Academy of Sciences of the Czech Republic
Nuclear Physics Institute
Department of radiopharmaceuticals

Review of nuclear data measurements on the cyclotron U-120M and our contribution to CRP project

Ondřej Lebeda

1ST COORDINATION RESEARCH MEETING ON *NUCLEAR DATA FOR CHARGED-PARTICLE MONITOR REACTIONS AND MEDICAL ISOTOPE PRODUCTION*, IAEA, VIENNA 3.–7. DECEMBER 2012

NUCLEAR PHYSICS INSTITUTE—A SHORT REVIEW

Nuclear Physics Institute of the Czech Academy of Sciences was founded in 1955 as a national centre for the basic and applied research in nuclear physics and related fields.

Today, it has 260 emploees, from those ca 90 researchers, 40 people with master degree and 30 PhD students.

It consists of seven following departments:

- Department of Theoretical Physics
- Department of Nuclear Spectroscopy (STAR, ALICE, KATRIN, HADES, NAA)
- Department of Neutron Physics *(*including *Tandetron* group*)*
- Department of Nuclear Reactions (astrophysics, neutron generators)
- Department of Radiation Dosimetry (DNA damage, dose calculations)
- Department of Accelerators *(cyclotron, microtron)*
- Department of Radiopharmaceuticals (founded 1997)

BACKGROUND AND CIRCUMSTANCES

- High need of the home-produced short-lived radiopharmaceuticals for Czech hospitals, in particular for PET, since 1995 triggered off interest in extension of the U-120M cyclotron use.
- Flexibility of the U-120M cyclotron for irradiation of both internal and external target systems (solid, liquid or gas targets) resulted in its continuous reconstruction and upgrade finished in 2003 by its conversion to H^-/D^- machine; it is by origin the only existing prototype built in Dubna in 1977.
- Availability of the reactor produced radionuclides by irradition at the LWR research reactor in the neighbouring Nuclear Research Institute, Řež allows for research of some reactor radionuclides based radiopharmaceuticals as well.

OUR APPROACH TO THE RADIONUCLIDES PRODUCTION FOR MEDICAL PURPOSES I

- Research, development and routine production of the radiopharmaceuticals labelled either by short-lived, or hardly available radionuclides with high potential in diagnostics and therapy
- Introduction or widespread of established methods in diagnostics into clinical practice in our country: PET – ^{18}F (FDG, FLT, F$^-$, FMISO, FET, FDOPA); SPECT – generator ^{81}Rb/^{81m}Kr, ^{123}I (I$^-$, MIBG)
- Research of therapeutic (^{67}Cu, ^{177}Lu, ^{211}At, ^{230}U) and diagnostic (^{44,47}Sc, ^{61,64}Cu, ^{86}Y, ^{68}Ga, ^{76}Br, ^{123,124}I, etc.) radionuclides and/or their compounds; involving interdisciplinary studies
- Since 2009, routine production of radiopharmaceuticals was transfered to RadioMedic Ltd., subsidiary company of NPI

OUR APPROACH TO THE RADIONUCLIDES PRODUCTION FOR MEDICAL PURPOSES II

- Since 2001, much attention has been paid to design, construction and operation of our own targets for production of medical radionuclides.
- In 2005, the potential of the cyclotron U-120 for measuring excitation functions was recognized again, and the first activities in this direction were started.
- Since 2001, we have developed our own targets for production of ^{18}F, ^{81,83}Rb, ^{61,64,67}Cu, ^{68}Ga, ^{86}Y, ^{123,124}I, ^{211}At and occasionally we produced other RN.
- Since 2004, we measured following excitation functions: ^{75}As(^{3}He,2n)^{76}Br, ^{nat}Mo(p,x) and ^{nat}Mo(d,x), ^{231}Pa(p,2n)^{230}U and ^{231}Pa(d,3n)^{230}U, ^{nat}Nd(p,x), ^{165}Ho(^{3}He,xn) and ^{159}Tb(^{3}He,x).

CYCLOTRON U-120M AND ITS UPGRADES

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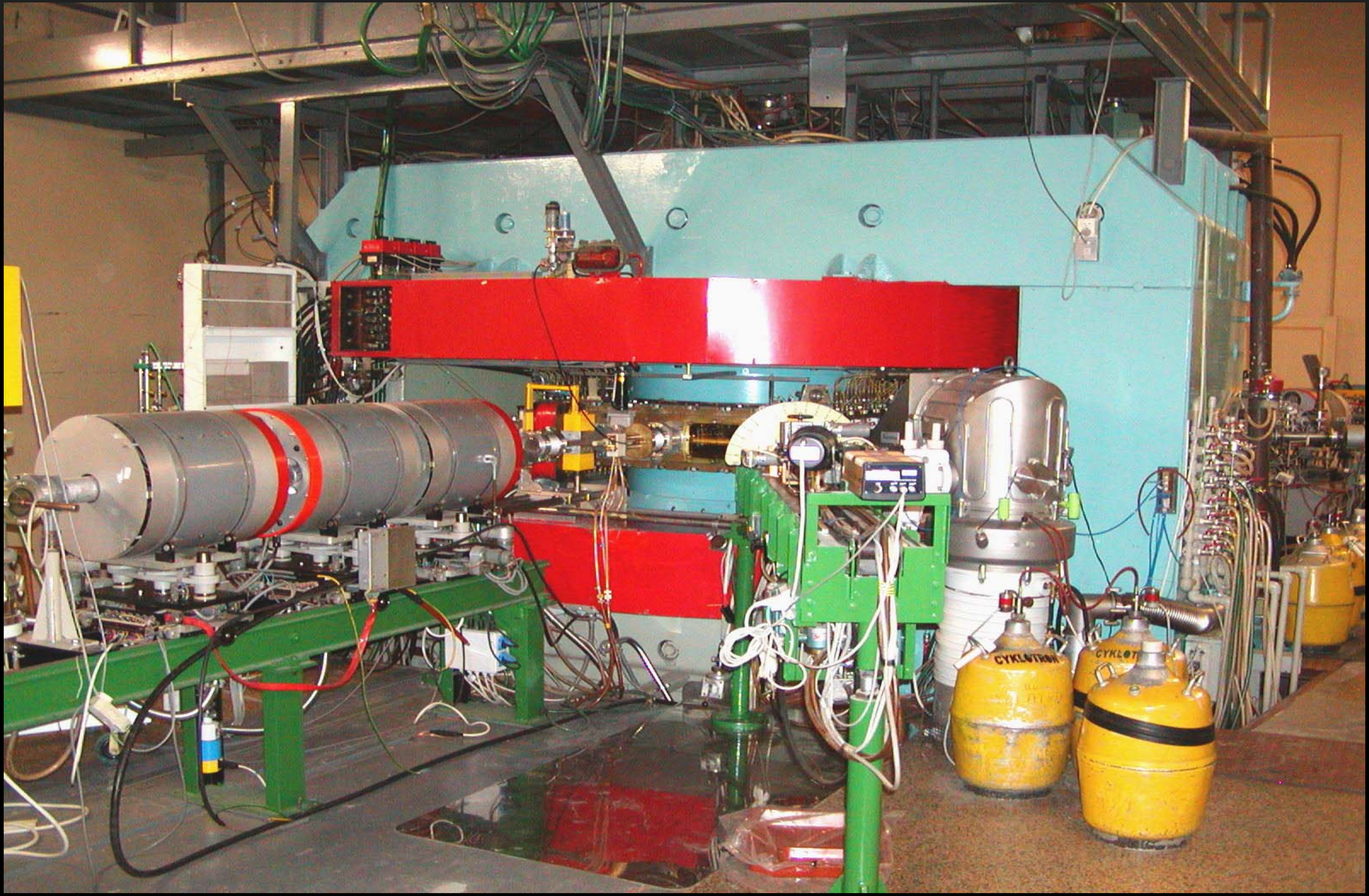
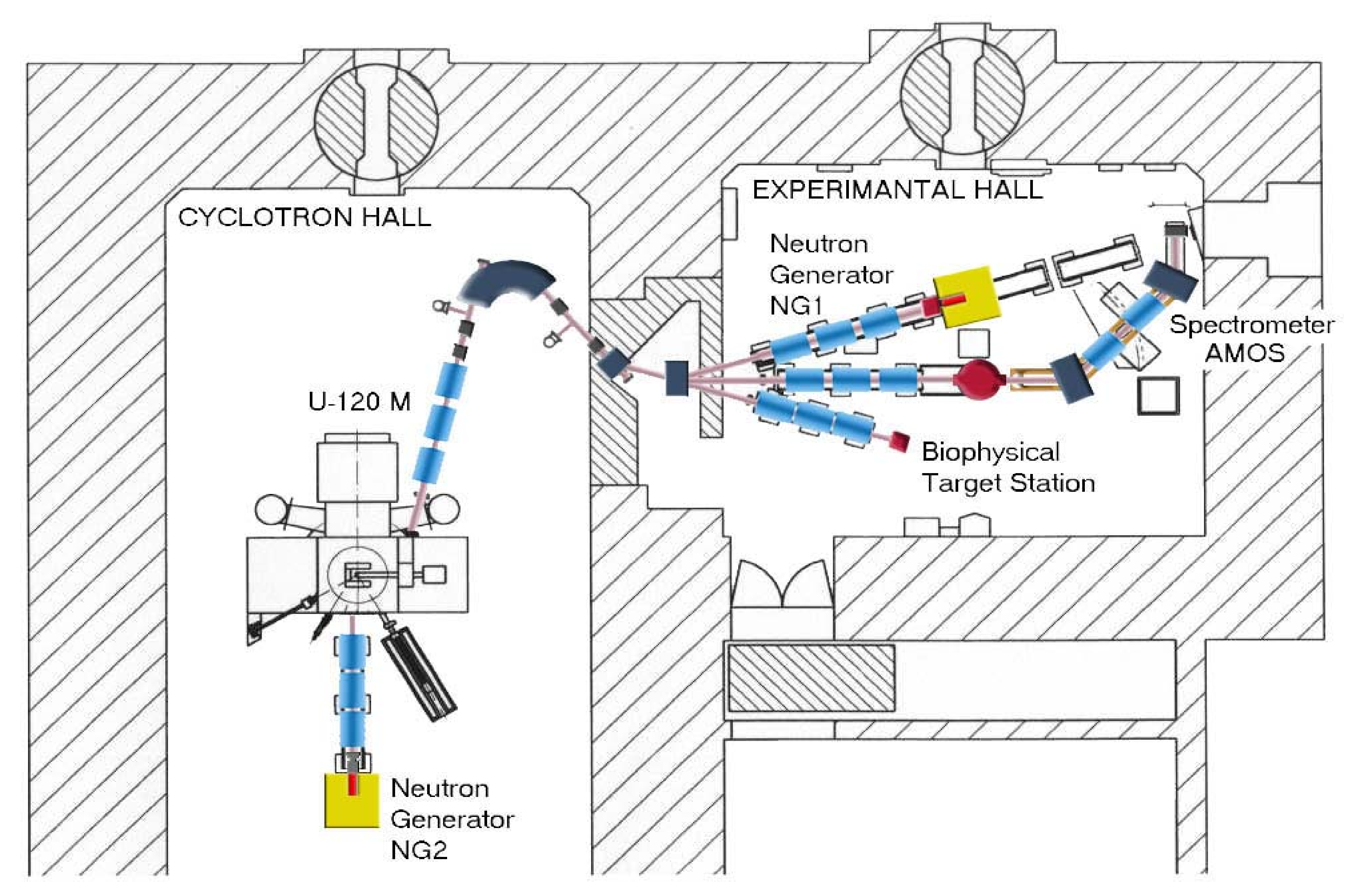
CYCLOTRON U-120M



LAYOUT OF THE CYCLOTRON U-120M



BEAM PARAMETERS

ion	E [MeV]	I_{max} [μA]
p (internal beam)	1–37	> 200
p (external beam)	6–25	5
H^-/H^+ (ext. beam)	6–37	50–30
d (internal beam)	2–20	> 80
d (external beam)	12–20	5
D^-/D^+ (ext. beam)	11–20	35–20
^{3}He (internal beam)	3–55	20
^{3}He (external beam)	18–52	2
α (internal beam)	4–40	40
α (external beam)	24–38	5

CONVERSION OF THE CYCLOTRON U-120M INTO H^-/D^- ACCELERATOR

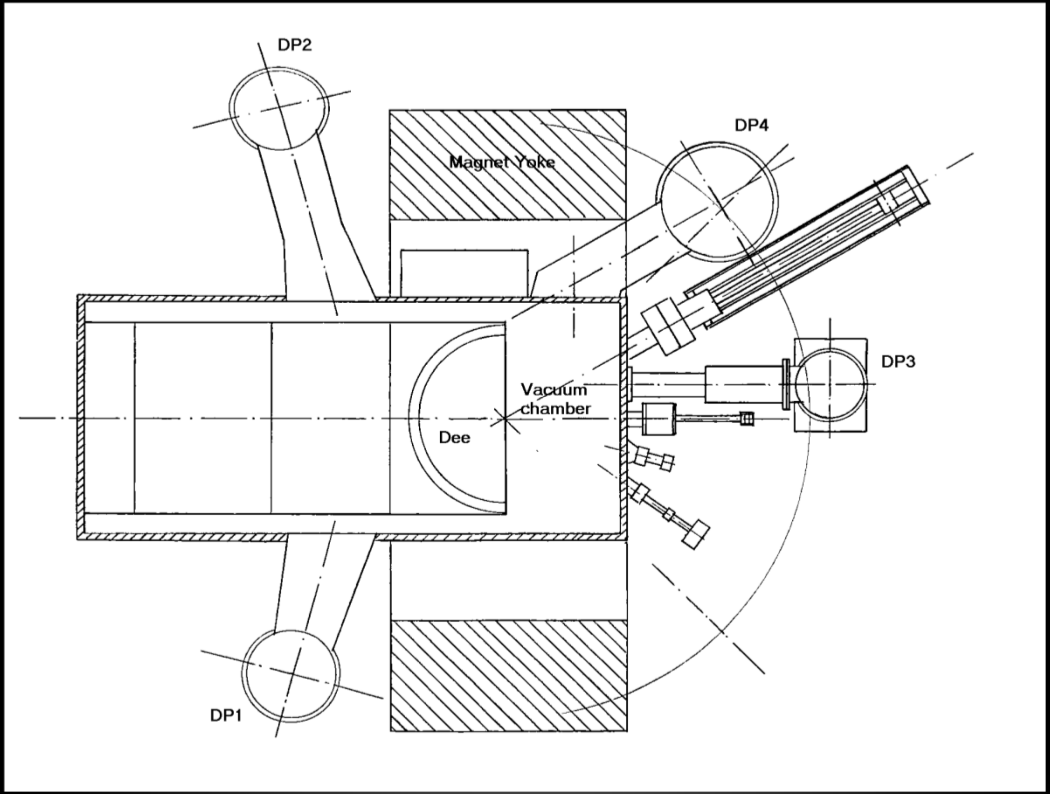
- New internal PIG ion source with a cold cathode
- Central region optimisation
- Employment of high effective beam extraction by means of the stripping method
- Project and implementing of a new beam line
- Upgrade of the cyclotron vacuum system

UPGRADE OF THE CYCLOTRON VACUUM SYSTEM

Originally not designed for negative ions (180°dee with a slit of 200 mm height, diffusion pump connection)

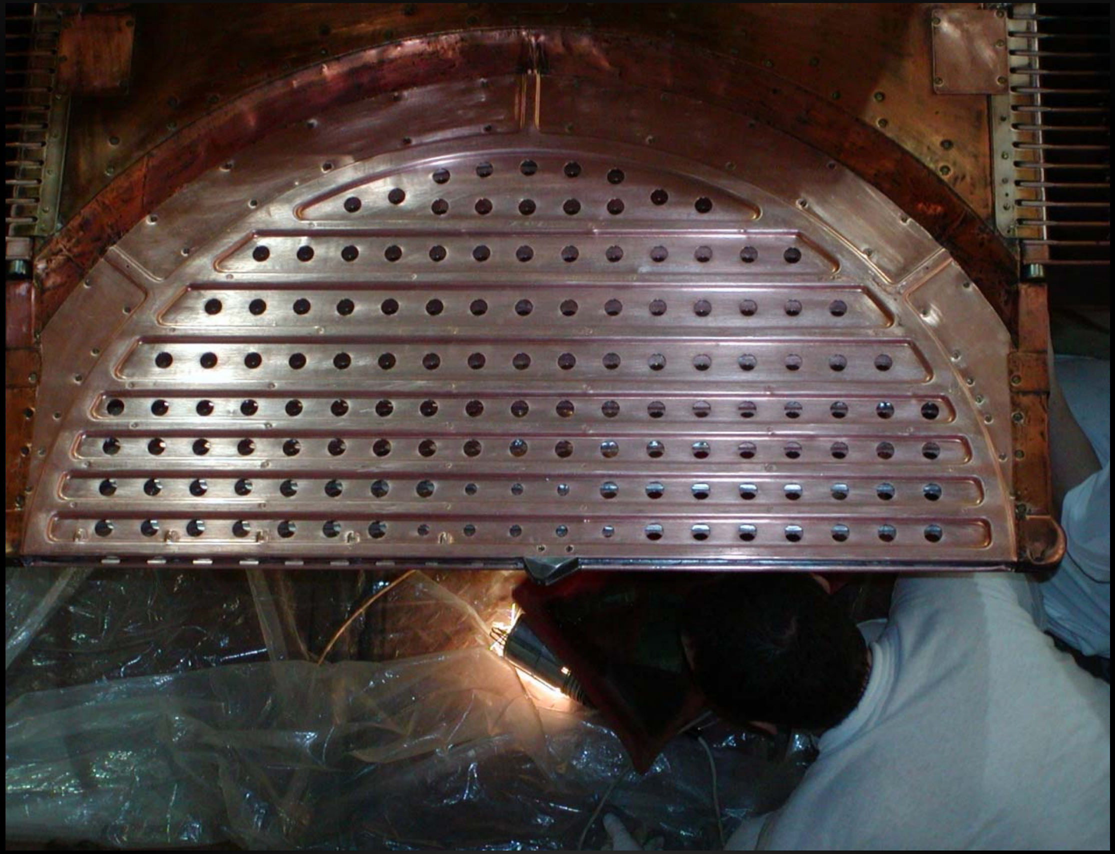
High beam losses of H^-/D^- ions on the residual gas (transamission ca 20 %)

Beam losses calculation → installation of two additional diffusion pumps

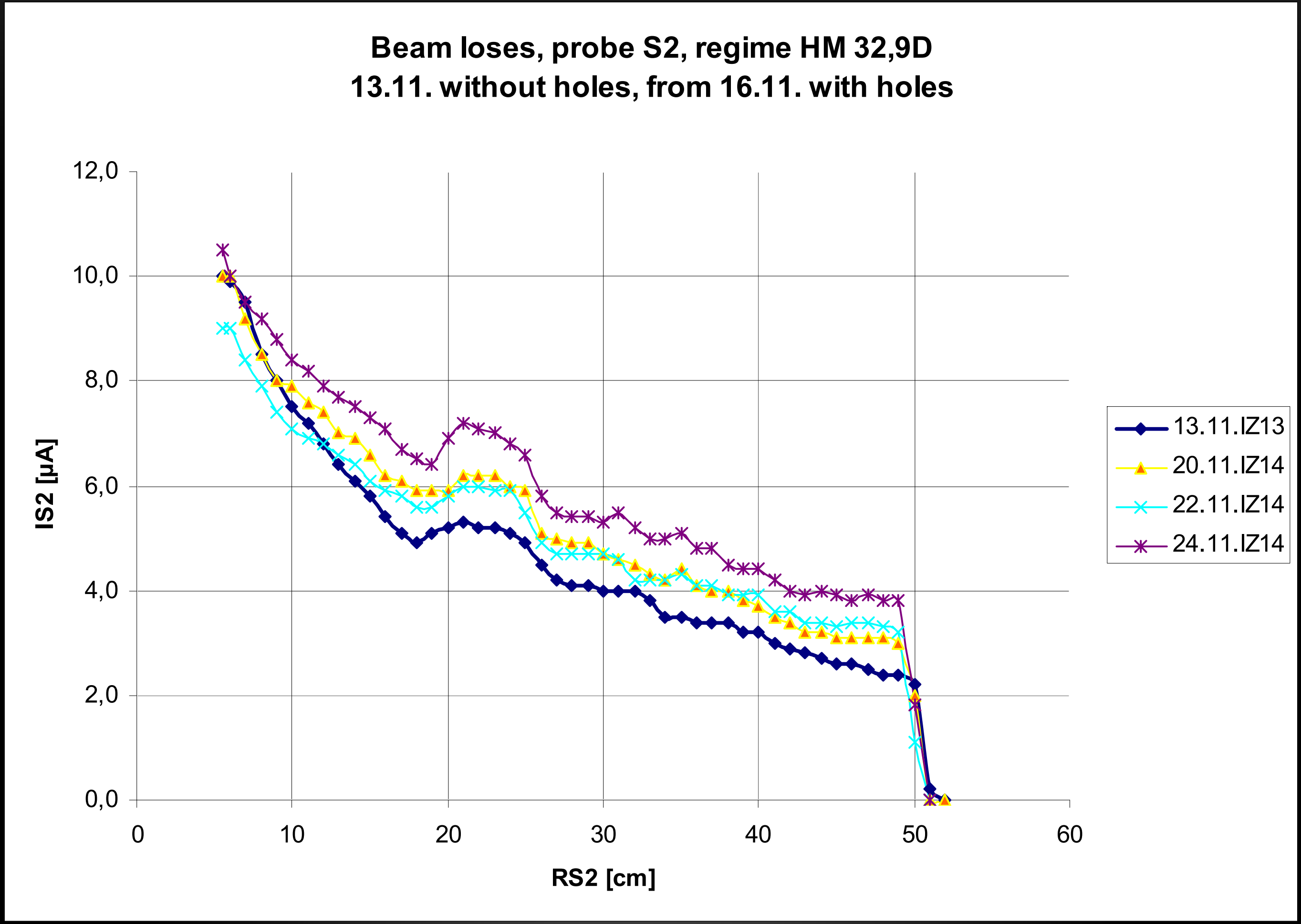


OLD-NEW DEE WITH HOLES

lower beam losses – approx. 20% shorter time for evacuation

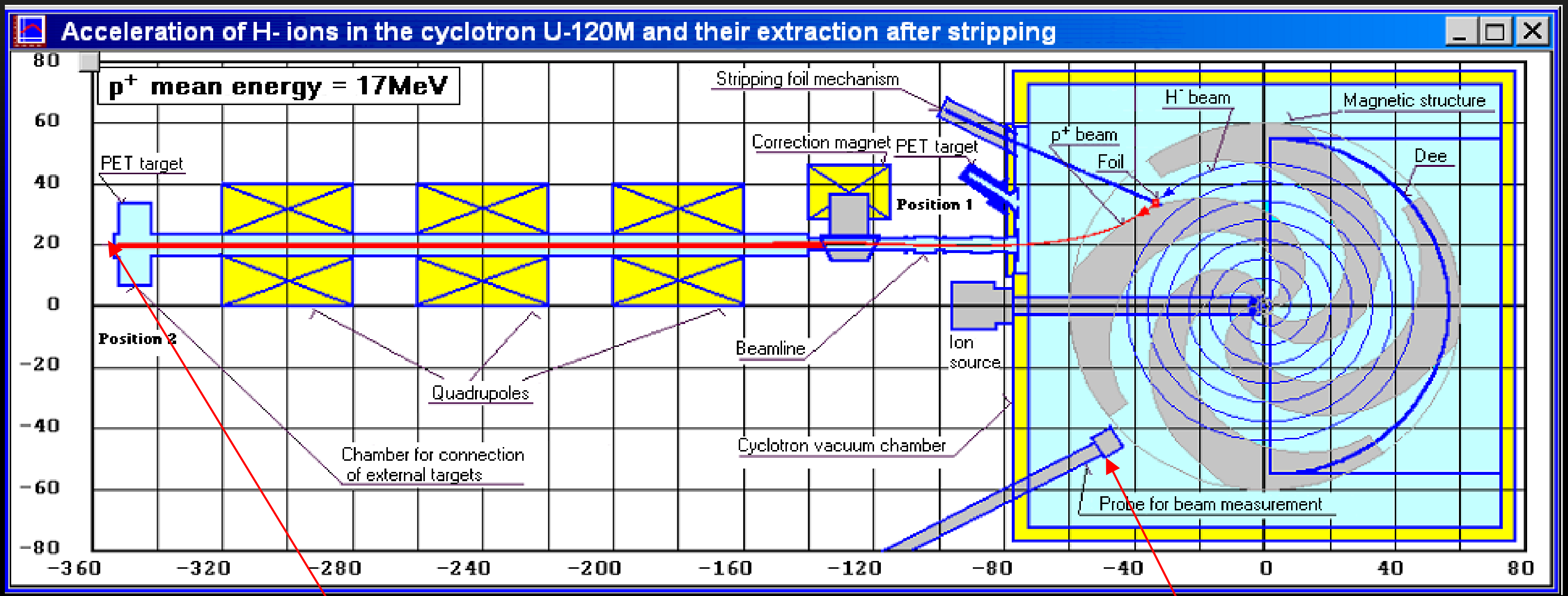


…AND POSITIVE IMPACT OF THE HOLES ON THE AVAILABLE BEAM CURRENT



TARGETS

POSITION OF THE TARGET SYSTEMS FOR RADIONUCLIDES PRODUCTION



Acceleration of H- ions in the cyclotron U-120M and their extraction after stripping

Position 1

a) target holder for cross-section measurements

b) liquid targets for ^{18}F, ^{68}Ga, ^{86}Y etc.

c) gaseous targets for ^{81,83}Rb and ^{123}I

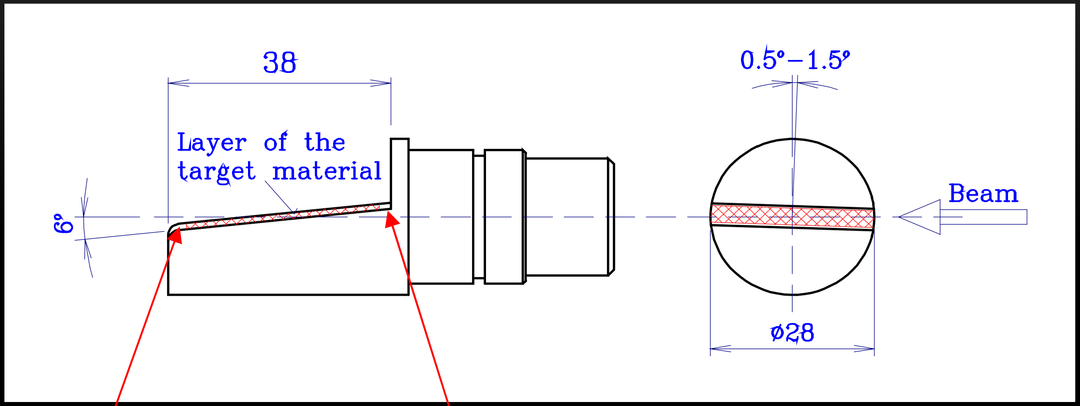
d) solid targets for ^{61,64,67}Cu, ^{86}Y, ^{124}I, ^{230}U and other non-conventional radionuclides

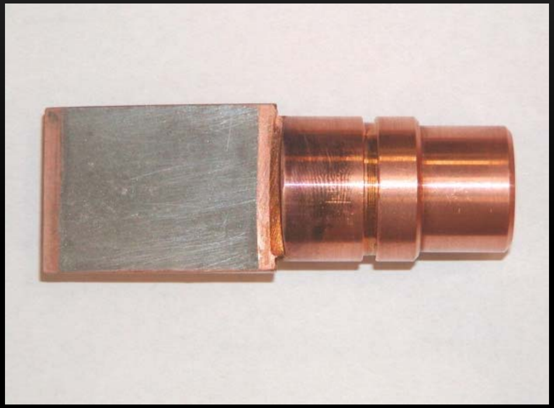
Position 2

^{68}Zn(p,2n)^{67}Ga
^{203}Tl(p,3n)^{201}Pb→^{201}Tl
^{112}Cd(p,2n)^{111}In
^{209}Bi(α,2n)^{211}At
^{209}Bi(p,2n)^{208}Po
recently for ^{61,64,67}Cu etc.

CYCLOTRON INTERNAL TARGETS I

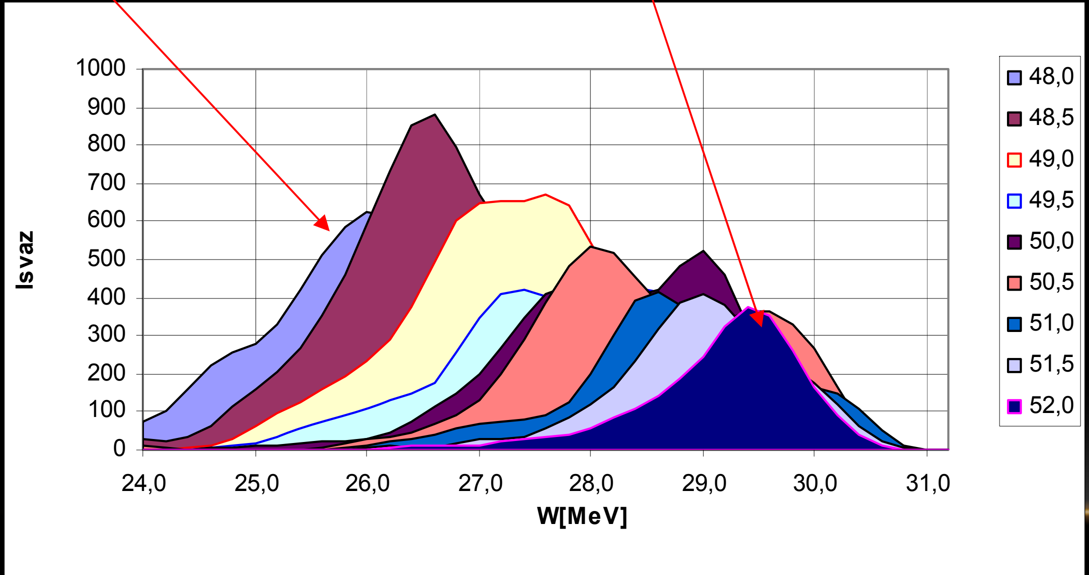
The original design from late 70ies





Radius 48cm

Radius 51.8cm



Beam energy distribution,

p^+, E=27.9MeV

Used for:

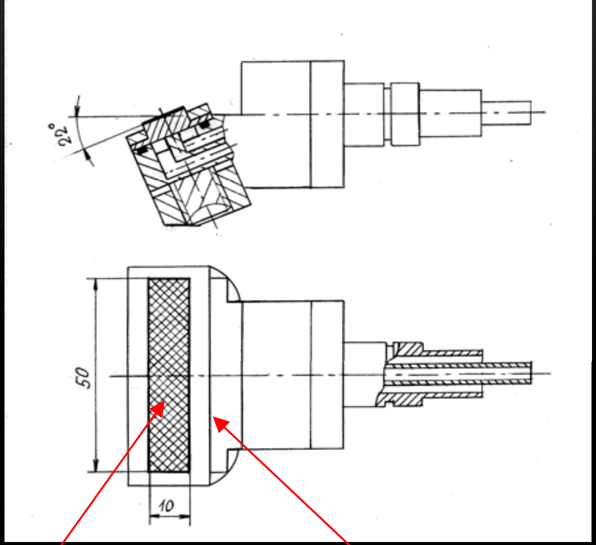
^{68}Zn(p,2n)^{67}Ga

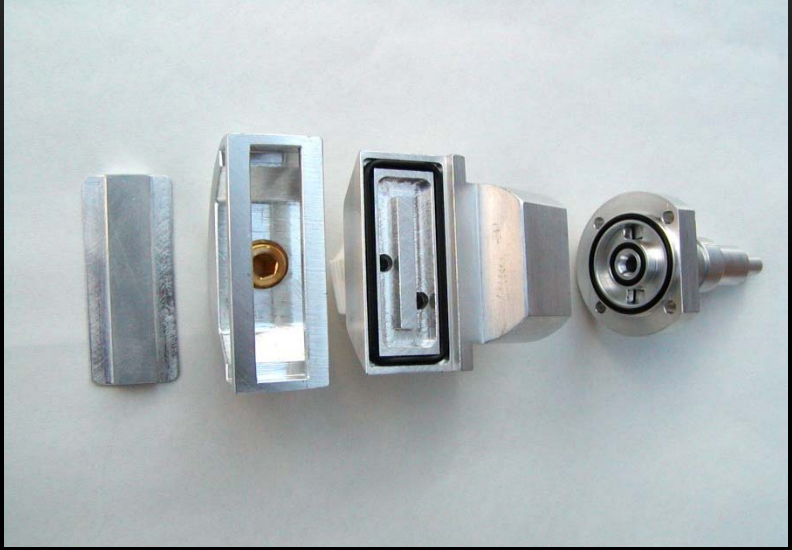
^{203}Tl(p,3n)^{201}Tl

^{112}Cd(p,2n)^{111}in

^{209}Bi(p,2n)^{208}Po

A NEW INTERNAL TARGET SYSTEM DESIGNED FOR PRODUCTION OF ^{211}At

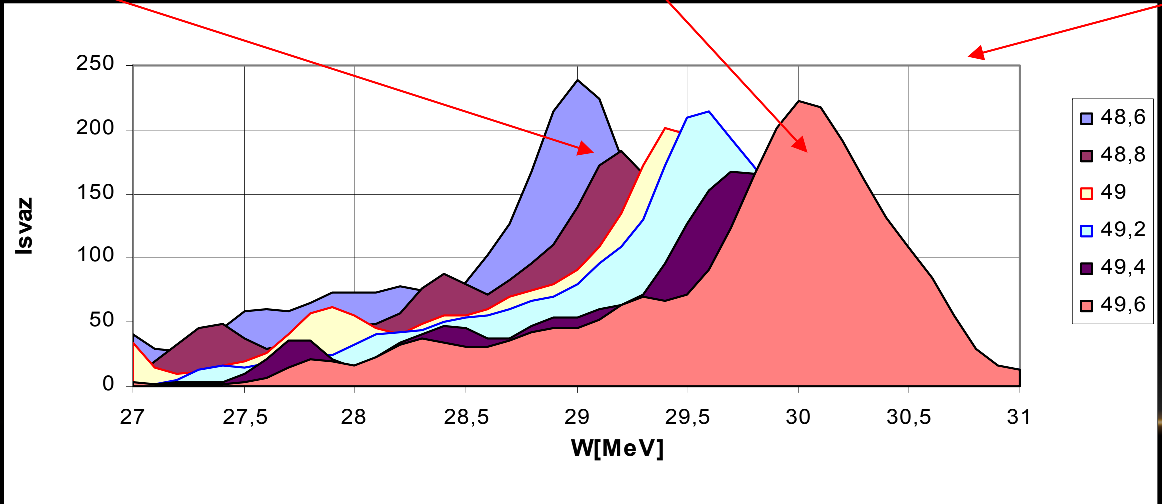




Radius 48.6cm

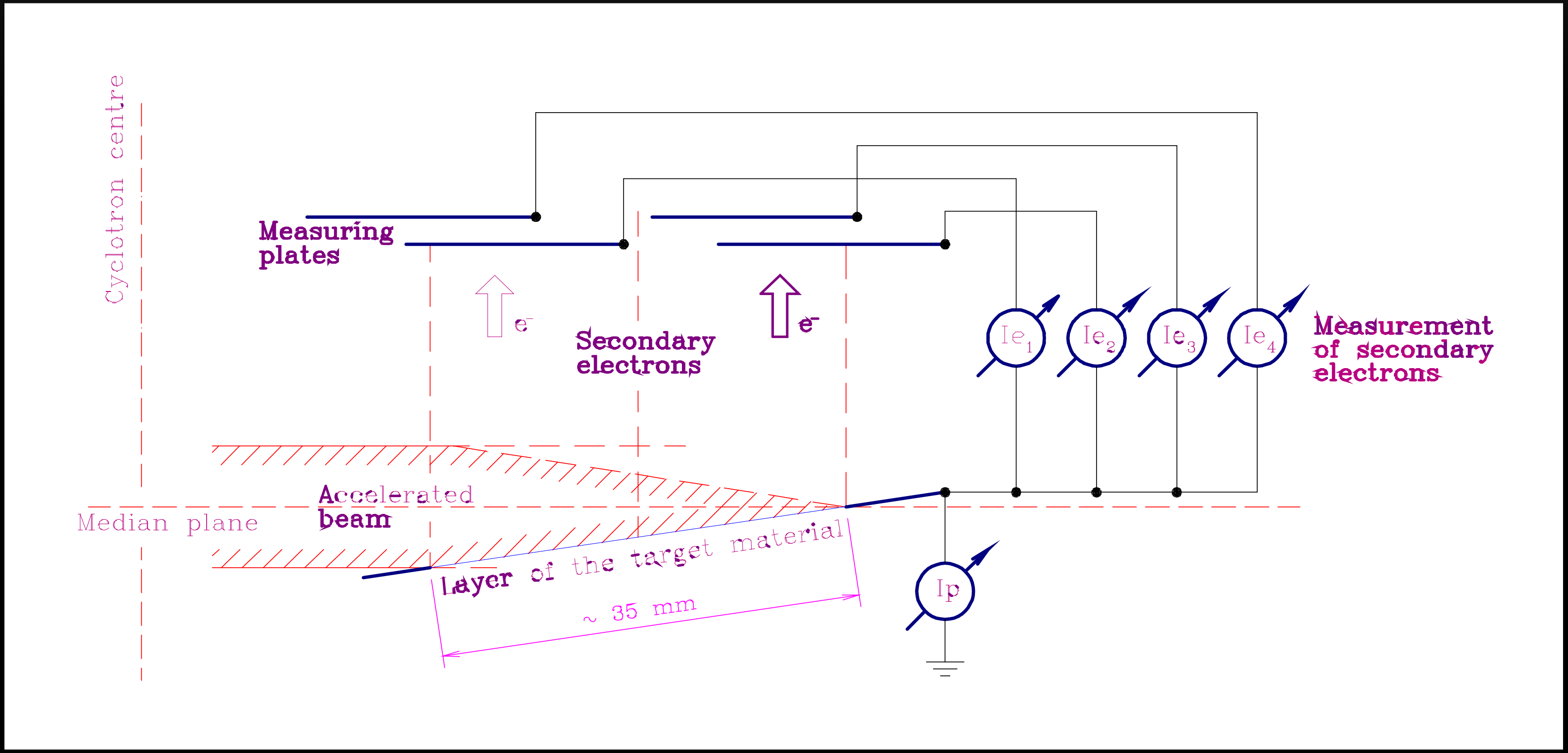
Radius 49.6cm

Radial beam energy distribution for 30.3 MeV alpha particles

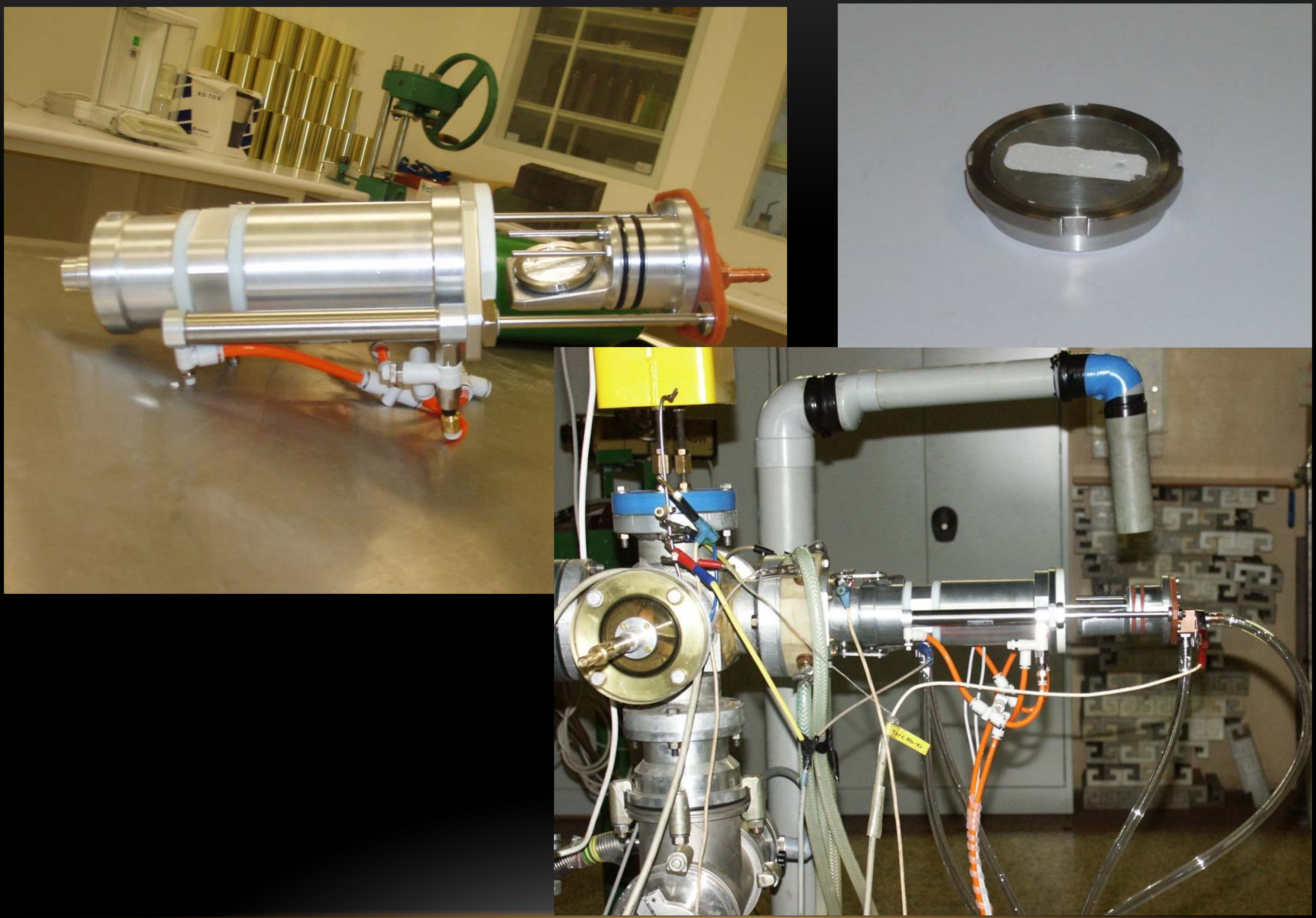


Thick target yield is equal to theoretical maximum available (400 MBq/μA), while keeping ^{210}At/^{211}At ratio below 10^{-3}

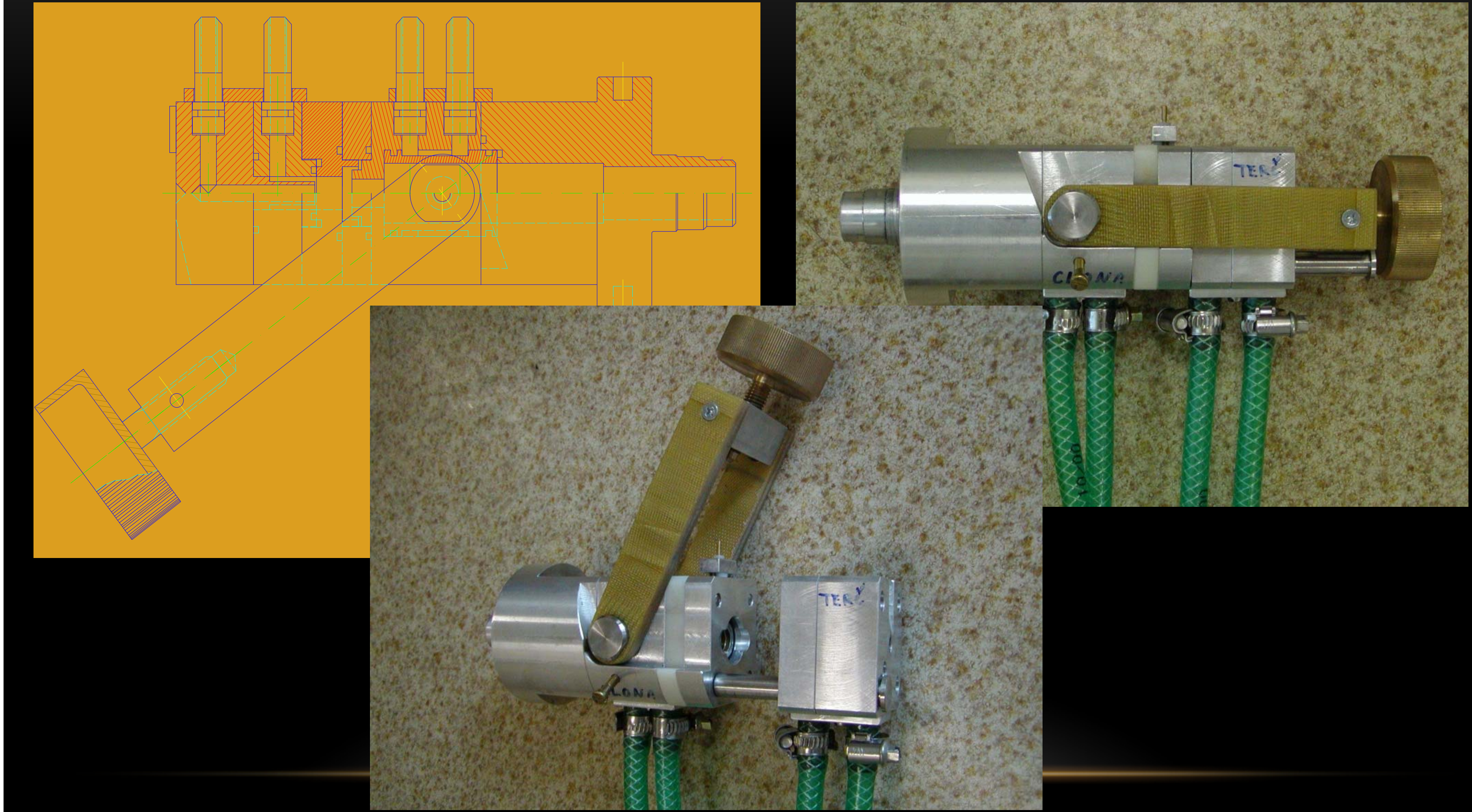
MONITORING OF THE BEAM DISTRIBUTION ON THE INTERNL TARGET SURFACE BY MEANS OF SECONDARY ELECTRONS



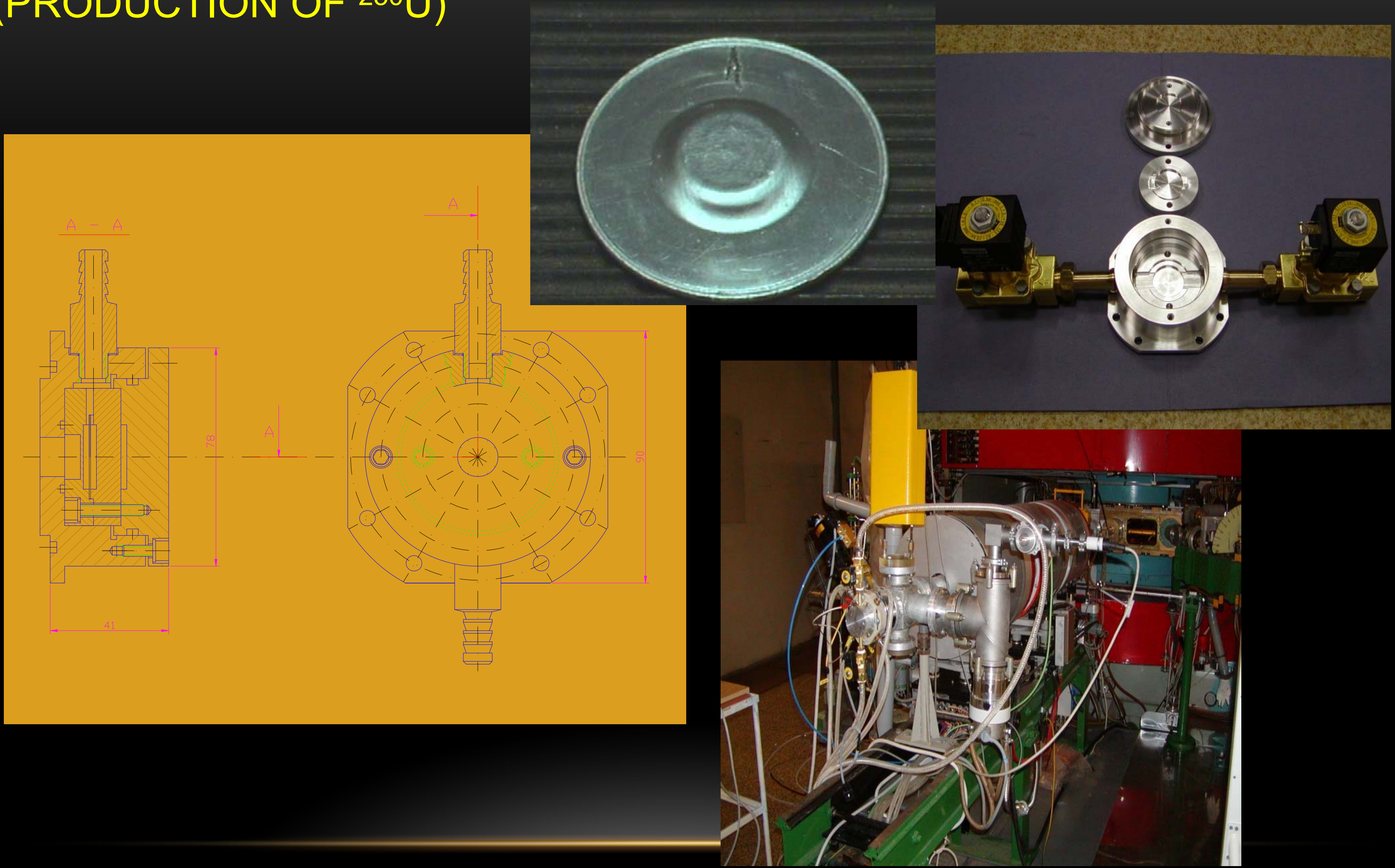
EXTERNAL TANGENTIAL (10 °) SOLID TARGETS FOR E.G. ^{124}I OR ^{86}Y



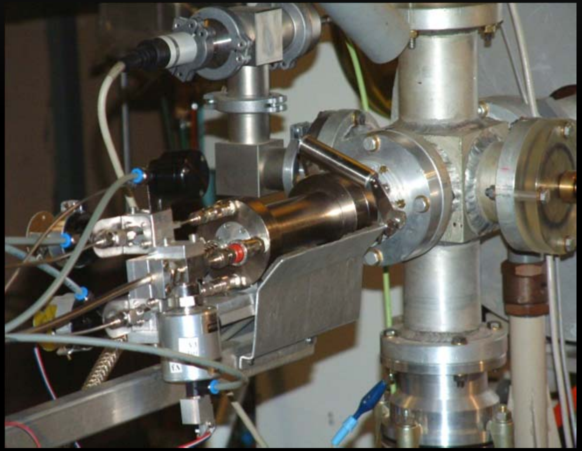
EXTERNAL PERPENDICULAR TARGET FOR CROSS-SECTION MEASUREMENTS AND FOR PRODUCTION OF SOME RN



EXTERNAL PERPENDICULAR SOLID TARGET WITH 4Π WATER COOLING (PRODUCTION OF ^{230}U)

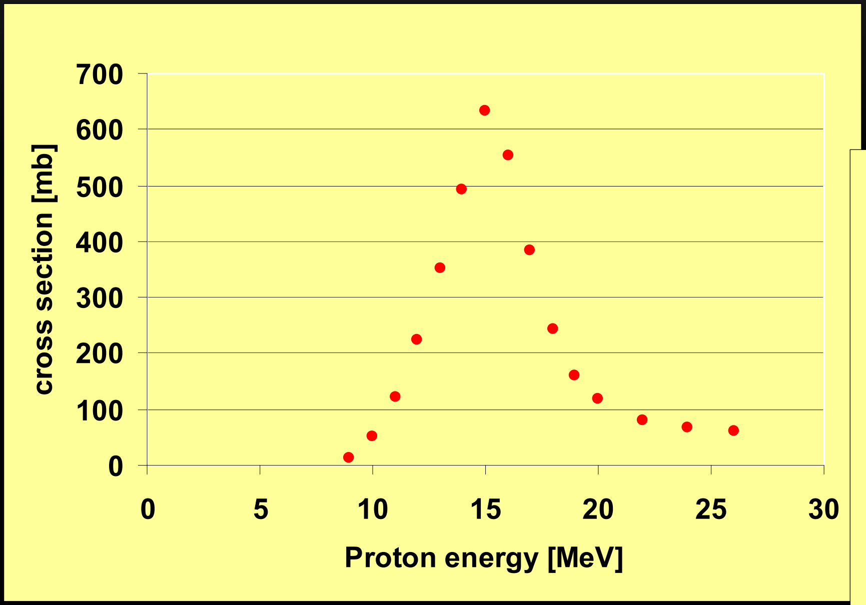


GAS TARGETS FOR ^{81,83}RB AND ^{123}I

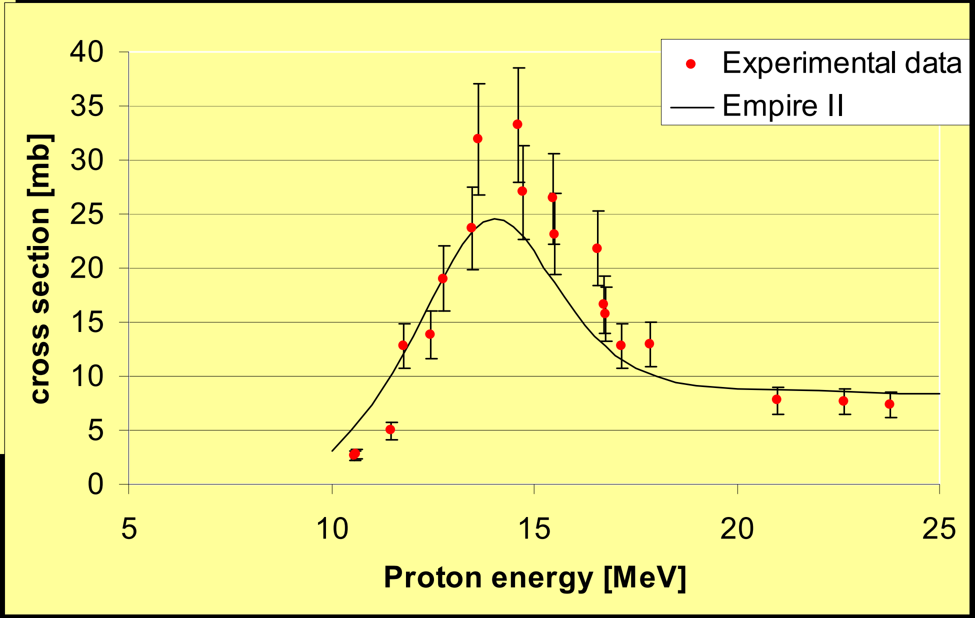


EXCITATION FUNCTIONS MEASUREMENTS

REACTION $^{231}Pa(p,2n)^{230}U$

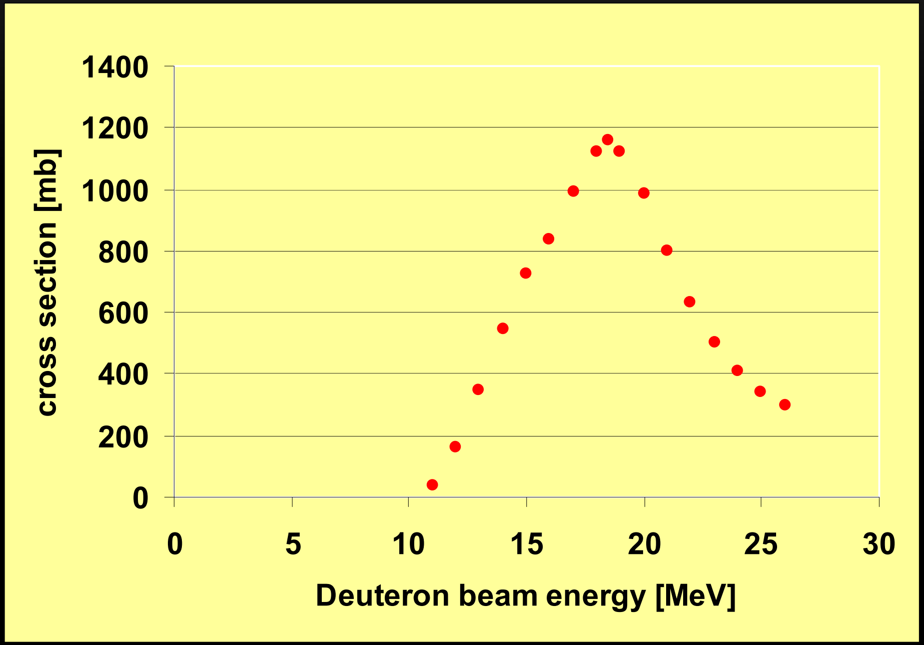


Alice code Lawrence
Livermore Laboratory



And the measured data…

REACTION ^{231}Pa(d,3n)^{230}U



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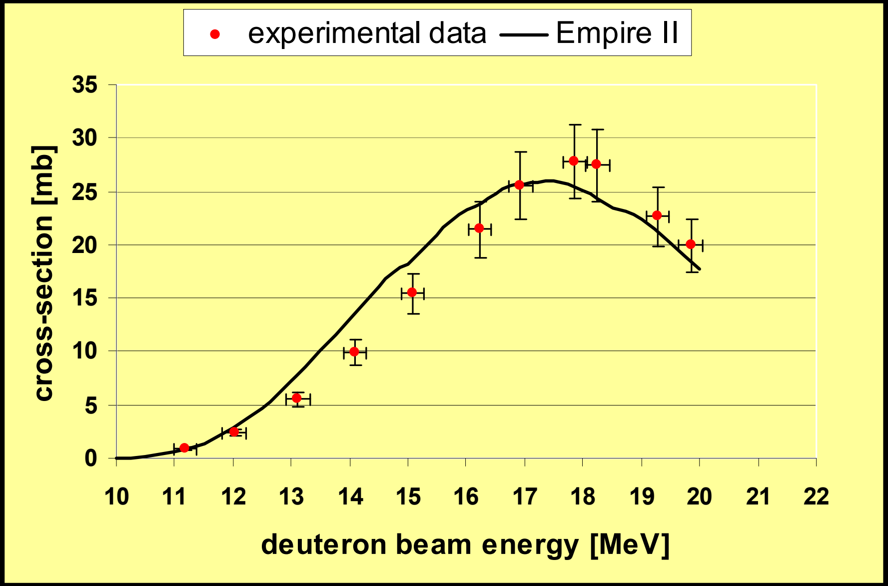


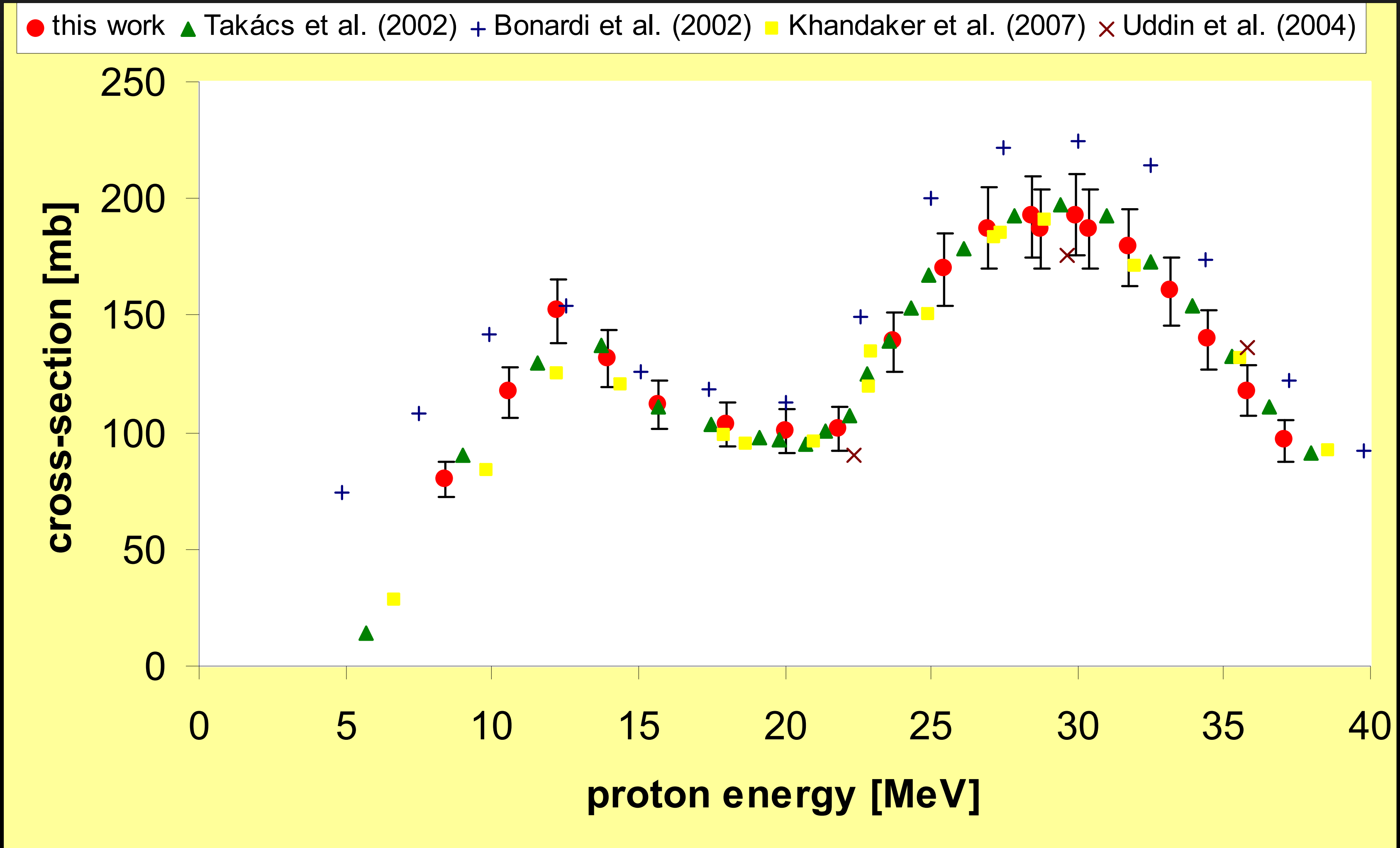
And the measured data…

THE ^{230}U PRODUCTION ROUTES AND THEIR COMPARISON

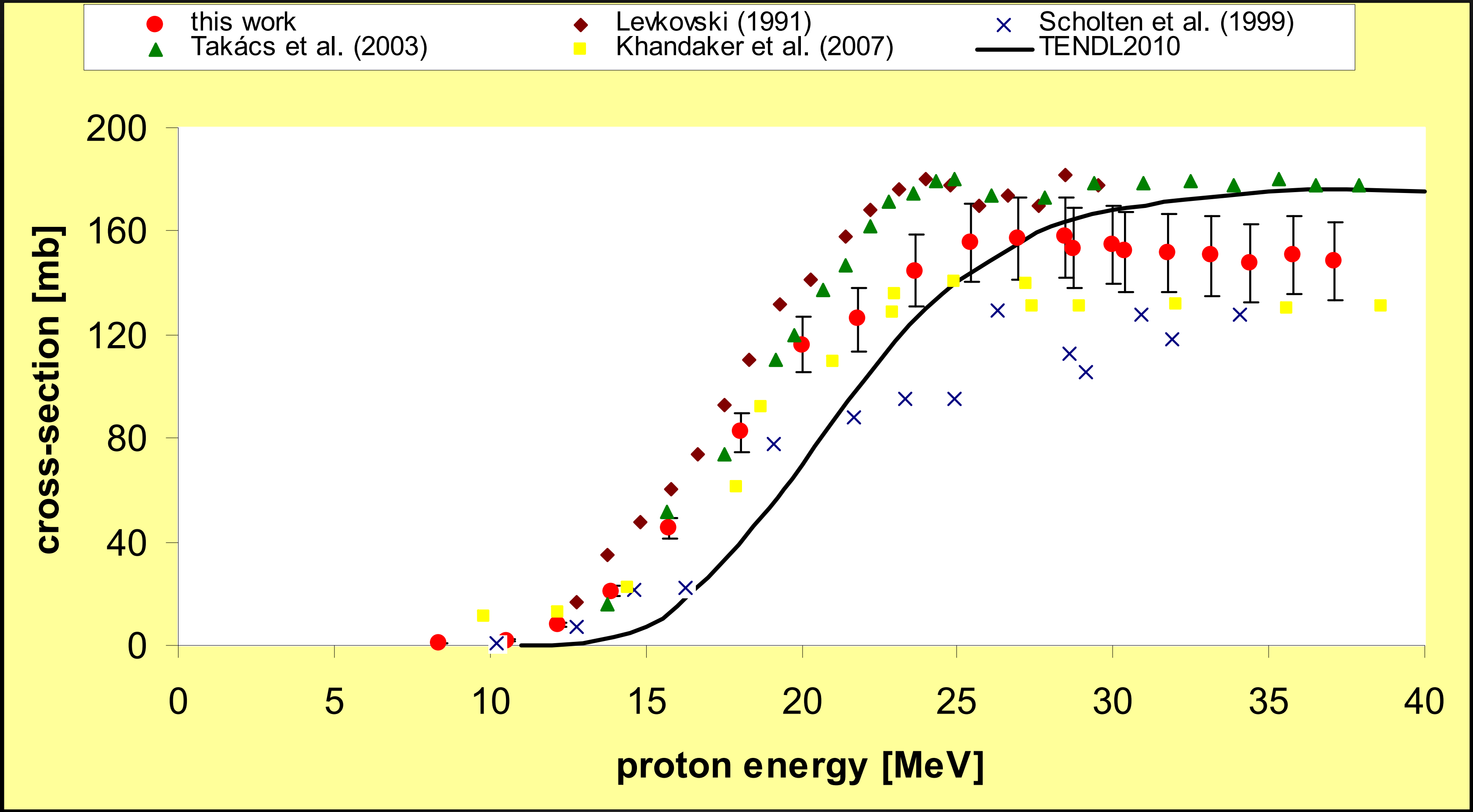
reaction	maximum cross-section [mb]	yield [MBq/µAh]
^{231}Pa(d,3n)	27.8 ± 3.4 (17.9 MeV)	0.119 (20.0→11.0 MeV, oxide)
^{231}Pa(p,2n)	33.2 ± 5.3 (14.6 MeV)	0.245 (24.0→10.5 MeV, oxide)
^{232}Th(p,3n) ^{230}Pa (17.4 d)	353 ± 15 (19.9 MeV)	8.4* (33.5 MeV)

*Thick target yield of ^{230}Pa. The maximum activity of ^{230}U is formed four weeks after end of irradiation via β^- decay of ^{230}Pa and corresponds to 2.82 % of the activity of ^{230}Pa initially produced. The available amount of ^{230}U corresponds thus to a yield of 0.24 MBq/µAh.

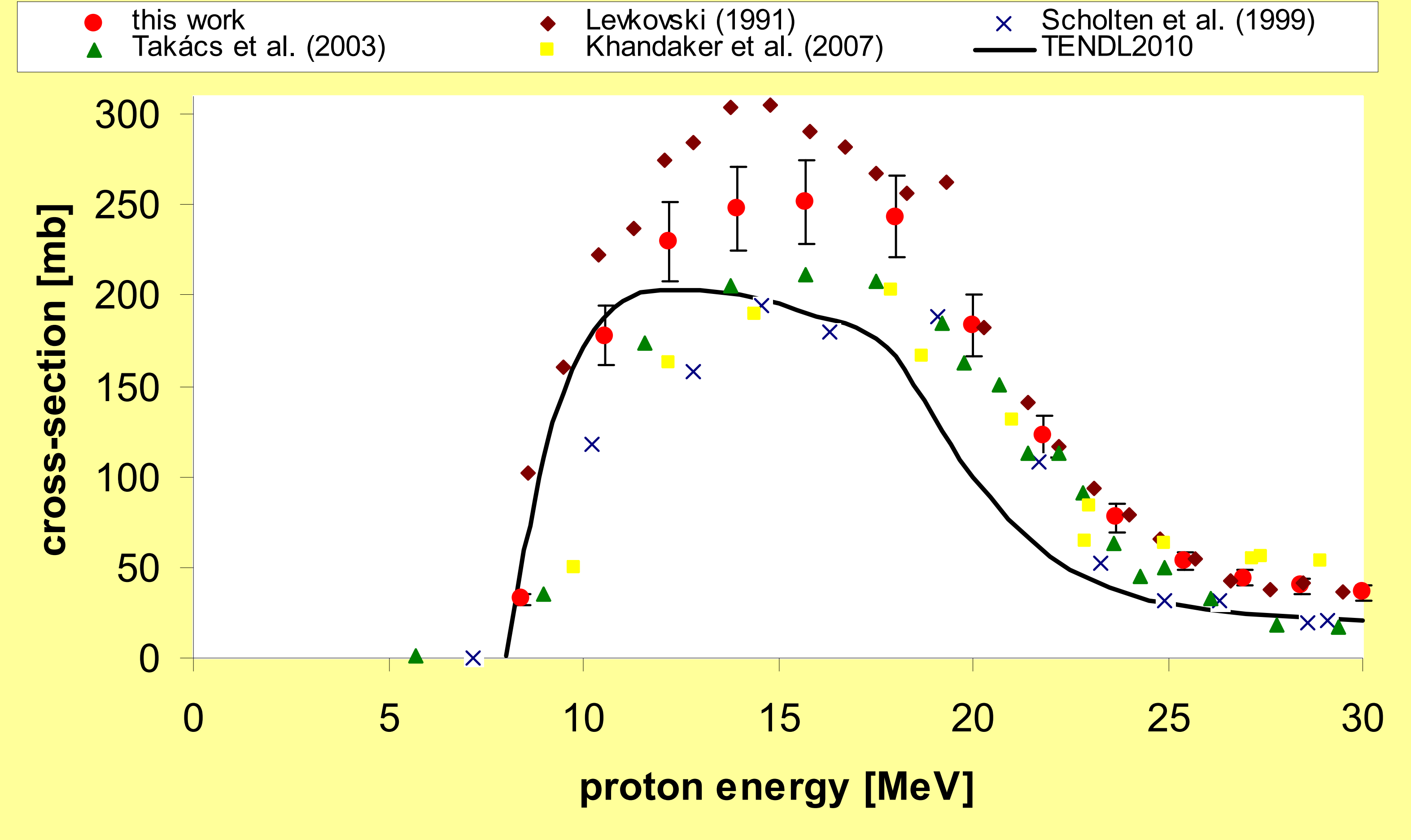
CROSS-SECTIONS FOR $^{nat}\mathrm{Mo}(p,x)^{96m+g}\mathrm{Tc}$



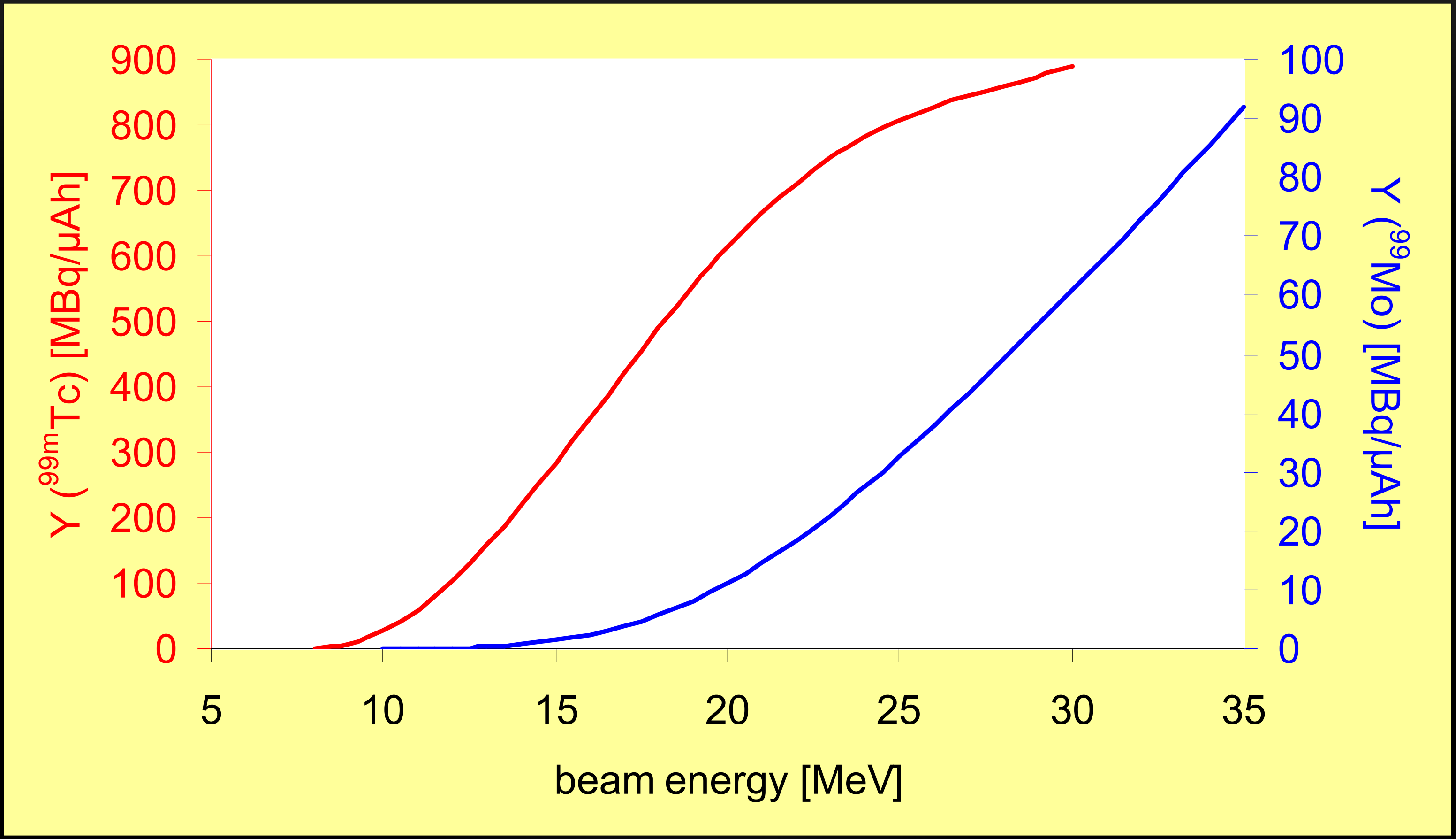
CROSS-SECTIONS FOR $^{100}Mo(p,x)^{99}Mo$



CROSS-SECTIONS FOR ^{100}Mo(p,2n)^{99m}Tc



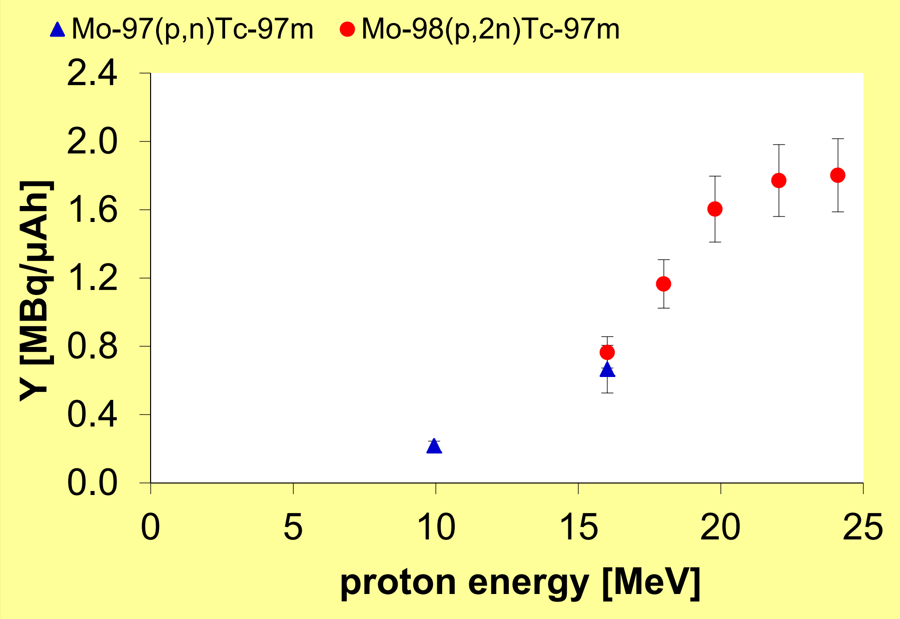
CALCULATED THICK TARGET YIELDS FOR ^{99}Mo AND ^{99m}Tc



DIRECT CYCLOTRON PRODUCTION OF ^{99m}Tc?

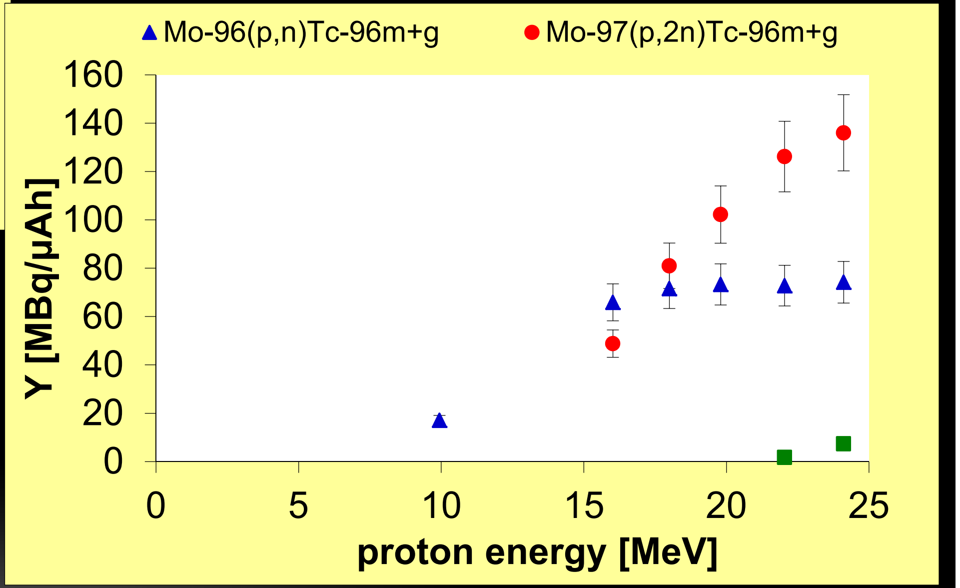
- Thick target of highly enriched ^{100}Mo, $E_p = 24 \rightarrow 10$ MeV, 500 μA, 6 h irradiation time results in ca 1.7 TBq of ^{99m}Tc.
- Assuming 6 h needed for target processing, quality control and delivery, one has ca 800 GBq in hospitals – daily consumption of large metropolitan area.
- The whole process requires optimizing the separation, quality control and isotopic composition of the enriched ^{100}Mo with respect to available radionuclidic purity.

AVAILABLE RADIONUCLIDIC PURITY OF ^{99m}Tc

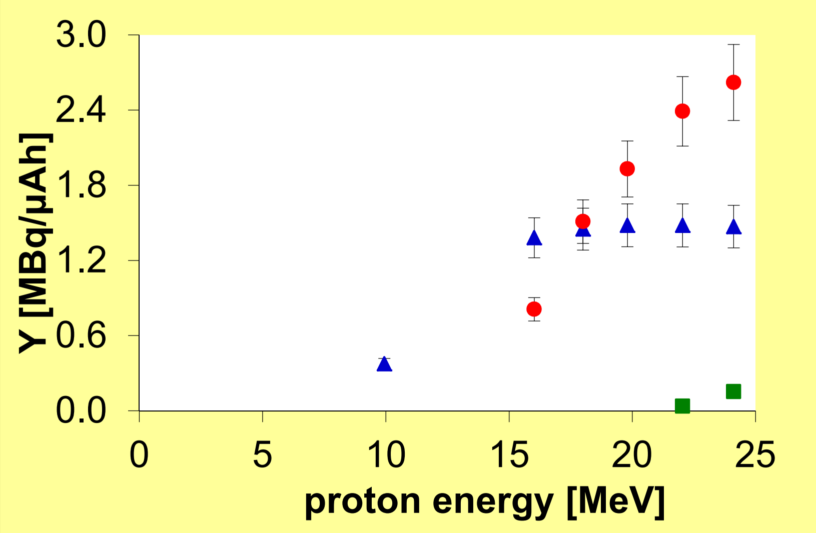


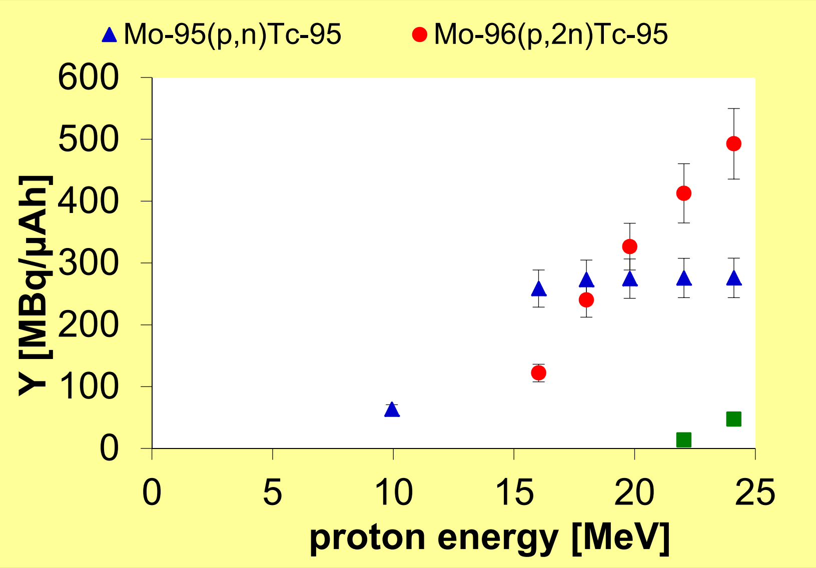
Pragmatic approach: measurement of the thick target yields for the main Tc impurities in the thick targets out of the highly enriched $^{95–98}$Mo in the critical energy region…

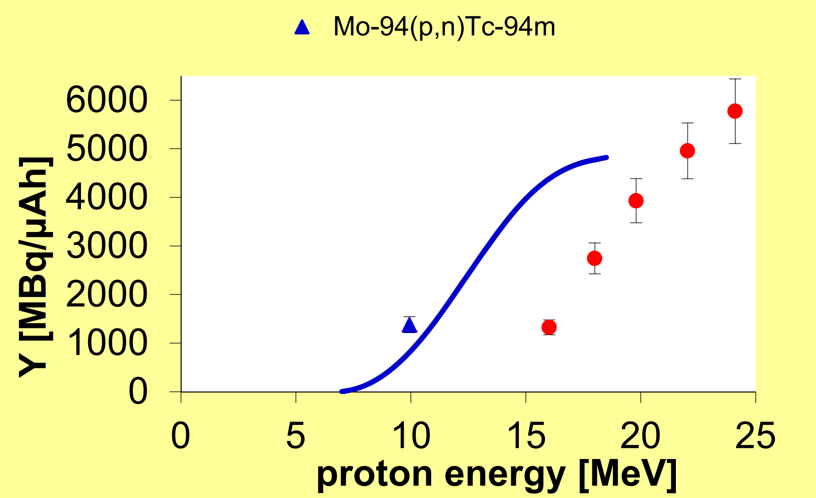
…and their comparison with measured content of radionuclidic impurities in highly enriched ^{100}Mo targets of known isotopic composition.

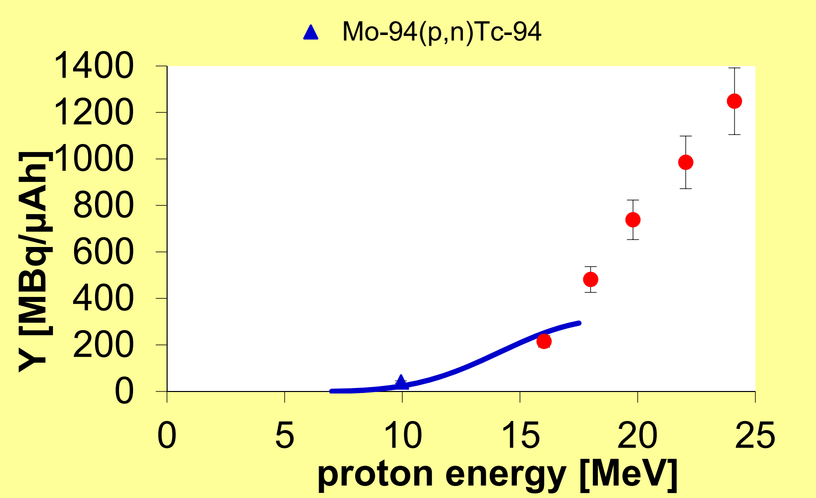


AVAILABLE RADIONUCLIDIC PURITY OF ^{99m}Tc









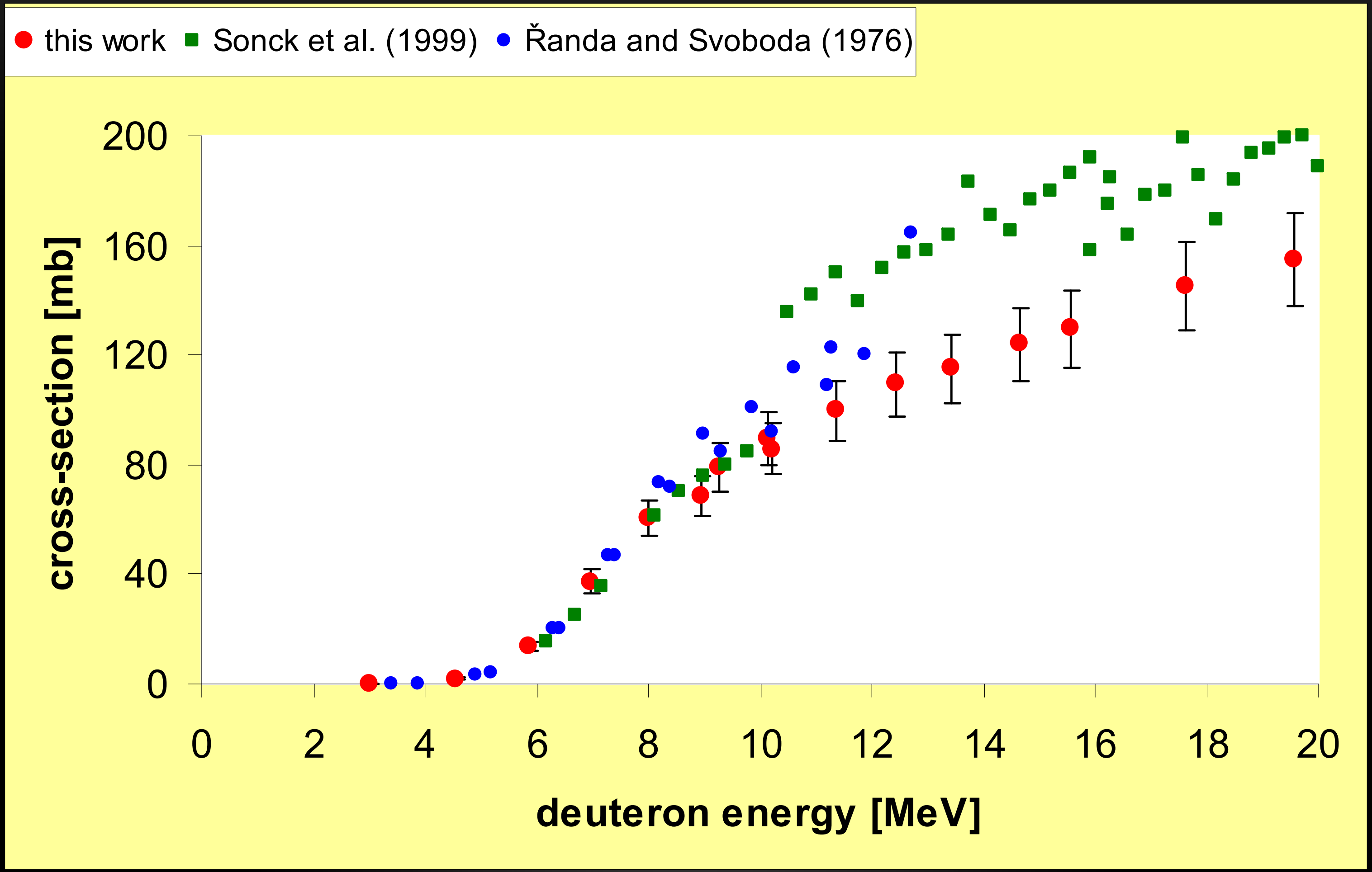
AVAILABLE RADIONUCLIDIC PURITY OF ^{99m}Tc CONCLUSIONS

Comparison of the thick target yields calculated from our data on previous six figures and those predicted by EMPIRE-3. The yields were calculated for the loss 24→10 MeV and the best available enrichment of ^{100}Mo (^{100}Mo 99.54 %, ^{98}Mo 0.41 %, ^{97}Mo 0.0016 %, ^{96}Mo 0.0012 %, ^{95}Mo 0.0076 %, ^{94}Mo 0.0051 % and ^{92}Mo 0.006 %). Relative activities A_{rel} were calculated for 6 h irradiation and 6 h cooling time:

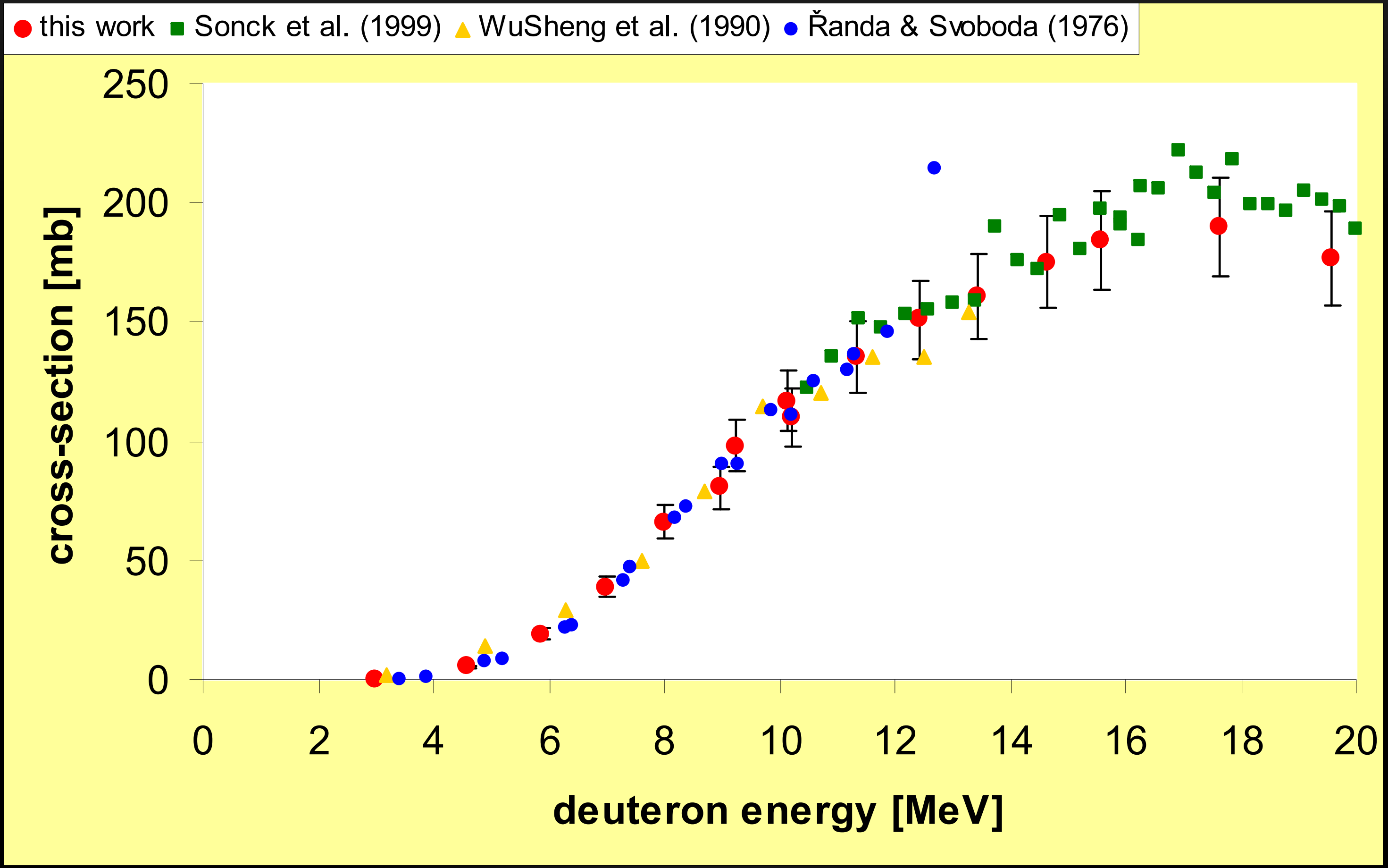
RN	^{99m}Tc	^{97m}Tc	$^{96m+g}$Tc	^{95m}Tc	^{95}Tc	^{94m}Tc	^{94}Tc
Y_{sat} (MBq/μA) – this work	6 508	23.3	4.98	0.543	0.660	0.848	0.798
Y_{sat} (MBq/μA) – EMPIRE-3	5 765	15.8	7.40	0.224	0.920	0.304	1.65
A_{rel} – this work (%)	99.97	0.0027	0.012	0.000094	0.0062	0.00043	0.012
A_{rel} – EMPIRE-3 (%)	99.94	0.0021	0.020	0.000044	0.0097	0.00017	0.028

The most critical impurities are ^{95}Tc (20.0 h) and $^{96m+g}$Tc (4.28 d), also due to their contribution to the increase of radiation burden of a patient. The non-isotopic impurities (^{99}Mo, ^{96}Nb, ^{97}Nb) can be efficiently separated from the product in the course of ^{99m}Tc separation from the target via extraction chromatography.

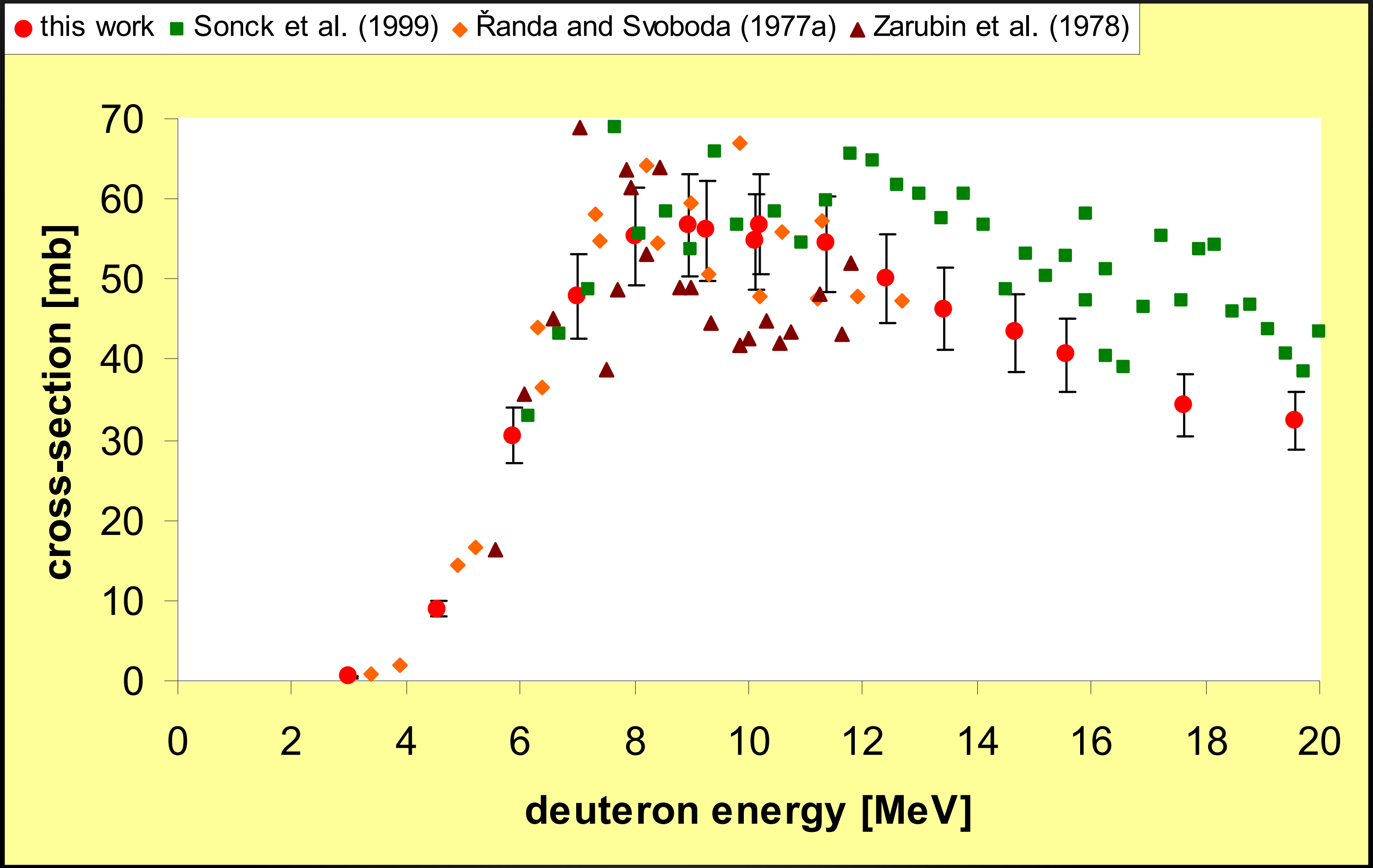
CROSS-SECTIONS FOR $^{nat}Mo(d,x)^{95}Tc$



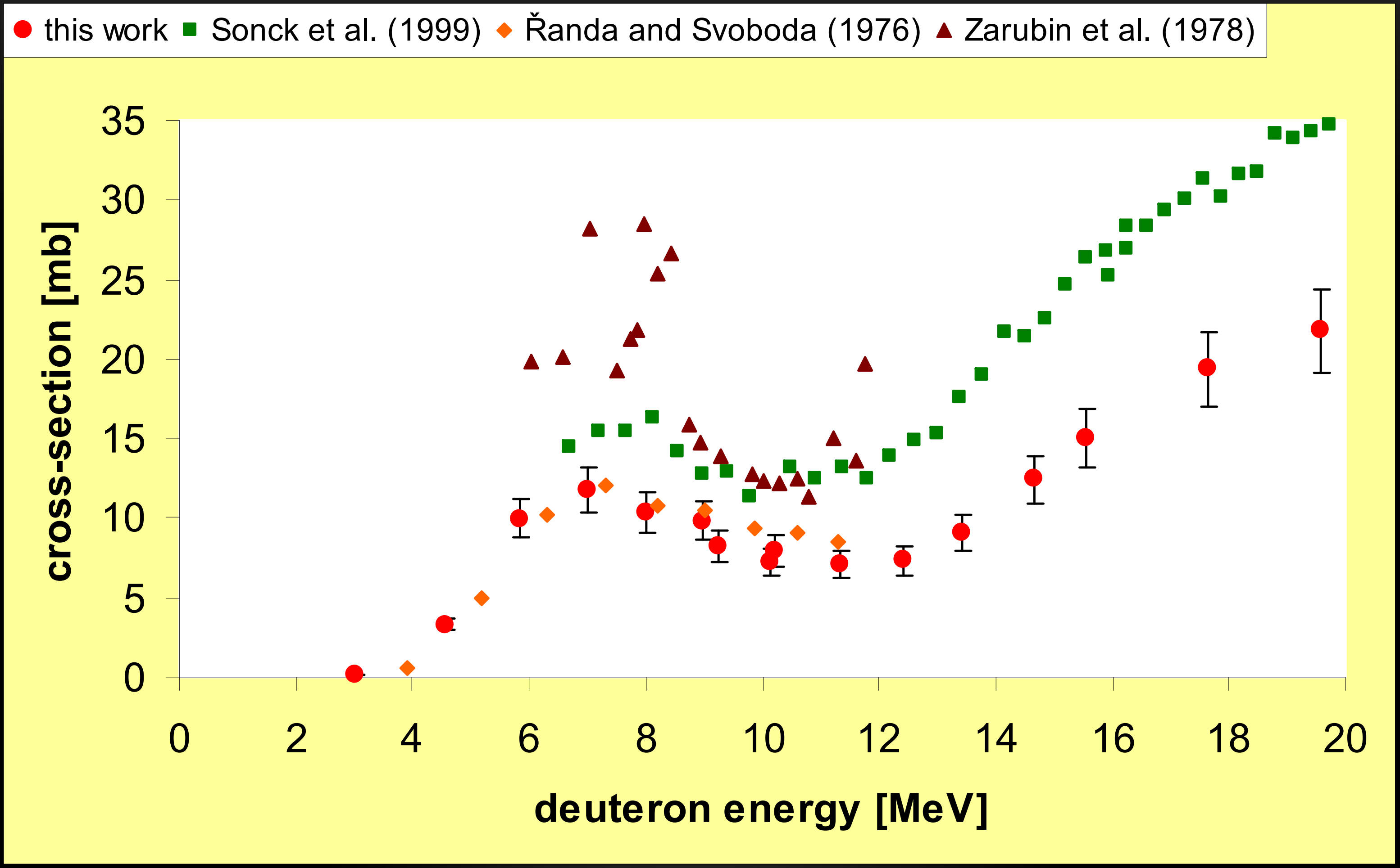
CROSS-SECTIONS FOR $^{nat}Mo(d,x)^{96m+g}Tc$



CROSS-SECTIONS FOR $^{nat}Mo(d,x)^{99}Mo$



CROSS-SECTIONS FOR $^{nat}Mo(d,x)^{99m}Tc$



RECENT ACTIVITIES

- Cross-sections measurement for activation products of proton irradiation of ^{nat}Nd – estimation of their activities induced by cosmic radiation in the Nd detector for the SNO (Sudbury Neutrino Project),

  Collaboration: TU dresden, NPI Řež, project is currently finished and data are published in Phys. Rev. C, however, a few data points below 10 MeV and over 30 MeV have been still measured and are currently evaluated.
- Cross-sections measurements for ^{165}Ho(^{3}He,xn) reactions – data are measured and evaluated – and for ^{159}Tb(^{3}He,x) reactions – data are measured and currently evaluated (project is supported by the IAEA)
- Development of target systems for routine production of ^{68}Ga and ^{61,67}Cu
- Determining the radionuclidic impurities present in the cyclotron produced ^{99m}Tc – together with ACSI, data were already published in Nucl. Med. Biol.

OUR CONTRIBUTION TO THE CRP PROPOSAL

Evaluation of the published cross-section data (in collaboration with others)

- Monitoring reactions: $^{nat}Mo(p,x)^{96m+g}Tc$
- SPECT radionuclides: $^{100}Mo(p,2n)^{99m}Tc$, $^{100}Mo(p,x)^{99}Mo$, $^{98}Mo(d,n)^{99m}Tc$, $^{100}Mo(d,3n)^{99m}Tc$, $^{98}Mo(d,p)^{99}Mo$ and $^{100}Mo(d,x)^{99}Mo$
- PET radionuclides: production routes for ^{61}Cu
- Therapeutic radionuclides: $^{231}Pa(p,2n)^{230}U$ and $^{231}Pa(d,3n)^{230}U$

New measurements using U-120M cyclotron

- SPECT radionuclides: $^{100}Mo(p,2n)^{99m}Tc$ and $^{100}Mo(p,x)^{99}Mo$ (on enriched ^{100}Mo)
- PET radionuclides: $^{64}Zn(p,\alpha)^{61}Cu$ (need for reliable decay data of ^{61}Cu), $^{75}As(p,3n)^{73}Se$ (need for reliable decay data of ^{73}Se), $^{89}Y(d,2n)^{89}Zr$