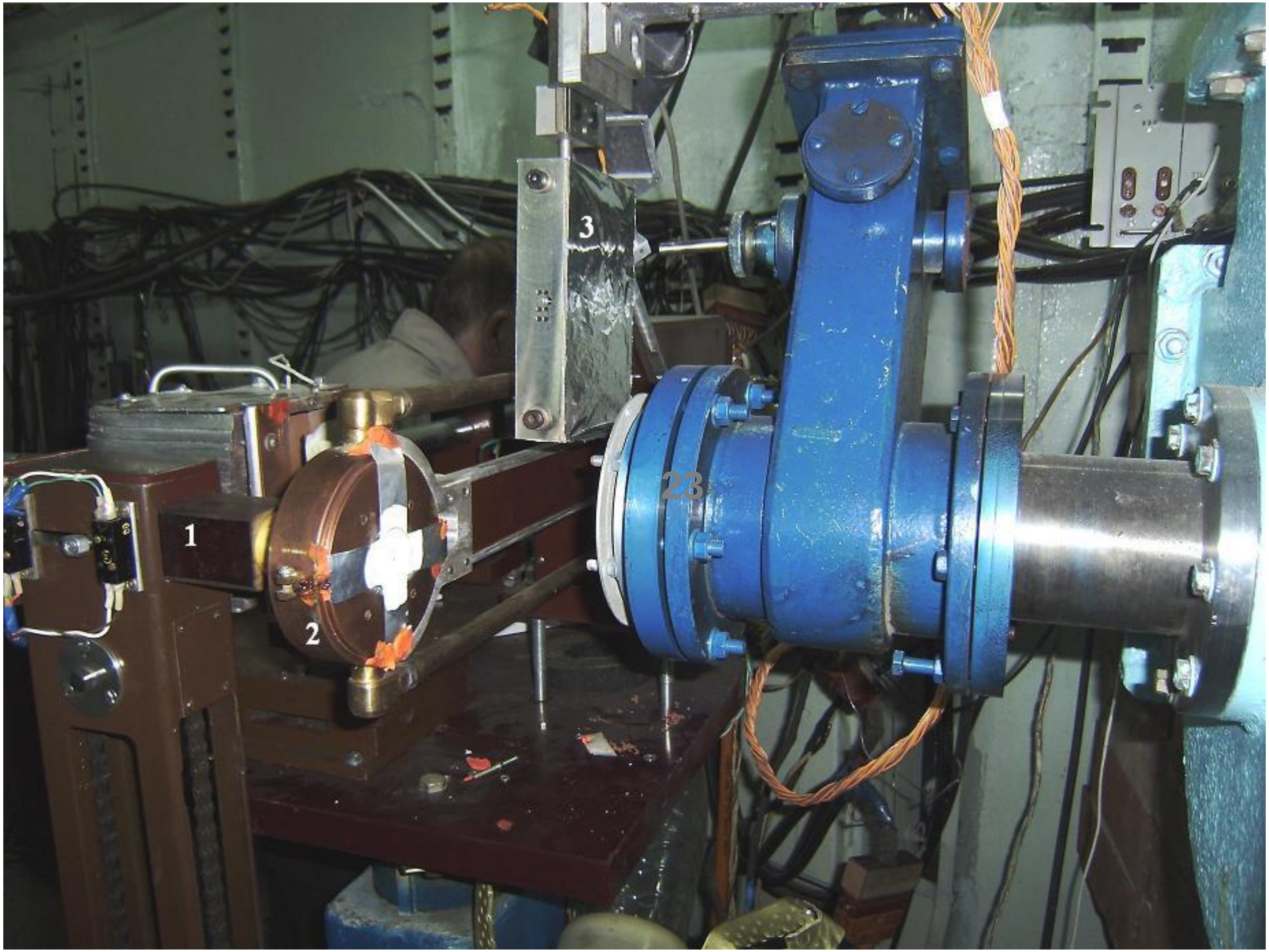
Parameter of improved accelerator

Parameter	before	after
Electron energy (MeV)	20	40
Beam current, μA	4.5	9.8
Beam size on the target, mm	20	13



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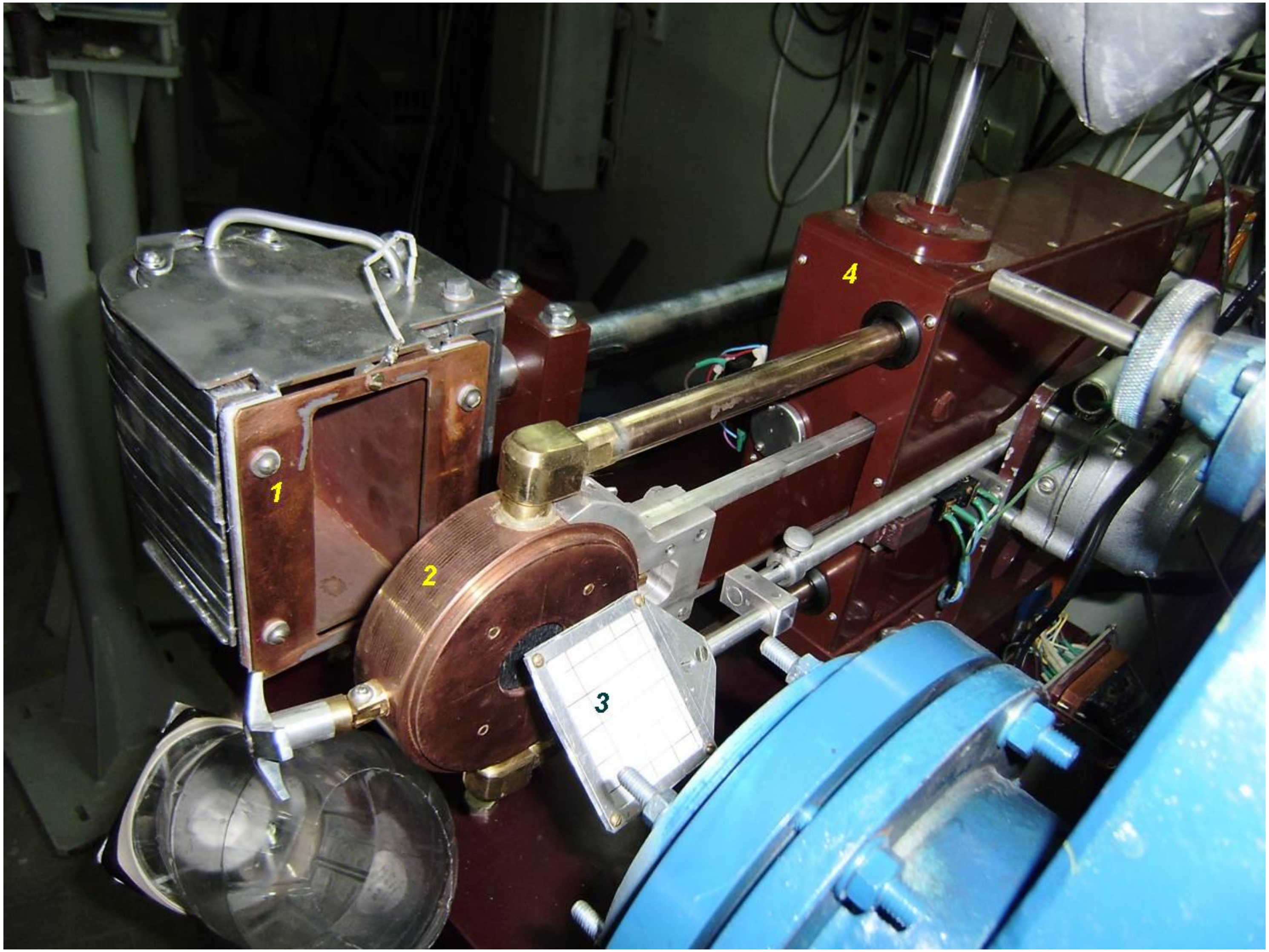

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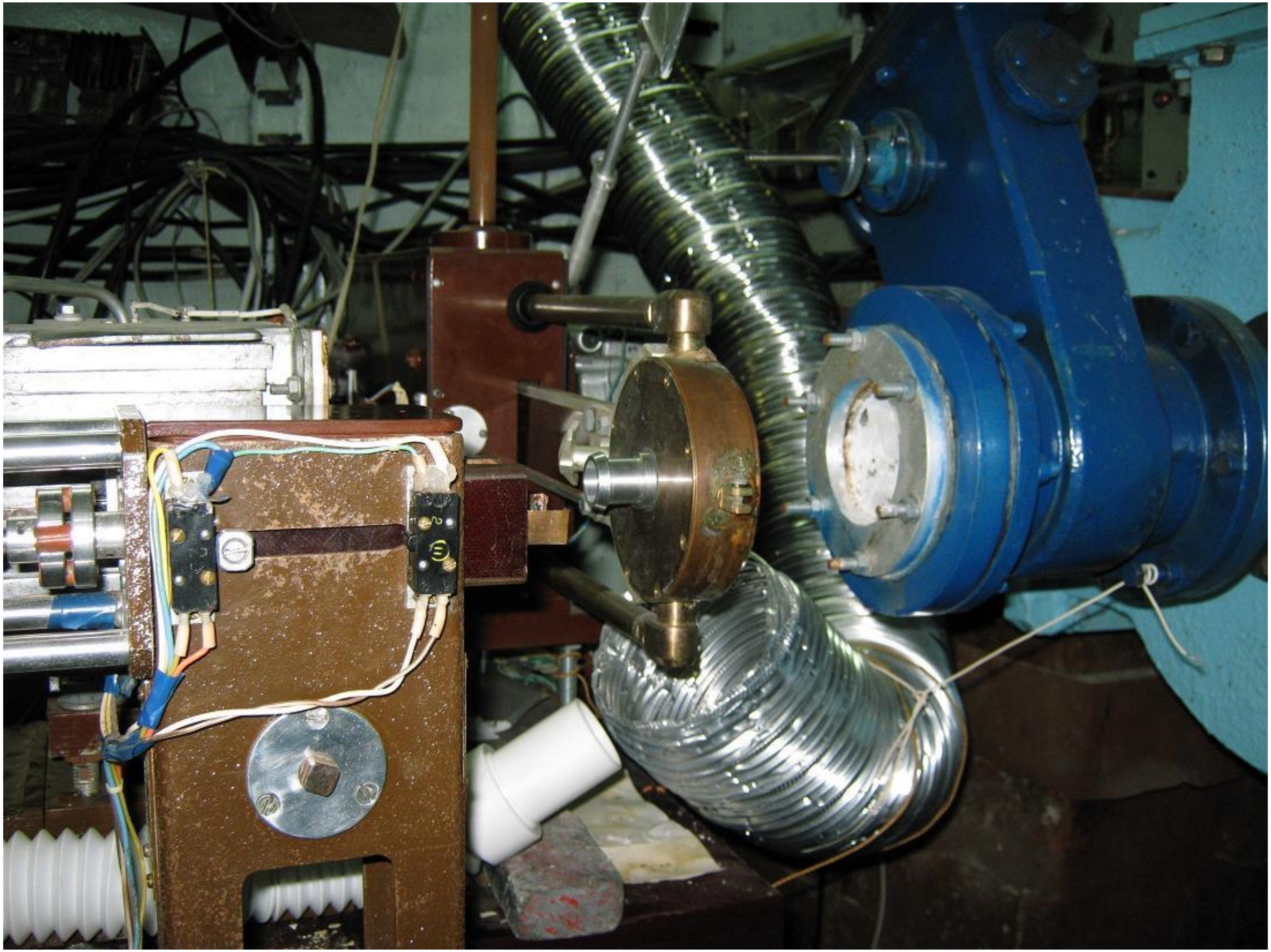

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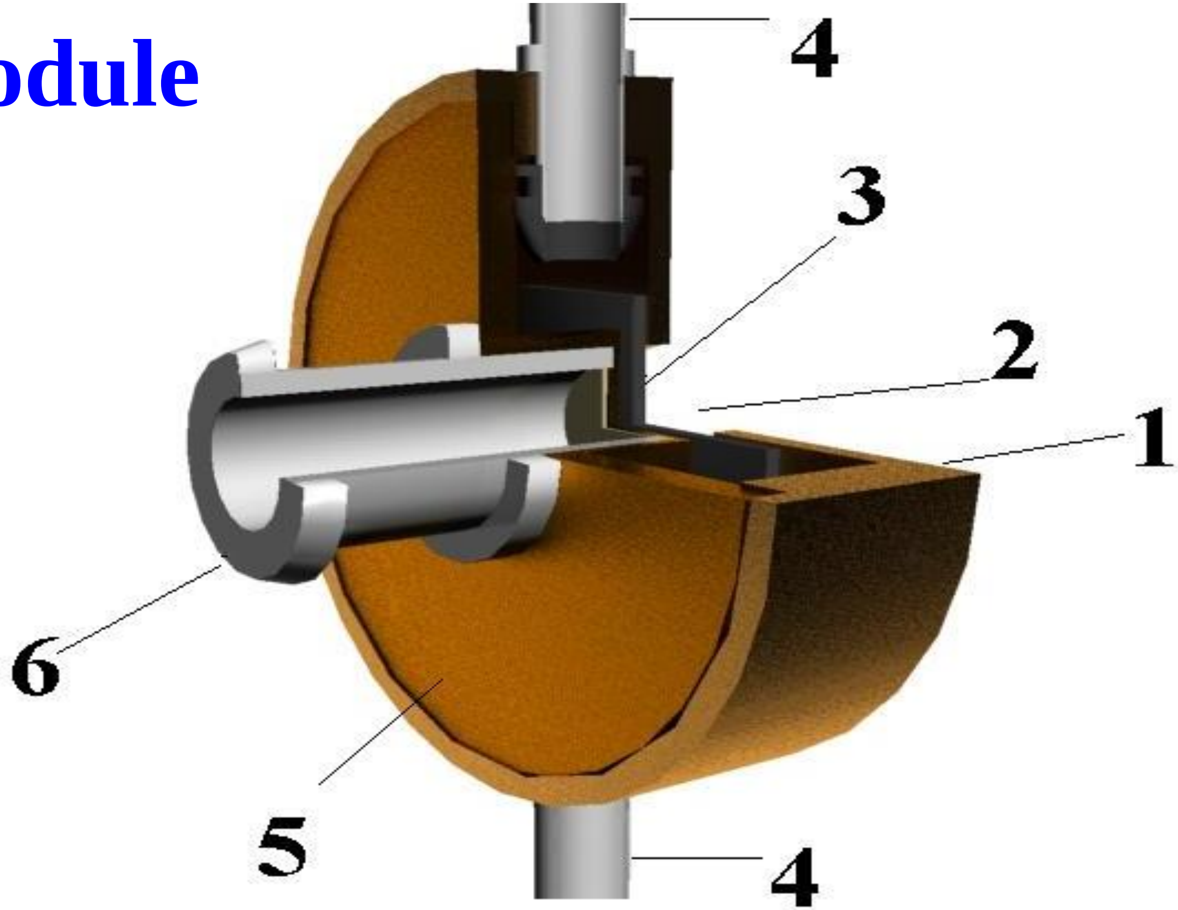
Target module



1 - frame, 2 - beam entrance window, 3 - tantalum plate, 4 – water cooling pipe, 5 – cover plate, 6 - target capsule

Target capsule for MoO_3 irradiation

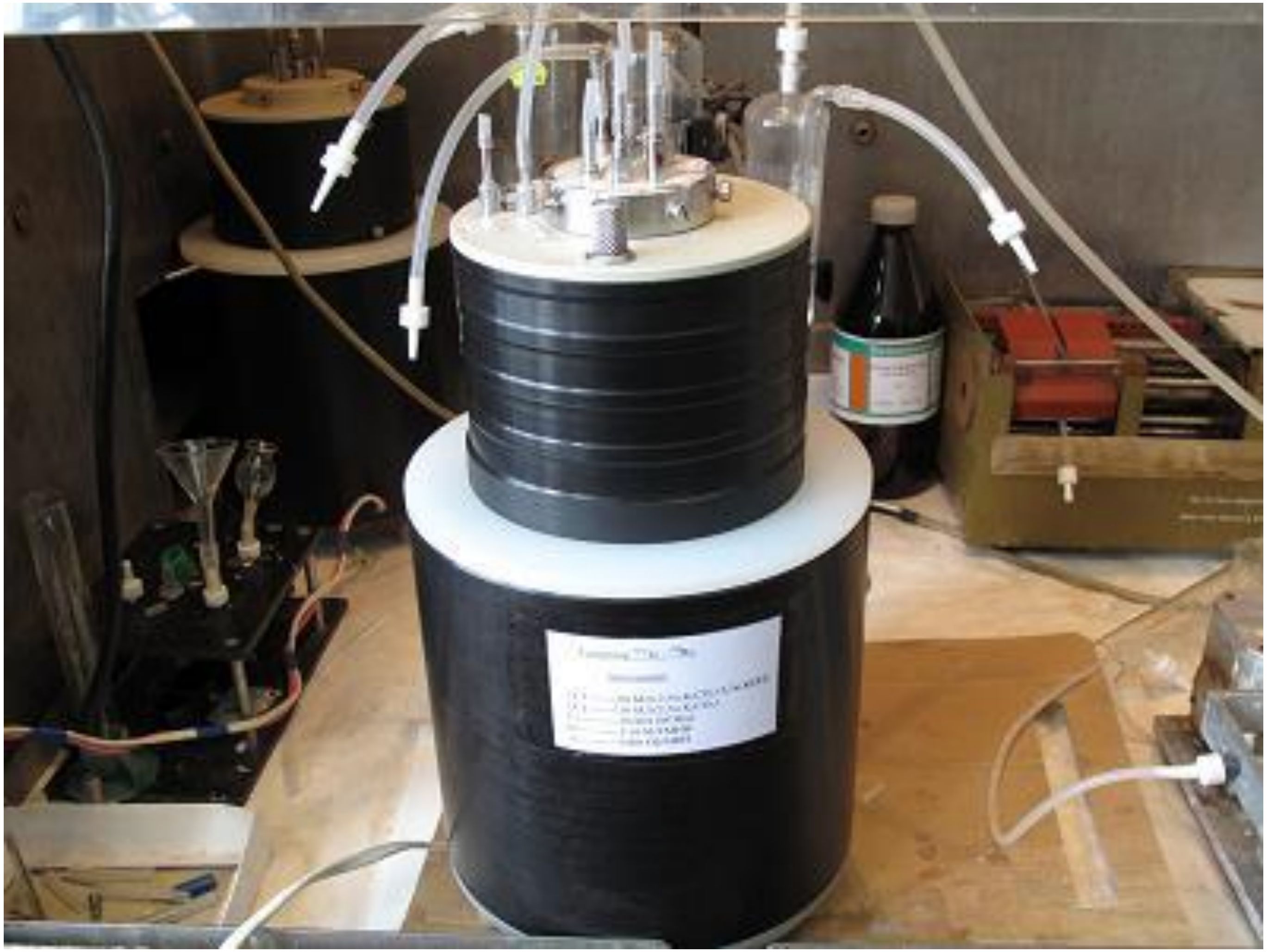
IRRADIATION MODE

The target – natural Molybdenum trioxide, weight up to 20 g.

The electron beam energy E=40±1 MeV, intensity on the target entrance window was ~9.5-10.5 mkA, beam size <15 mm.

One of the main parameter by production of radioisotopes under electron beam is the specified activity normalized to mass unit of irradiated material, unit of beam current and unit of time – Bk/mg·µA·h. The data published from different experiments have very big dispersion – from 90 to 3200 Bq/mg·µA·h. Results from presenting experiment is ~3000 Bq/mg·µA·h which is in close to the maximum value of world data.

Tc direct extraction method (MEK)



- **Irradiated material e.g. MoO_3 solved in alkali, then added MEK either, dissolves ONLY Tc. The mixture of 2 solutions is established – one with ONLY Mo, next with ONLY Tc. And their densities are strongly different so that centrifuge method is working well to separate them from each other!**

This extractor is built in A.N.Frumkin Institute of physical chemistry and electrochemistry, authors Alexander and Oleg Filyanin (now they have created a EXTRACTOR LTD private company)

and full scale equipment – in a factory "MedRadioPreparat"

COMMERCIAL ESTIMATION OF PRODUCTION

Mass of irradiating material	**20g**
Type of irradiating material	**$^{100}MoO_3$**
Duration of irradiation	**100 h**
Beam current	**10 mkA**

(3000Bq/mkA*mg*h) * $2*10^4$mg*10mkA*10^2h=
$6*10^{10}$Bq = 0.8 Ci on the end of irradiation.

- Extracting 98mTc from irradiated material during 6-7 days using centrifuge extractor one can “milk” total up to 2-3 Ci of activity.
- That mean ~9-12 Ci per months.
- This activity should completely cover the demand of Armenian clinics now and in a nearest future – taking into account serious estimated growth of needs.

^{123} Iodine production technology

Accelerator based method of ^{123}I production

$\gamma + {}^{124}Xe \rightarrow {}^{123}Xe + n$ threshold of reaction – 8.3 MeV

$\downarrow$

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

The effective cross-section for this reaction is rather high; for photons of approximately 15 MeV the cross section is 450 mbarn. So the effective energy of electrons should be 25-35 MeV.

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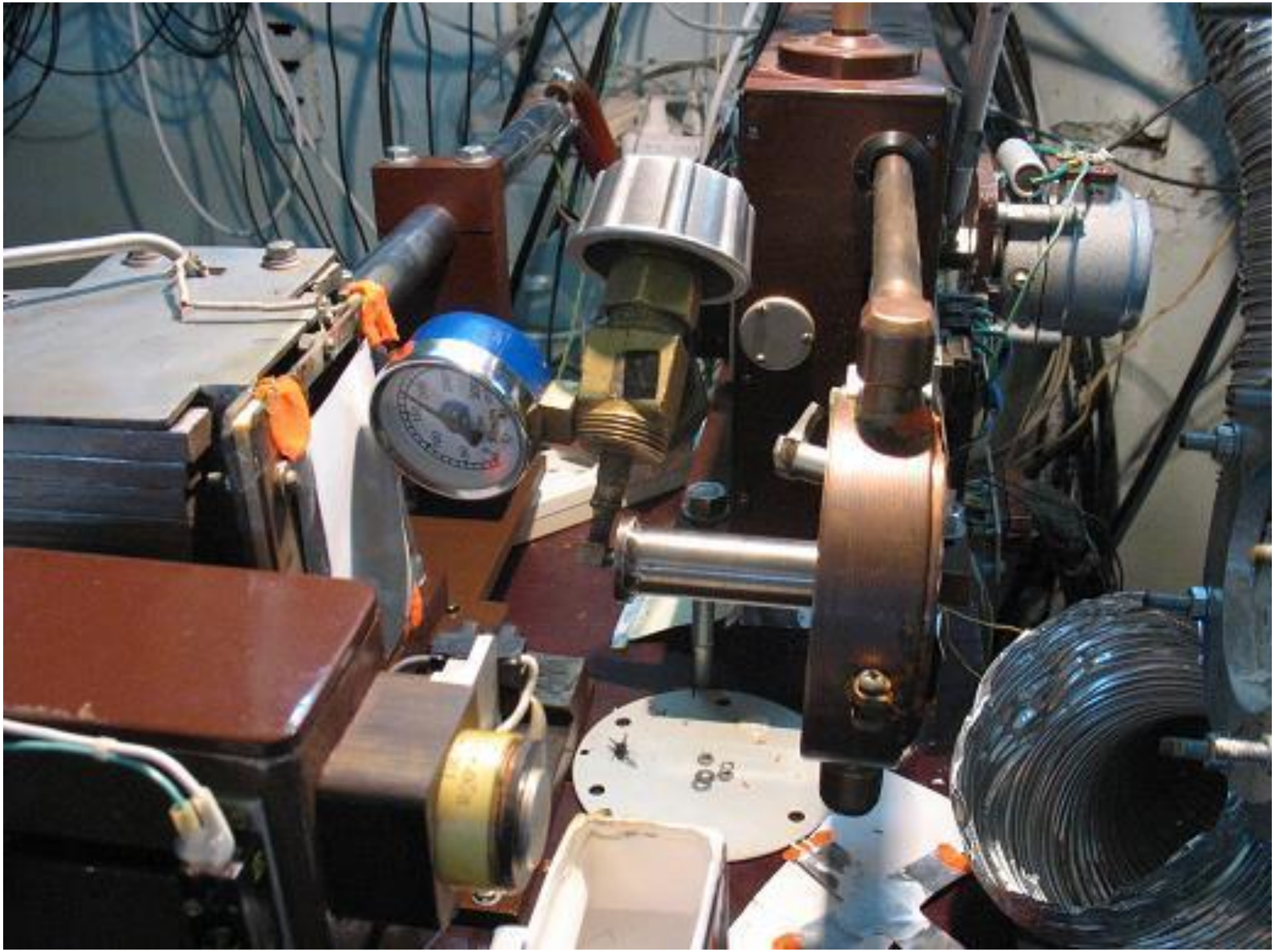
Xe target



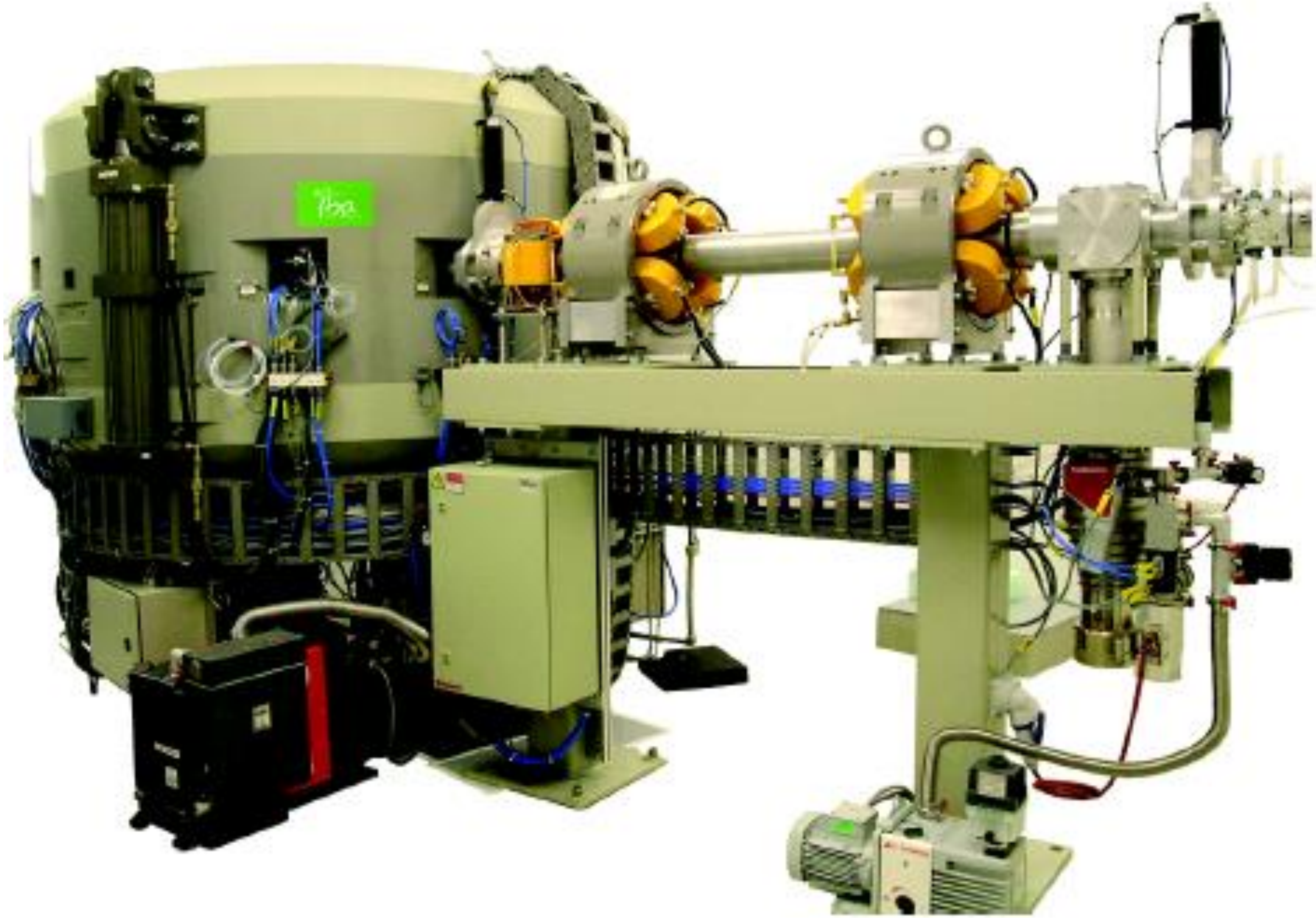
The main often use parameter of yield of irradiation is the total activity after irradiation normalized to the amount of target material (for pure ^{124}Xe), beam current and exposition time - duration of irradiation.

And we got

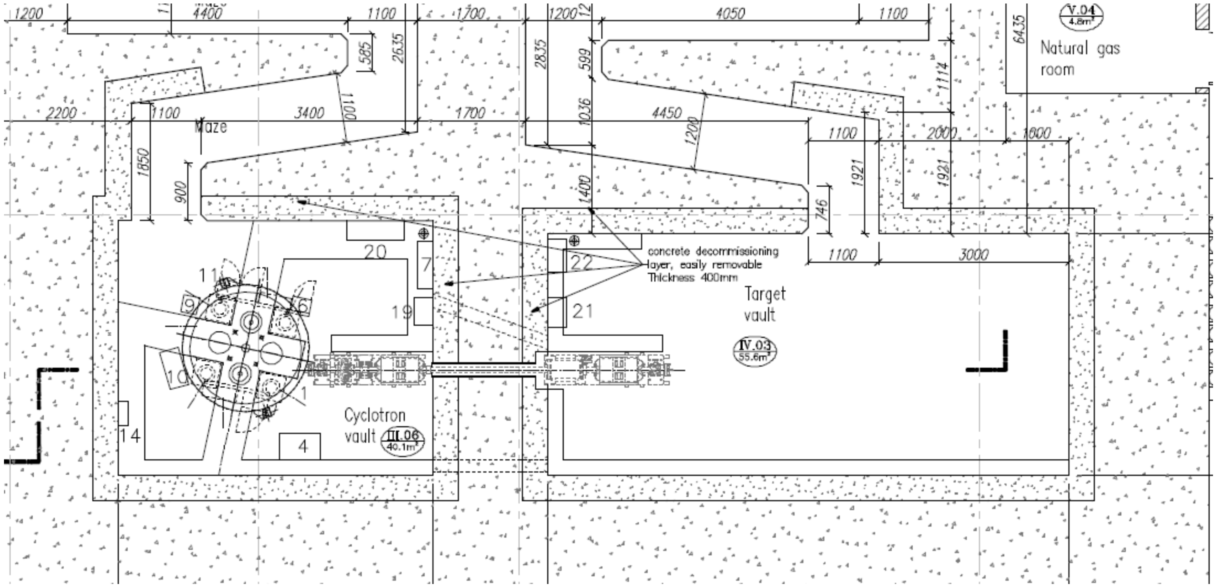
$$A_{tot} = 7*10^5 Bq \sim 20\ mcCi$$

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

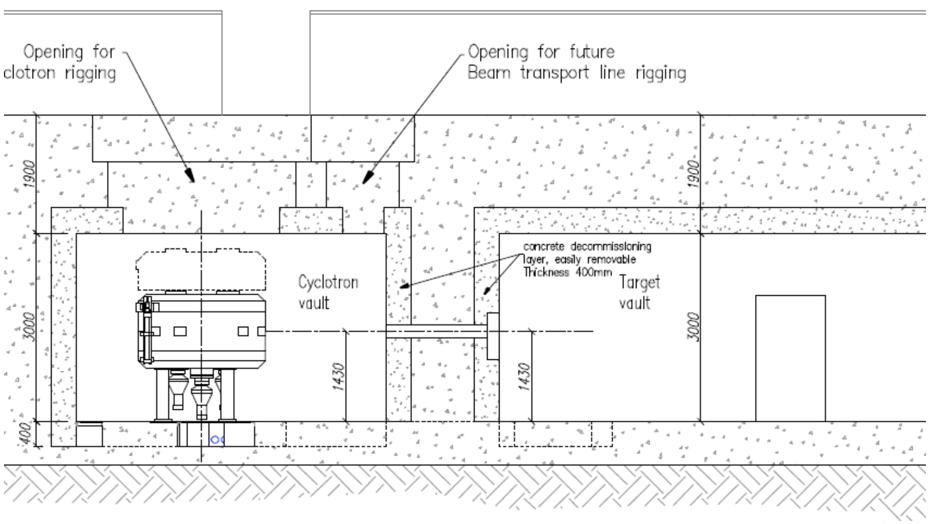
Cyclotron based activity



C18/18



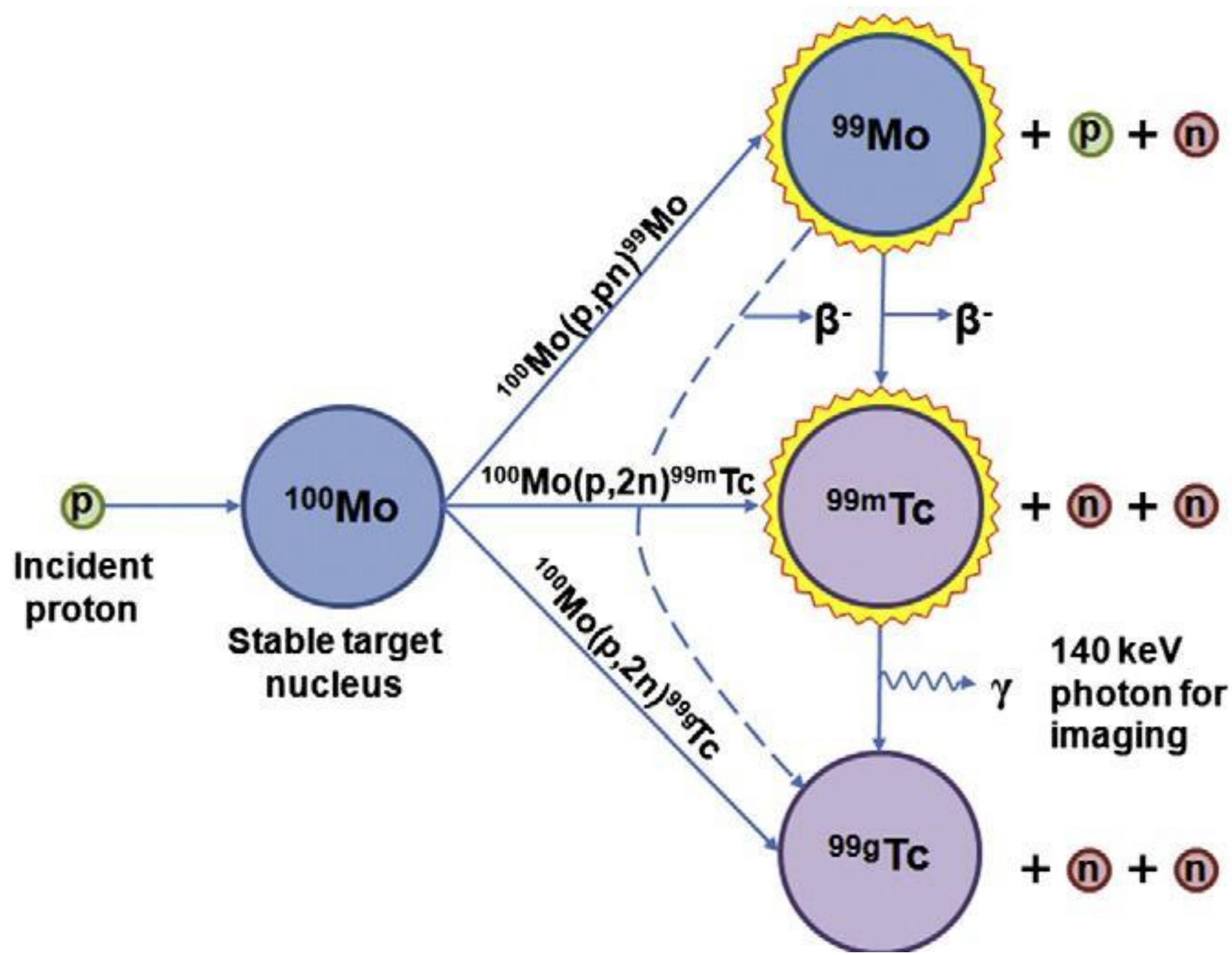
Maze
concrete decommissioning
layer, easily removable
Thickness 400mm
Target
vault
Cyclotron
vault
Natural gas
room



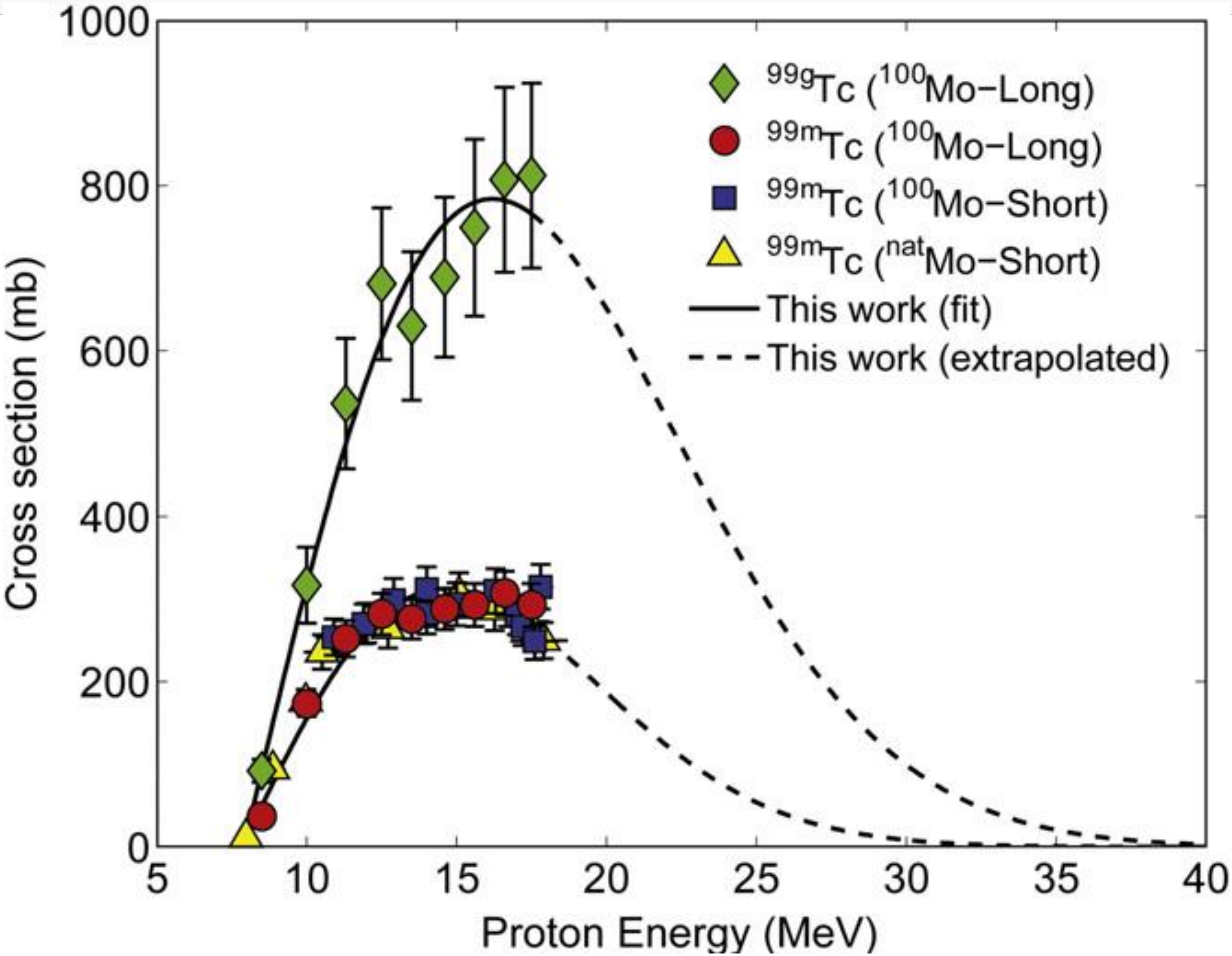
Opening for
clotron rigging
Opening for future
Beam transport line rigging
Cyclotron
vault
concrete decommissioning
layer, easily removable
Thickness 400mm
Target
vault

$^{100}MoO_3(p,2n)^{99m}Tc$ and $^{100}Mo(p,2n)^{99m}Tc$ reaction should be investigated under 18 MeV proton beam from C18/18 cyclotron.

The second one is more promising providing much higher yield.



99Mo
+ p + n
100Mo(p,pn)99Mo
β-
β-
p
100Mo
100Mo(p,2n)99mTc
99mTc
+ n + n
Incident proton
Stable target nucleus
100Mo(p,2n)99gTc
γ
140 keV photon for imaging
99gTc
+ n + n



Cross-sections of 99gTc and 99mTc production

Yield estimation

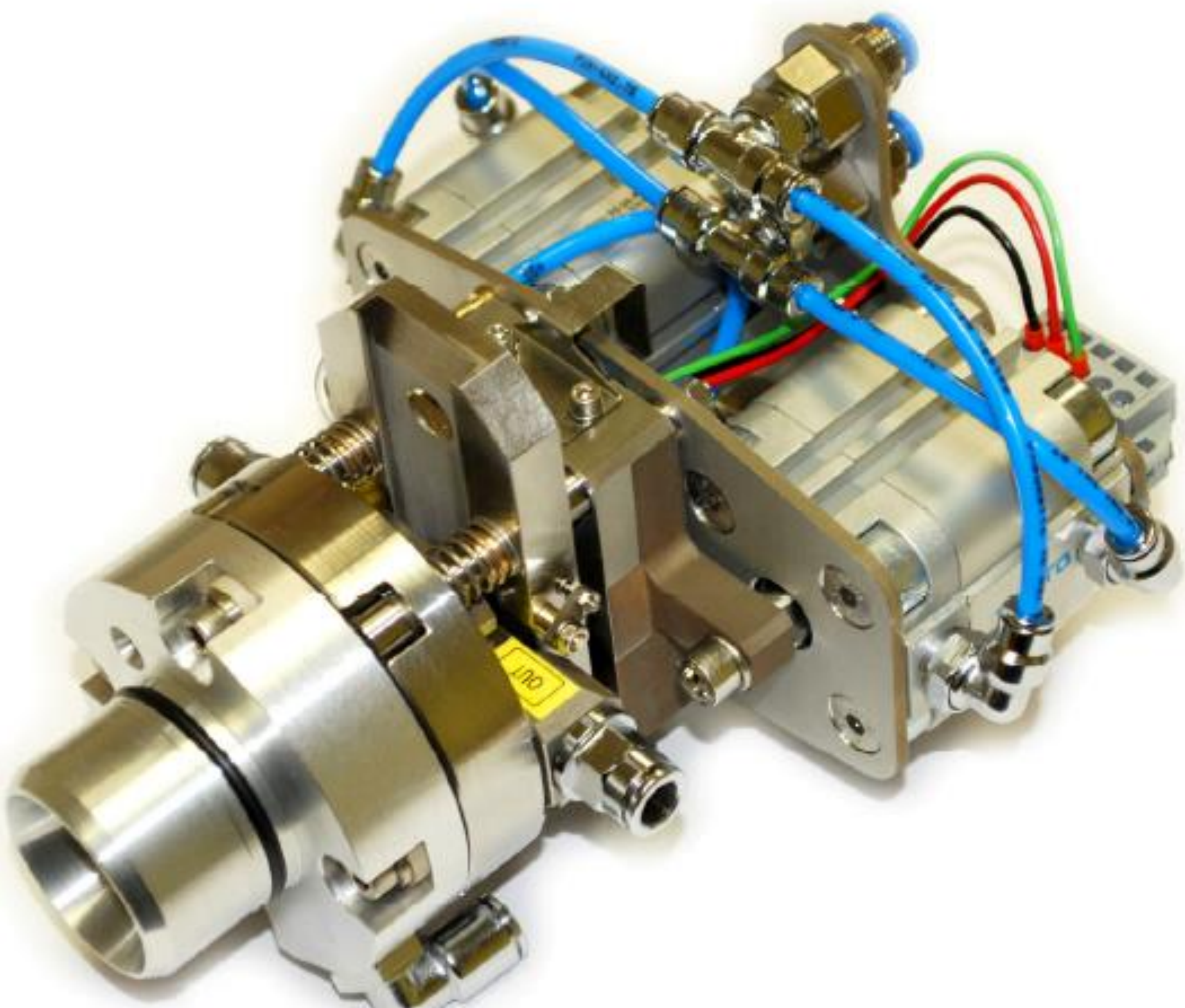
Results from other experimental groups shows e.g. 1.6 TBq yield of 99mTc for a 6 hours, 500µA, 22→10 MeV irradiation. In our case it will be 3 hours, 35 µA, 17→10 MeV so that totally 2*14*1.7=47 times less,

means 1.6 TBq :47=34GBq ≈1Ci! (EOB)

Even taking into account the time is required to extract 99mTc and deliver to consumer (clinics) this activity is more than daily demand of all 3 Armenian clinics use this isotope.

One of the very actual tasks is a target preparation following many required parameters such as hardness, thermo conductivity etc. We were going investigate an option of different composites gluing Mo powder. On of the option was silver powder like compound. Unsuccessful!

Nirta Solid Compact (COmpact Solid Target Irradiation System)



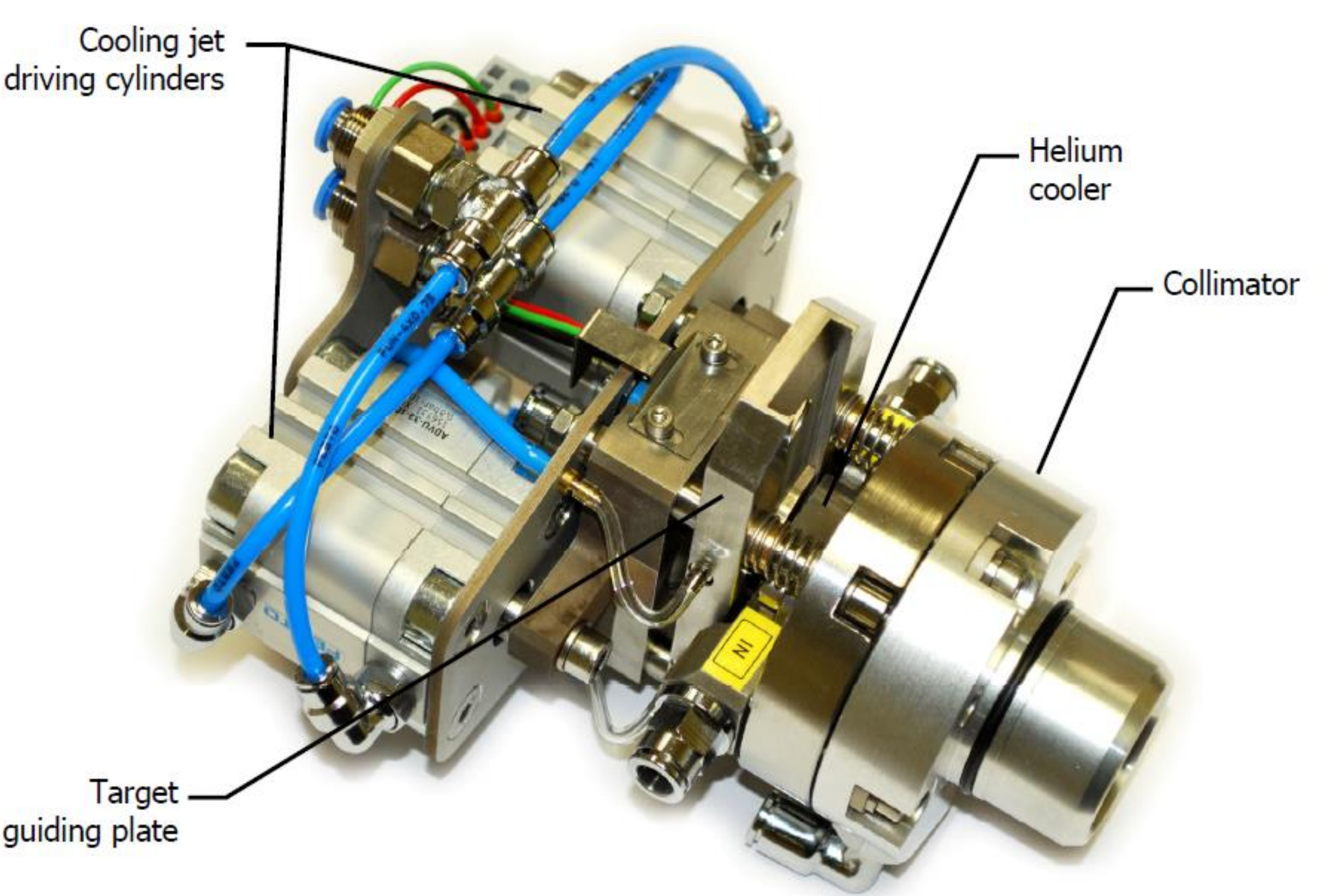
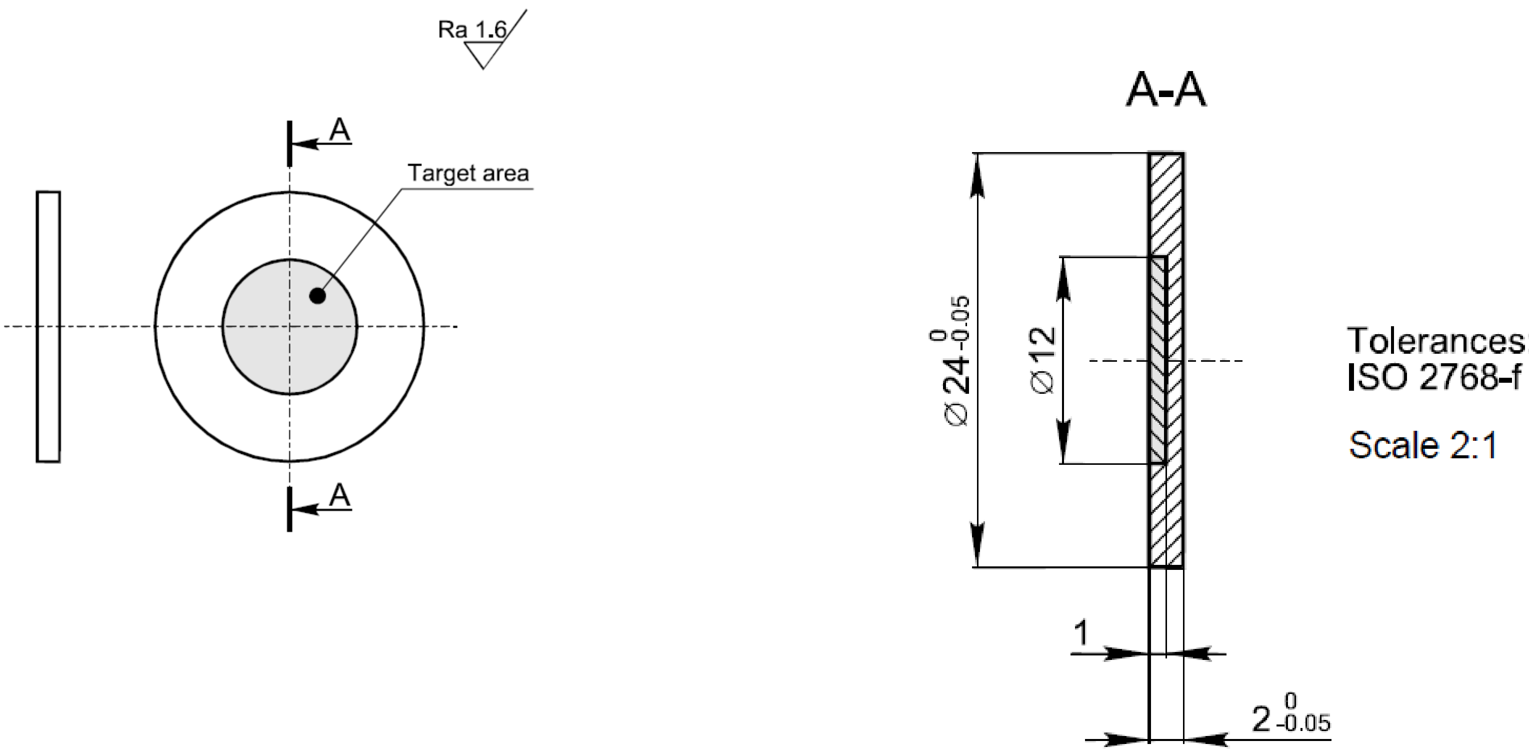
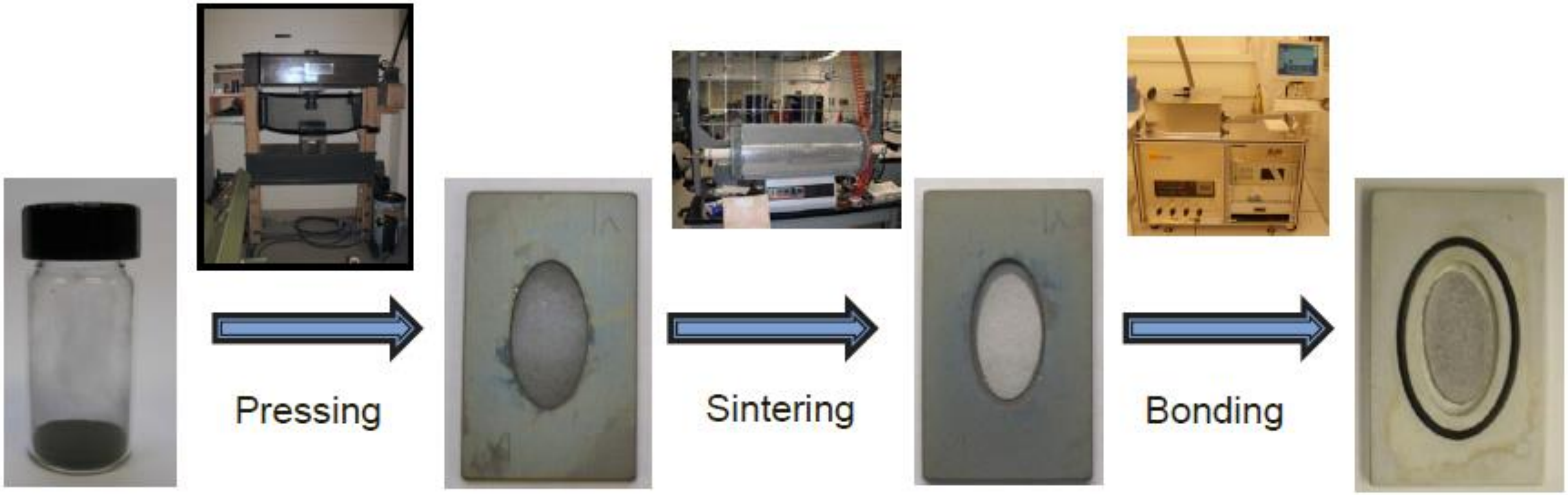

Cooling jet
driving cylinders
Helium
cooler
Collimator
Target
guiding plate

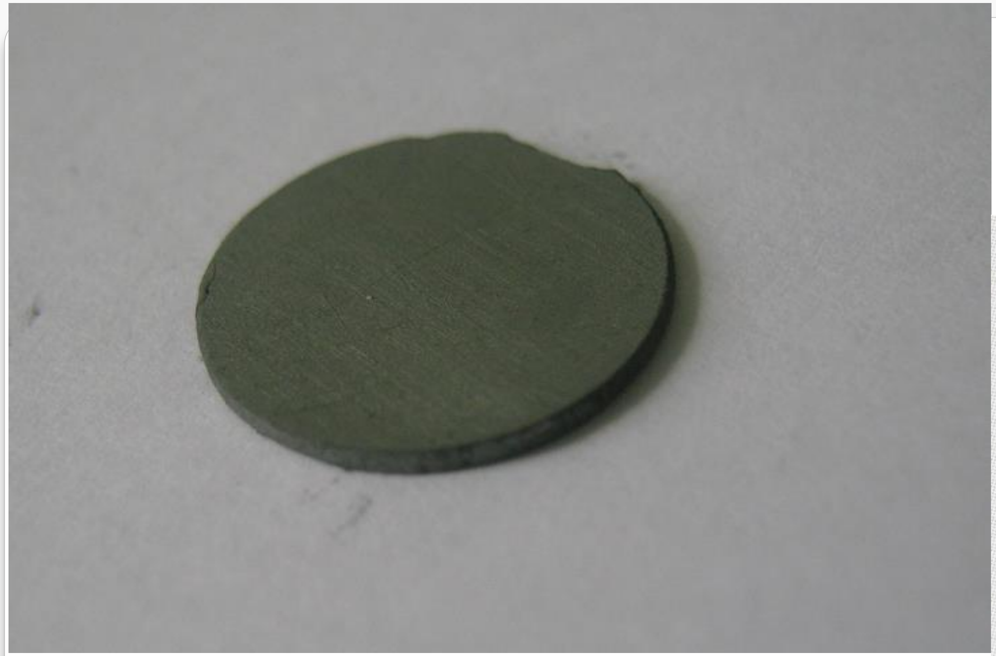
Table 1.1. Summary of technical characteristics.

Specifications
Height: 126 mm Width: 175 mm Length: 194 mm Mass: 3.0 kg
Performance
Max. beam power: 500 W Min. beam spot: 8 mm FWHM Target disk size: Ø24×2 mm^2 Effective target spot: Ø12 mm
Cooling fluids consumption
Helium: 60 $dm^3 \cdot min^{-1}$ @ 0.2 MPa Deionized water: 16 $dm^3 \cdot min^{-1}$ Coolant pressure: 0.5 MPa
Compressed air
Oil-free clean air @ 0.5 MPa
Operating conditions
Temperature: from +15 to +30 °C Humidity: from 0 to 75 % RH

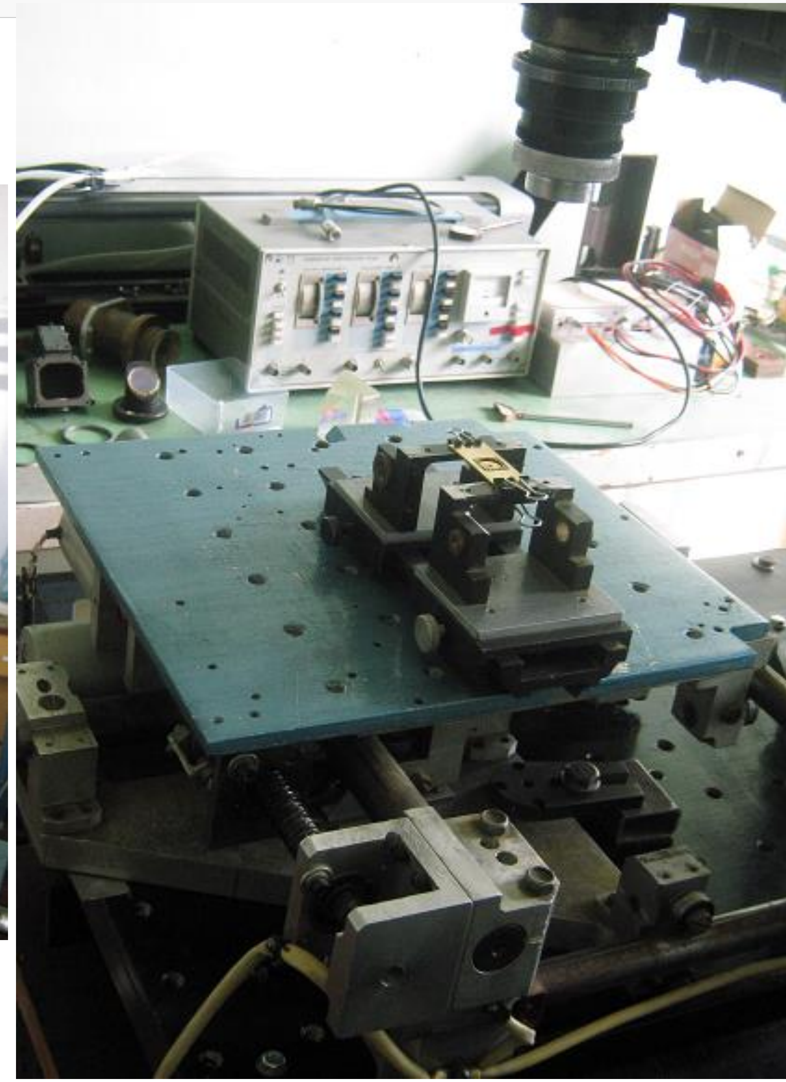

Ra 1.6
A
Target area
A
A-A
Ø 24 0 -0.05
Ø12
1
2 0 -0.05
Tolerances:
ISO 2768-f
Scale 2:1

Widely used technology of Mo target pellet preparation





Left – separate pellet from pressed Mo powder, right – Mo pressed inside the target disc.

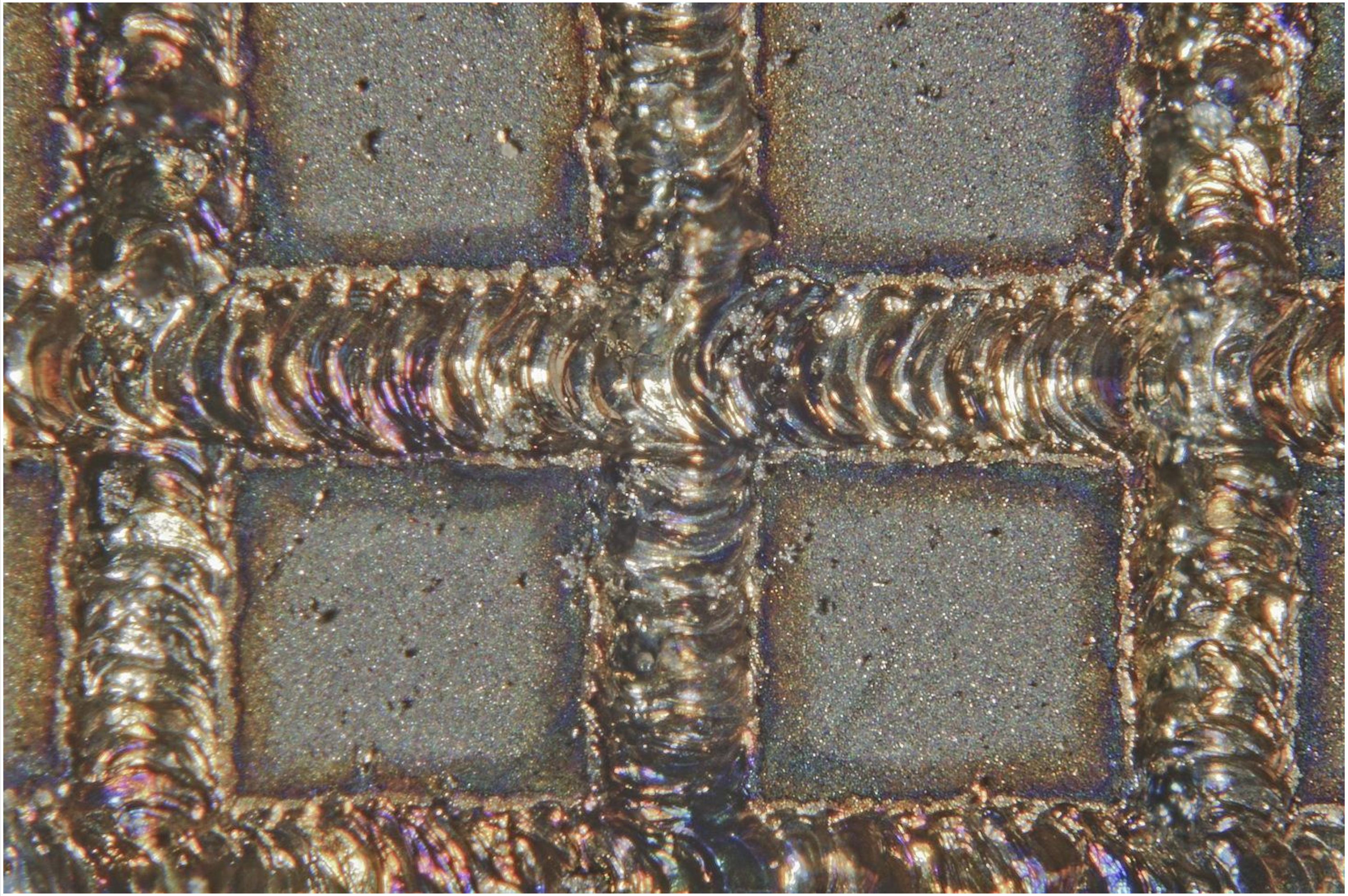


Left - laser layout for Mo pellet processing. 1 – solid state laser, 2 – beam expander. Right - XY movable table with step motors controlled by computer.

The layout for Mo pellet processing is based on the solid state pulse-periodic laser with following parameters:

Wave length	**1.06 μm**
Pulse energy	**250 MJ**
Repetition frequency	**40 Hz**
Pulse length	**200 μs**

Then one side of that pellet was processing under laser beam. These grooves of the Mo powder became to melted metallic solid state are working like metallic fixtures in concrete providing enough high mechanical strength and thermal conductivity.



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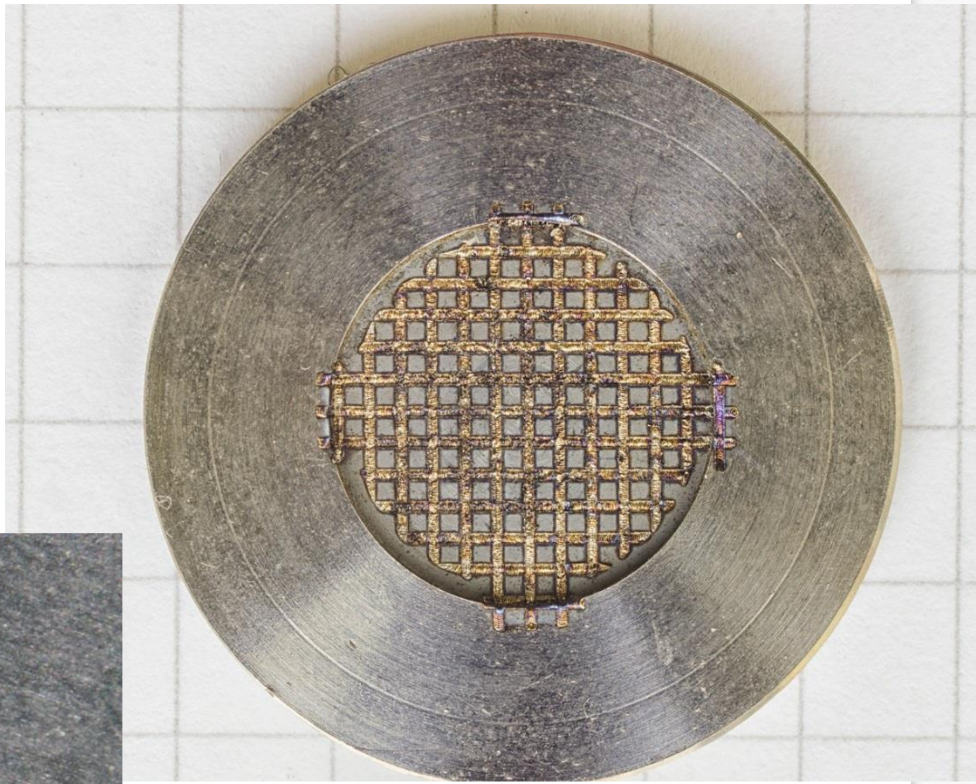

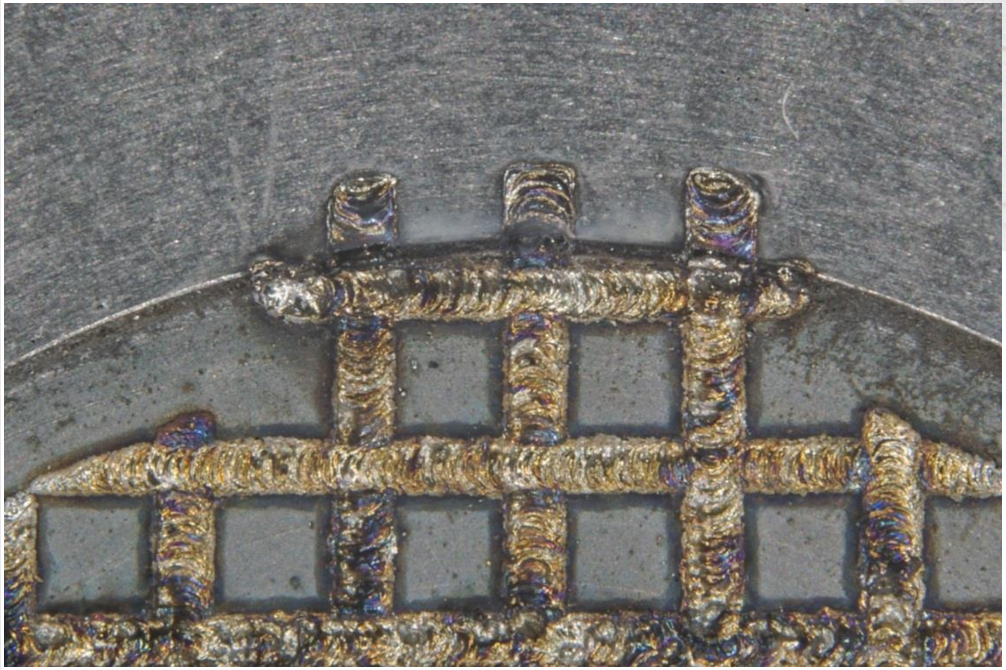

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- **Material – titanium foil with ~300mkm of thickness, processed by laser beam.**

Titanium disc with structured net and pressed Mo powder

OUTLOOK

AANL (YerPhI) started the activity of isotopes production technology just a few years ago in general using present linear electron accelerator;

- During last years technology of 2 types of isotopes were investigated, positive results were achieved;
- Results were reported in international conferences and published. Last publication is -
- R. Avagyan, A. Avetisyan, I. Kerobyan, R. Dallakyan Photo-Production Of 99Mo/99mTc With Electron Linear Accelerator Beam. Nuclear Medicine and Biology, 41(2014), 705-709

A new C18/18 cyclotron will be commissioned soon (October-November 2014) which we will use also for ^{99m}Tc direct production technology master and development – with a target of real production and covering the demand of Armenian clinics.

The activity under electron beam was done under support from Armenian state scientific budget, ISTC A-1444 and CNCP(ISTC) A-1785 partner project.

The current activity devoted to direct production of 99mTc under C18 proton beam is under financial support of Armenian state scientific budget and IAEA CRP “Accelerator-based Alternatives to Non-HEU production of Mo-99/Tc-99m” program (Contract number 18029).

Thanks for attention!

http://isotope.yerphi.am/index_en.html