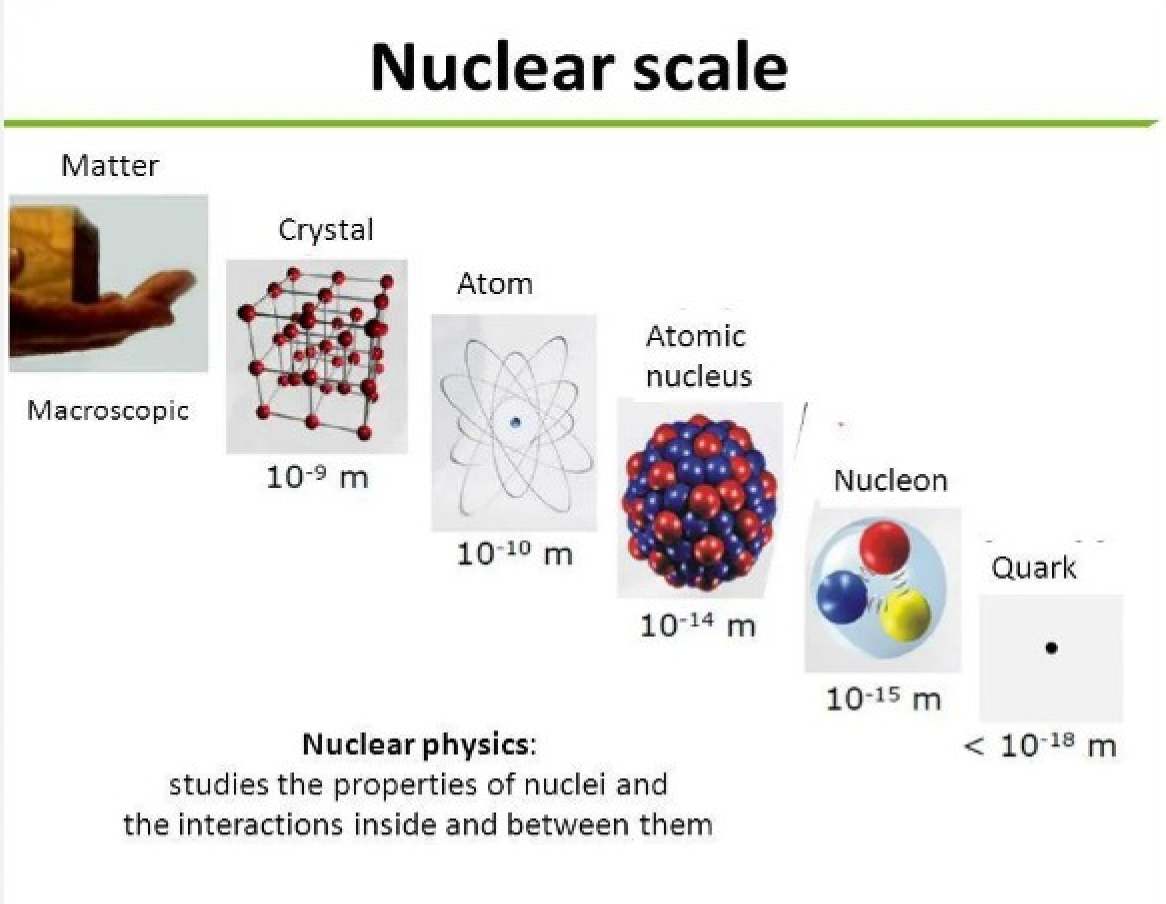
THE HENRYK NIEWODNICZAŃSKI
INSTITUTE OF NUCLEAR PHYSICS
POLISH ACADEMY OF SCIENCES

Medical Radioisotopes Study Using AIC-144 Cyclotron

dr Arshiya Anees Ahmed (NZ64)

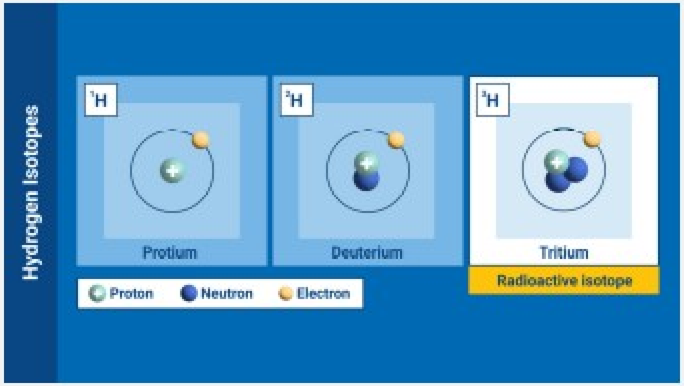
27-02-2025

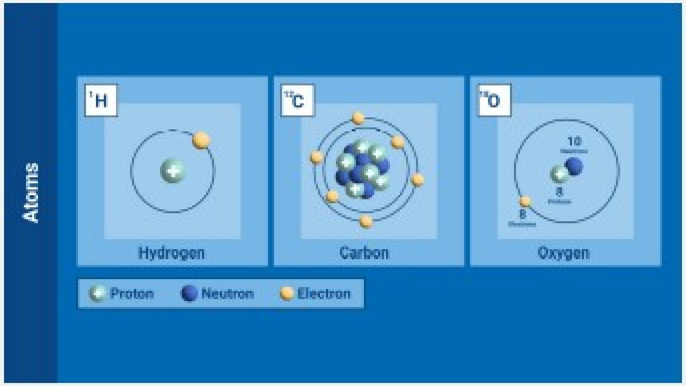
Isotopes



Nuclear scale

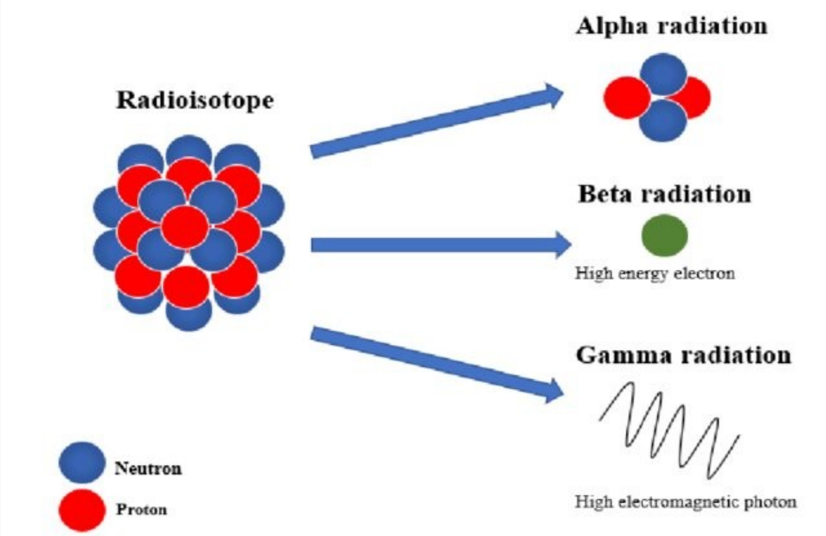
Nuclear physics:
studies the properties of nuclei and
the interactions inside and between them

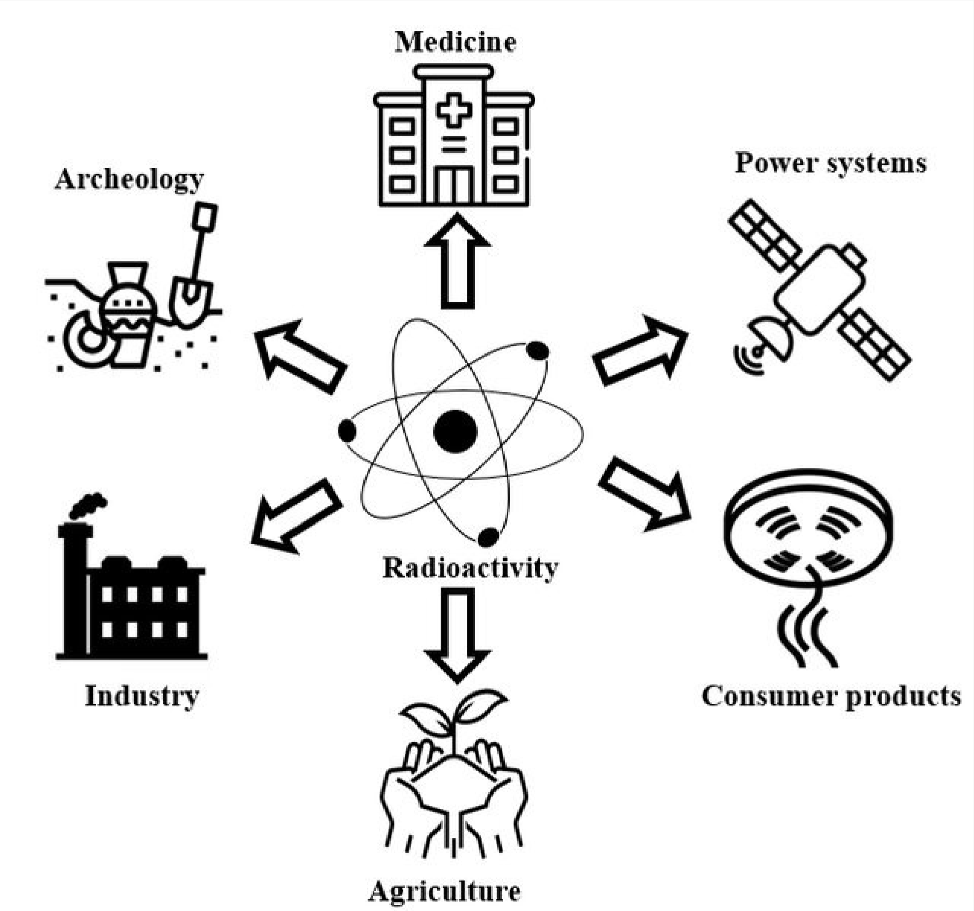




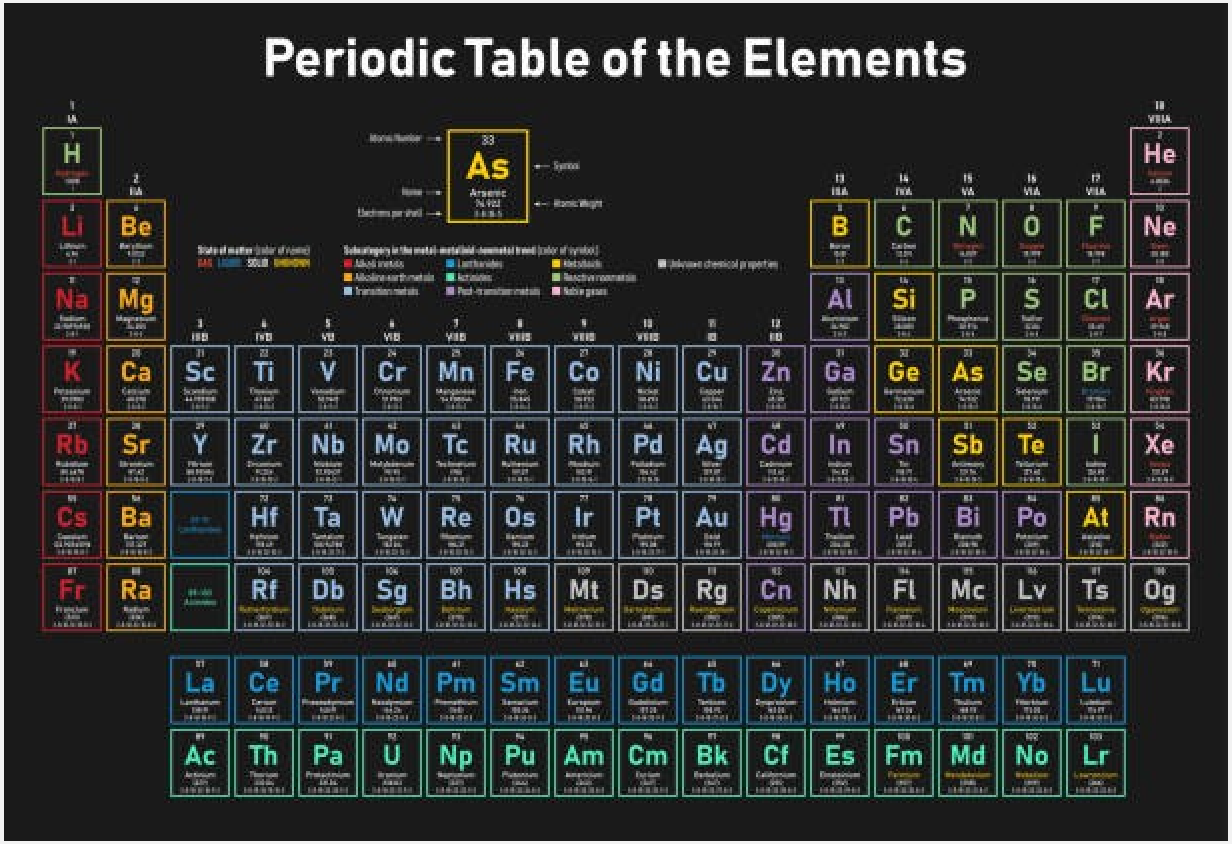
Sourcec: https://www.iaea.org/newscenter/news/what-are-isotopes

Radioisotopes





Radioisotopes for Medicine



118 elements

94 naturally occurring

254 stable isotopes

> 3000 radioisotopes

84 seen in nature

Radioisotopes for Medicine

Selection criteria

→ Should emit only the radiation required for its medical application

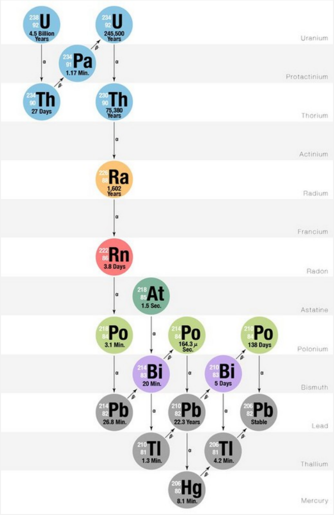
increase the radiation dose

→ Should have $T_{1/2}$ in corresponding to the medical procedure

Should decay to stable or very long-lived isotope

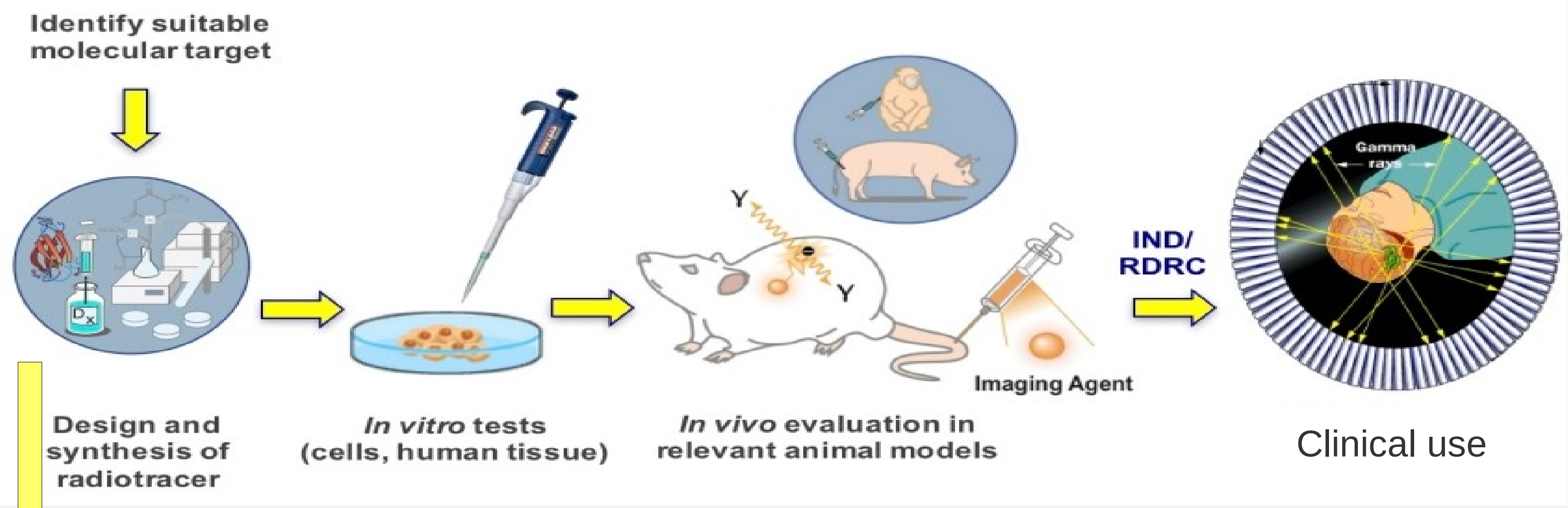
→ Should easily build stable complexes with desired radiotracers

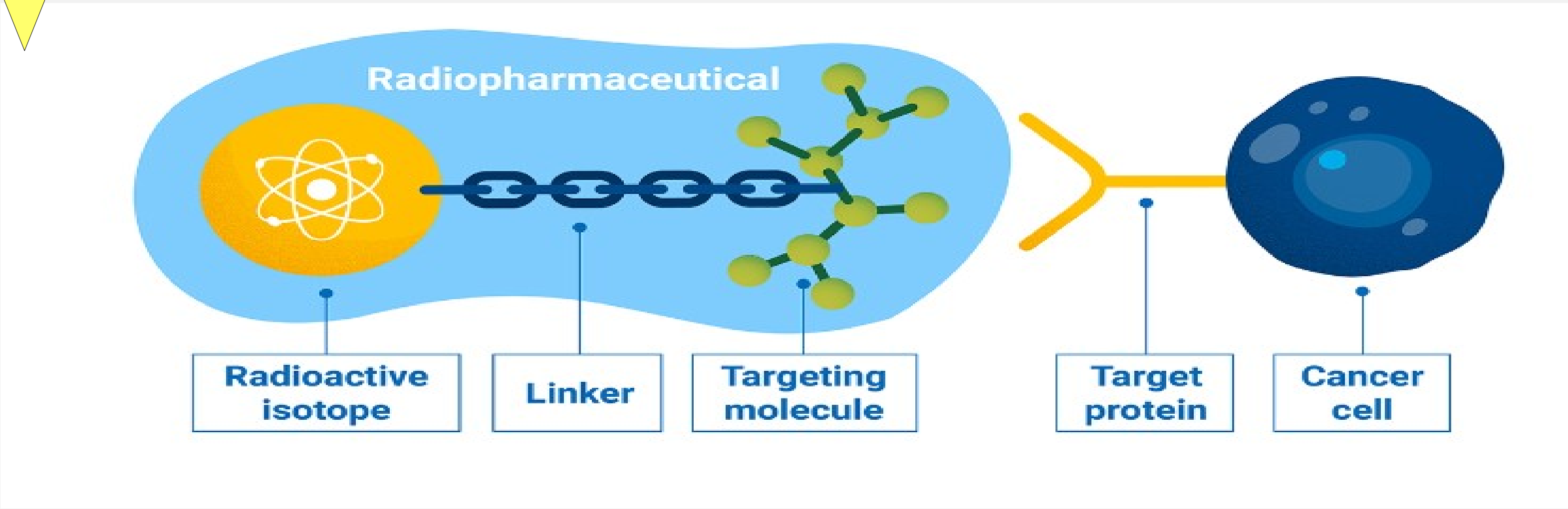
→ should have a feasible, cost-effective, and safe production route



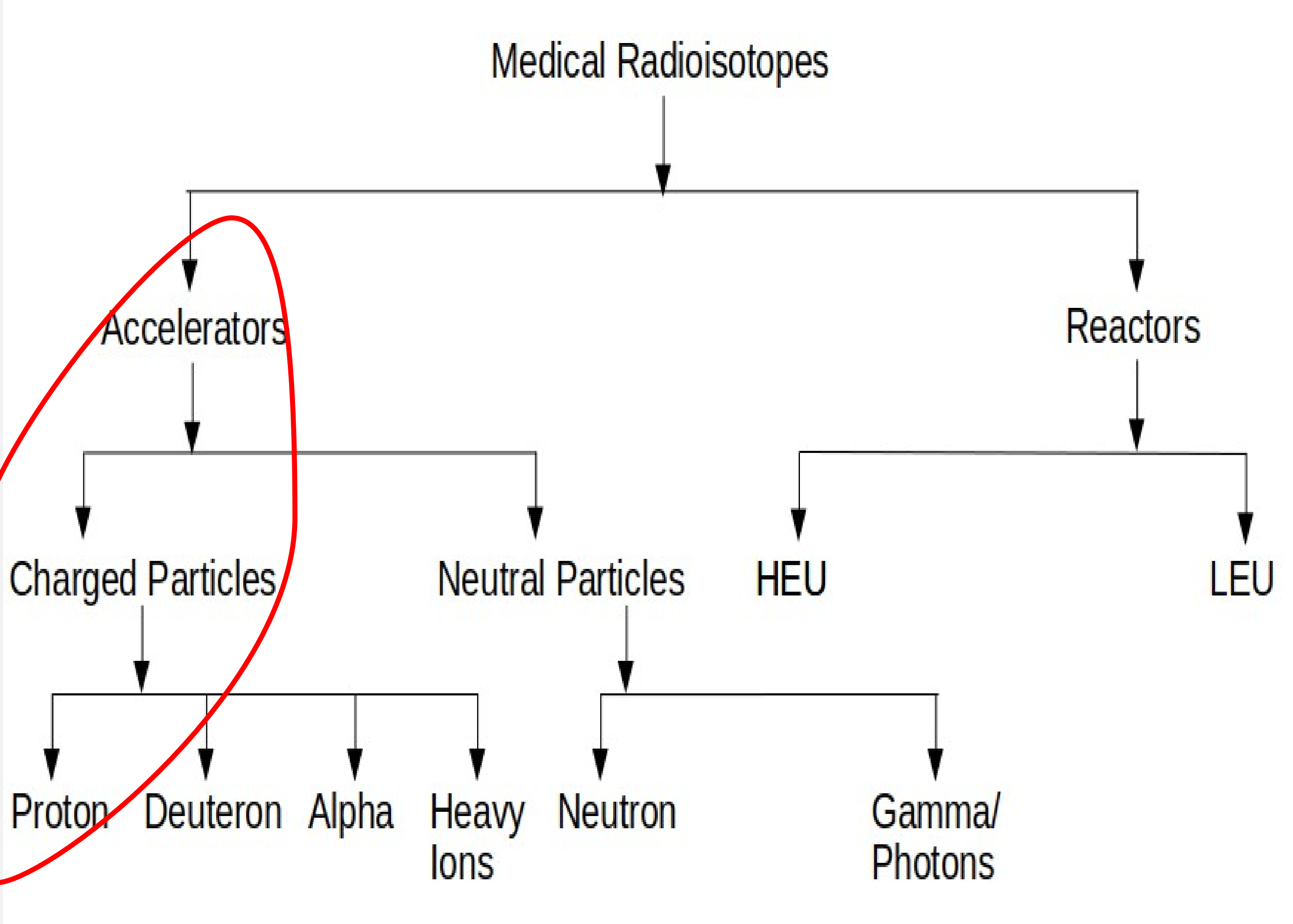
< 50 radioisotopes

Radioisotopes for Medicine





Methods of Radioisotope Production



Motivation

Isotope shortage looms after reactor shutdown | The Star

NRU Canada

IAEA assesses ageing management at Dutch research reactor : Regulation &...

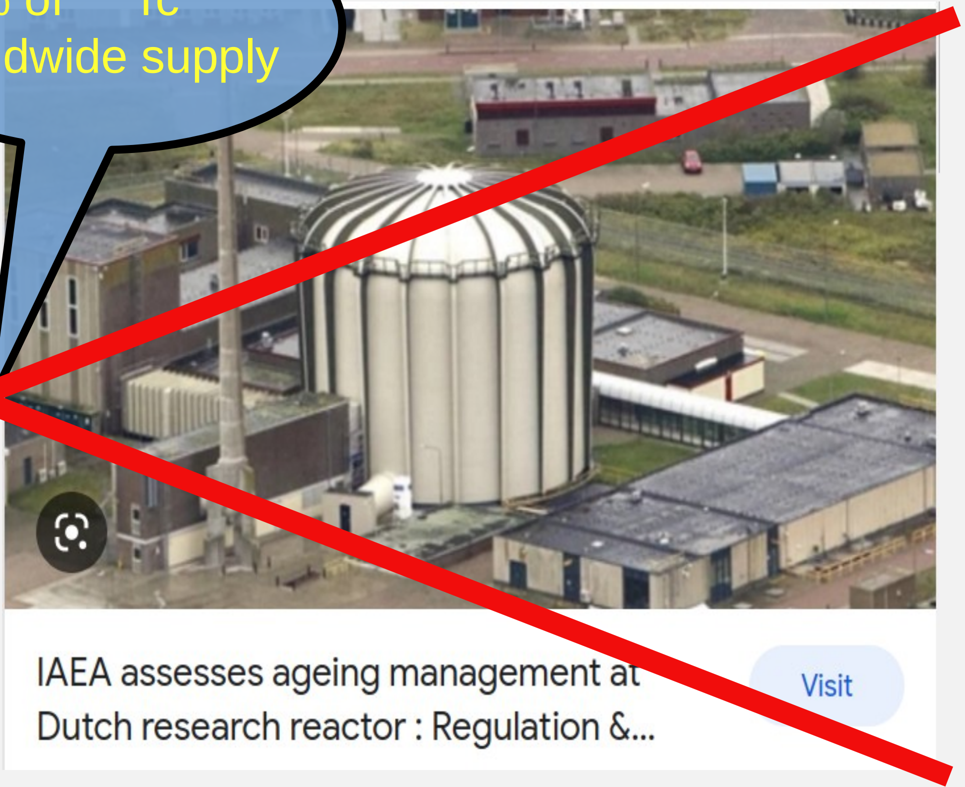
HFR Netherlands

Motivation

60% of ^{99m}Tc worldwide supply


Isotope shortage looms after reactor shutdown | The Star

NRU Canada


IAEA assesses ageing management at Dutch research reactor : Regulation &...

HFR Netherlands

https://www.thestar.com/news/canada/2009/05/19/isotope_shortage_looms_after_reactor_shutdown.html
https://www.world-nuclear-news.org/Articles/IAEA-assesses-ageing-management-at-Dutch-research

Motivation

OPINION

NATURE|Vol 457|29 January 2009

ESSAY

Accelerating production of medical isotopes

The global problem of a safe and reliable supply of radioactive isotopes for use in critical hospital procedures can be solved with accelerators, not nuclear reactors, says **Thomas Ruth**.

Physicians and patients around the world are increasingly anxious about the shortage of nuclear isotopes used in medical imaging. A single radionuclide — technetium-99m (^{99m}Tc) — is used in four-fifths of all such imaging procedures worldwide. Yet its supply is remarkably fragile. In 2007, the unanticipated closure of a single nuclear-reactor facility in Canada slashed isotope stocks in North American hospitals by about 80%, causing much panic and the cancellation of 50,000 medical procedures over five weeks. Some patients went into surgery without the scans their doctors usually rely on. The medical-isotope supply came back online, but the fragility of the system did not improve. In 2008, isotope shortages struck again.

Shockingly, there are no clear plans in place for how to tackle this problem. My colleagues and I see viable mid-term and long-term solutions. Each relies on a very different plan. But both involve accelerators, rather than reactors.

Nuclear medicine, developed following the Second World War, relies on the injection of a radioactive compound into the bloodstream, and instruments that can then detect and map, in three dimensions, the distribution of the injected radioactivity and its decay products. It is used primarily to locate tumours in the body, monitor cardiac function following heart attacks, map blood flow in the brain, and guide surgery. About 70,000 diagnostic images are taken each day, worldwide.

Some 85% of the ^{99m}Tc used in Europe and North America comes from the decay of molybdenum-99 (^{99}Mo) made at just two reactor facilities: the High Flux Reactor in Petten, the Netherlands, and the National Research Universal reactor in Chalk River, Ontario, Canada. Supplies are shipped continuously to hospitals. Stockpiling the ^{99}Mo radioisotope for more than a couple of days is impossible, as it has a half-life of just 66 hours.

In November 2007, the Chalk Ri
ity was closed for one month ov
regulatory dispute over its mainten
shutdown and subsequent isotope
became the subject of such a publ
that the Canadian government or
reactor to restart; the president of th
Nuclear Safety Commission, who ha
the shutdown, was removed from he
in the process. Then in August 2008
tor in Petten was closed because o
the coolant system. There couldn't
a worse time: the four next-largest
including Chalk River, were alrea

for unrelated reasons. The press latched on

Canada's ageing Chalk River nuclear reactor (top) is pr
closures; supplies of medical isotopes for diagnoses (b

536

© 2009 Macmillan Publishers Limited. All ri

ARTICLE DE FOND

A SHORT TERM SOLUTION TO THE MEDICAL ISOTOPE CRISIS VIA DIRECT PRODUCTION OF TC-99M AT LOW ENERGY: A PIECE OF THE PUZZLE

BY THOMAS J. RUTH, TRIUMF

The recent unexpected shutdown of the Chalk River, Canada reactor has caused a major disruption in the supply of the most important radionuclide used in medicine today, Mo-99. Mo-99 is the source of Tc-99m used in more than 80% of all nuclear medicine imaging procedures. There are only 5 reactors that are presently used in the production of Mo-99 and all of these reactors are over forty years old, the one in Chalk River, the NRU, is 52 years old. The NRU and the HFR reactor in the Netherlands account for more than 60% of the world's supply. The NRU is closed because of a heavy water leak in the containment vessel releasing tritiated water into the holding tank. The HFR reactor had a leak in a coolant pipe earlier in 2009 and is due for an extended shutdown in 2010 to repair this leak.

With these shutdowns the supply of Mo-99 has caused major shortages around the world causing major challenges in diagnosing patients with heart disease and cancer.

With most solutions for obtaining a reliable supply of Mo-99 taking 5 or more years, short term solutions need to be examined. Some of the long term solutions involve the use of accelerators including using electron linacs to generate photon beams for photo induced fission of natural uranium or photo induced neutron emission on Mo-100 yielding low specific activity Mo-99. Other proposals include the use of proton spallation sources to generate secondary neutrons for neutron induced fission of uranium-235. However these large projects require several years of planning and construction before the conceptual ideas can become a reality and would not be able to supply commercial quantities of Mo-99 before 2016-2020.

SUMMARY

The shutdown of the NRU reactor in Chalk River, Ontario, and the planned shutdown of the HFR reactor in the Netherlands in 2010, has caused major shortages in the supply of Mo-99 around the world, causing major challenges in diagnosing patients with heart disease and cancer.

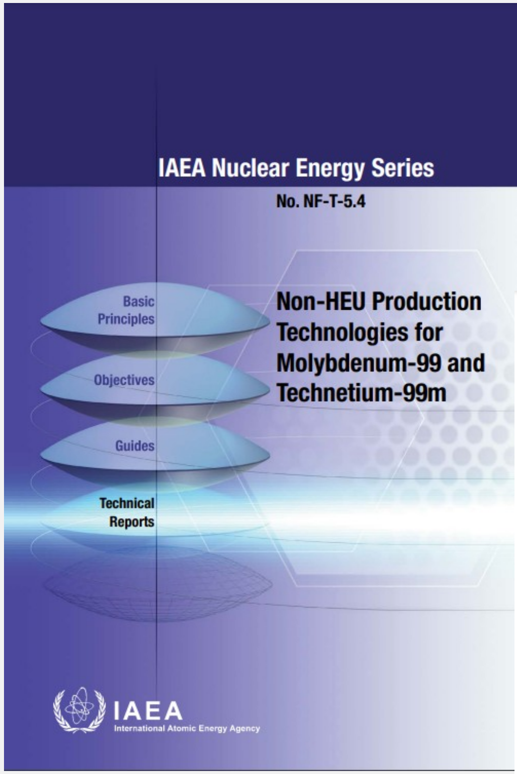
In the recent National Academy of Sciences report *Medical Isotope Production without Highly Enriched Uranium* [1], it was suggested that direct production of Tc-99m could be used to alleviate shortages in regions close to a low energy cyclotron. It turns out that the ^{100}Mo(p,2n)^{99m}Tc reaction peaks at around 16 MeV and the entire useful excitation function is covered from about 15 MeV to 24 MeV. (see Figure 1) From the literature it appears that the production rate for this reaction is 17 mCi/µAh. [2-7] At this rate it is possible for existing low energy cyclotrons to produce tens of curies of Tc-99m per day at somewhat modest beam currents (100 µA protons). Thus existing cyclotrons such as those with proton energies of 17-19 MeV could produce significant amounts of Tc-99m for local use on a daily basis. The chemistry for isolating Tc-99m from the Mo-100 target is fairly straightforward and less complex than what is used to extract Mo-99 from the fission products and allows for the recycling of the Mo-100 for subsequent irradiations [8]

Fig.1 Production cross section for the ^{100}Mo(p,2n) ^{99m}Tc reaction. Exfor, Nuclear Data Center, BNL.

While this approach is not a *fix* it does provide for an alternative that could be implemented in the short term to alleviate demands for Tc-99m from generator produced Mo-99. Such a relief would allow for the scarce Mo-99 generators to be used in locations more distant from the cyclotrons. Another layer of sophistication that should be

Tom Ruth
<truth@triumf.ca>,
Director, PET
Programme,
TRIUMF,
4004 Wesbrook Mall,
Vancouver, BC,
V6T2A3

LA PHYSIQUE AU CANADA / Vol. 66, No. 1 (jan. à mars 2010) • **15**



IAEA Nuclear Energy Series

No. NF-T-5.4

Basic Principles

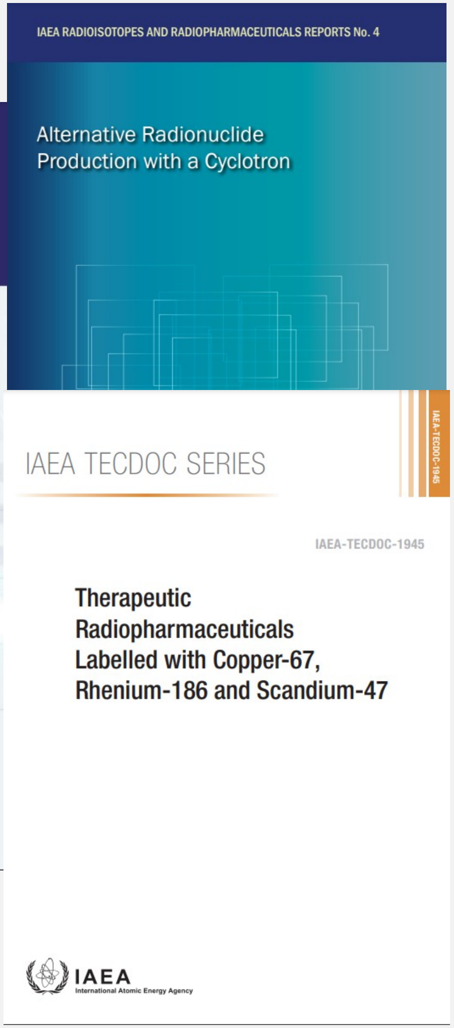
Objectives

Guides

Technical Reports

Non-HEU Production Technologies for Molybdenum-99 and Technetium-99m

IAEA
International Atomic Energy Agency



IAEA RADIOISOTOPES AND RADIOPHARMACEUTICALS REPORTS No. 4

Alternative Radionuclide Production with a Cyclotron

IAEA TECDOC SERIES

IAEA-TECDOC-1945

IAEA-TECDOC-1945

Therapeutic Radiopharmaceuticals Labelled with Copper-67, Rhenium-186 and Scandium-47

IAEA
International Atomic Energy Agency

T.J. Ruth Nature 457, (2009)
T.J. Ruth, La Physique AU Canada 66, 15 (2010)
https://www-pub.iaea.org/MTCD/publications/PDF/TE-1945web.pdf
https://www-pub.iaea.org/MTCD/Publications/PDF/Pub1589_web.pdf
https://www-pub.iaea.org/MTCD/publications/PDF/P1937_web.pdf

Facility

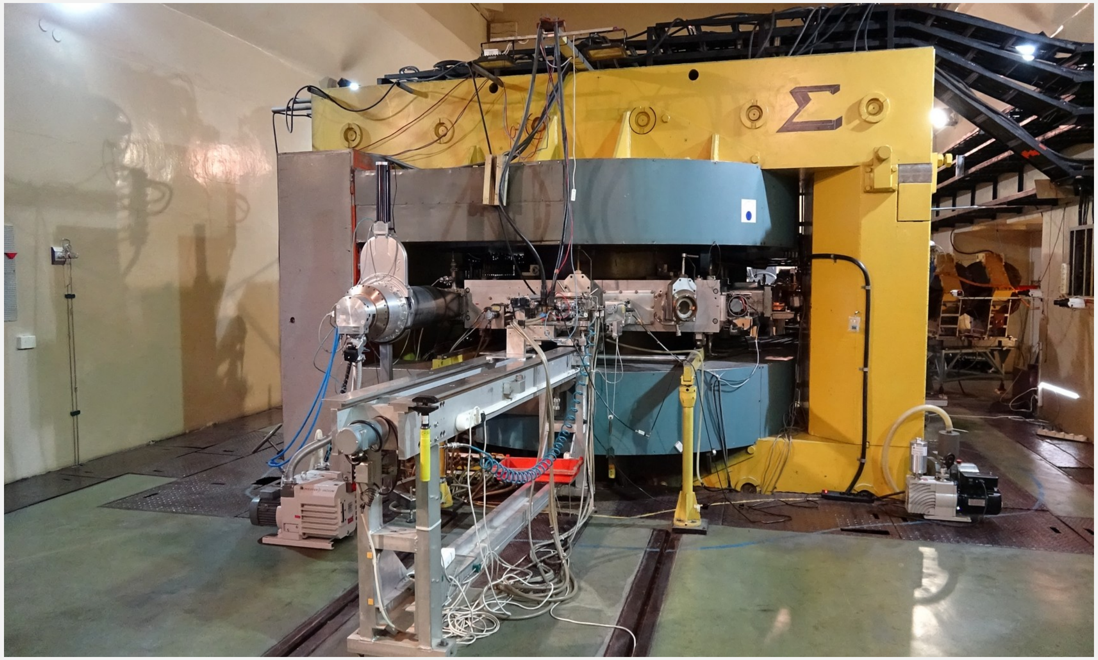


Fig: Cyclotron AIC-144, IFJ-PAN Cracow, Poland

- **Proton Beam parameters**

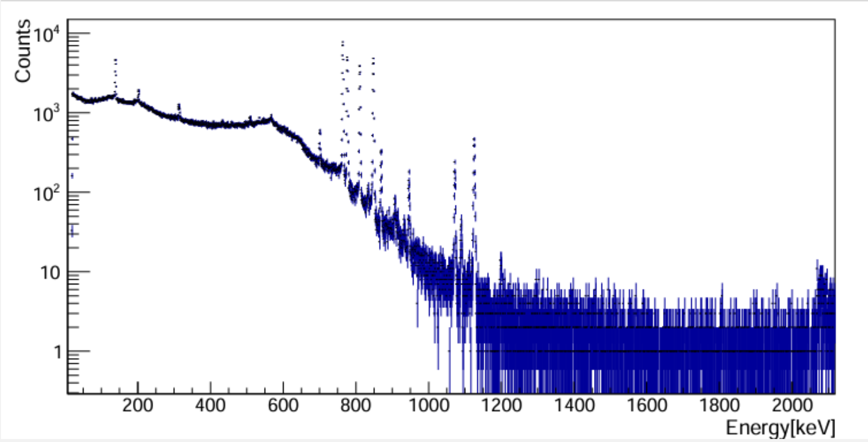
☐Energy – 60 MeV

☐ Current –10 - 30 nA

- Low Z materials are used to degrade the beam energy

Facility

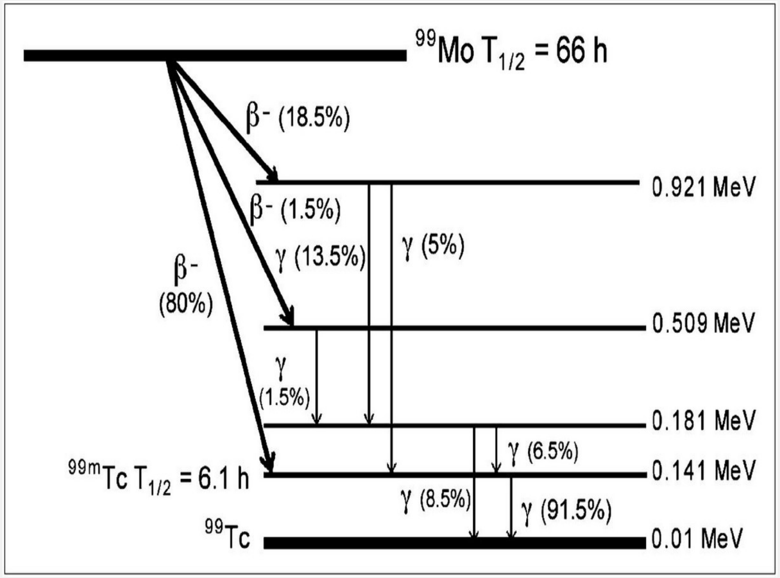
Energy and efficiency calibrated HPGe detector was employed to for gamma-spectroscopy.



Gamma spectra of one of the irradiated targets

Calibration sources => ^{241}Am, ^{133}Ba, ^{109}Cd, ^{60}Co, ^{137}Cs, ^{152}Eu, and ^{22}Na

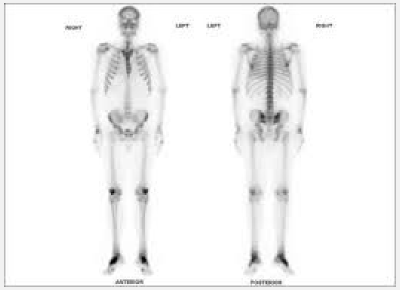
^{99}Mo/^{99m}Tc



→ ^{99m}Tc is widely used radioactive “tracer isotope”

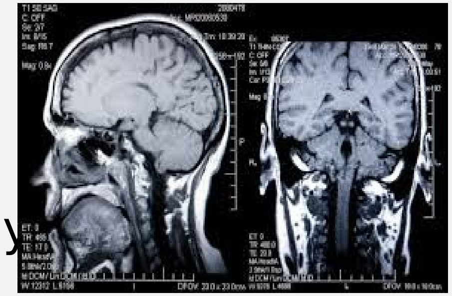
→ Used in more than 80% nuclear medicine imaging procedure

Examples:



Bone scan

SPECT scanning



Brain imaging

$\tau_{(99Mo)}$ = 66 h → Decays to ^{99m}Tc

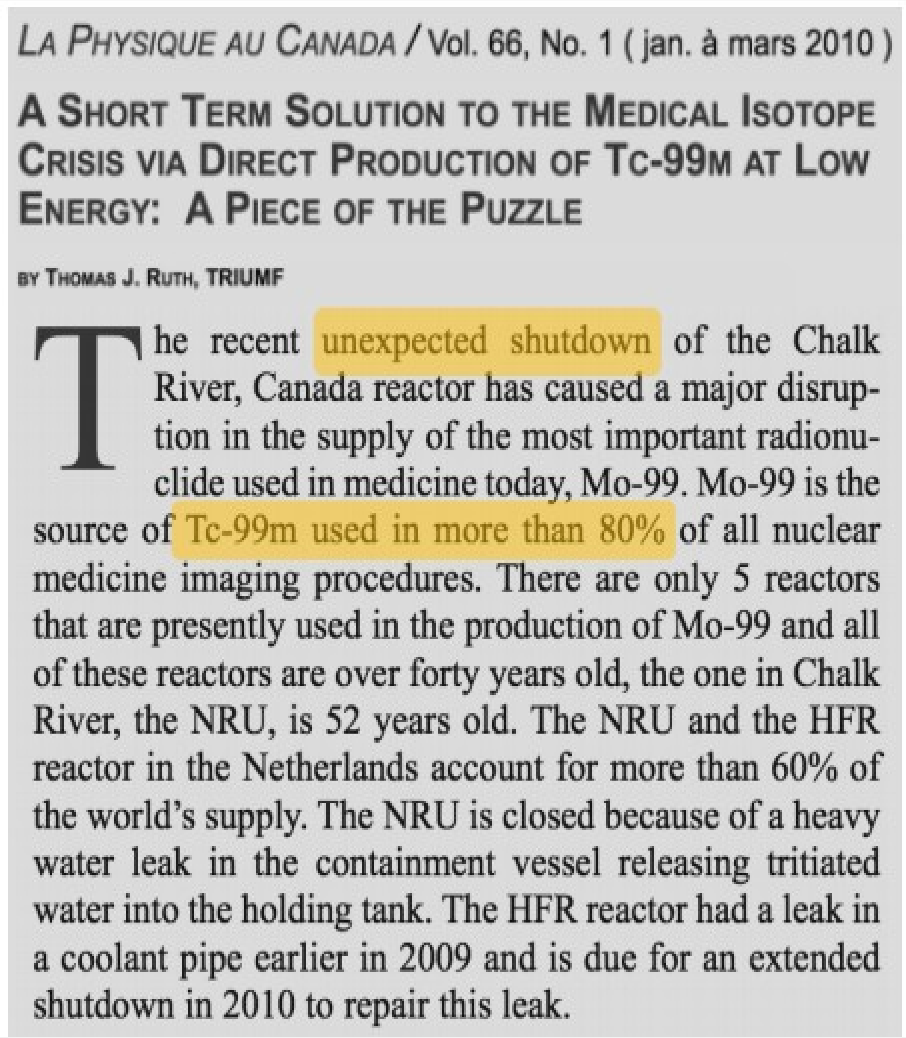
$\tau_{(99mTc)}$ = 6.01 h → fast removal from patient’s body

https://www.medgadget.com/2007/10/symbia_e_series_spect_imager.html

https://www.semc.org/services-directory/imaging-radiology/diagnostic-imaging-center/nuclear-medicine/bone-scan

https://www.britannica.com/science/brain-scanning

^{99}Mo/^{99m}Tc



LA PHYSIQUE AU CANADA / Vol. 66, No. 1 (jan. à mars 2010)

A SHORT TERM SOLUTION TO THE MEDICAL ISOTOPE CRISIS VIA DIRECT PRODUCTION OF TC-99M AT LOW ENERGY: A PIECE OF THE PUZZLE

BY THOMAS J. RUTH, TRIUMF

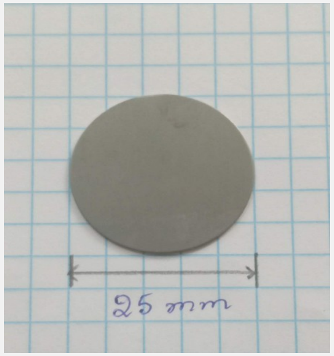
The recent unexpected shutdown of the Chalk River, Canada reactor has caused a major disruption in the supply of the most important radionuclide used in medicine today, Mo-99. Mo-99 is the source of Tc-99m used in more than 80% of all nuclear medicine imaging procedures. There are only 5 reactors that are presently used in the production of Mo-99 and all of these reactors are over forty years old, the one in Chalk River, the NRU, is 52 years old. The NRU and the HFR reactor in the Netherlands account for more than 60% of the world's supply. The NRU is closed because of a heavy water leak in the containment vessel releasing tritiated water into the holding tank. The HFR reactor had a leak in a coolant pipe earlier in 2009 and is due for an extended shutdown in 2010 to repair this leak.

To over come the shortfall IAEA meeting (2010, in Vienna)

- 14 research group assigned
- ^{100}Mo (p,x) ^{99m}Tc/^{99}Mo is best short-term solution

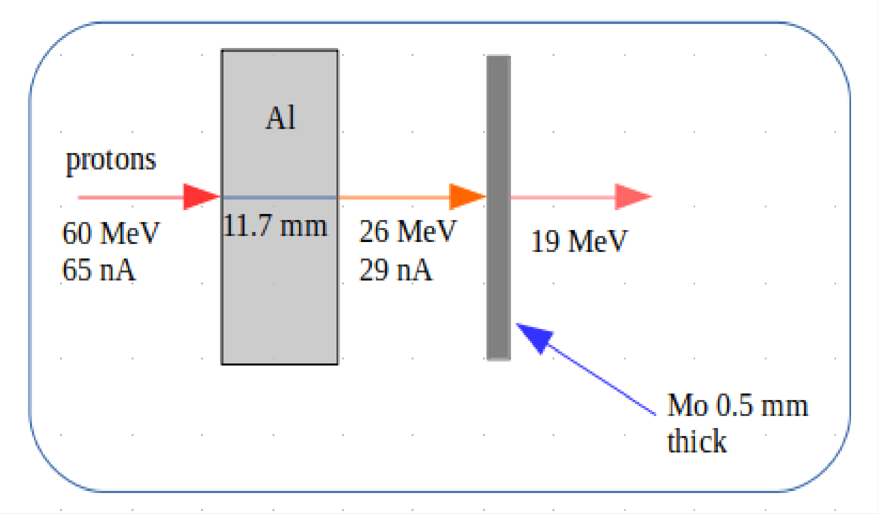
Reported experimental cross section found large discrepancy for proton induced reactions

Single target irradiation



Isotope	Abundance	Isotope	Abundance
^{92}Mo	14.65%	^{97}Mo	9.58%
^{94}Mo	9.19%	^{98}Mo	24.29%
^{95}Mo	15.87%	^{100}Mo	9.74%
^{96}Mo	16.67%	-----	-----

Mo with natural abundance with 0.5 mm thick and 25 mm diameter metallic disc used as target



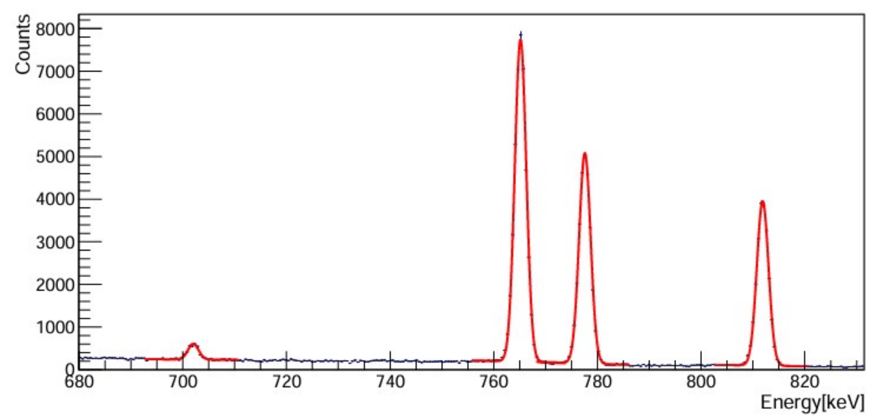
Experimental details

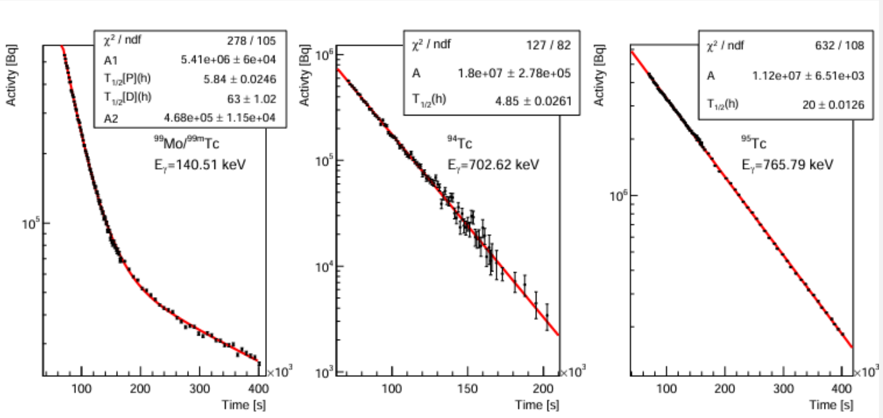
→ Energy range 19-26 MeV

→ 5 hours of irradiation

→ 18 hours of cooling time

Data analysis





$$A_{i,j} = \frac{\dot{n}_{i,j}}{f_j \epsilon_j \tau_j (1 - e^{-t_{\mathrm{meas},i}/\tau_j})},$$

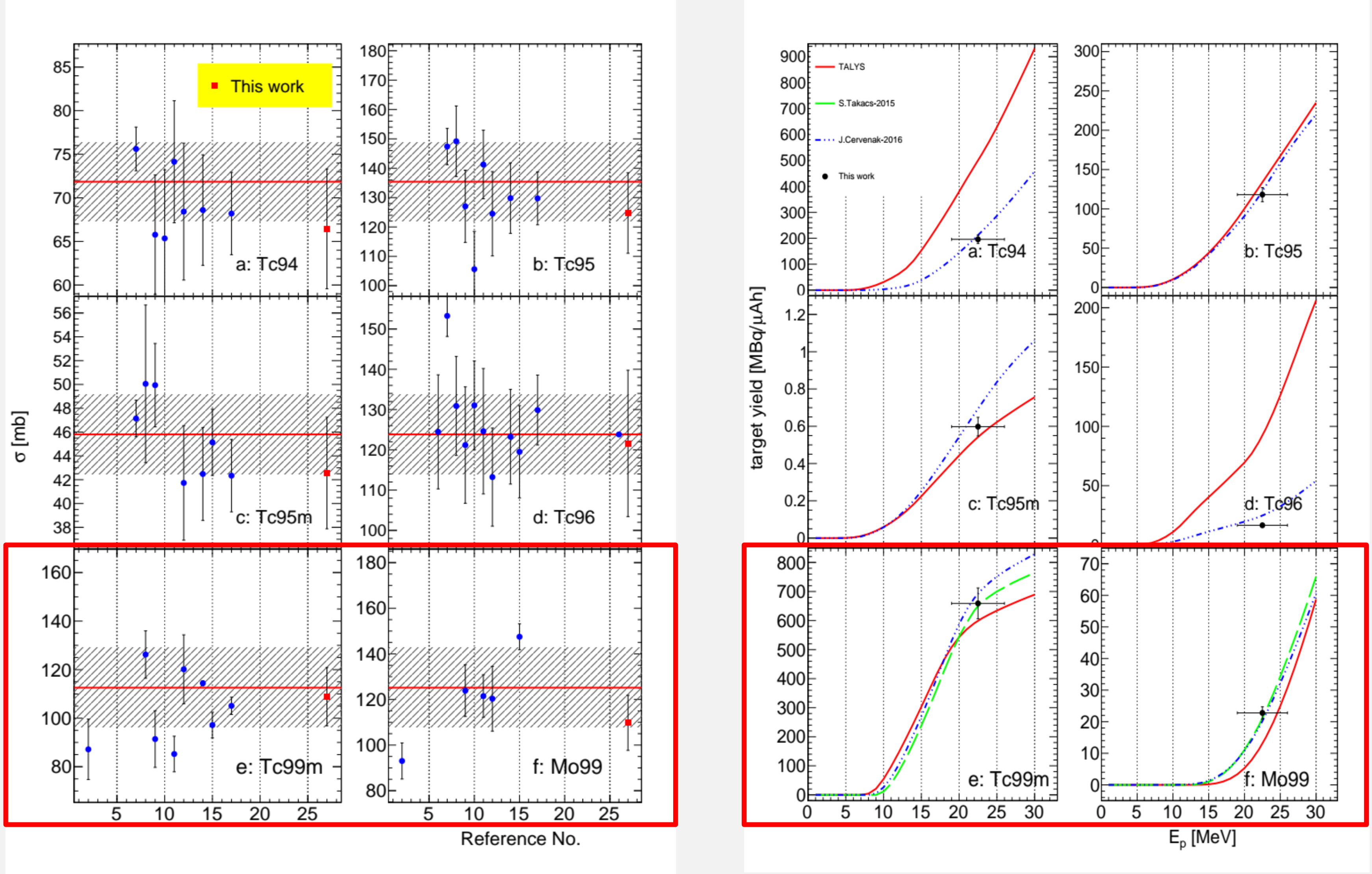
Reaction cross section and target yield

$$\sigma(E) = \frac{Z \cdot e \cdot M \cdot A_{\mathrm{EOB}}}{H \cdot N_A \cdot \rho \cdot d \cdot I \cdot (1 - e^{(-\lambda \cdot t_{irr})})}.$$

$$TY(E) = \frac{A_{\mathrm{EOB}}}{I \cdot \tau \cdot (1 - e^{-\lambda \cdot t_{irr}})}.$$

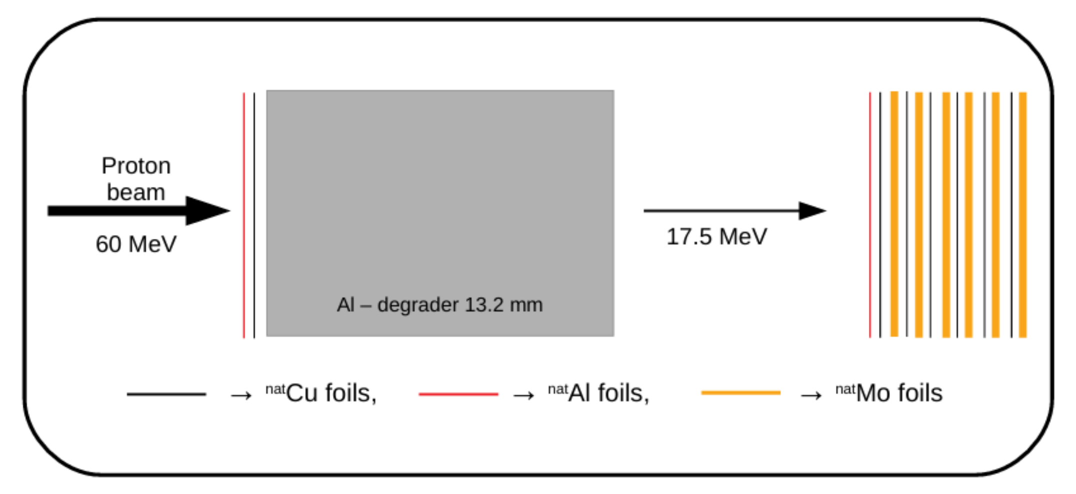
- Z atomic number of the projectile
- e elementary charge
- M atomic mass of the target material
- H abundance of the target
- N_A Avogadro's number
- ρ target density [g/cm^3]
- d target thickness [μm]
- I beam current [μA]
- λ decay constant of the radioisotope [s^{-1}] and
- t_{irr} irradiation time [s].

Single target irradiation



Cross section of radionuclide produced through $^{nat/100}$Mo (p, x) reactions averaged over the proton energy range 19-26 MeV where panels a, b, c, d, e and f respectively represent cross sections of ^{94}Tc, ^{95}Tc, ^{95m}Tc, ^{96}Tc, ^{99m}Tc and ^{99}Mo. The Grey band represents standard deviation of literature data.

Stack-foil activation



→ Energy range 0-17 MeV

→ 5 hours of irradiation

→ 2 hours of cooling time

→ Stack foil activation technique

→ Cu foils are used to monitor the beam current.

Stack-foil activation

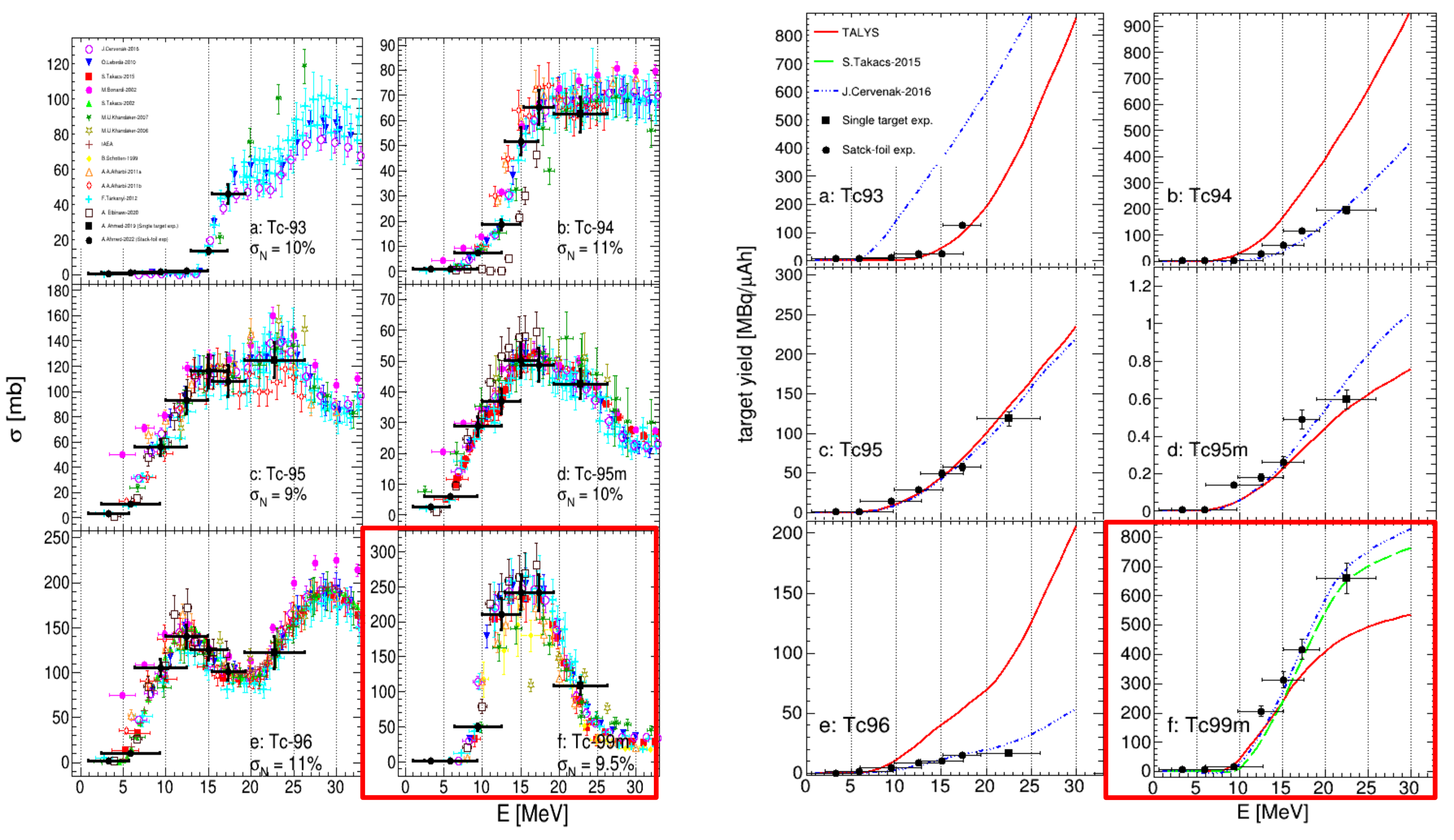


Fig.: Production cross-section and yield of ^{nat}Mo(p, x) reactions. Here, the horizontal error bars represent the range of energy degradation within the ^{nat}Mo target.

Stack-foil activation

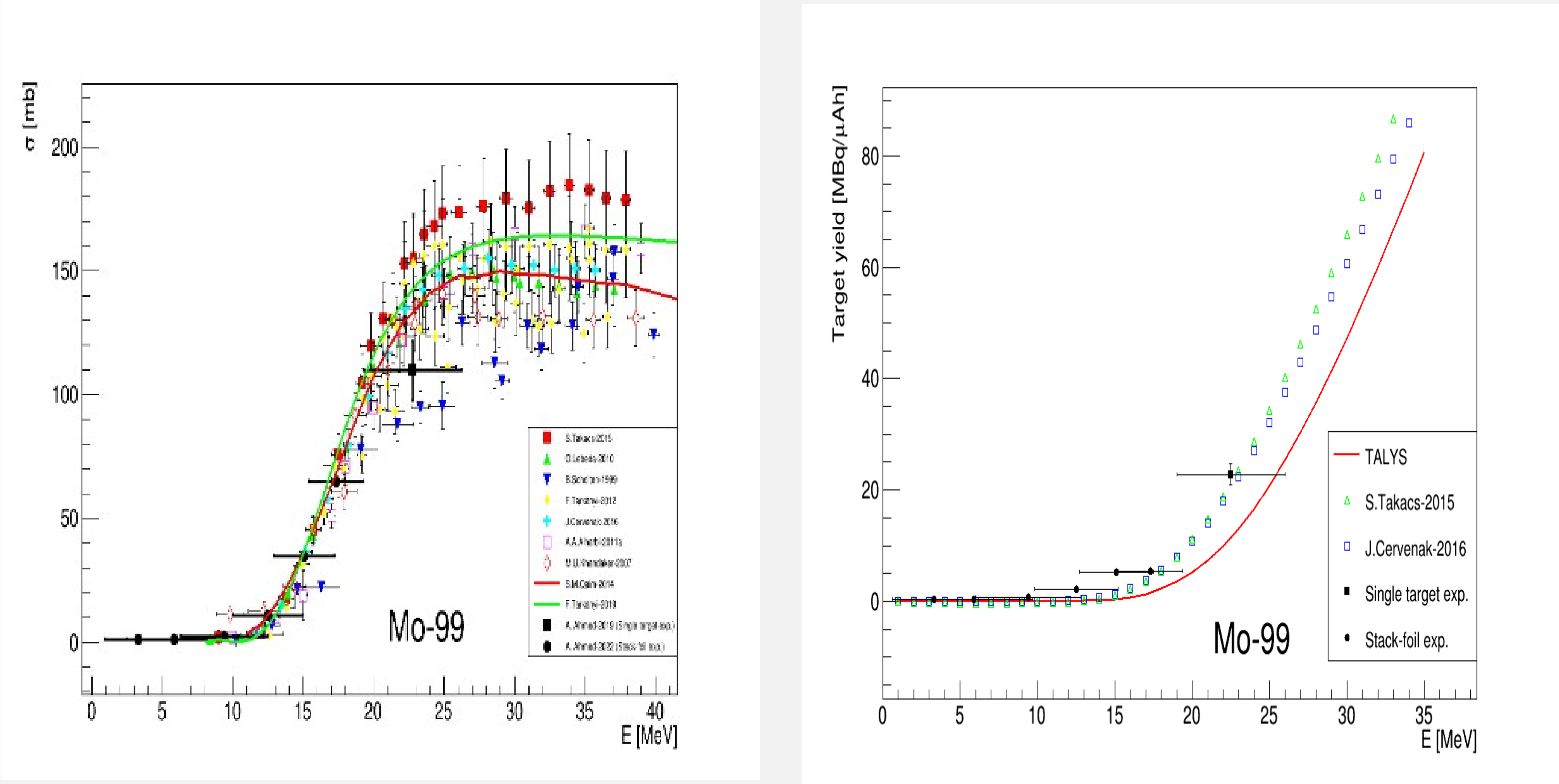


Fig.: Production cross-section and yield of ^{nat}Mo(p, x)^{99}Mo reactions. Here, the horizontal error bars represent the range of energy degradation within the ^{nat}Mo target.

^{47}Sc radioisotope

Look for ^{99m}Tc like radionuclides

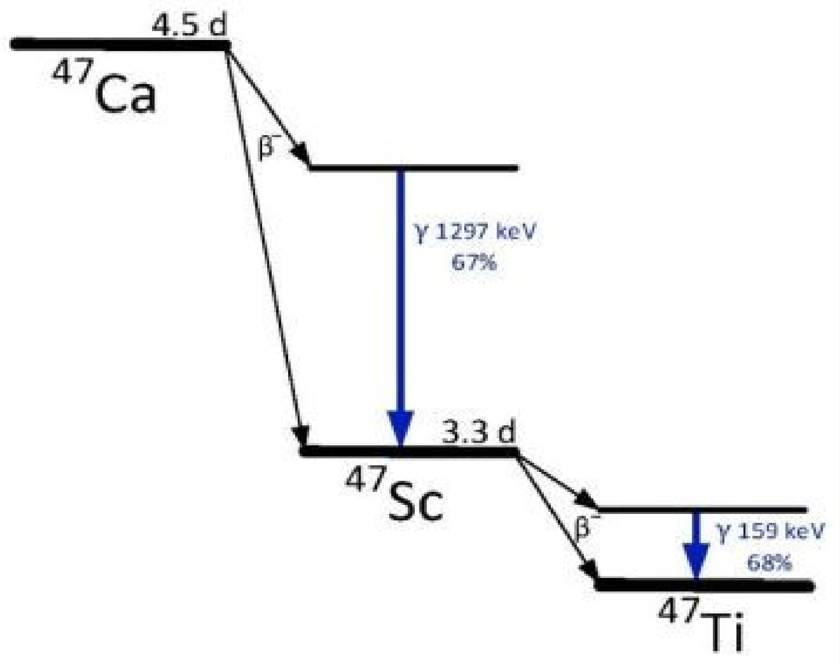


Fig: Decay scheme of ^{47}Sc

→ $T_{1/2}(^{47}Sc)$ = 3.3 days

→ E_γ = 159 keV

→ E_β = 440, 600 keV

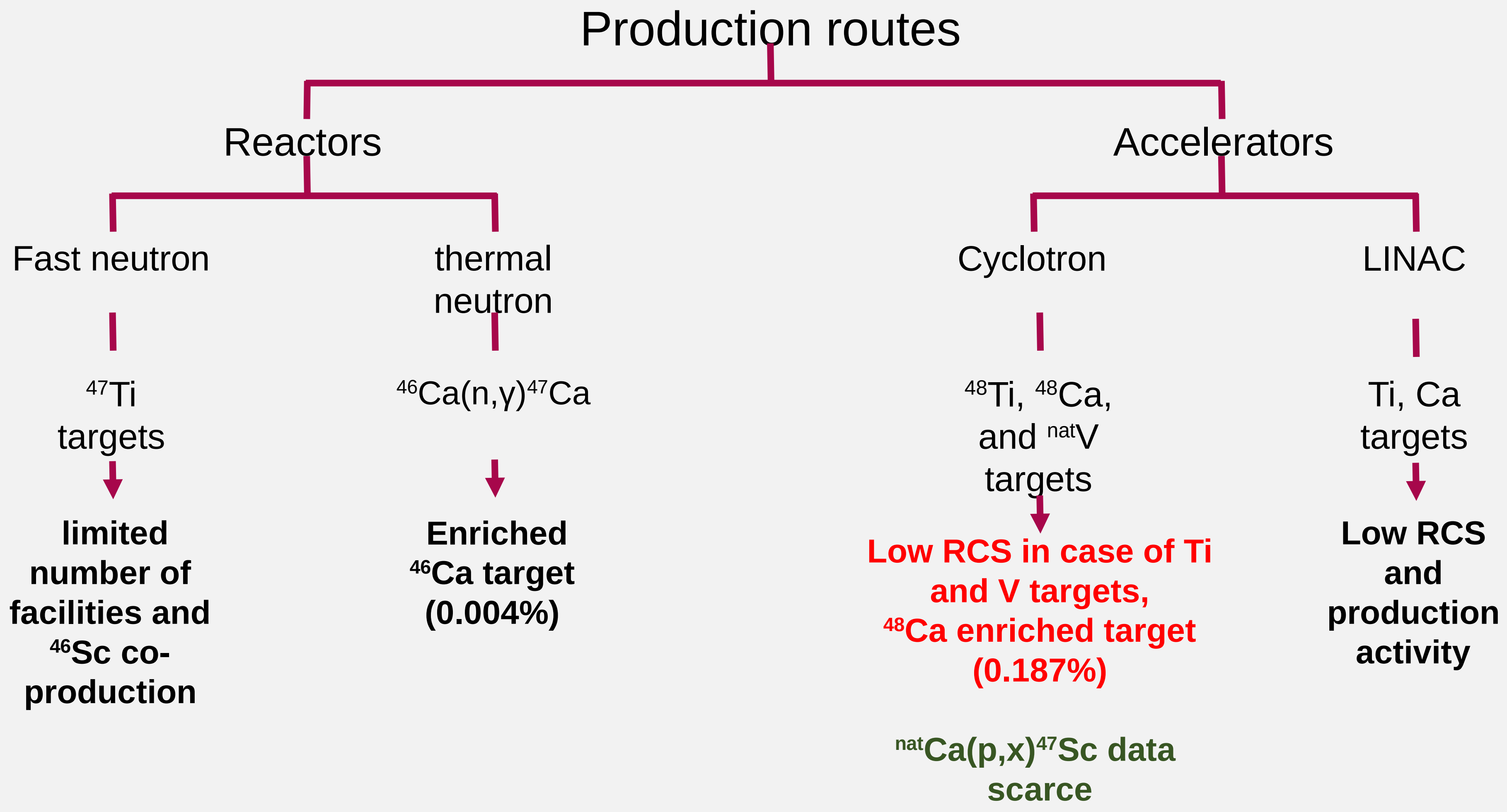
→ ^{47}Ca/^{47}Sc generator

→ Chemistry similar to ^{177}Lu

→ ^{44,47}Sc pair or ^{47}Sc good theranostic radionuclides

https://www.chemistry.msu.edu/faculty-research/faculty-members/severin-greg.aspx

^{47}Sc radioisotope



Production routes

Reactors

Fast neutron

^{47}Ti targets

limited number of facilities and ^{46}Sc co-production

thermal neutron

^{46}Ca(n,γ)^{47}Ca

Enriched ^{46}Ca target (0.004%)

Accelerators

Cyclotron

^{48}Ti, ^{48}Ca, and ^{nat}V targets

Low RCS in case of Ti and V targets, ^{48}Ca enriched target (0.187%)

^{nat}Ca(p,x)^{47}Sc data scarce

LINAC

Ti, Ca targets

Low RCS and production activity

https://doi.org/10.1186/s41181-021-00131-2

^{47}Sc radioisotope

Experimental details

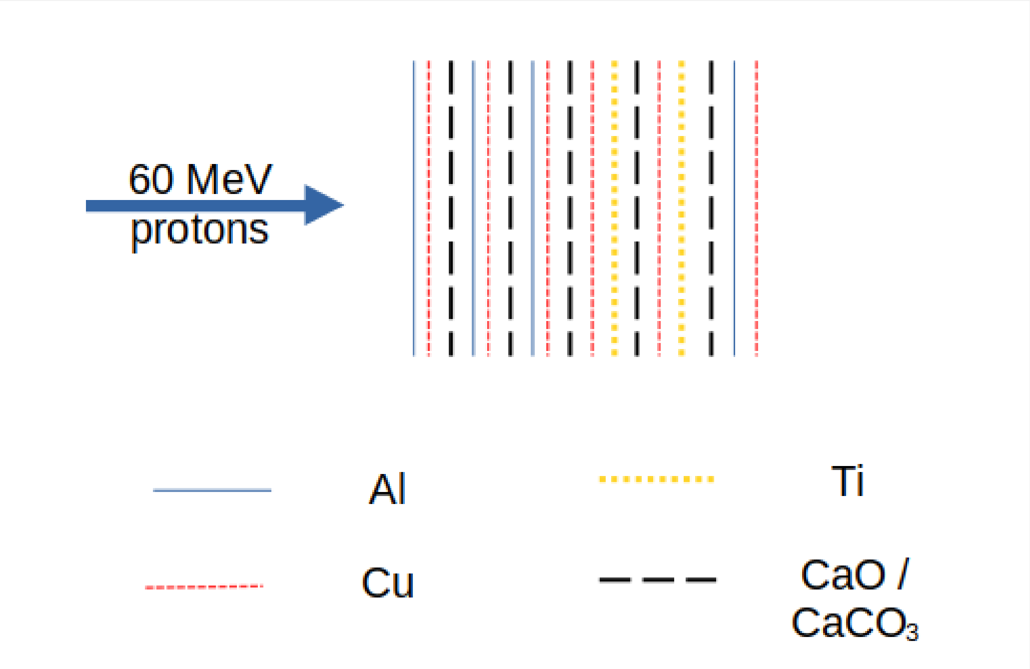
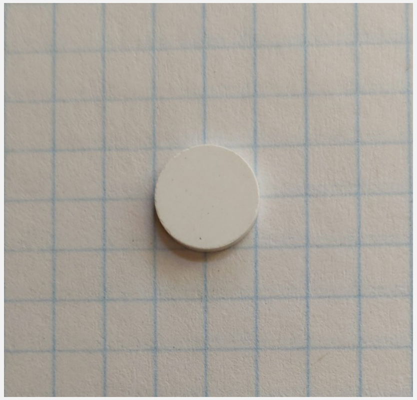


Fig: Schematics stack foil activation method



Monitoring reactions

→ ^{nat}Al (p,x) ^{22,24}Na

→ ^{nat}Cu (p,x) ^{56,58}Co, ^{65}Zn

→ ^{nat}Ti (p,x) ^{48}V

^{47}Sc radioisotope

Ca Targets

Table: Isotopic abundance of ^{nat}Ca

Isotopes	Abundance (%)
^{40}Ca	96.941
^{42}Ca	0.647
^{43}Ca	0.135
^{44}Ca	2.086
^{46}Ca	0.004
^{48}Ca	0.187

Table: Chemical admixtures in the Ca compounds

Elements	Content (%)	
	CaO	$CaCO_3$
Cl		0.01
SO_4		0.1
As	0.0003	0.0005
Ba		0.01
Zn	0.002	0.01
Cu	0.001	0.001
Pb	0.001	0.0001
K		0.05
Na		0.05
Sr		0.1
Fe		0.003

^{47}Sc radioisotope

CaO

→ **16 – 60 MeV** proton energy range

→ 5 h irradiation

→ **34.4 nA** beam current

→ 15 data points

→ Target dimesions

0.10 – 0.21 g

0.7 ± 0.3 mm thick

10.0 ± 0.1 mm diameter

$CaCO_3$

→ **0 – 61 MeV** proton energy range

→ 5 h 15 min irradiation

→ **26.8 nA** beam current

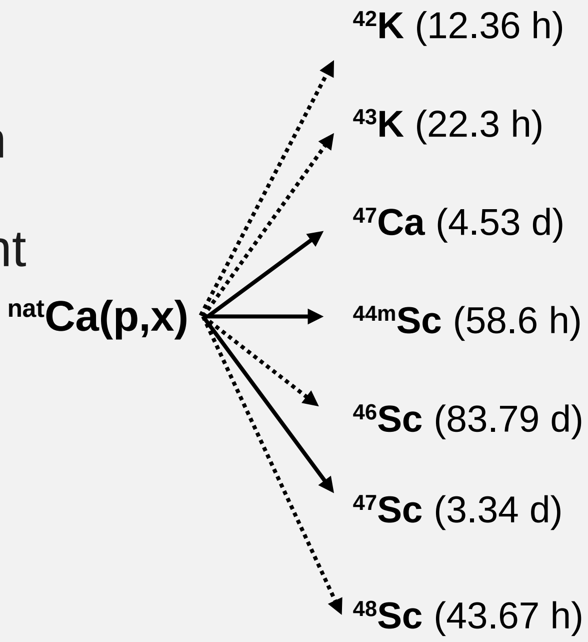
→ 17 data points

→ Target dimensions

0.10 – 0.22 g

0.7 ± 0.2 mm

10.0 ± 0.1 mm diameter



^{nat}Ca(p,x)

^{42}K (12.36 h)

^{43}K (22.3 h)

^{47}Ca (4.53 d)

^{44m}Sc (58.6 h)

^{46}Sc (83.79 d)

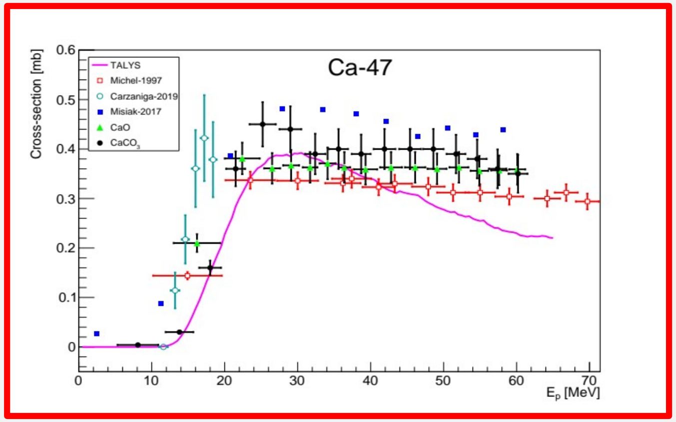
^{47}Sc (3.34 d)

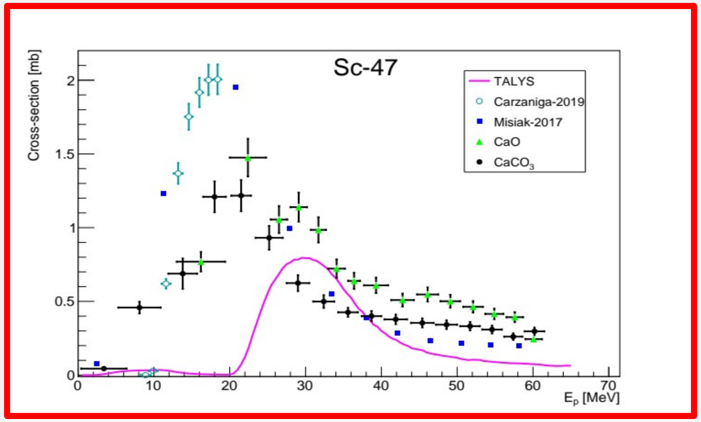
^{48}Sc (43.67 h)

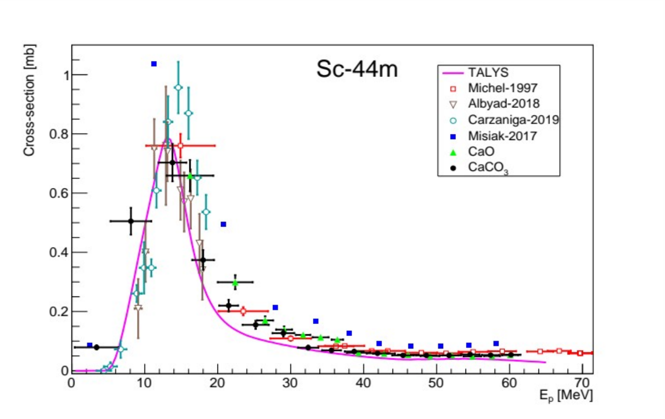
^{47}Sc radioisotope

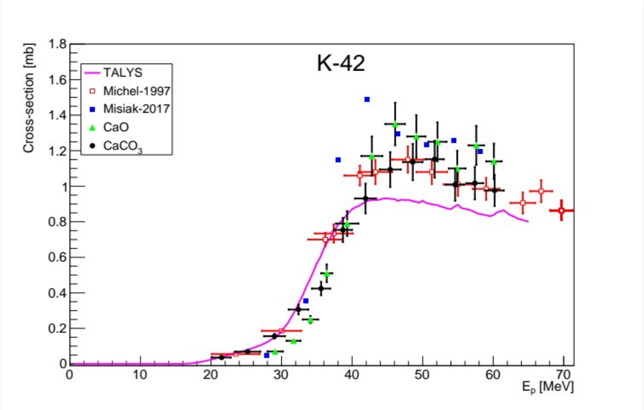
Results

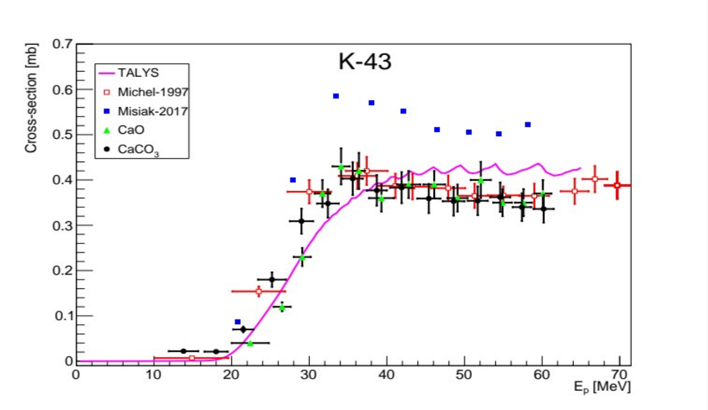
Reaction cross-sections

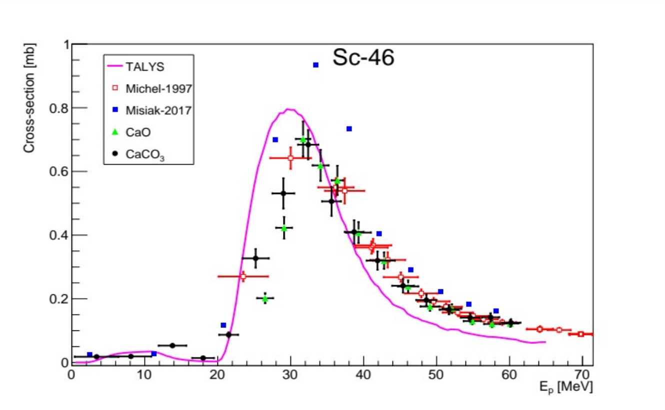






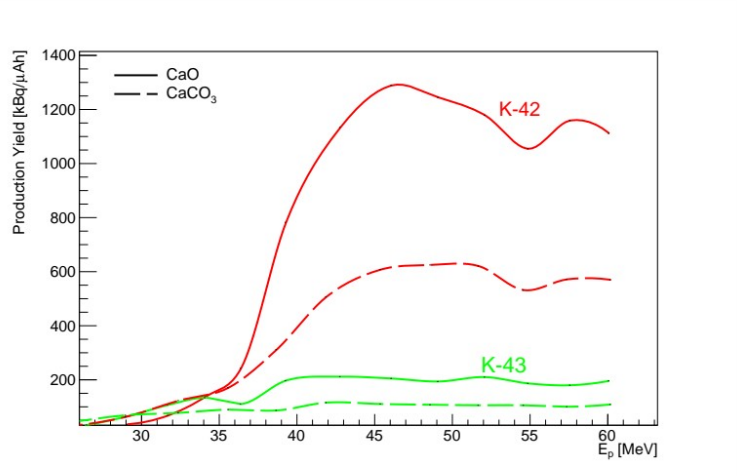


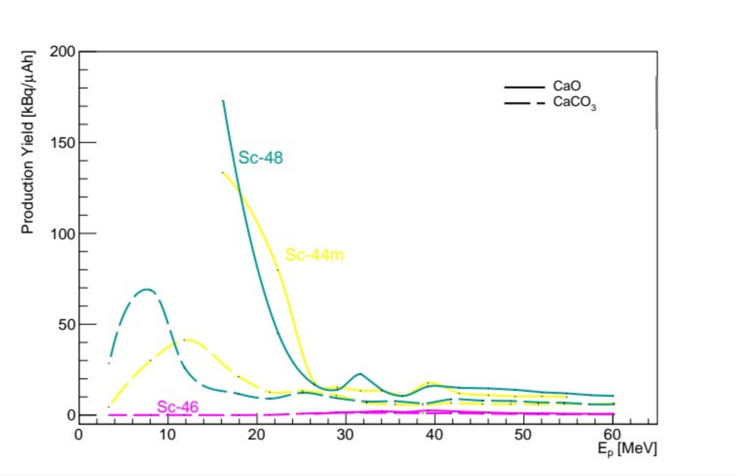


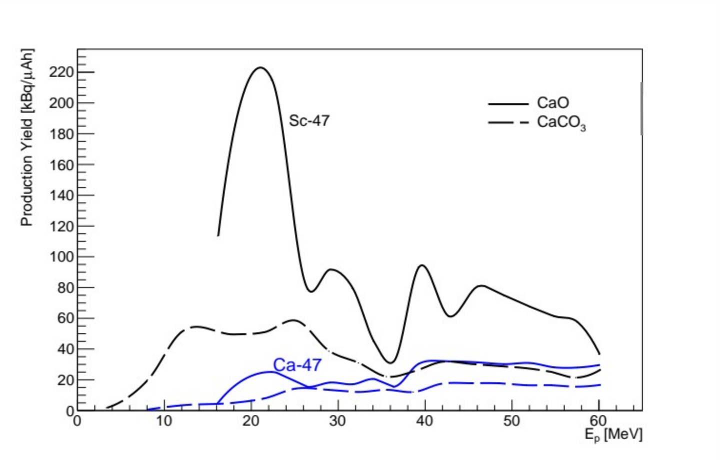


^{47}Sc radioisotope

Target yield







Ge (p,x) reactions

Experimental details

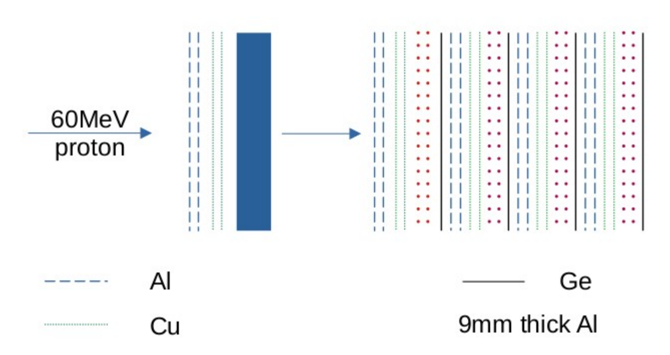


Fig: Schematics of one of the experiments using Ge targets

^{70}Ge

^{nat}Ge

Isotopes	Abundance (%)	
	^{nat}Ge	^{70}Ge
^{70}Ge	20.37	95.56
^{72}Ge	27.31	4.36
^{73}Ge	7.76	0.04
^{74}Ge	36.73	0.03
^{76}Ge	7.83	0.01

Ge (p,x) reactions

^{nat}Ge

- → **14 – 60 MeV** proton energy range
- → 5 h irradiation
- → 18.5 **nA** beam current
- → 10 data points
- → Target dimesions

  0.11 – 0.29 g

  1.1 ± 0.3 mm and 0.5 ± 0.1 thick

  8.0 ± 0.1 mm diameter

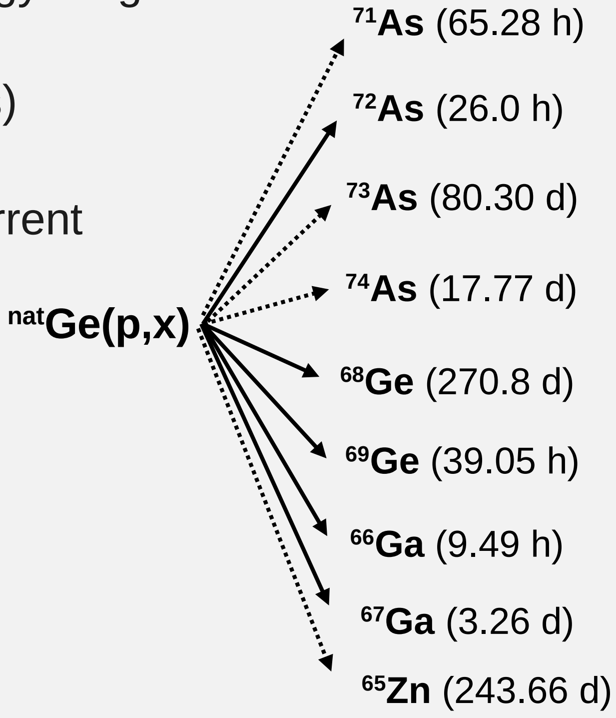
^{70}Ge (95%)

- → 4 – **53 MeV** proton energy range
- → 5 h irradiation (2 satges)
- → 0.4 and 10 **nA** beam current
- → 8 data points
- → Target dimensions

  0.45 ± 0.01 g

  1.0 ± 0.2 mm

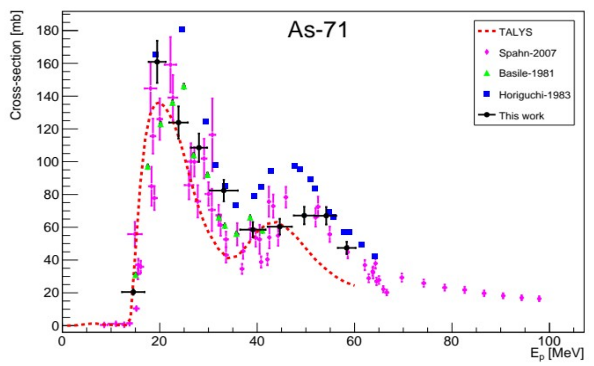
  10.0 ± 0.1 mm diameter

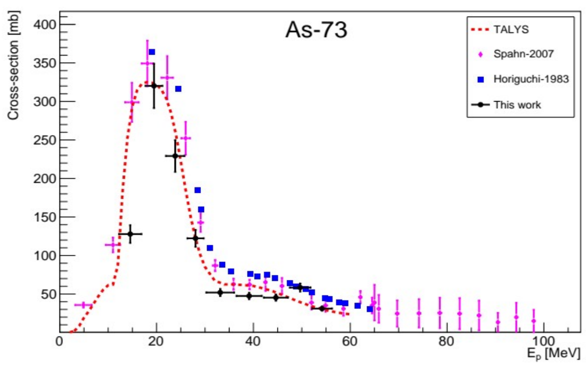


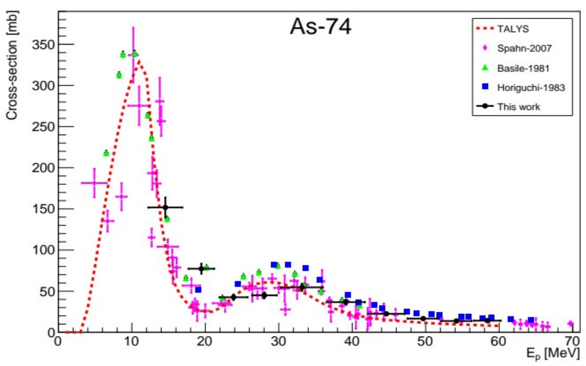
^{nat}Ge (p,x) reactions

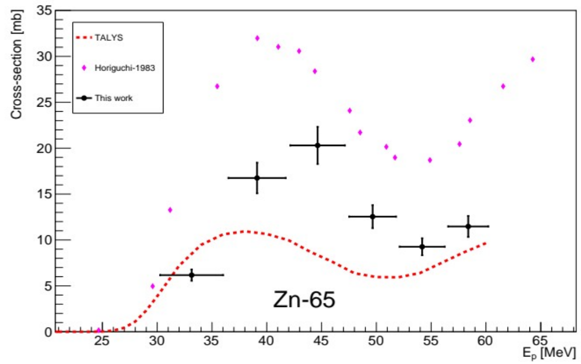
Results

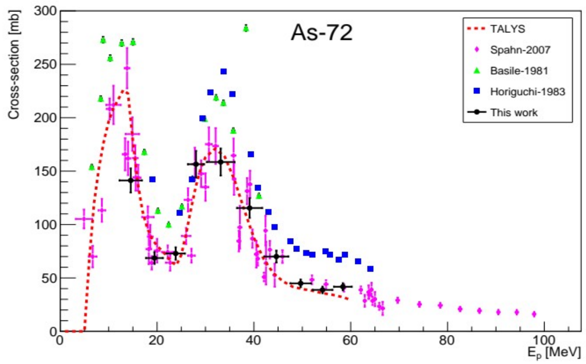
Reaction cross-sections









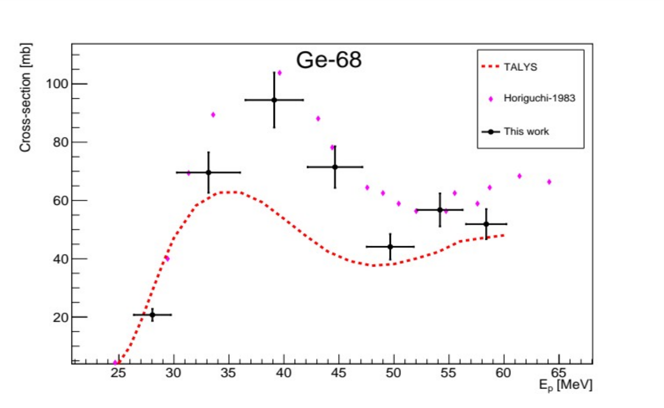


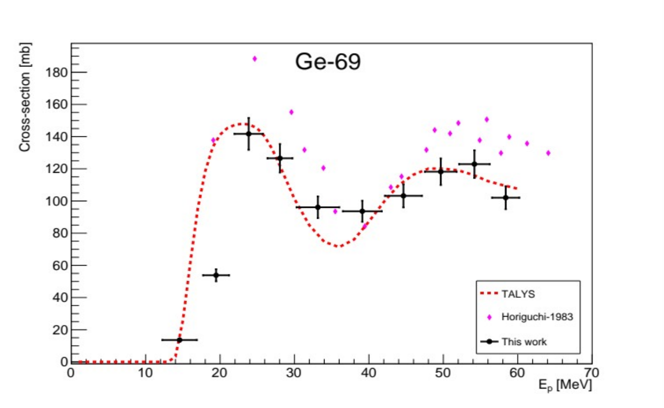
^{72}As Promising positron emitters

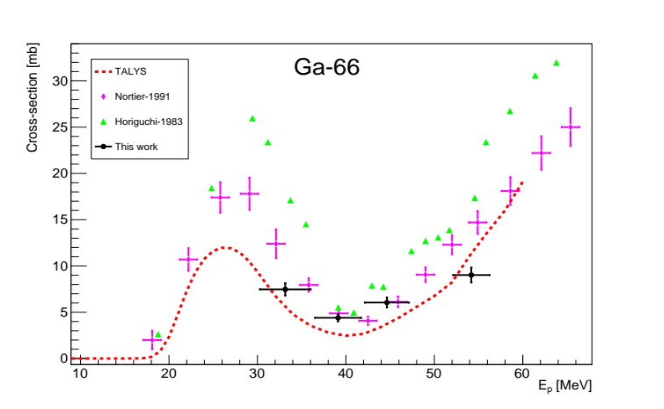
^{nat}Ge (p,x) reactions

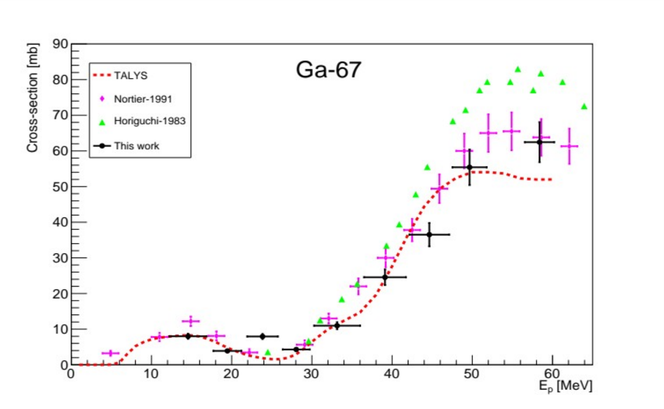
Results

Reaction cross-sections







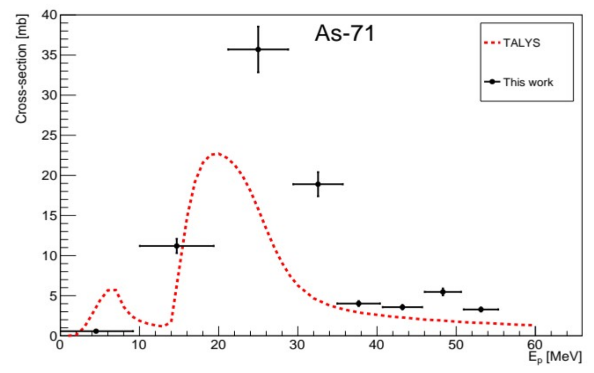


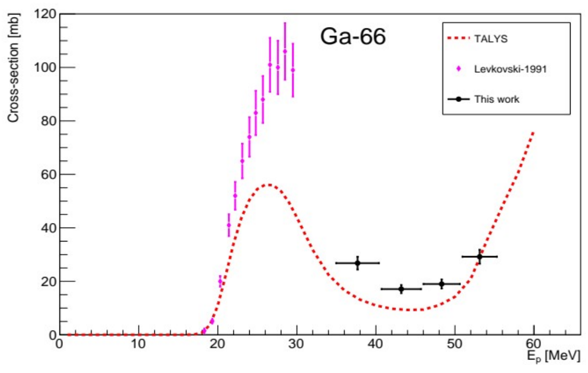
- ^{66,67}Ga, ^{69}Ge are Promising positron emitters
- ^{68}Ge will be the radio generator for ^{68}Ga

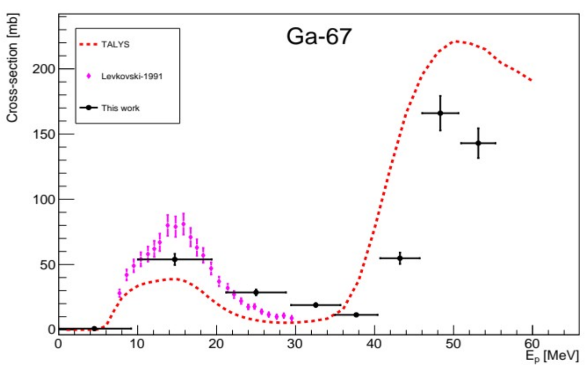
^{70}Ge (p,x) reactions

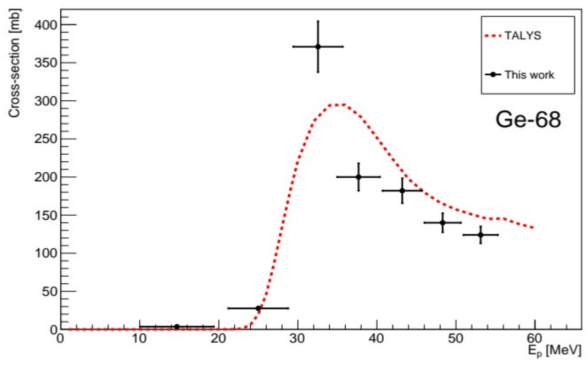
Results

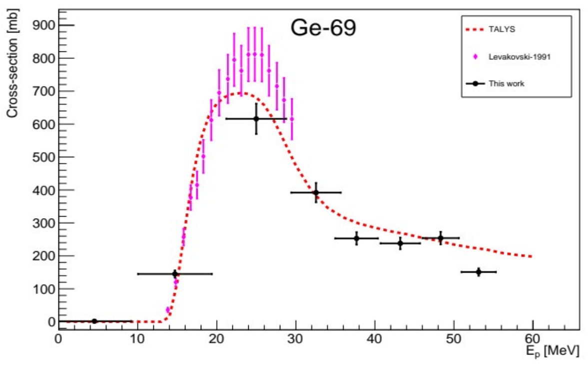
Reaction cross-sections











Conclusions

→ Experiments using proton beam of AIC-144 accelerator on different target materials are conducted for the study of production of radioisotopes was conducted.

→ It was demonstrated that use of ^{nat}Mo target could provide very pure ^{99}Mo source for extraction of ^{99m}Tc with standard methods.

→ Proton-induced reaction cross-section data for ^{47}Sc medical radionuclide was measured on ^{nat}CaO and ^{nat}CaCO$_3$ materials

→ CaO target are more favorable

→ Using ^{nat}Ge target one could produce multiple medical radionuclides such ^{72}As, ^{66,67}Ga, and ^{68,69}Ge

→ https://doi.org/10.1016/j.radphyschem.2025.112594
https://doi.org/10.1088/1361-6471/ada8c6
https://doi.org/10.1016/j.radphyschem.2023.111290
https://doi.org/10.1016/j.radphyschem.2023.110821
https://doi.org/10.1016/j.radphyschem.2021.109774
https://doi.org/10.5506/AphysPolB.50.1583

Thank You

References

2. S. Takács et al. Nucl. Instrum. Meth. 2002; B 198: 183-196.

3. M. Bonard et al. Appl. Radiat. Isot. 2002; 57: 617-635.

6. A. A.Alharbi et al. Radiochim. Acta 2011 99: 763-770.

7. A. A.Alharbi et al. Radioisotopes – Applications in Bio-Medical Science. Prof. Nirmal Singh (Ed.), ISBN: 978-953-307-748-2.

8. F. Tárkányi et al. Nucl. Instrum. Meth. 2012; B280: 45-73.

9. P. Chodash et al. Appl. Radiat. Isot. 2011; 69: 1447-1452

10. S. M. Qaim Nucl. Med. Biol. 2017; 44: 31-49.

11. O. Lebeda et al. Appl. Radiat. Isot. 2010; 68: 2355-2365.

12. S. Takács et al. Nucl. Instrum. Meth. 2015; B347: 26-38.

13. K. Szkliniarz et al. Modern Phys. Letters. A 2017; 32(17):

1740012-1-1740012-11.

14. J. Červenák et al. Nucl. Instrum. Meth. 2016; B380: 32-49.

15. S. M. Qaim et al. Appl. Radiat. Isot. 2014; 85: 101-113.

17. M. C. Lagunas-Solar et al. Appl Radiat Isot 1991; 42(7): 643-657.

26. Experimental nuclear reaction data (EX-FOR), 2018. Database version of November 29.2018. Available at:

https://www-nds.iaea.org/exfor/exfor.htm