The Production of Medical Isotopes

A DEDICATED VALUE OF INTERNATIONAL COOPERATION:
"Overcoming current shortage of medical isotopes"

CAND meets TPU

1. Introduction to Structural Reliability in Nuclear Engineering

CAND SEMINAR 2013
Sao Paulo

In the course of our meetings, we discussed current global shortcomings of Technetium Te-99m

"The shutdown of the (Canadian) NRU reactor has triggered a global shortage in nuclear medical isotopes (mainly molybdenum-99), which has made the situation particularly problematic from a medical standpoint.Technetium-99m (Tc-99m), which is derived from Mo-99, is used for the vast majority of nuclear medical procedures – primarily cardiac imaging …"

"The medical isotope shortage is an ongoing issue of national and global concern"

Cited from: Mohamed Zakzouk, *The medical Isotope Shortage: Cause, Effects and Options*, Library of Parliament PRB 09-04E, 2009

TECHNETIUM ^{99m}Tc

ISOTOPE	Half-lives in days		
	$T_{Physical}$	$T_{Biological}$	$T_{Effective}$
^{99m}Tc	0,25	1,00	0,20

Physical half-life T_{p}:

With $1/T_e = 1/T_p + 1/T_b$

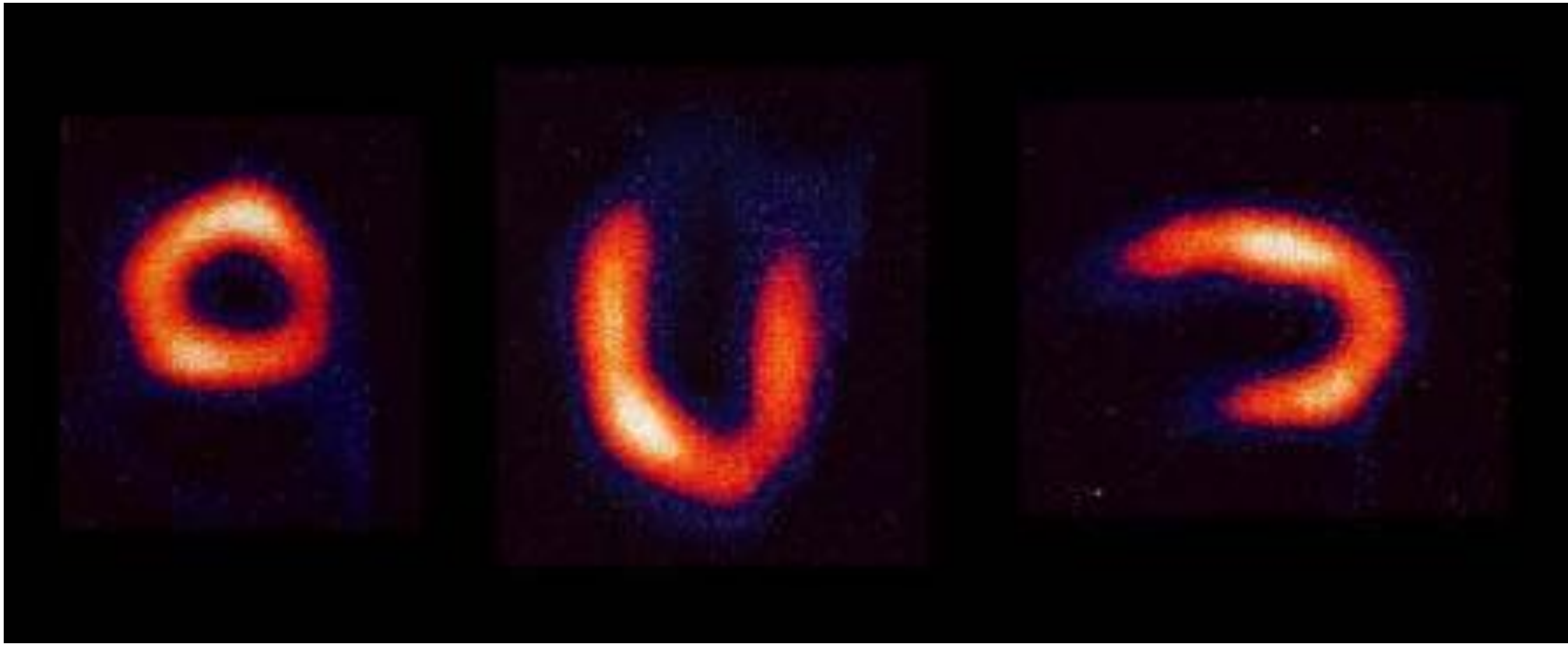
The radioactive half-life is physically determined and unaffected by the physical or chemical conditions around it.

Biological half-life T_{b}:

In a living organism, the biological half-life is determined by the rate of excretion.

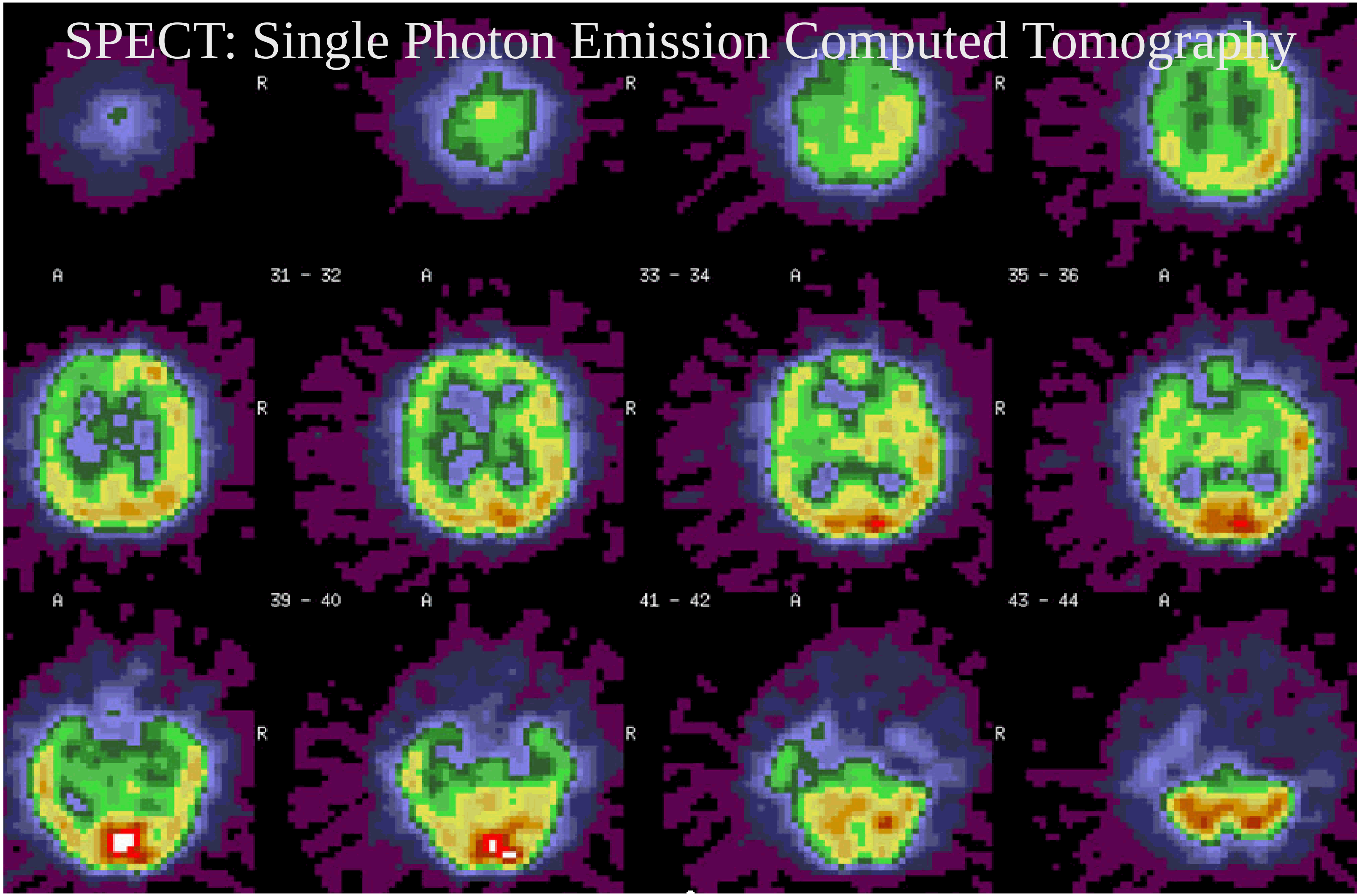
Technetium, ^{99m}Tc, is one of the favorites for diagnostic scans because of short physical and biological half-lives. It clears from the body very quickly after the imaging procedures

Myocardial Infusion Imaging



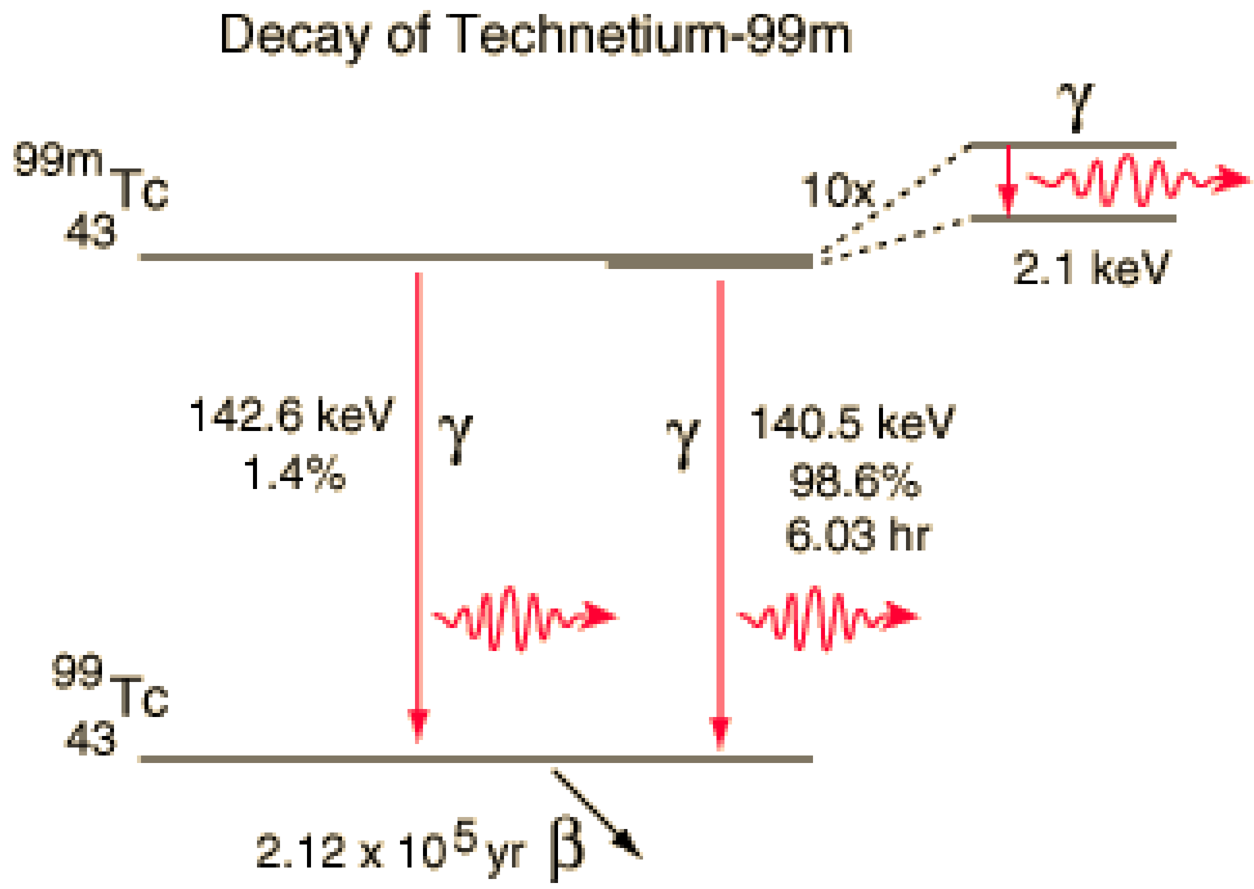
Assessment of blood infusion by images of the blood flow in the heart muscle

BRAIN SPECT WITH TECHNETIUM ^{99m}Tc



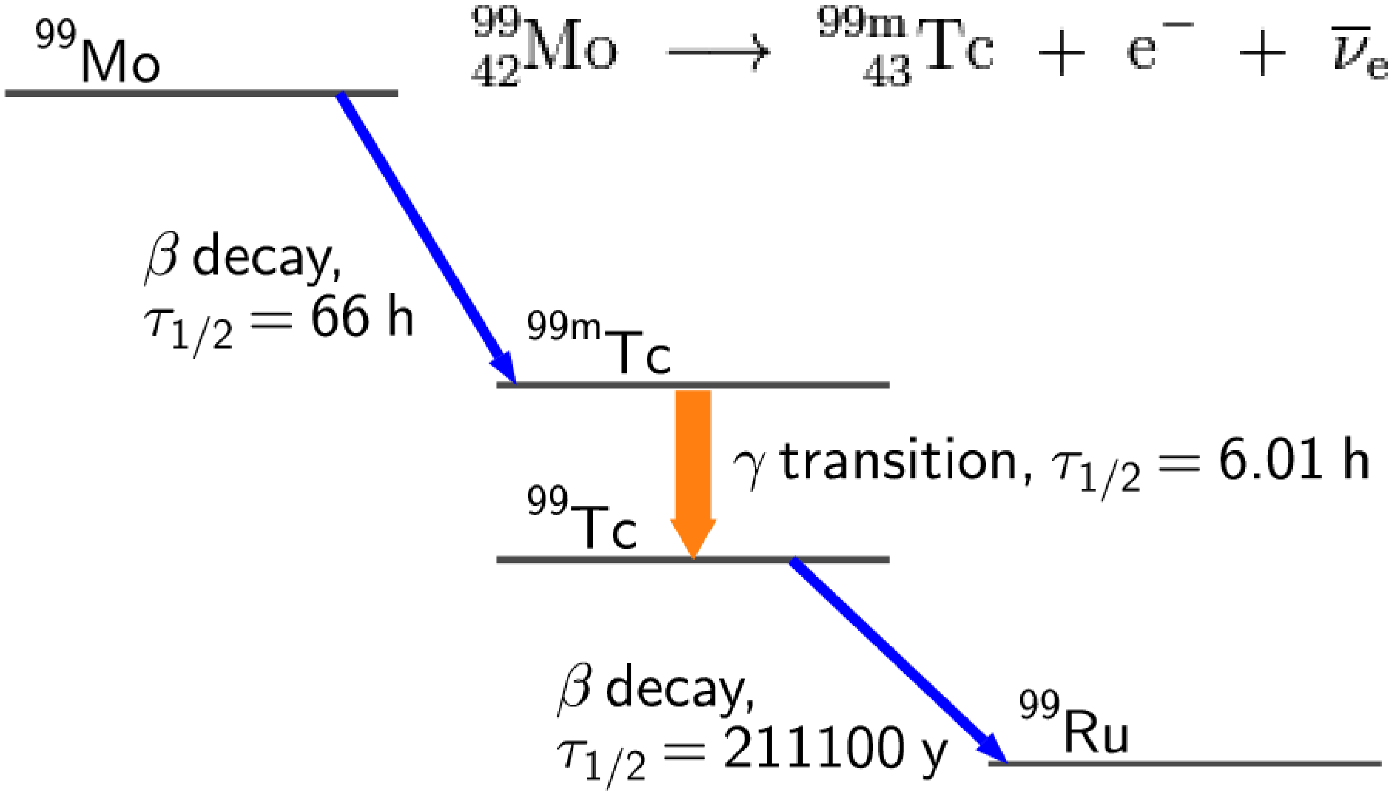
Brain SPECT with Technetium-99m-Bicisate intravenous injection during balloon occlusion of the right carotid artery

TECHNETIUM ^{99m}Tc



The half-life for γ-emission of the excited state of technetium isotope ^{99m}Tc is extremely long. Such states are called metastable (m)

PARENT ISOTOPE MOLYBDENUM-99



PARENT ISOTOPE MOLYBDENUM-99

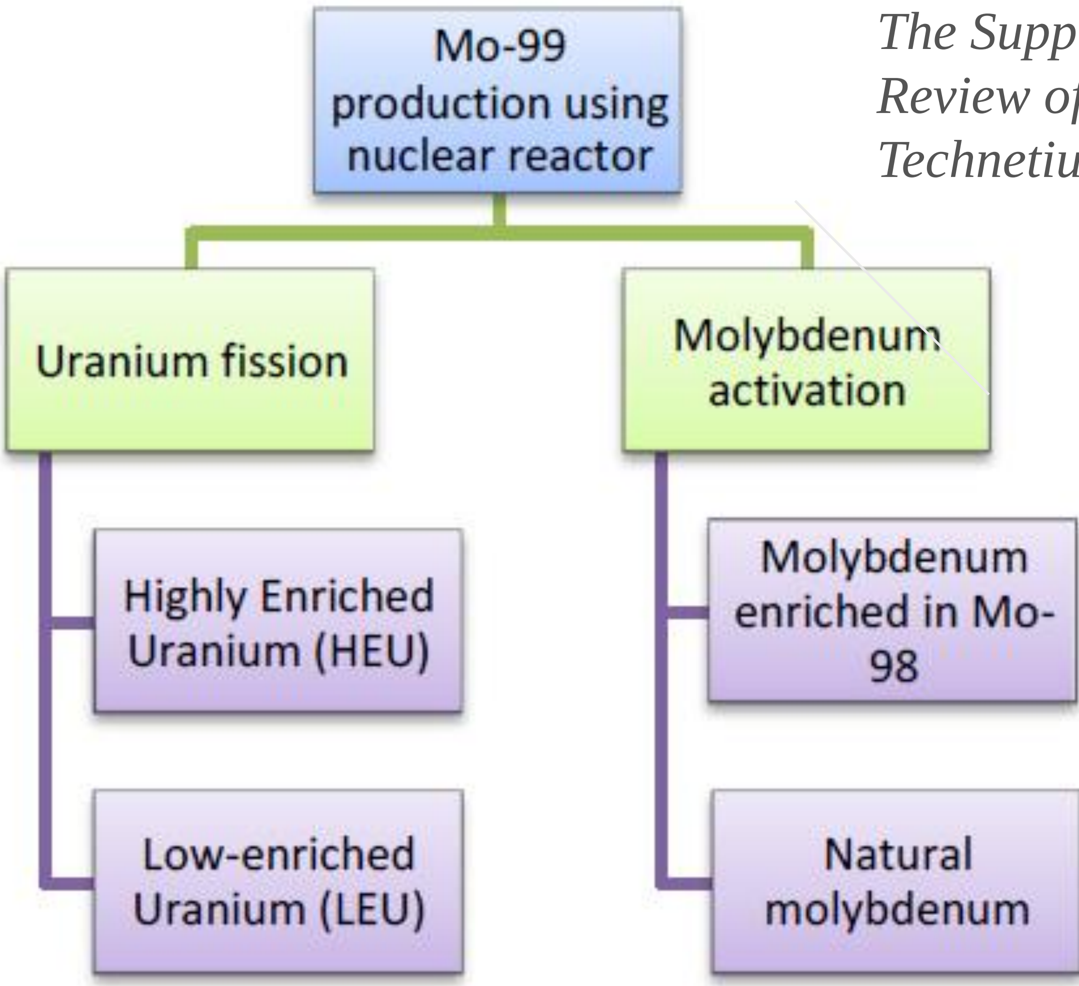
The tracer-isotope $^{99m}_{43}\mathbf{Tc}$ can be produced by eluting it from the parent isotope $^{99}_{42}\mathbf{Mo}$
The Technetium-99m generators ("COWS") can be eluted several times a day for about a week.

$^{99}_{42}$Mo cannot be stockpiled for use.
It must be made at least on a weekly basis to ensure continuous availability

PRODUCTION OF TECHNETIUM ^{99m}Tc

https://www.oecd-nea.org/

The Supply of Medical Radioisotopes: Review of Potential Molybdenum-99/ Technetium-99m Production Technologies



Mo-99 production using accelerators

A scientific approach only

Neutron stripping from Mo-100

Reactor-based ^{99}Mo Production Technologies

PRODUCTION OF TECHNETIUM ^{99m}Tc

	FISSION (U-235) $^{235}U(n,f)^{99}Mo$		CAPTURE $^{98}Mo(n,\gamma)^{99}Mo$	
	Non-enriched (1)	Enriched (2)	Non-enriched	Enriched
SPECIFIC ACTIVITY (PRODUCTION YIELD)	high	< 10^4 Ci/g very high	< 2 Ci/g very low	< 10 Ci/g low
ECONOMICS	US$ 735 to 1100 per 6-day curie	most attractive: USD 555 to 850 per 6-day curie	ONLY REGIONAL SUPPLY	
PROLIFERATION RESISTANCE	Standard; processing of target materials	weapon grade materials	high; processing of target material	high; enrichment of Molybdenum

Small scale indigenous Mo-99 production in research reactors (pool type) bridge regional supplier gaps at reasonable costs and investments;
The technique can be realized and installed by short-term R&D projects

PRODUCTION OF TECHNETIUM ^{99m}Tc – A PROLIFERATION ISSUE

Coordinated Research Projects (CRPs)

Developing Techniques for Small Scale Indigenous Mo-99 Production Using Low Enriched Uranium (LEU) Fission or Neutron Activation
(Initiated in 2005 – completed in 2011)

The CRP involved eight technology "providers"/agreement holders (Argentina, Brazil, India, Indonesia, Korea, Poland and the USA) and six technology "recipients"/contract holders (Chile, Egypt, Kazakhstan, Libya, Pakistan and Romania) Technology providers are intended to assist recipients in becoming small-scale producers of Mo-99 from LEU sources through the provision of materials and expertise. See also: IAEA Nuclear Energy Series publication

PRODUCTION OF TECHNETIUM ^{99m}Tc – A PROLIFERATION ISSUE

Upcoming Mo-99 IAEA Meetings

27–28 January 2014

Technical Meeting on Conversion Planning for ^{99}Mo Production Facilities from HEU to LEU, IAEA Headquarters, Vienna

15–17 October 2014

Technical Meeting of the International Working Group to Support the Transition of ^{99}Mo Production away from the Use of Highly Enriched Uranium

PRODUCTION OF TECHNETIUM ^{99m}Tc – A PROLIFERATION ISSUE

Any new Mo-99 production facilities should be based on LEU.

The conversion of existing Mo-99 facilities is technically feasible, although certain technical and financial/economic issues will have to be addressed.

PRODUCTION OF TECHNETIUM ^{99m}Tc – A JOINT INITIATIVE

?Can we benefit from each other?

There is a shortage in molybdenum 99

There are two research reactors of pool type

There are experienced scientists and technicians

There are international scientific cooperation agreements

Can we speed up the development of a small scale Mo-99 production and the full supply chain of medical Technetium-99m generators?

Processing of the Mo-99 for Radiopharmaceutical Use

Step 1: Mo-99 small scale production by neutron capture
Enriched Mo-98 target is irradiated by neutrons
with specific spectral characteristics

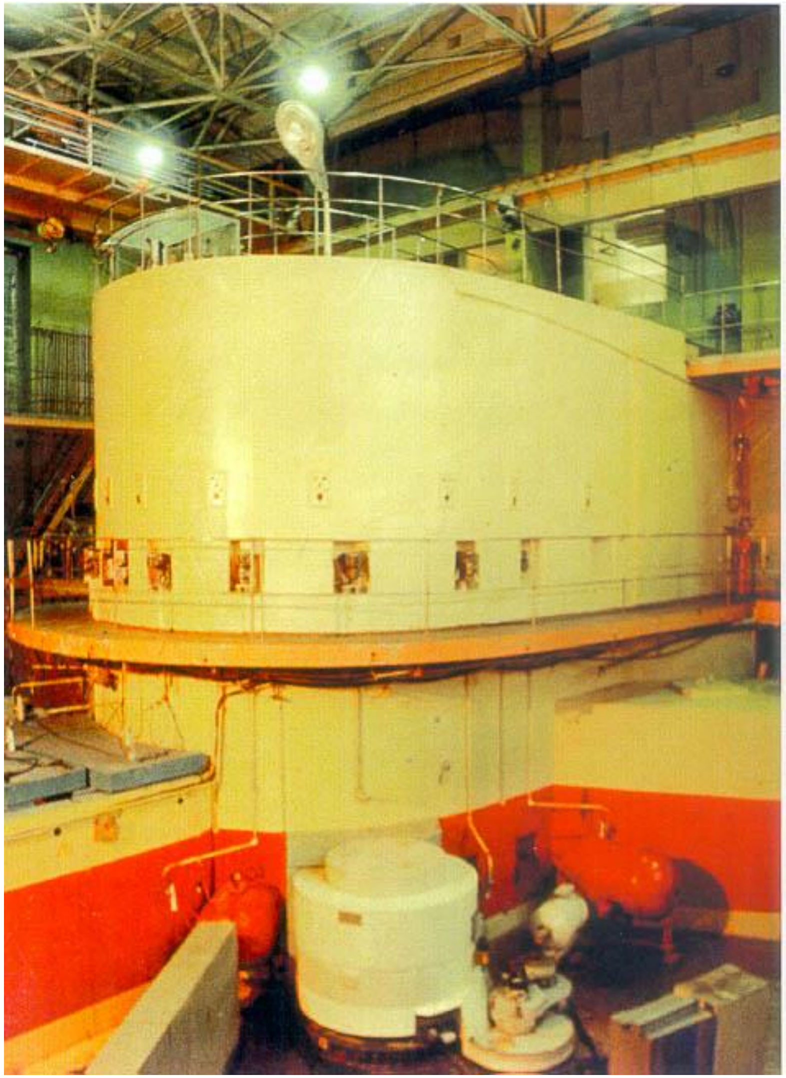
Step 2: Processors
Product is purified
almost not necessary for highly enriched Mo-98 targets – no waste problem
(If produced by uranium fission, separation from other fission products)

Step 3: Generators
The purified product is incorporated into the Mo-99 (Technetium) generator

Step 4: Nuclear pharmacy
Nuclear pharmacy experts compound and dispense technetium –based products

Step 5: Delivery to customer
Finally the nuclear pharmaceutical is delivered to a nuclear medicine facility for administration to the patient.

TPU Nuclear Reactor IRT-T



Light water pool reactor

Thermal power - 6 MW

Number of channels:
horizontal - 10
vertical – 14

Nuclear Reactor Core

Flux of Thermal Neutrons

in central channels:

$1{,}7 \cdot 10^{14}$ n/(cm$^2 \cdot$s)

in peripheral channels:

$(2\text{-}\ 5) \cdot 10^{13}$ n/(cm$^2 \cdot$s)

Specific activity ^{99}Mo

(after 100 hours of irradiation):

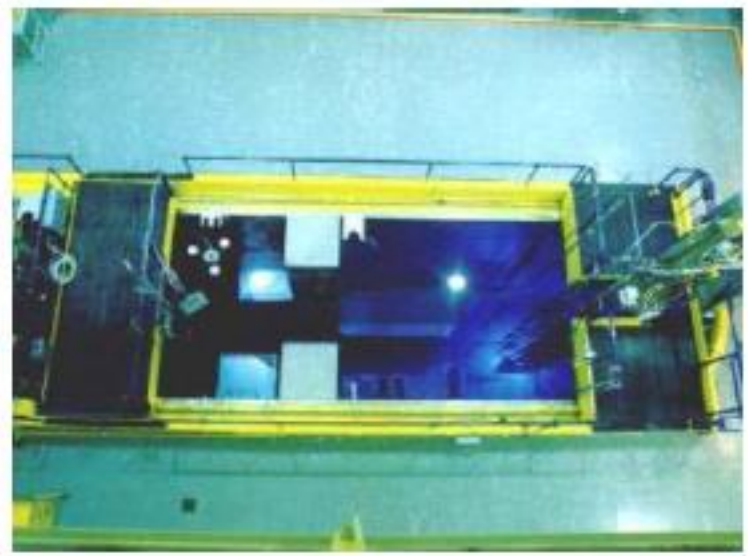
2 Ci/g on natural molybdenum

10 Ci/g – on enriched ^{98}Mo (98,6 %)

PRODUCTION OF TECHNETIUM ^{99m}Tc

IEA-R1 Research Reactor

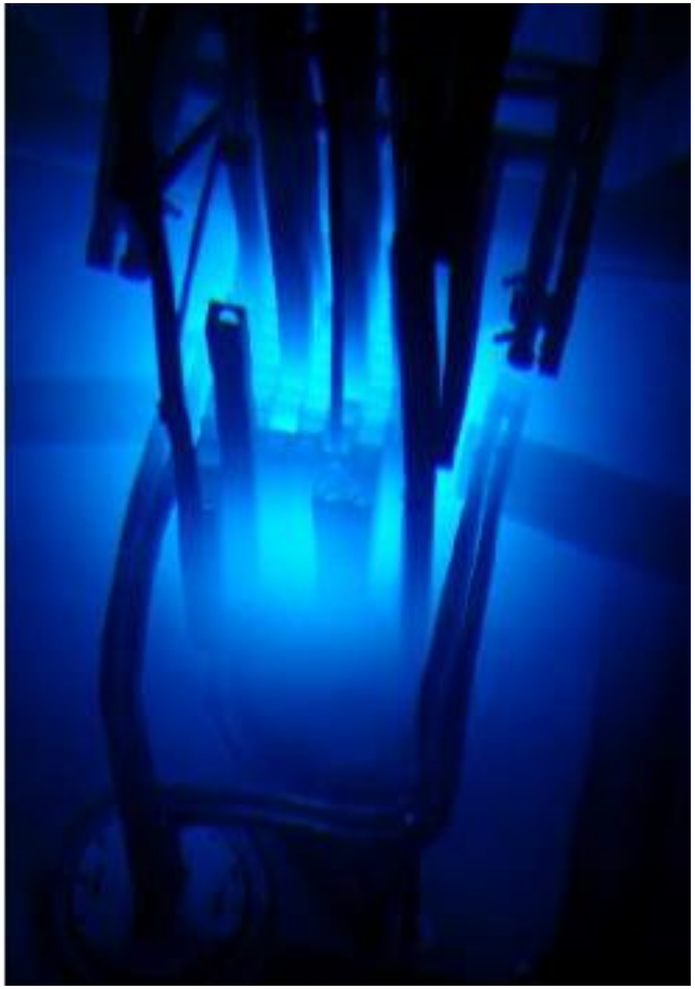
- Pool type research reactor, Babcock & Wilcox project.
- Installed at the previous Atomic Energy Institute (IEA), presently the Nuclear and Energy Research Institute (IPEN) of the Brazilian Nuclear Energy Commission site, in Sao Paulo, inside the Sao Paulo University Campus,
- The reactor achieved its first criticality on September 16, 1957.
- 5 MW of maximum power (originally 2 MW)
- The reactor originally used 93% enriched U-Al fuel elements, but now it uses 20% enriched uranium U_3Si_2-Al dispersion fuel produced at IPEN.



PRODUCTION OF TECHNETIUM ^{99m}Tc

IEA-R1 Research Reactor

Radioisotope	Total Activity per year (Ci)	Users* per year	Comments
Mo-99	20,000	300	imported
I-131	2,000	260	50% imported 50% IEA-R1
Cr-51	1	7	imported
Sm-153	21	50	100% IEA-R1



DEVELOPMENT OF TECHNETIUM-99M GENERATORS AND RADIOPHARMACEUTICALS

NATIONAL RESEARCH TOMSK POLYTECHNIC UNIVERSITY

National Research Tomsk Polytechnic University

Radiopharmaceutical production is in function for more than 20 years. The production includes all steps, the Mo-99 production, the generators, the nuclear pharmacy, and the delivery to the hospitals.

Clinics of the vast region from Yuzhno-Sakhalinsk to Samara are provided with generators.

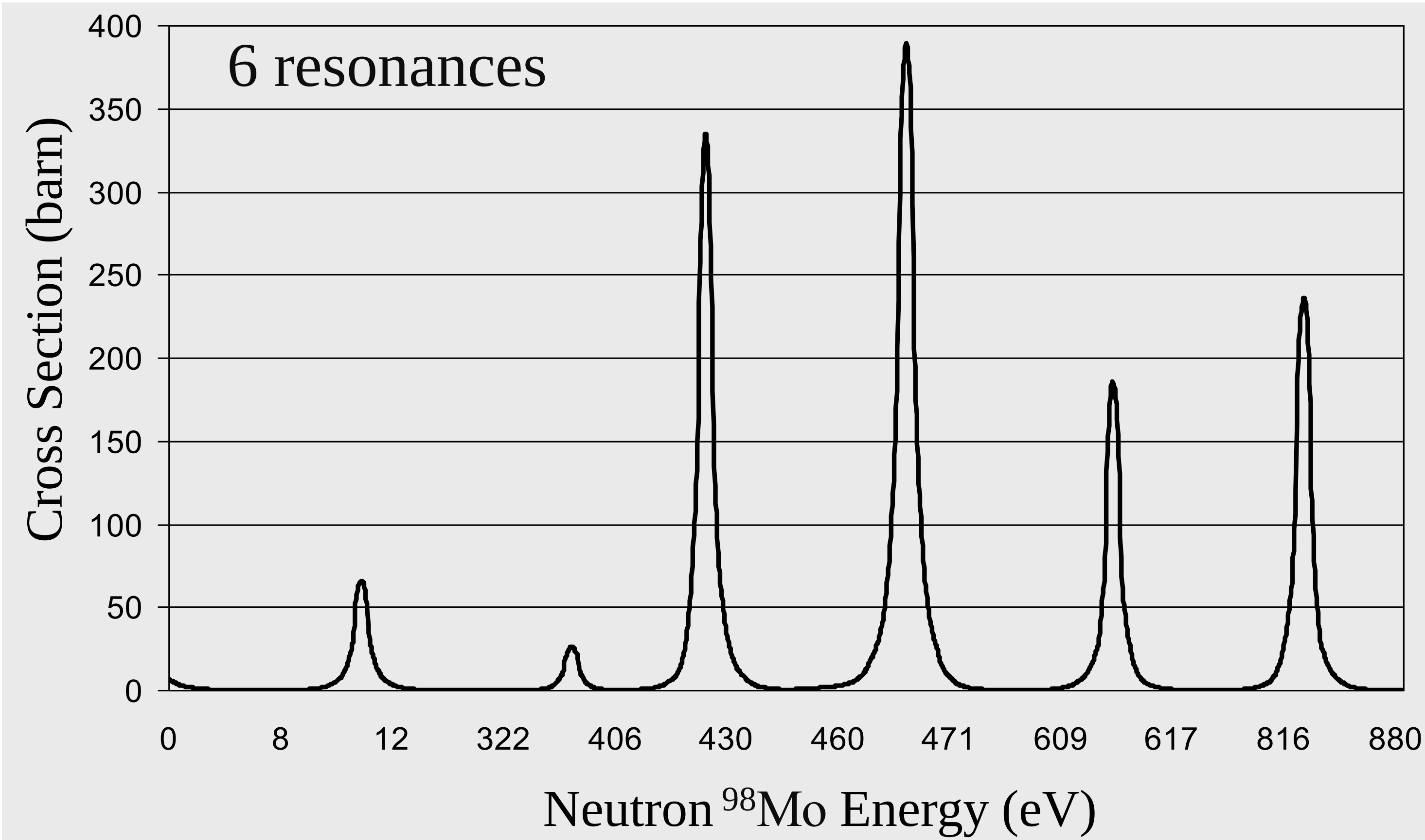
TPU R&D PROJECT

EFFECTIVE MOLYBDENUM-99 GENERATION BY OPTIMIZED RESONANCE NEUTRON CAPTURE

OBJECTIVES & TASKS

- **Assessment of Mo isotope contributions to the neutron resonance capture value**
- **Measurement of the effective cross section**
  $^{98}Mo(n, \gamma)^{99}Mo$
  for natural and enriched Mo-targets irradiated in epithermal flux
- **Determination of increasing specific activity of ^{99}Mo under irradiation of natural and enriched Mo**

Cross-section $^{98}Mo\ (n,\gamma)\ ^{99}Mo$



Effective Cross Section $^{98}Mo(n,\gamma)^{99}Mo$

$\sigma^* = \sigma + kI$ (Effective Cross Section)

σ = 0,13 barn: thermal neutron cross-section
I = 6,9 barn: resonance integral of ^{98}Mo

Beryllium neutron traps are used (layer thickness of 20-90 mm) in order to moderate fast neutrons to resonance level.

Results of Experiential Studies of Neutron Activation ^{98}Mo

σ*

in peripheral channel VEC-6: 0,195 barn

in central channel -1: 0,700 barn

This allows to accumulate the specific activity

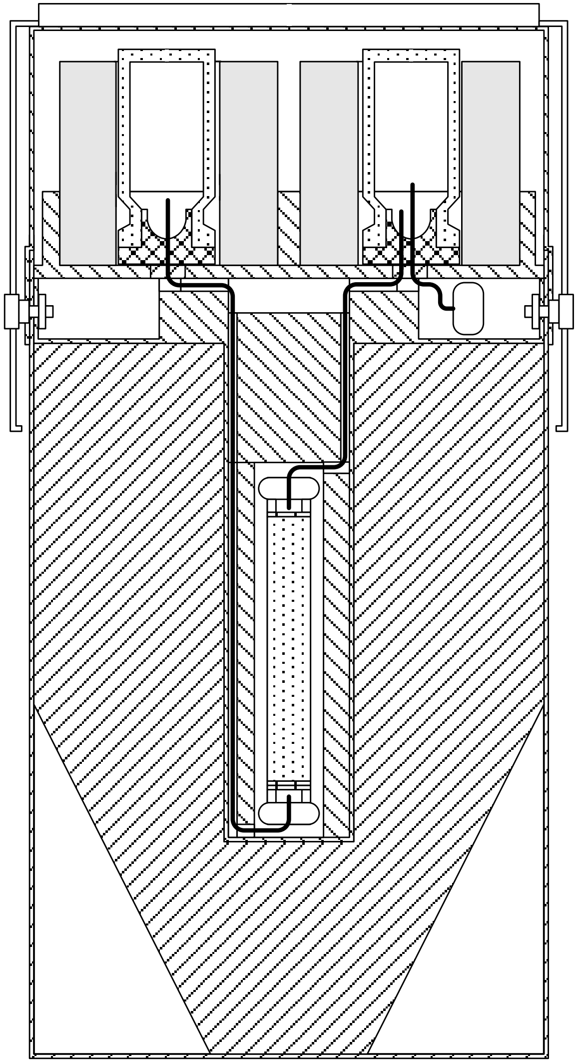
^{99}Mo ~ 10-12 Ci/g

for 100-120 hours of irradiation

when using molybdenum-98 with enrichment 98,6%.

Design of Technetium 99м Sorption Generator

Column with aluminum oxide
in shielding container and two flasks:
vacuum and with normal saline



Discovery of physical laws of increasing sorptive capacity of aluminum oxides

Technetium-99м
Automated Module

Performance Requirements for Technetium-99m Generators TPU Research Institute of Nuclear Physics

Nr.	Generator type	Height, mm	Activity ^{99}Mo, Ci	Receipt time, min	Yield ^{99м}Tc, %
1	Coaxial	450	5	120	80
2	Multiple cycle extraction	270	15-20	90	75-90
3	Small size	110	1-2	60	50-70
4	Extraction-chromatographic	110	1-2	25	75-85

6 RU patents obtained

^{99m}Tc Labeled Compounds

R&D OBJECTIVES

^{99m}Tc labeled antibiotics

diagnostics of suppurative inflammation

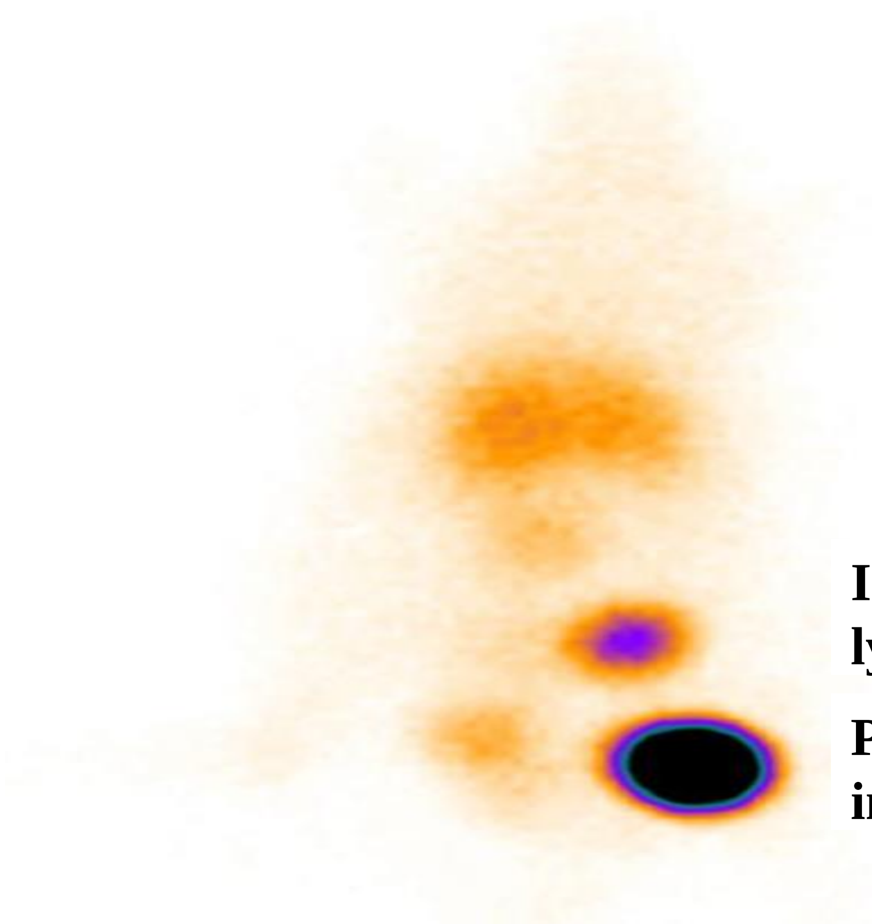
^{99m}Tc labeled glucose

diagnostics of oncological diseases

Various nanocolloids for lymphoscintigraphy

Scintigram of a Rat

2 hours after injection of nanocolloid Fe@C. %.



CONCLUSIONS

RUSSIAN – BRAZILIAN
SCIENTIFIC COOPERATION

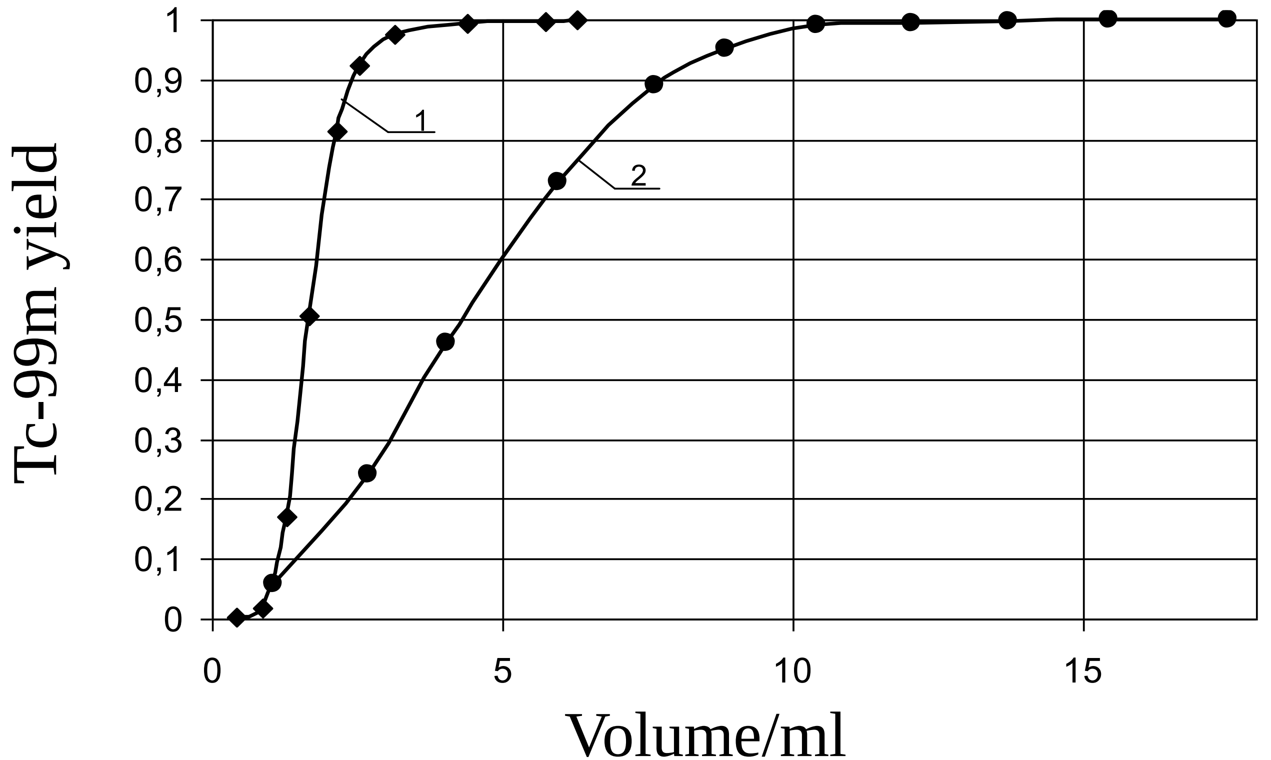
?

US$ 500,000-2 years

MATCHING FUND PROJECTS
(exchange of ideas, scientists, students)


Thank you
for
your attention

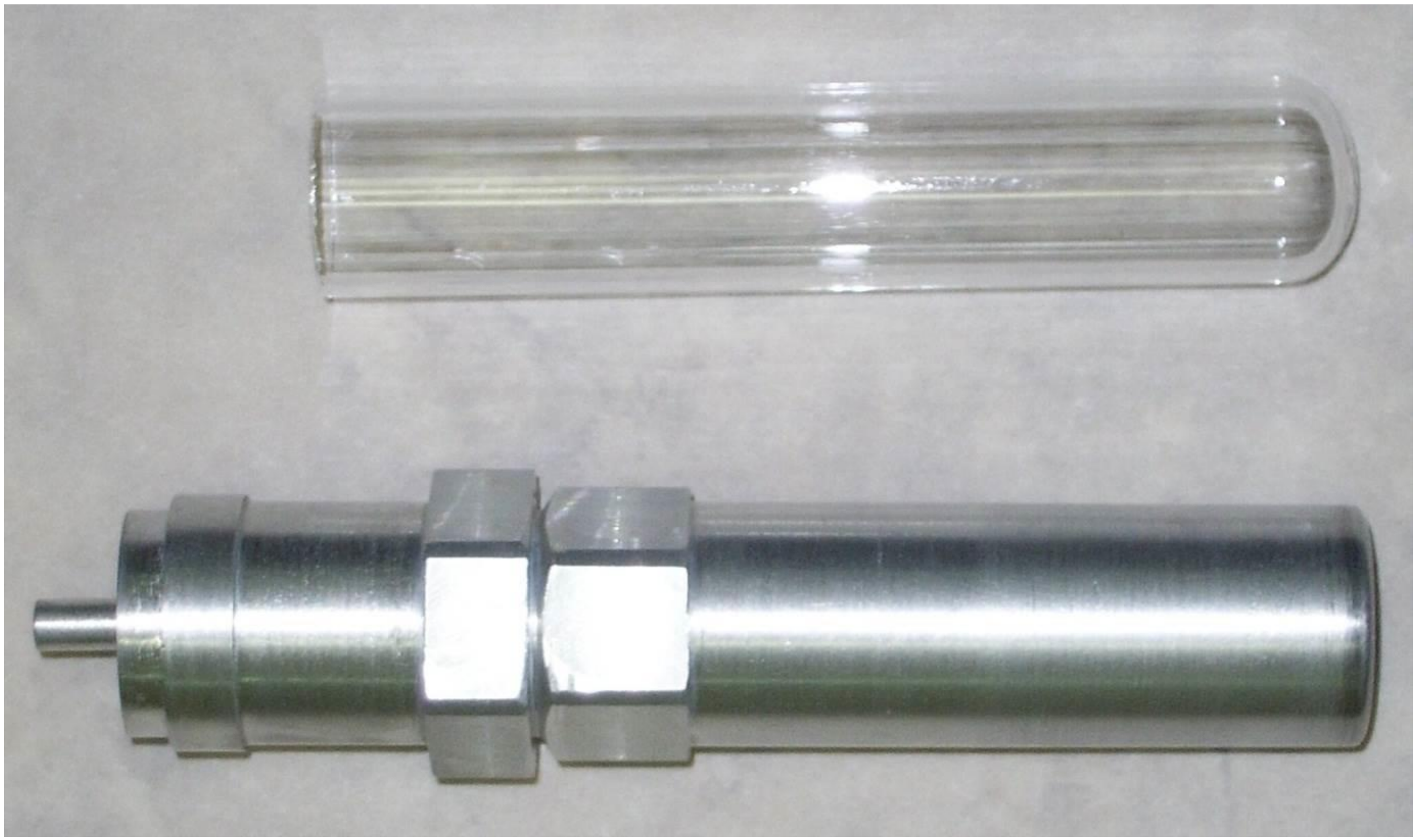
Elution Profiles



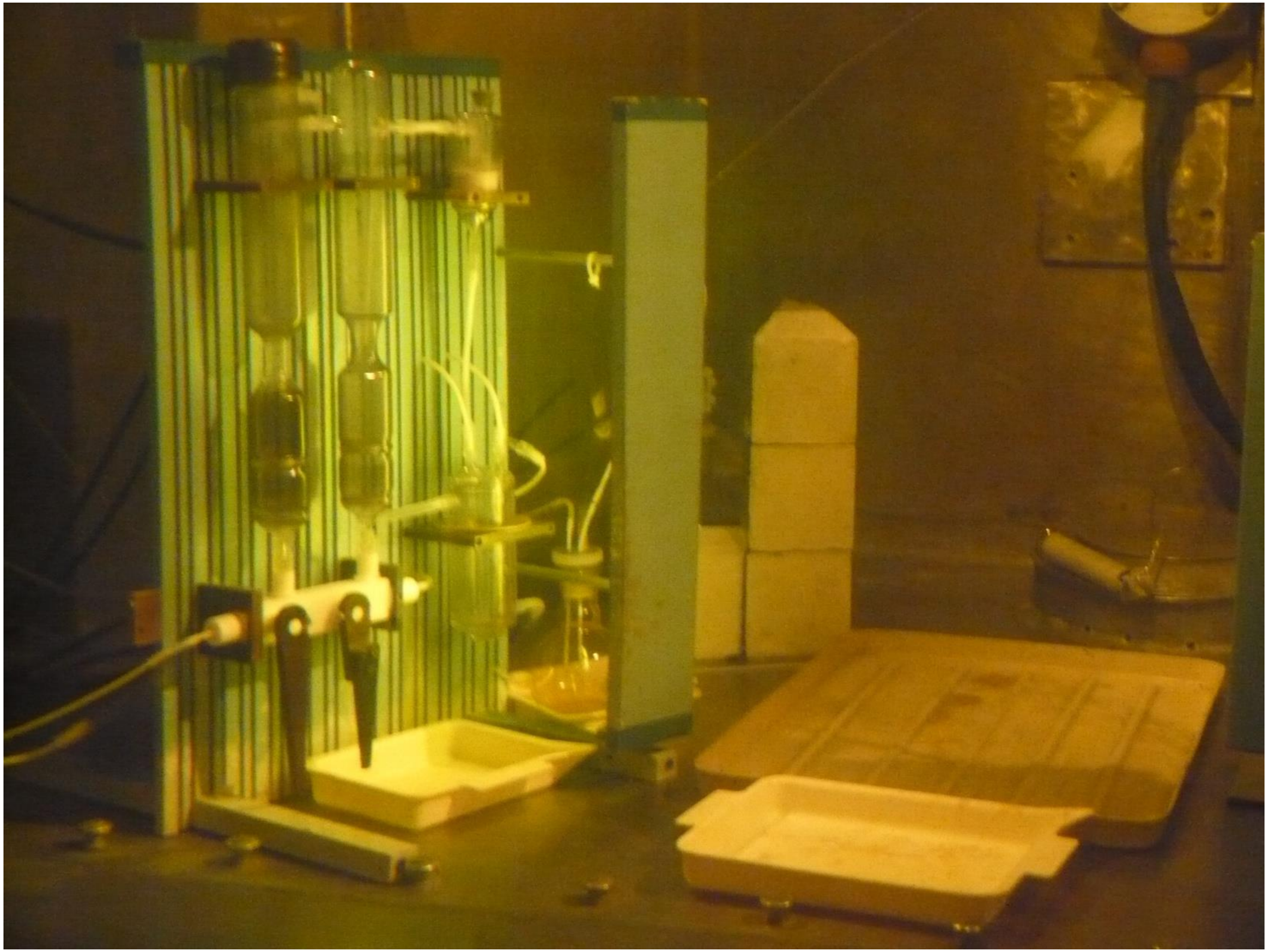
^{99m}Tc yield dependent on elution volume

- **1 – generator based on debris ^{99}Mo with sorbent mass Al_2O_3 ~ 1,5 g;**
- **2 – generator of (n,γ)^{99}Mo with sorbent mass 7 g.**

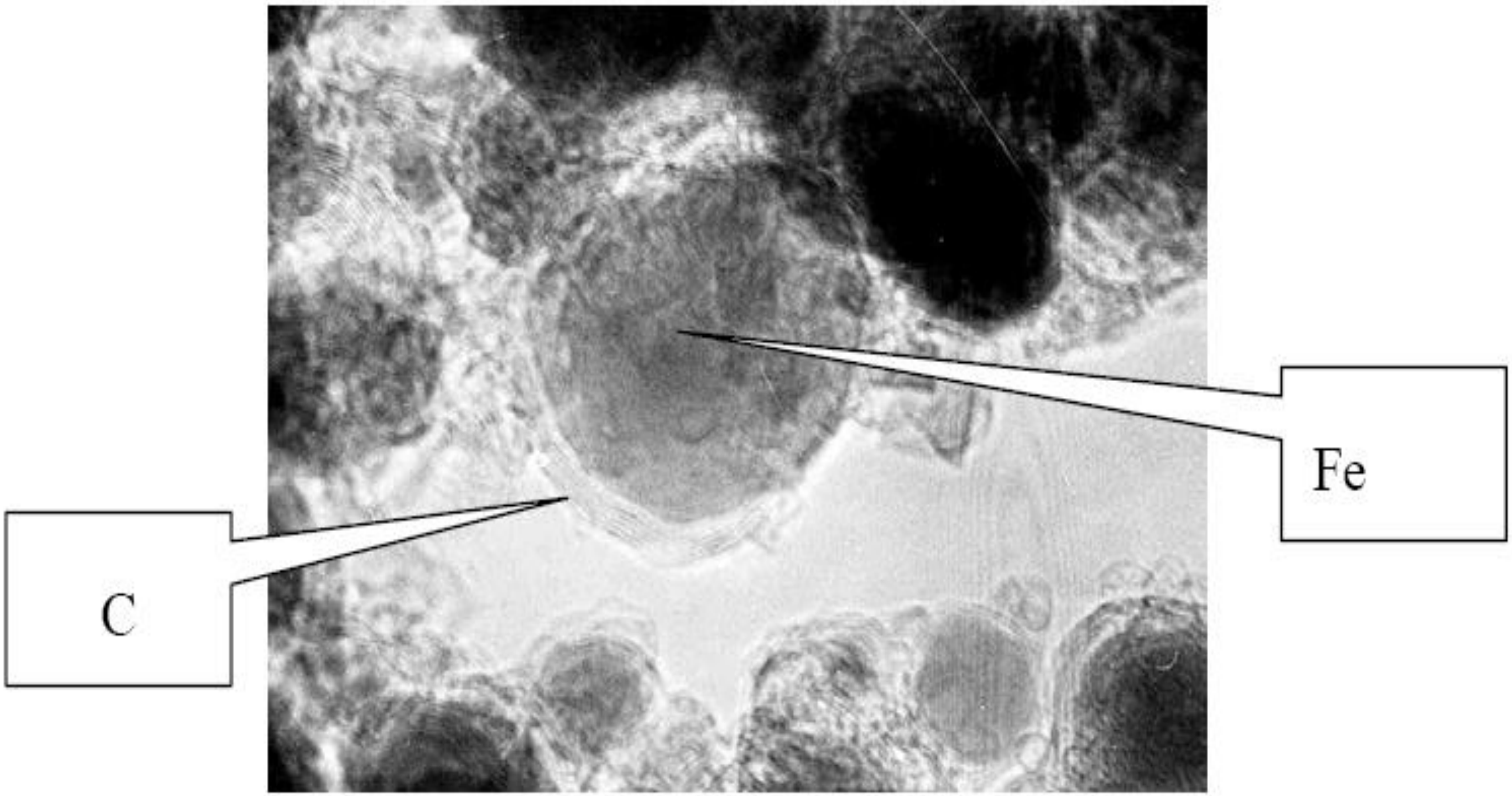
Target Construction for Irradiation of Enriched (98,6 %) Oxide MoO_3



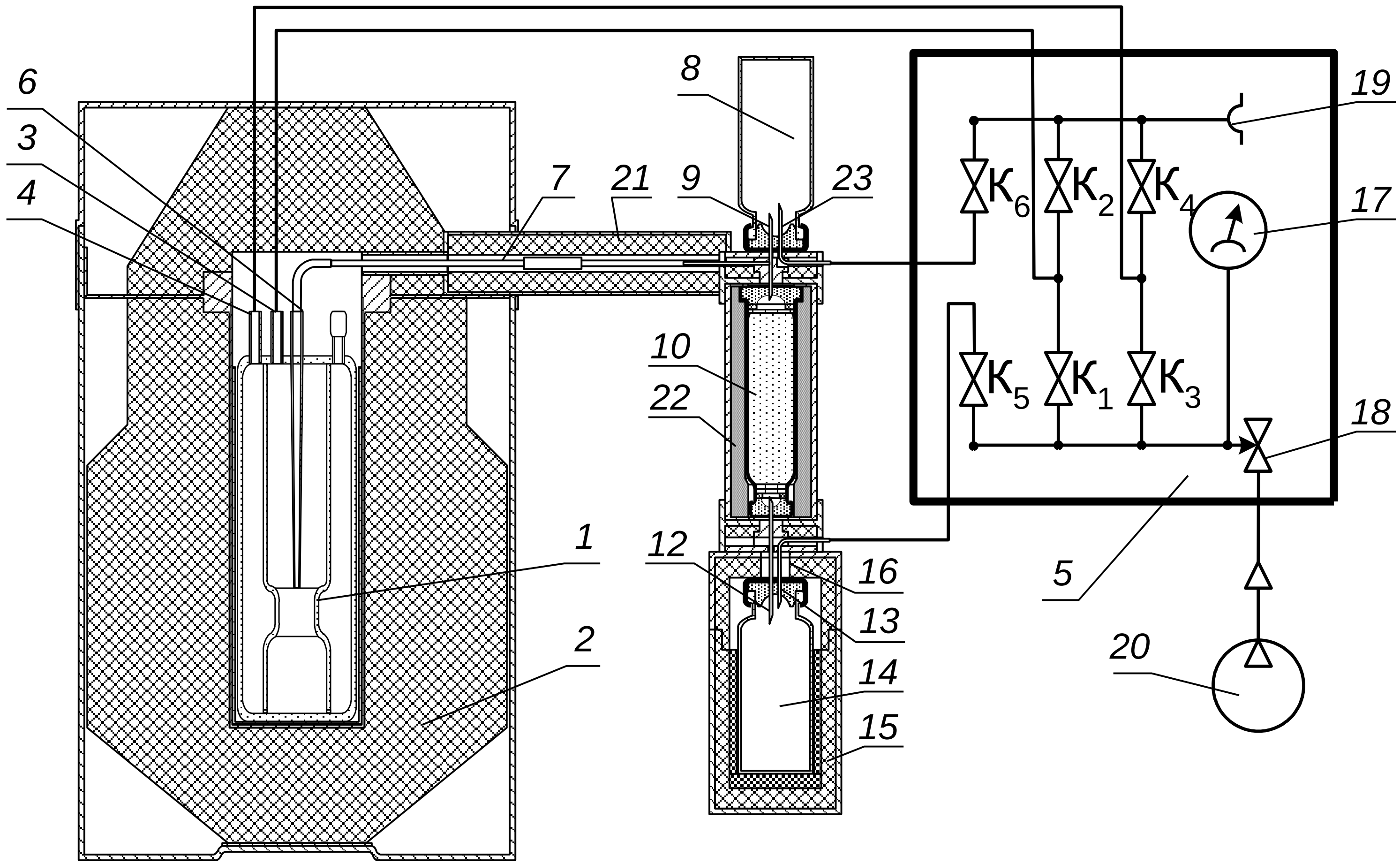
Technetium-99м Stationary Extraction Generator (ИРТ-Т, Tomsk)



Picture of Iron Carbon Particles Fe@C



Design of Technetium-99м Extraction-chromatographic Generator



Production Complex

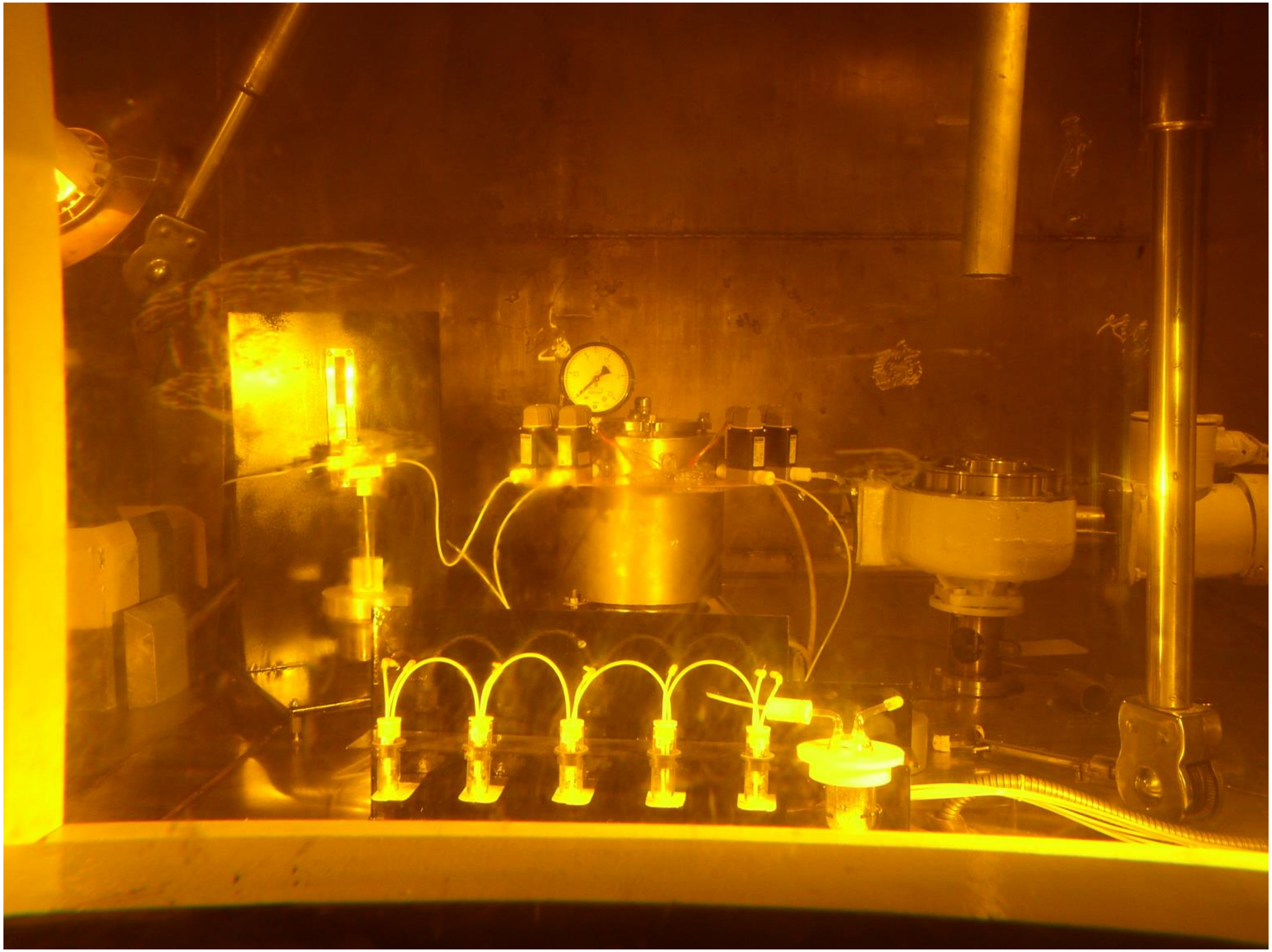
Preparation and Assembly of Generator Columns with Communications

Preparation of Al_2O_3, Columns and Communications

Generator Assembly

Hot cell Control Room

Hot cell



Analytical Laboratory

Microbiological Control Laboratory

Microclimate Control