

# Status of Cyclotron Laboratory at Institute for Nuclear Research and Nuclear Energy

- › Project goals
- › Cyclotron @ INRNE
- ›  $^{18}\text{F}$  production & activation of components

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 INRNE-BAS

# Key Points about the Cyclotron Project

- › A “green field” market oriented infrastructure for GMP production of **medical radioisotopes and radiopharmaceuticals** with major R&D activities in the fields.
  
- › Enables high level **fundamental and applied research with radioisotopes/radiotracers** in life sciences, industry, pharmacy and medicine. A contribution of the nuclear and particle community to the other fields of science in Bulgaria.
  
- › With **basic capabilities** for materials and electronics **irradiation**, beam diagnostics, detector testing, experimental equipment development.
  
- › **Training** within the R&D program in **radiochemistry, radiation protection**, and experimental **nuclear physics** for the **nuclear energy and radioactive waste management industry and nuclear medicine** in Bulgaria.

# TR-24, ACSI (EBCO), Canada

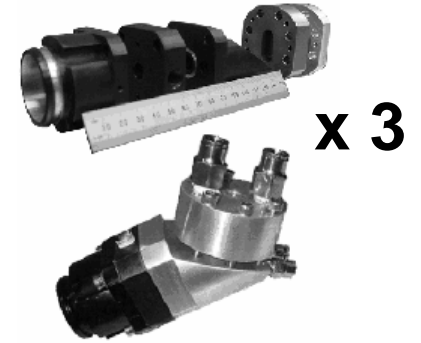
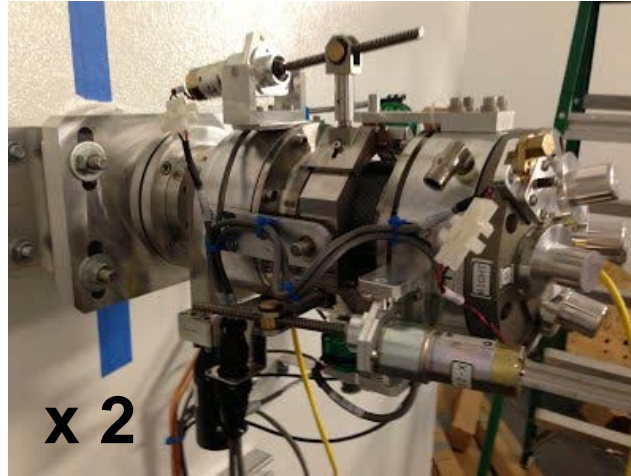


- › Accelerates H- ions
- › Extraction by stripping foils
- › **Beam Energy: 15 – 24 MeV**
- › **Beam Current: 400  $\mu$ A**
- › **Upgradeable to 1 mA**
  
- › Dual Beam Extraction
- › External CUSP ion source
- › Turbomolecular and cryo vacuum pumps
- › Vacuum:  $5 \cdot 10^{-7}$  –  $10^{-6}$  Torr

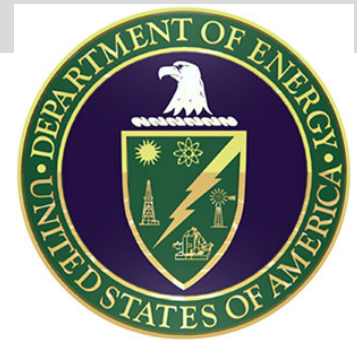
**PET:  $^{11}\text{C}$ ,  $^{13}\text{N}$ ,  $^{15}\text{O}$ ,  $^{18}\text{F}$ ,  $^{124}\text{I}$ ,  $^{64}\text{Cu}$ ,  $^{68}\text{Ge}$**

**SPECT:  $^{123}\text{I}$ ,  $^{111}\text{In}$ ,  $^{67}\text{Ga}$ ,  $^{57}\text{Co}$ ,  $^{99\text{m}}\text{Tc}$**

# Beamlines, targets and target stations for PET&SPECT radioisotopes production



# Financial Support for the Project



“АЕЦ КОЗЛОДУЙ” ЕАД  
KOZLODUY NPP PLC



Donations from DOE of USA and Kozloduy NPP.

# Government support

Prime Minister visit at INRNE-BAS 27.10.2016



Business plan showing the feasibility of such a facility (2015).

# Cyclotron (1)

- › FAT done in August 2015



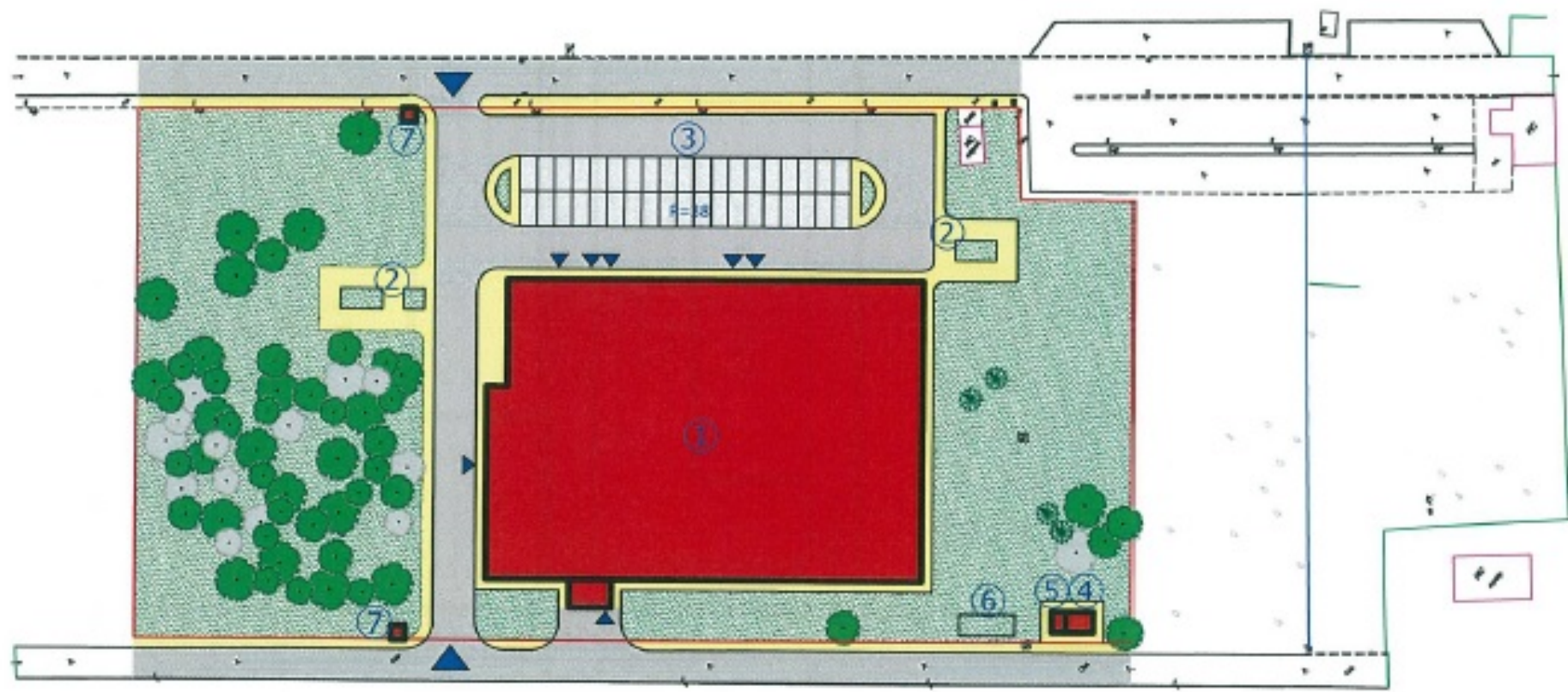
# Cyclotron (2)

› Delivery – January 2016





# Vision for the building layout



← Former research reactor

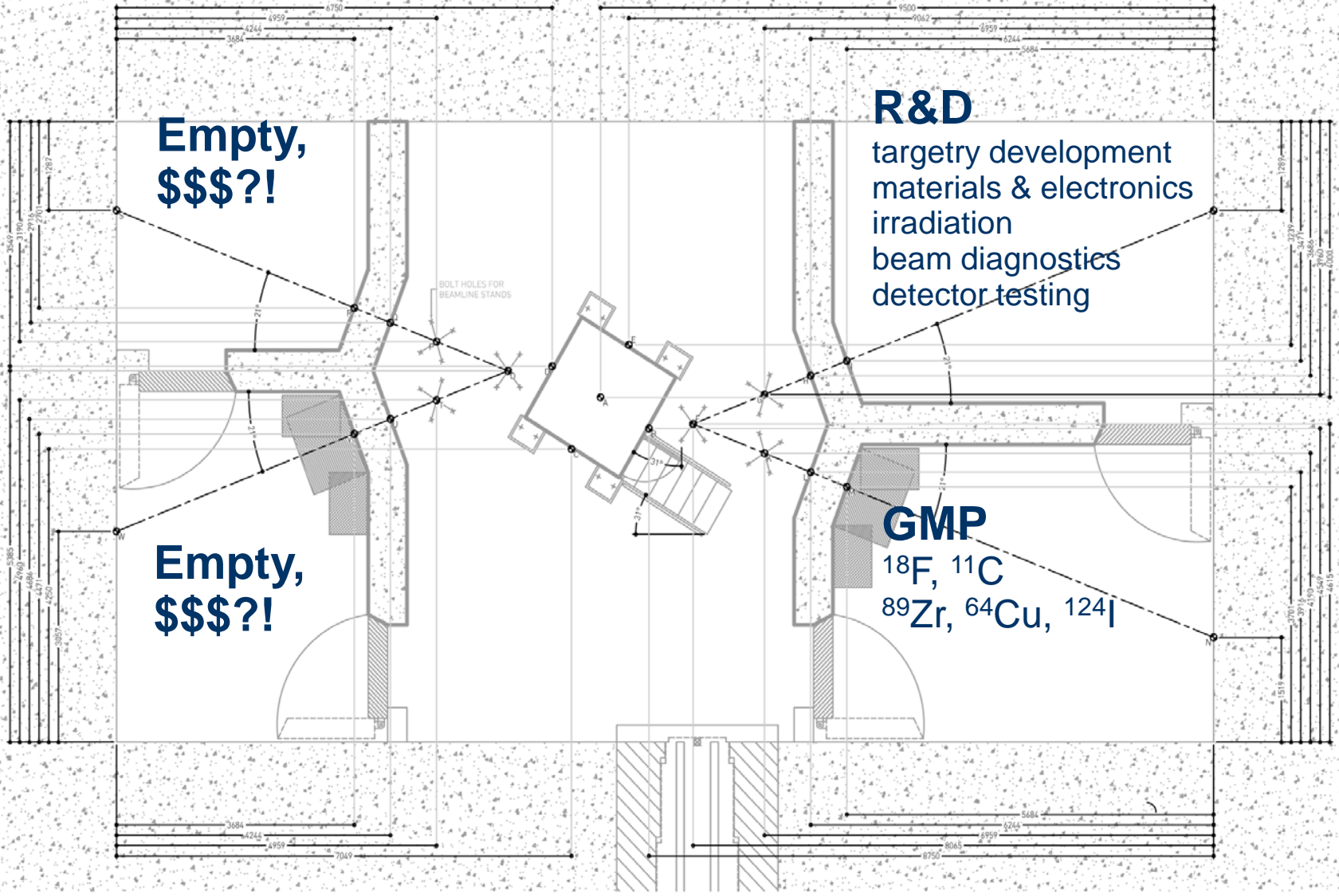
INRNE →

Close to major roads – 4 hospitals nearby, airport, highways to N/E part of Bulgaria.

# Cyclotron vault layout

Synthesis units (GMP/R&D)

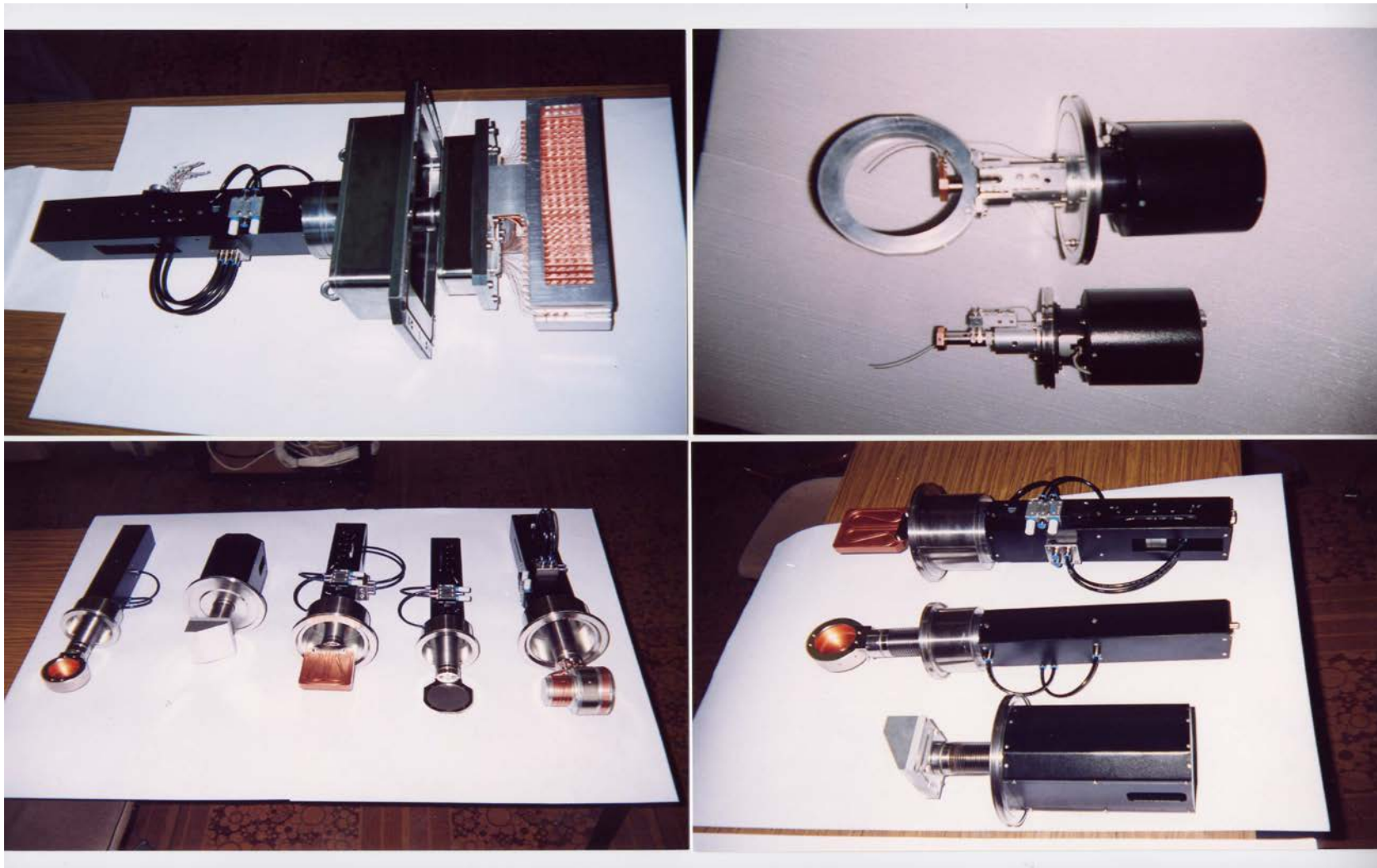
Synthesis units (GMP/R&D)



Till 1989 radioisotopes production at the **Research Nuclear Reactor IRT-2000**:

- › **Sealed radioactive sources**:  $^{60}\text{Co}$ ,  $^{75}\text{Se}$  and  $^{192}\text{Ir}$  used for gamma-defectoscopy control, charging of gamma relays in testing equipment.
- › **Short living isotopes**:  $^{18}\text{F}$ ,  $^{42}\text{K}$ ,  $^{24}\text{Na}$ ,  $^{64}\text{Cu}$ ,  $^{82}\text{Br}$ ,  $^{140}\text{La}$  for application in industry, criminology, biology, medicine, etc.
- › **Radioactive sources** of  $^{198}\text{Au}$ ,  $^{90}\text{Y}$ ,  $^{182}\text{Ta}$ ,  $^{192}\text{Ir}$  for treatment of certain types of malignant tumors.
- › **12 products** of great value for medical usage.
- › Before EU GMP, INRNE used to **produce cold kits for  $^{99\text{m}}\text{Tc}$  and distribute them to hospitals** (**MDP** for skeletal metastases, **MDP-RPC** for labeling of **RBC**, **PYROPHOSPHATE** for myocardial imaging, etc).

# Beam Diagnostics Modules. In-house technical design. Workshop for Development and Production/Physics.



## Evaluate internal hazards:

- › Nuclides in target body
- › Define nuclides expected to be produced over the operation time of the machine and the vault
- › Check vault radiation specs w.r.t. neutrons and gamma rays
- › Define cooling time - short lived nuclides (airborn  $^{41}\text{Ar}$ ?)
- › Check operators dose rate

Monte-Carlo approach

FLUKA used for simulations

- › Emission and transport of secondary particles due to primary nuclear reaction
  - › low energy neutron transport
  - › takes into account the geometry of the impinging beam (e.g. point source)
- › Assessment of the produced residual nuclei
- › Possibility to score the same physics process at different irradiation & cooling times
  - › buildup and decay of waste
  
- › Not possible to include missing X-section libraries

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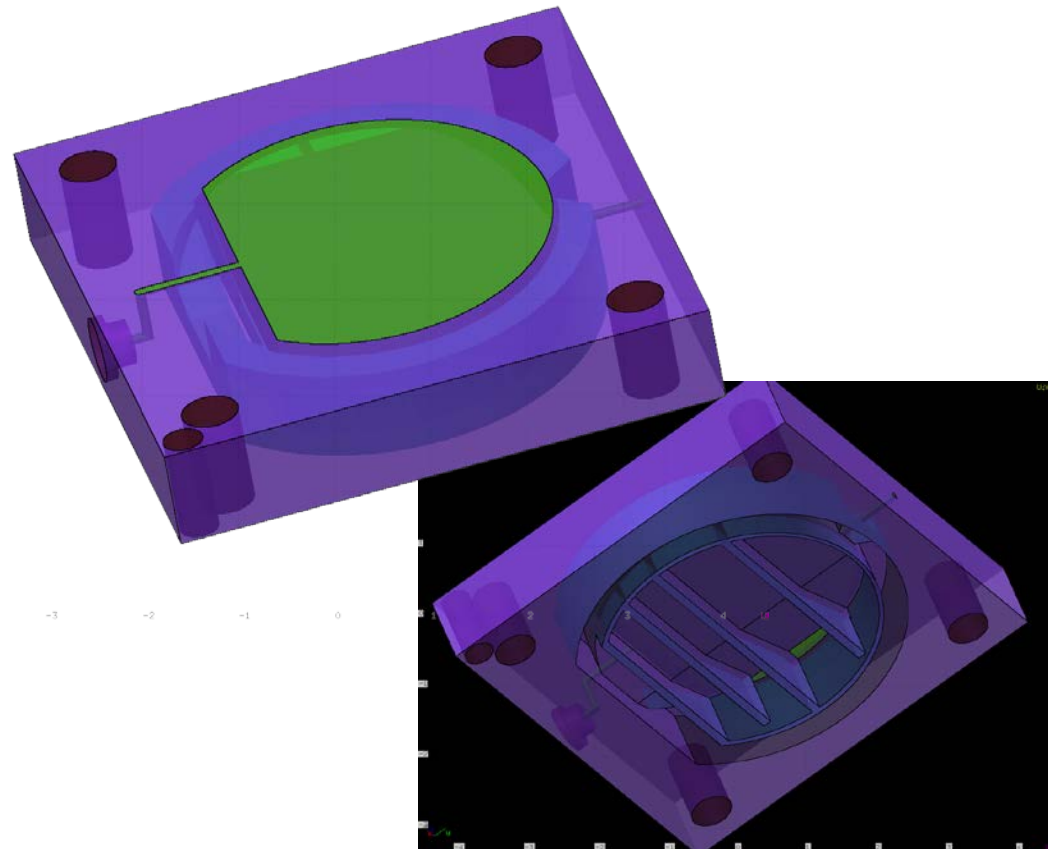
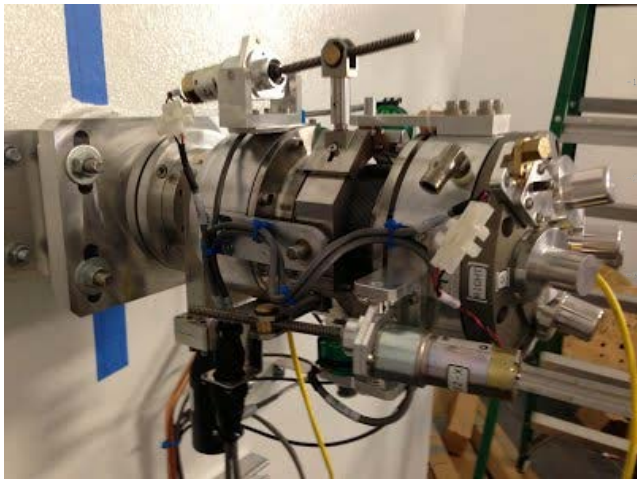
## Two-step approach to estimate fluence/waste within the vault

- › Simulate **target** irradiation, assess secondary particles
  - ›  $(p, n)$ ,  $(p, \gamma)$
- › Use **secondary particles as source** irradiating vault components

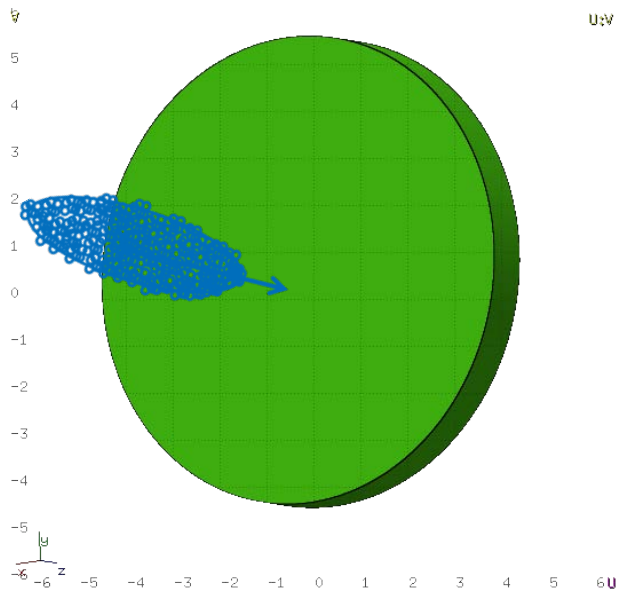
# $^{18}\text{F}$ high-current liquid target



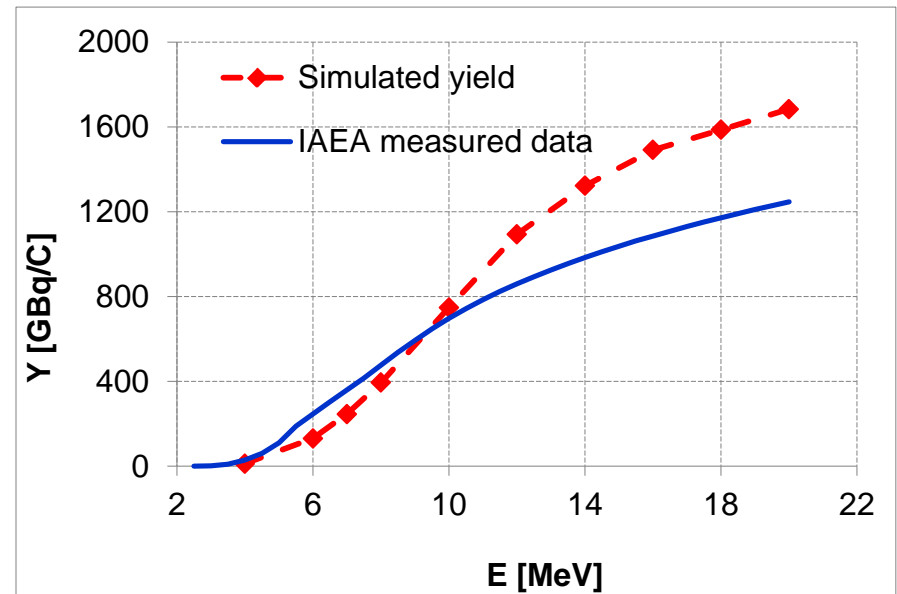
- > Delivered 3.8 mL targets
- > Check thick target yield in  $^{18}\text{O}(p, n)^{18}\text{F}$
- > Pipe secondary particles to be used as source irradiating the vault



# Check the FLUKA Monte-Carlo methodics



A proton beam (various **E**, fixed **I**) impinges on a simple target



**Thick target** – the reaction takes place with the volume of enriched water.

The lower the beam energy, the better the agreement:

- » Real beam not gaussian in any plane, not point-like, no experimental data on phase space
- » The FLUKA model is limited in terms of energy

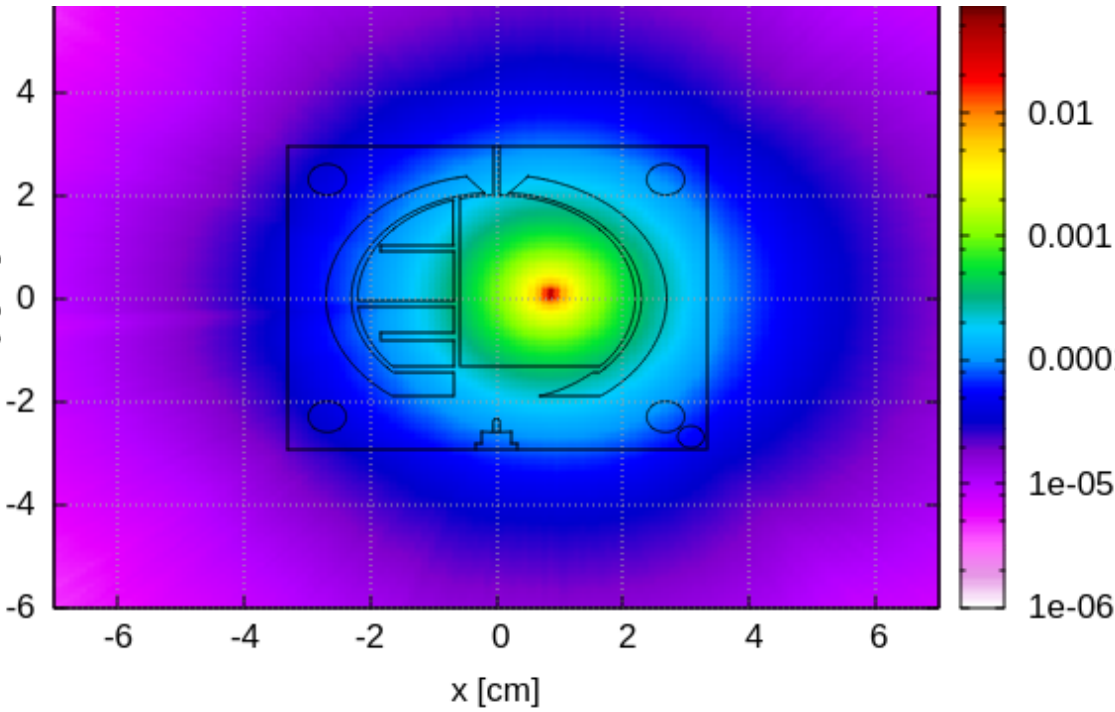
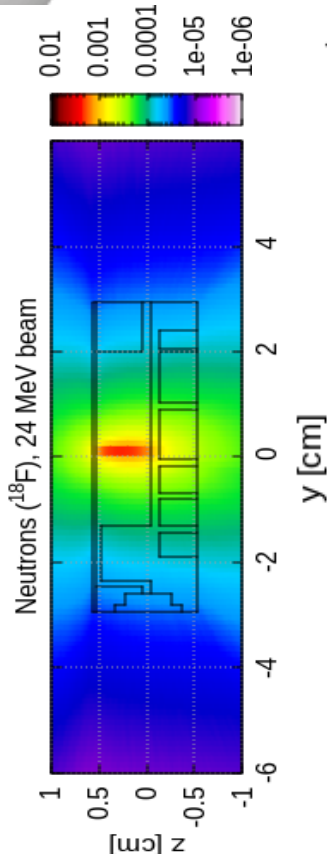
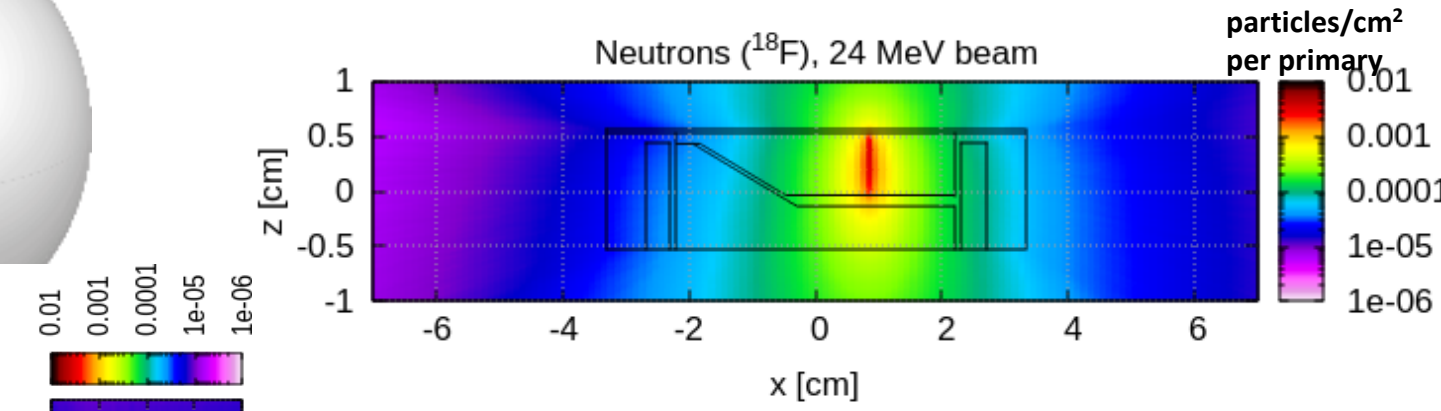
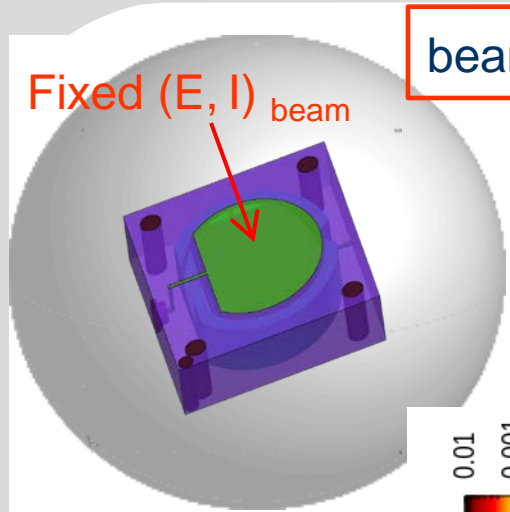


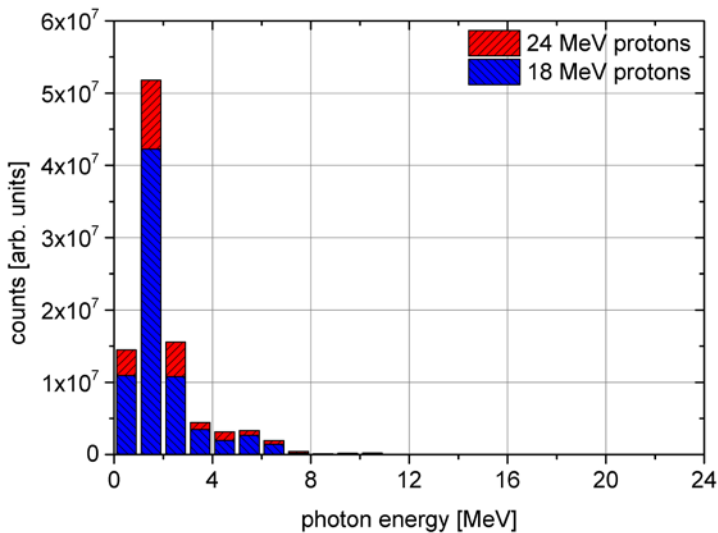
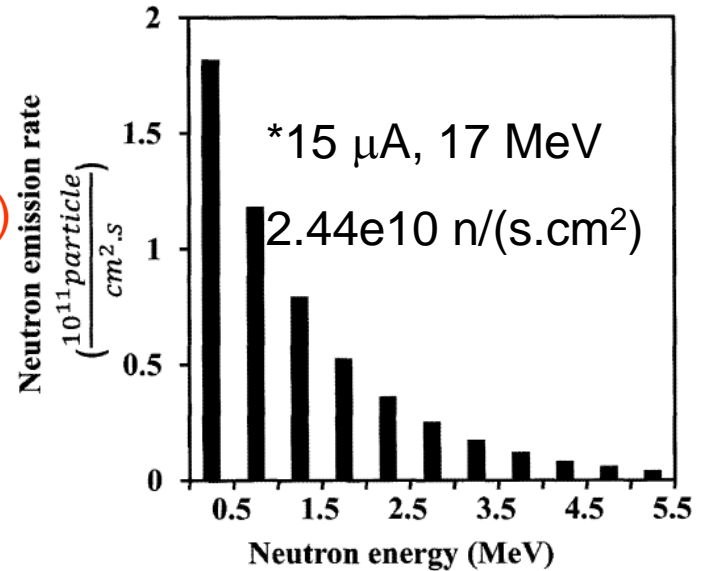
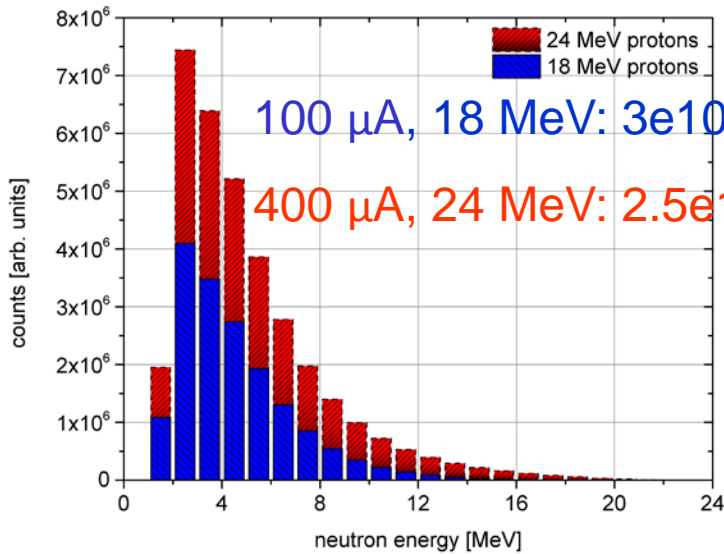
# Secondary particles – real target

## A. Density distribution

beam orientation w.r.t. target

rate of emission of secondaries

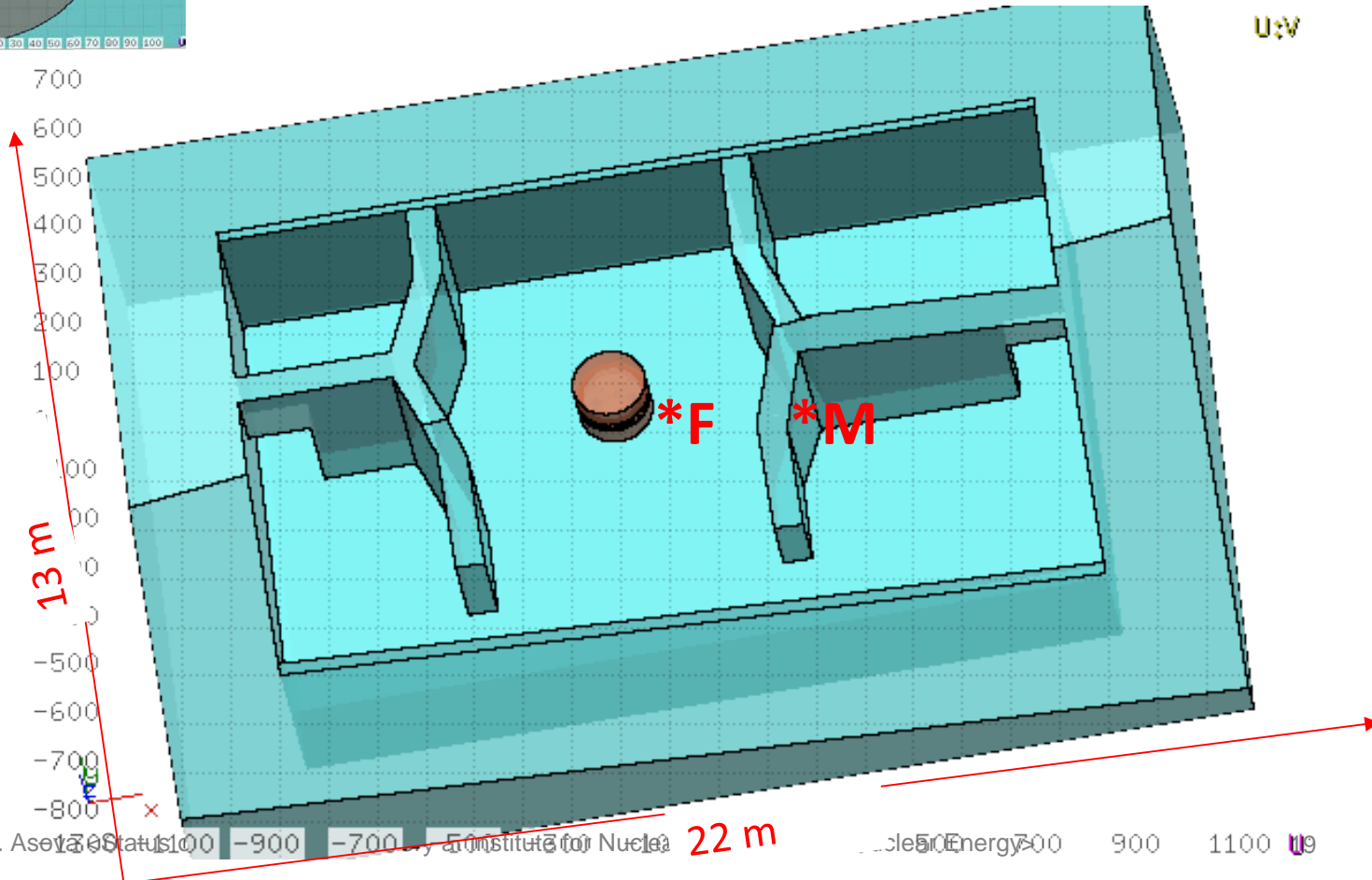
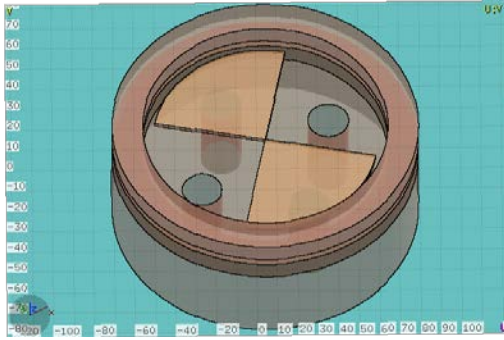




\*Sadat-Eshkevar et al, Assessment of the staff absorbed dose related to cyclotron operation and service in the production of <sup>18</sup>F radiopharmaceuticals, *Nukleonika* 2012; 57 (3):407-410

# The vault with the cyclotron

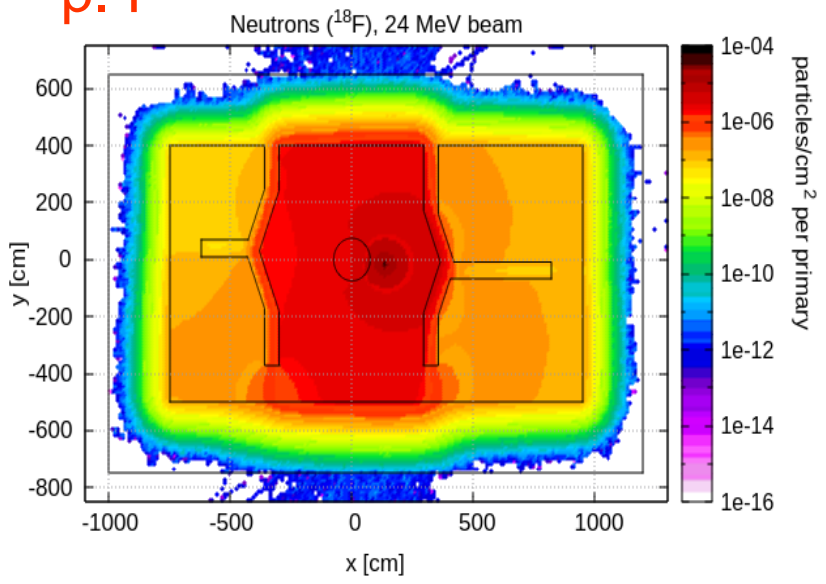
External targets in a  $^{18}\text{F}$ -dedicated cave (\*)



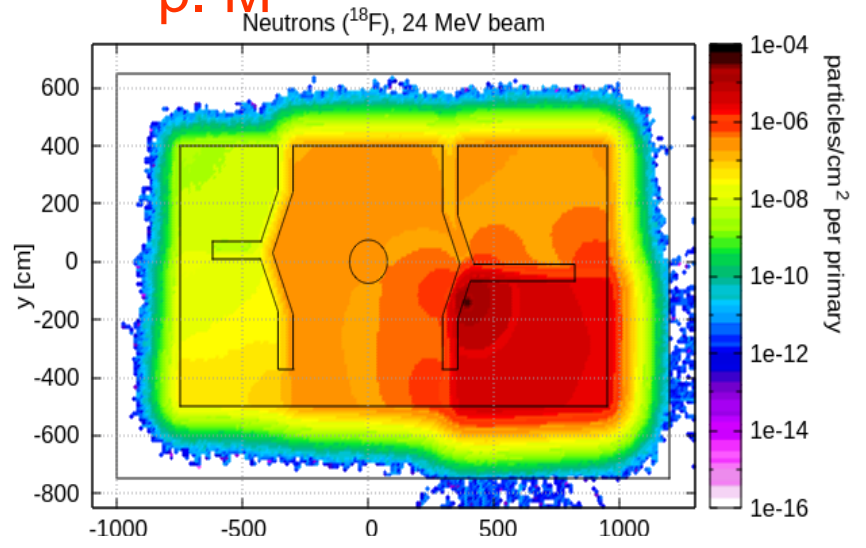
# Neutron fields

No additional shielding around the targets. High-density concrete used.

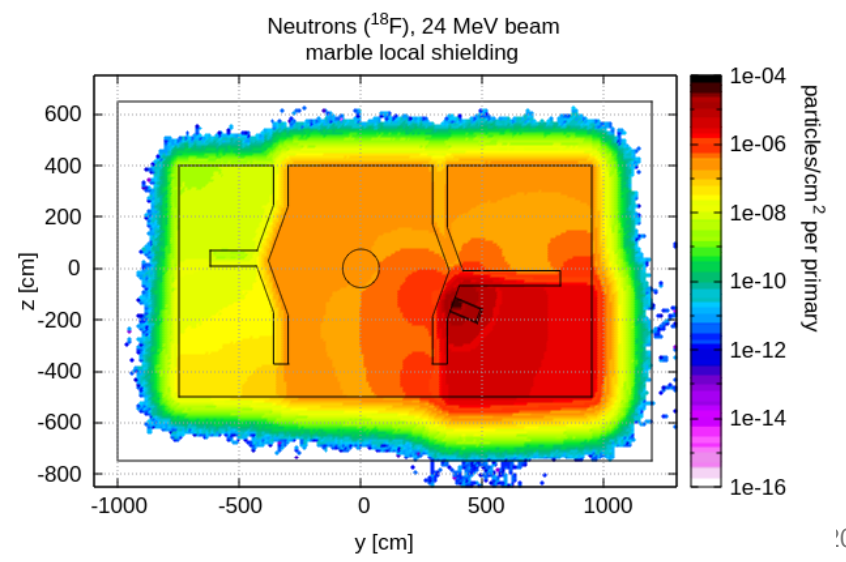
p. F

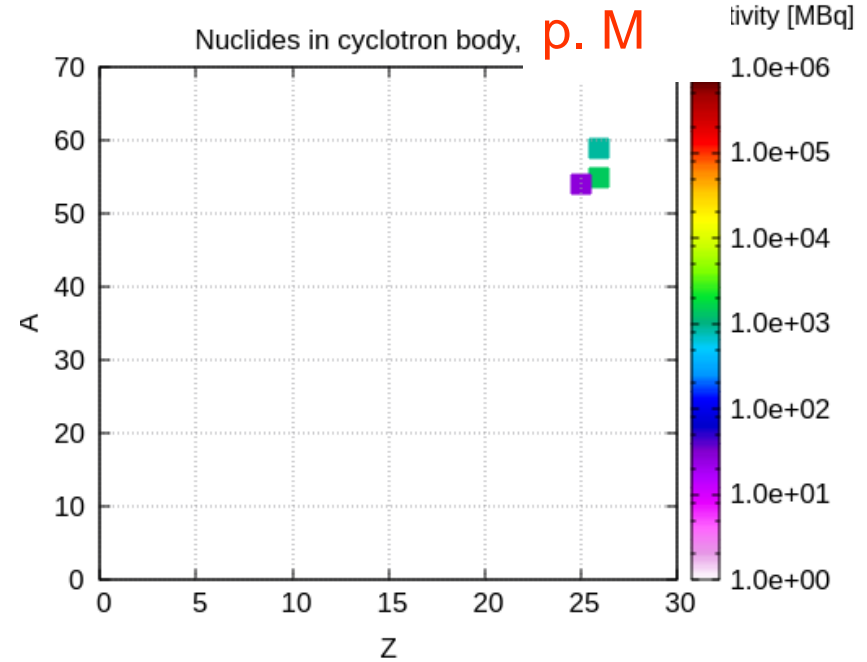
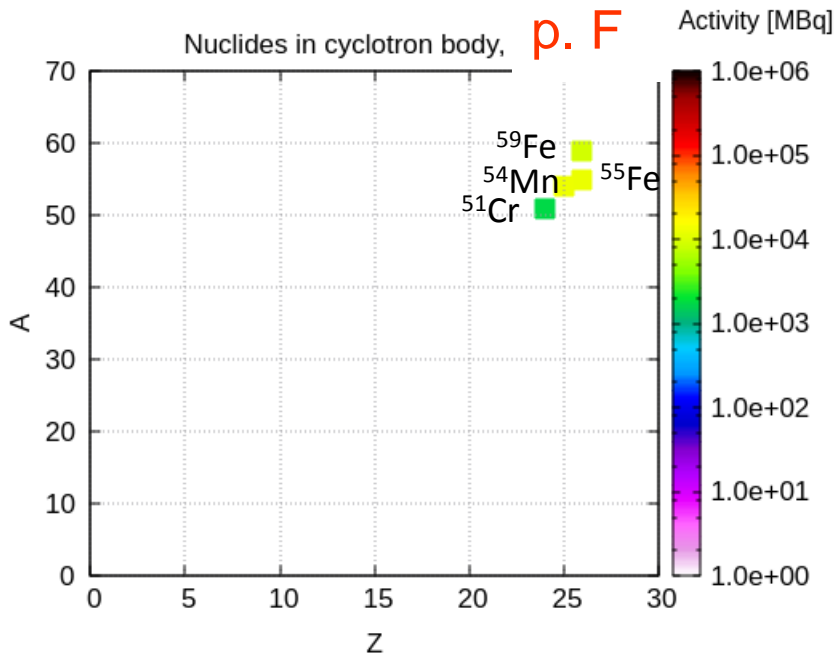


p. M



Marble-enriched shielding  
around the target. **→**  
Thickness not optimized!

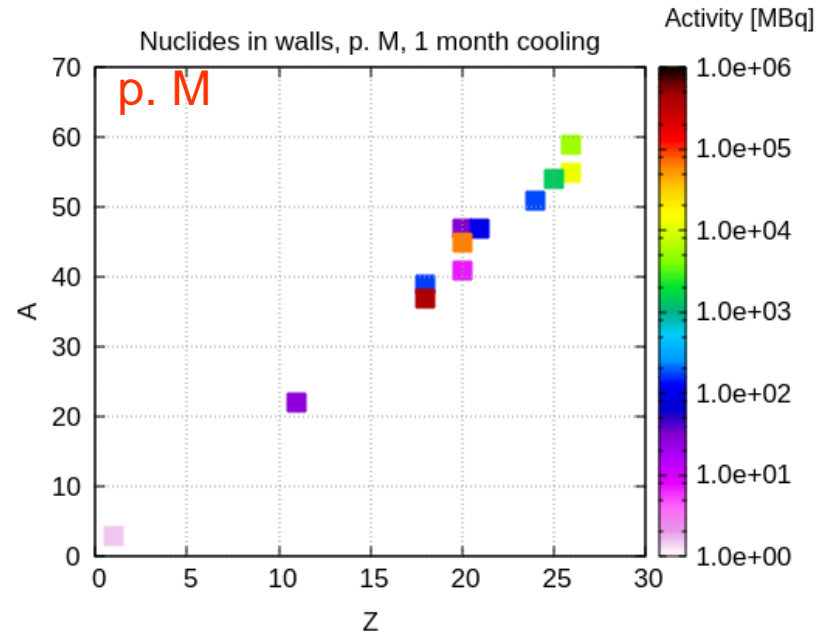
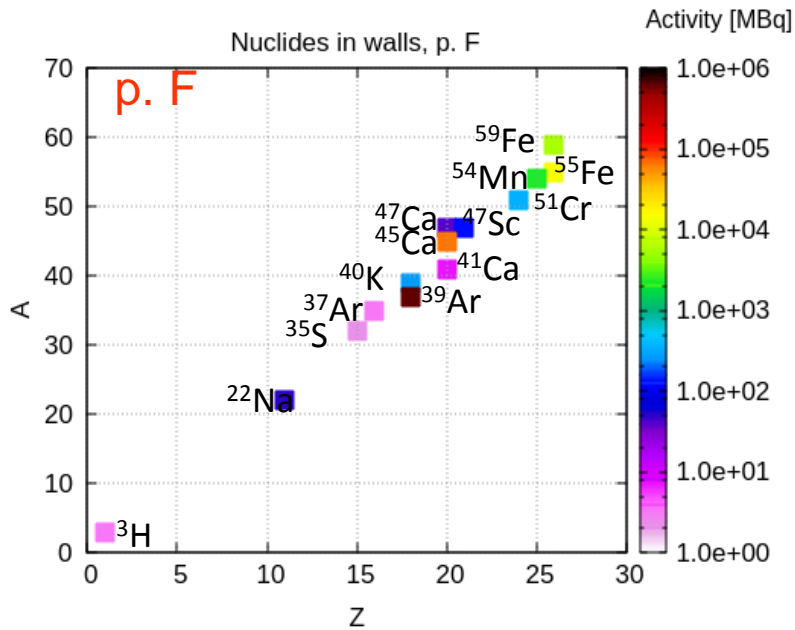




- $^{55}\text{Fe}$  ( $t_{1/2} = 2.7$  y)
- $^{53}\text{Mn}$  ( $t_{1/2} = 3.7\text{e}6$  y)
- $^{56}\text{Mn}$  ( $t_{1/2} = 2.6$  h)
- $^{59}\text{Fe}$  ( $t_{1/2} = 44.5$  d)
- $^{54}\text{Mn}$  ( $t_{1/2} = 312$  d)

p. M preferable w.r.t. cyclotron contamination.

# Nuclides in vault, irradiation for 6 h/d for a month @ 400 $\mu$ A, 24 MeV



$^{59}\text{Fe}$  ( $t_{1/2} = 44$  d)

$^{53}\text{Mn}$  ( $t_{1/2} = 3.7\text{e}6$  y)

$^{45}\text{Ca}$  ( $t_{1/2} = 163$  d)

$^{51}\text{Cr}$  ( $t_{1/2} = 27$  d)

$^{54}\text{Mn}$  ( $t_{1/2} = 312$  d)

$^{37}\text{Ar}$  ( $t_{1/2} = 35$  d)...

Almost no difference in walls contamination between p. M and p. F (score outer walls?).

# Nuclides in vault, irradiation for 6 h/d for a month @ 400 $\mu$ A, 24 MeV

walls

after EOB

3 weeks cooling

		after EOB	3 weeks cooling	
$^{59}\text{F}$	44 d	8 GBq		
$^{56}\text{Mn}$	2.6 h	0.6 GBq		
$^{55}\text{Fe}$	2.7 y	13 GBq		
$^{54}\text{Mn}$	312 d	1.4 GBq		
$^{53}\text{Mn}$	3.7e6 y	15 Bq		
$^{51}\text{Cr}$	28 d	0.3 GBq		1 year
$^{49}\text{Sc}$	57 m	1 MBq		
$^{47}\text{Sc}$	3 d	1.9 GBq		
$^{47}\text{Ca}$	4.5 d	2 GBq		
$^{45}\text{Ca}$	163 d	69 GBq		
$^{41}\text{Ca}$	1e5 y	6.7 MBq		
$^{43}\text{K}$	22 h	0.3 GBq		
$^{42}\text{K}$	12.4 h	858 GBq		
$^{39}\text{Ar}$	269 y	167 MBq	4.6 kBq	
<b><math>^{41}\text{Ar}</math></b>	<b>109 m</b>	<b>10 MBq</b>	<b>42 MBq / 1 GBq</b>	1 day

# Summary

- › Major problem – “researchers dislike wasting time and inspiration on infrastructure projects”. They also lack skills and knowledge required to run an infrastructure investment project. The solution:
  - » seek consultants until “BEAM-ON” time and partnership with well established radiopharmaceutical companies and foreign R&D institutions
- › Land for the facility granted by BAS, geological survey done.
- › The building for the cyclotron facility – ongoing call for public tenders.
- › Monte-Carlo procedure needed for Bulgarian Nuclear Regulatory Agency
  - » model of the vault complete unless something changes
  - » more simulations to come
    - » vault with local target shielding, with marble concrete, activation in depth in the walls, etc.
    - » more isotopes to be checked –  $^{67, 68} \text{Ga}$ ,  $^{111} \text{In}$ ,  $^{64} \text{Cu}$ , etc.
- › Design a solid target station capable to work with the beam load delivered by the cyclotron – far future.
- › Nuclear physics – far future.

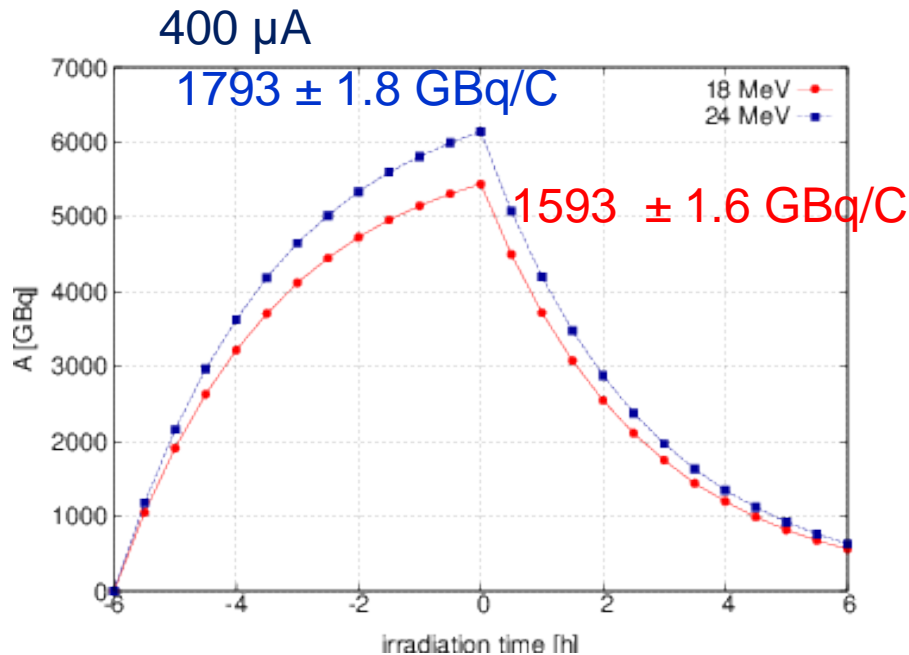


Thank you for the attention!

# Thick target yield

Cross-check FLUKA calculations with published experimental data

- › 100 and 400  $\mu\text{A}$  for 18 and 24 MeV
  - » results normalized to particle charge ( $Y_{100 \mu\text{A}} \sim Y_{400 \mu\text{A}}$  depending on the beam energy)



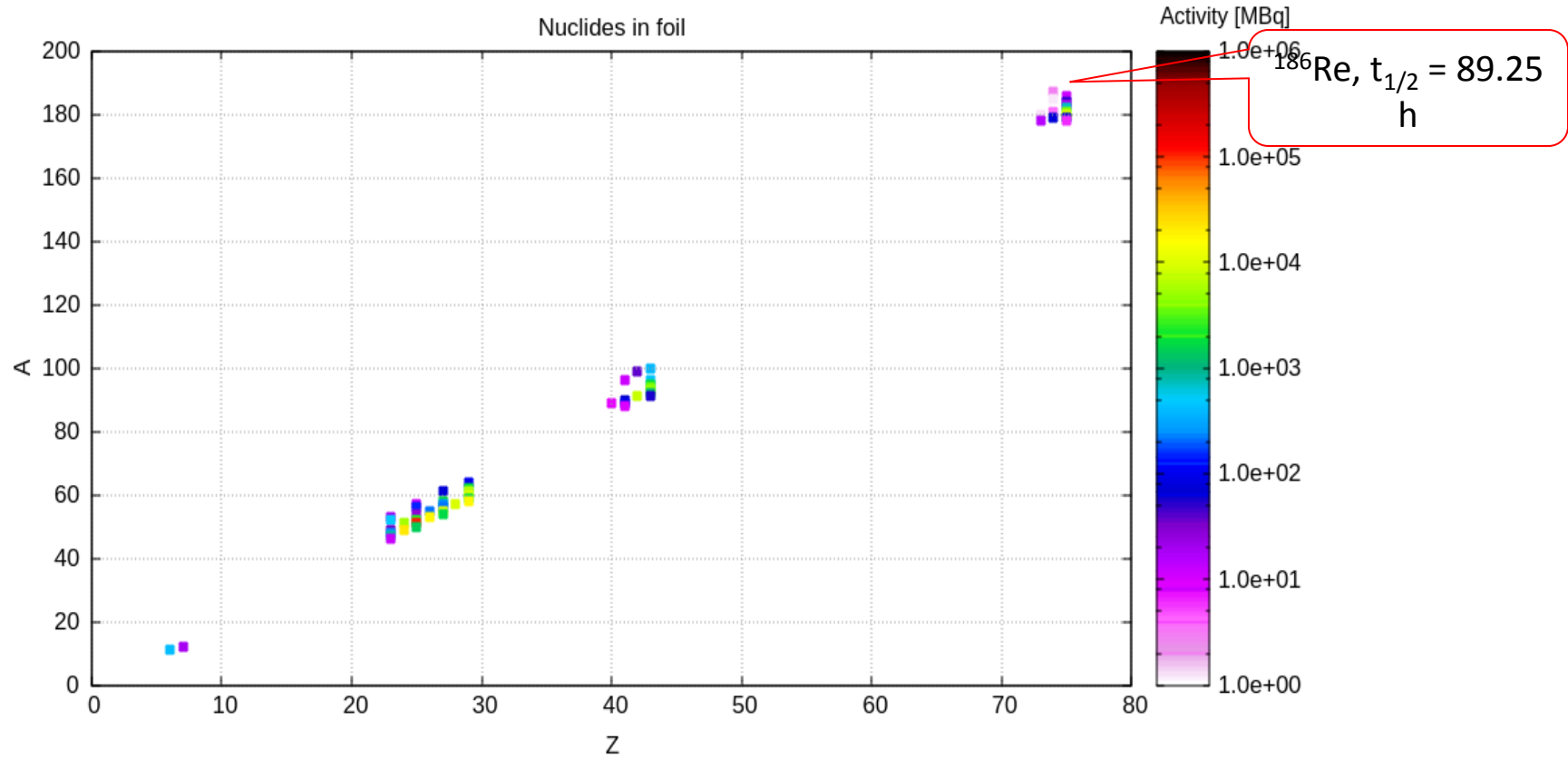
IAEA data (IAEA-TECDOC-1211):

18 MeV: 1171 GBq/C measured

24 MeV - no data.

# Nuclides in Havar foil

After irradiation with 400  $\mu\text{A}$  @ 24 MeV, 6 h



$^{186}\text{W}$  (p, n)  $^{186}\text{Re}$  – liver cancer treatment

$^{93}\text{Mo}$  ( $t_{1/2} = 4\text{e}3$  y)

$^{57}\text{Co}$  ( $t_{1/2} = 272$  d)

$^{55}\text{Fe}$  ( $t_{1/2} = 2.7$  y)

# Nuclides in Havar foil

After irradiation with 400  $\mu$ A @ 24 MeV, 6 h

		Exemption limit
$^{185}\text{W}$	75 d	5.6 MBq / 10 MBq
$^{181}\text{W}$	121 d	7 MBq / 10 MBq
$^{96}\text{Tc}$	4.3 d	126 MBq / 1 MBq
$^{93}\text{Mo}$	4e3 y	0.6 Bq / 0.1 GBq
$^{59}\text{Fe}$	44 d	558 MBq / 1 MBq
$^{58}\text{Co}$	71 d	2.7 MBq / 1 MBq
$^{56}\text{Mn}$	2.6 h	18 MBq / 0.1 MBq
$^{56}\text{Co}$	77 d	0.1 MBq / 0.1 MBq
$^{55}\text{Fe}$	2.7 y	0.03 MBq / 1 MBq
$^{54}\text{Mn}$	312 d	0.7 MBq
$^{52}\text{Mn}$	5 d	71 MBq / 0.1 MBq
$^{51}\text{Cr}$	28 d	23 MBq / 10 MBq
$^3\text{H}$	12.3 y	88 MBq / 1 GBq

137 days  
in storage