Theranostic Radioisotope production Techniques with High Current Cyclotrons

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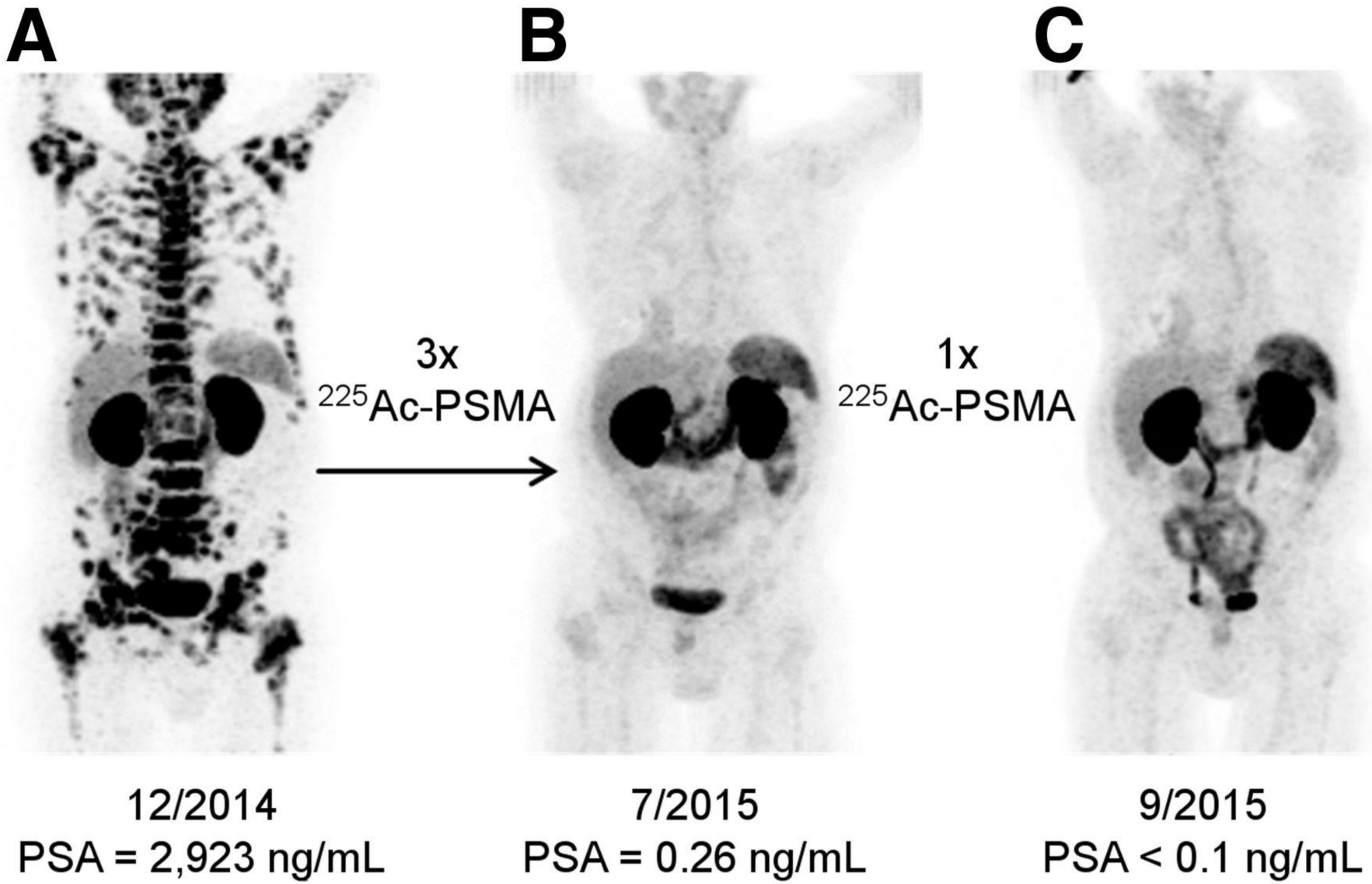
1. Concentrate on treating disease   Theranostics Background Information
2. IBS potential isotopes
3. Key cyclotron features
4. Key targetry features
5. Neutron production too.
6. Case examples
    1. Lu177
    2. BNCT

Summary

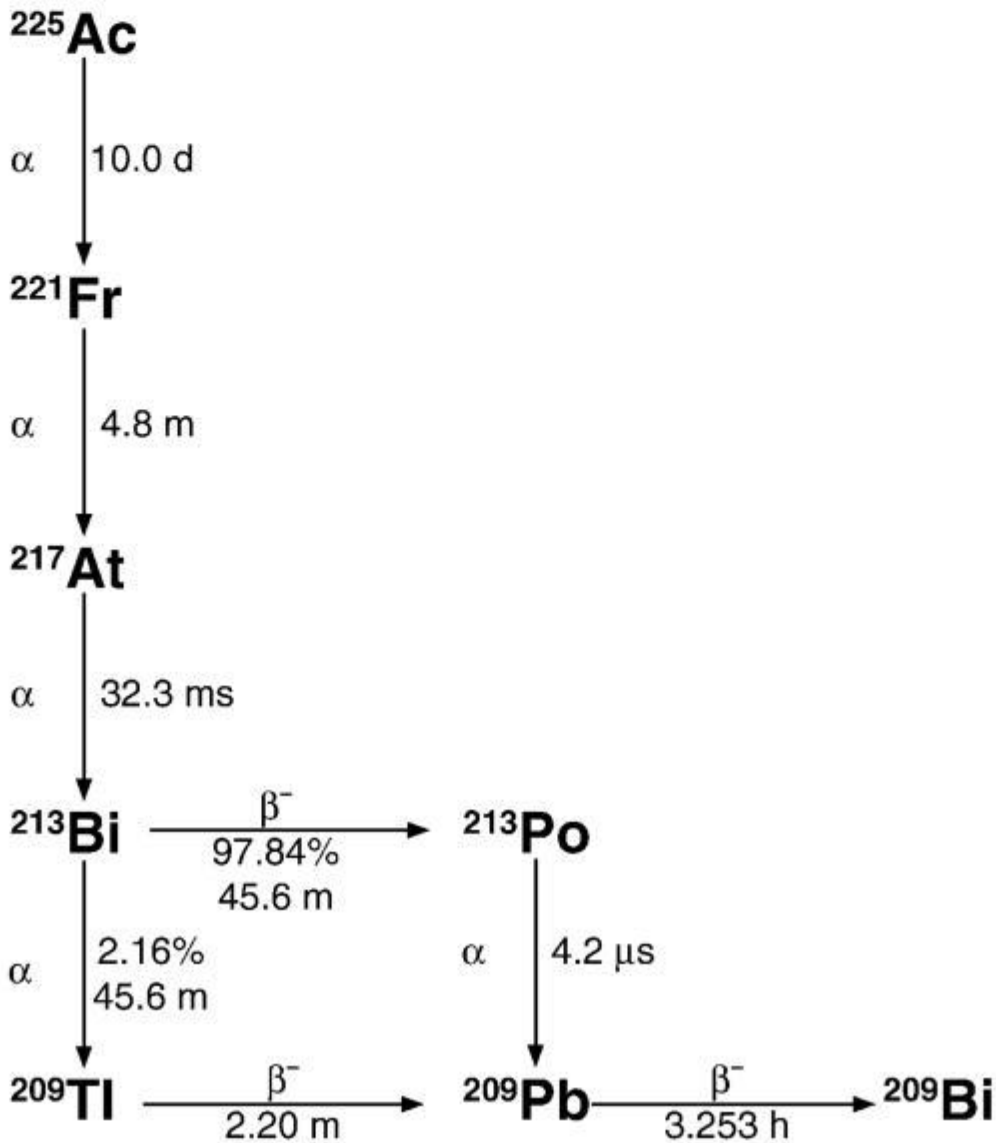
*sponsored by TeamBest



68Ga-PSMA-11 PET/CT scans of patient A. Pretherapeutic tumor spread (A), restaging 2 mo after third cycle of 225Ac-PSMA-617 (B), and restaging 2 mo after one additional consolidation therapy (C). Clemens Kratochwil et al. J Nucl Med 2016;57:1941-1944

The Journal of NUCLEAR MEDICINE

Ac^{225} Details



Ac 225 decay chain.

Alpha Energy
MeV

5.9

6.3

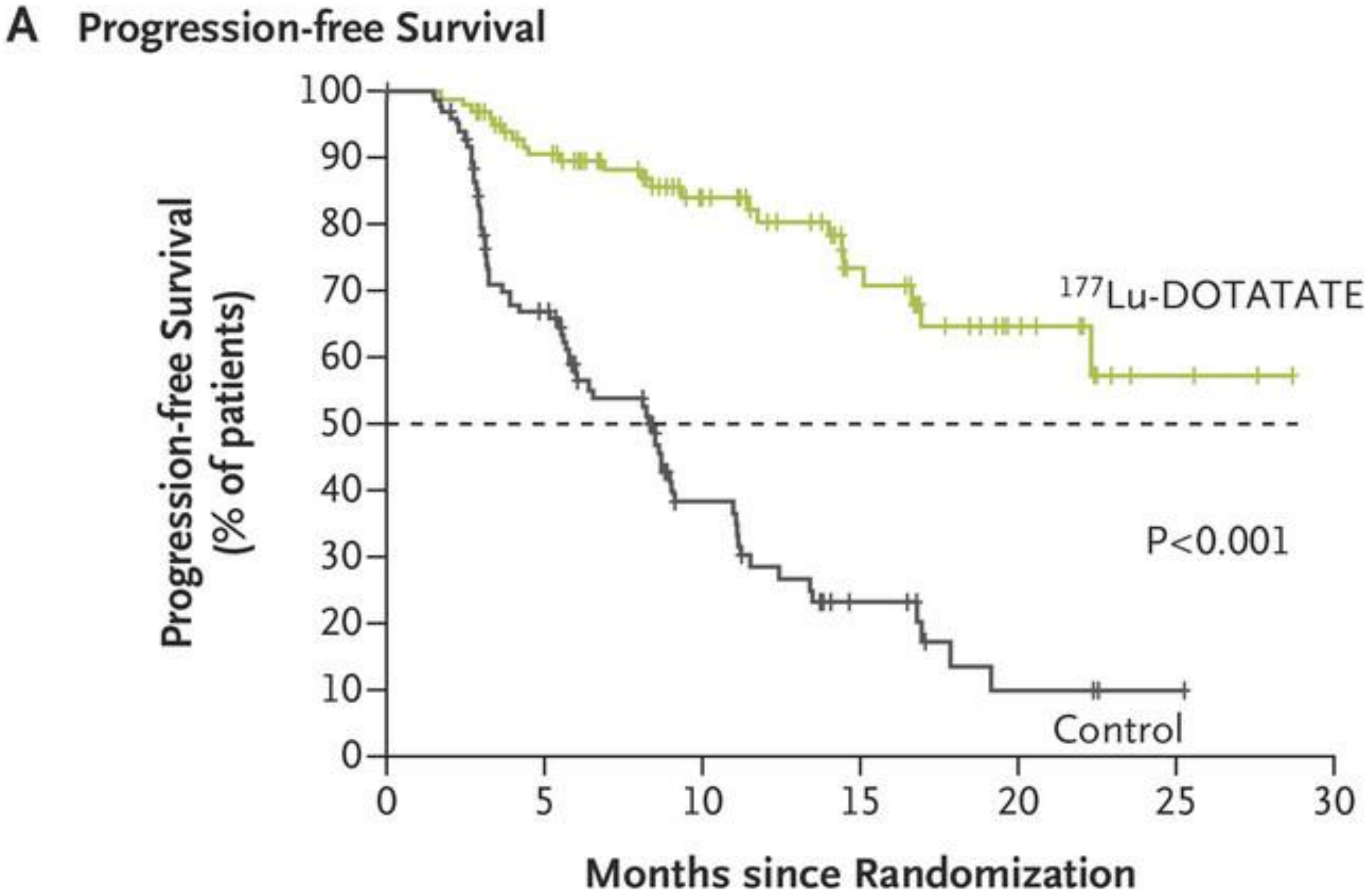
7.2

8.5

nominal Range in
Muscle
46 uM

Nominal Injection Dosage

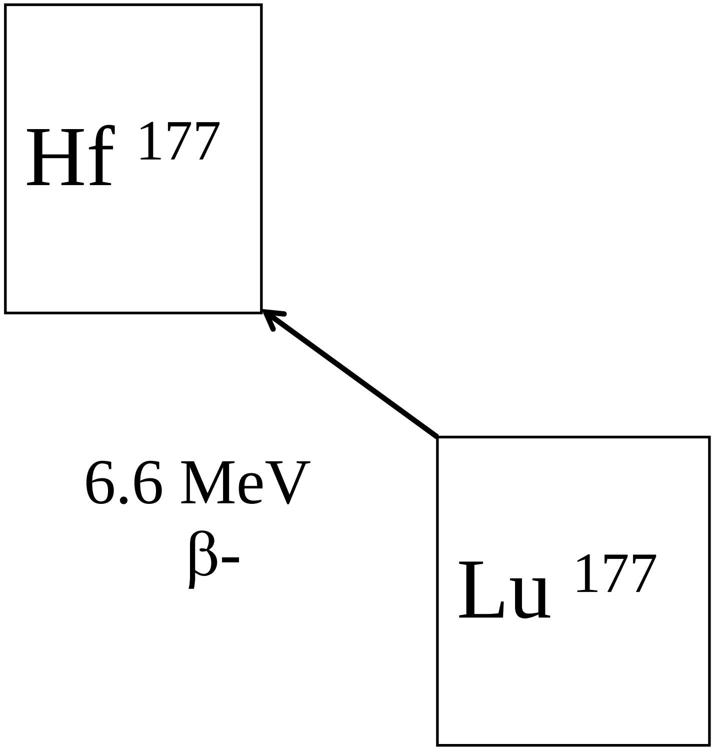
100 KBq/kgBW
Or
6 MBq (160 mCi)



Lutathera Therapy

Strosberg J et al. N Engl J Med 2017;376:125-135.

Luticium Details



Nominal Injection Dosage

7.4 MBq (200 mCi)

Range in water ~ 3 mm

Theranostic Pairs

isotope for image	isotope for therapy
^{64}Cu (12.7 h)	^{67}Cu (2.6 d, 141 keV)
^{44}Sc (3.9 h)	^{47}Sc (3.3 d, 162 keV)
^{86}Y (14.7 h)	^{90}Y* (2.7 d, 934 keV)
^{68}Ga (1.1 h)	^{67}Ga (3.3 d, 12 keV)
^{72}As (26.0 h)	^{76}As (26 h, 1070 keV) ^{77}As* (39 h, 225 keV)

Need pairs but select carefully

Therapy

^{211}At $t_{1/2}$ = 7.2 h

^{225}Ac $t_{1/2}$ = 10.0 d

^{223}Ra $t_{1/2}$ =11.4d

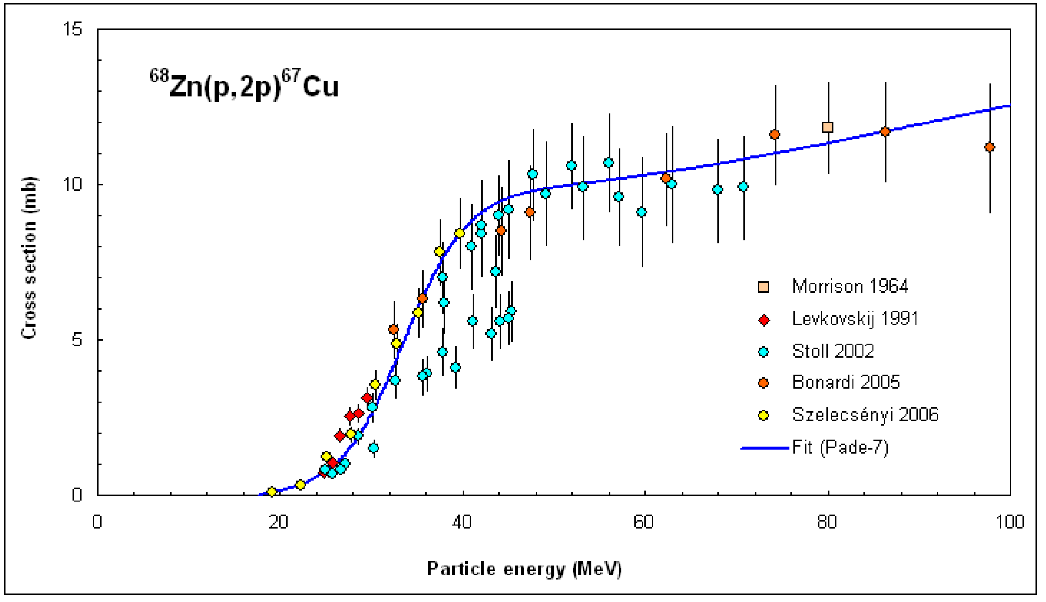
^{111}In $t_{1/2}$ = 2.81 d

reaction	isotope for image
$^{64}Ni(p,n)^{64}Cu$ T=15 MeV	^{64}Cu (12.7 h)
$^{44}Ca(p,n)^{44}Sc$ T=15MeV	^{44}Sc (3.9 h)
$^{86}Sr(p,n)^{86}Y$ T=15 MeV	^{86}Y (14.7 h)
$^{69}Ga(p,2n)^{68}Ge$ T=35 Mev	^{68}Ga (1.1 h)
$^{68}Zn(p,n)^{68}Ga$ T=15 MeV	
$^{72}Ge(p,n)^{72}As$ T=15 MeV	^{72}As (26.0 h)
$^{70}Ge(p,n)^{70}As$ T=15 (53min)	

isotope for therapy	reaction
^{67}Cu (2.6 d, 141 keV)	^{68}Zn(p,2p)^{67}Cu T=70MeV
^{47}Sc (3.3 d, 162 keV)	^{48}Ti(p,2p)^{47}Sc T= 70 MeV
^{90}Y* (2.7 d, 934 keV)	reactor or ^{91}Zr(p,2p) T=70
^{67}Ga (3.3 d, 12 keV)	^{68}Zn(p,2n)^{67}Ga T=45 MeV
^{76}As (26 h, 1070 keV)	^{76}Ge(p,n)^{76}As
^{77}As* (39 h, 225 keV)	^{78}Se(p,2p)^{77}As
	Bi209 (li6,4n)Rn211
^{211}At $t_{1/2}$ = 7.2 h	Bi209(alpha,2n) 35 MeV
^{225}Ac $t_{1/2}$ = 10.0 d	^{226}Ra(p,2n)^{225}Ac T=35 MeV
	^{232}Th p spallation 100 MeV
^{223}Ra $t_{1/2}$ =11.4d	beta decay of ^{223}Fr and Ra^{226} (p,alpha)reaction
^{111}In $t_{1/2}$ = 2.81 d	electron conversion ^{112}Cd(p,2n) T=35 MeV

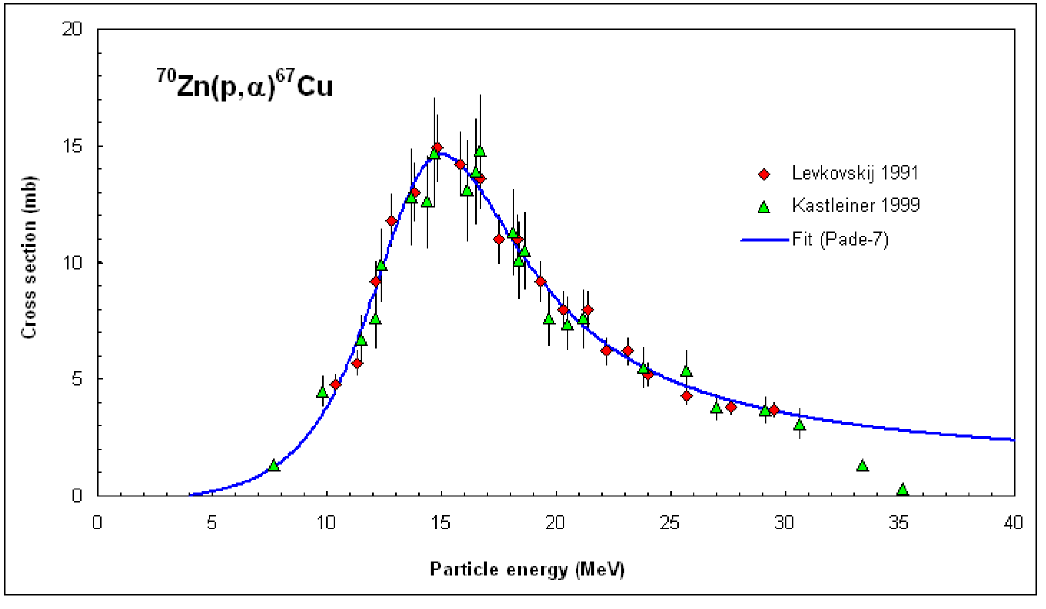
Theranostics

Cu^{67} Production



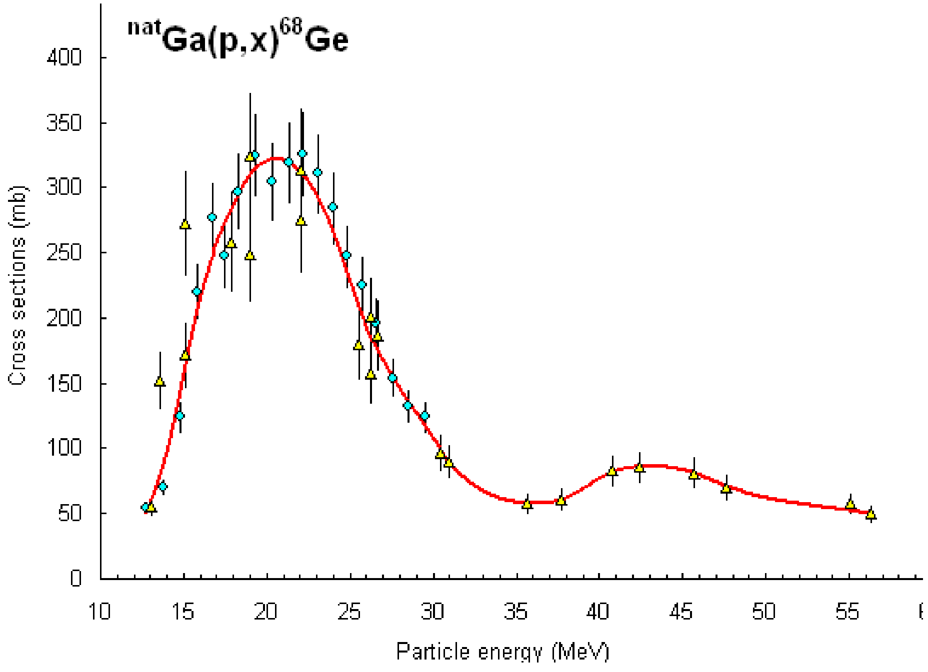
Yield is 30 MBq/uAhr at 70 MeV

isotopic abundance
Zn68 19%
Zn70 0.6%

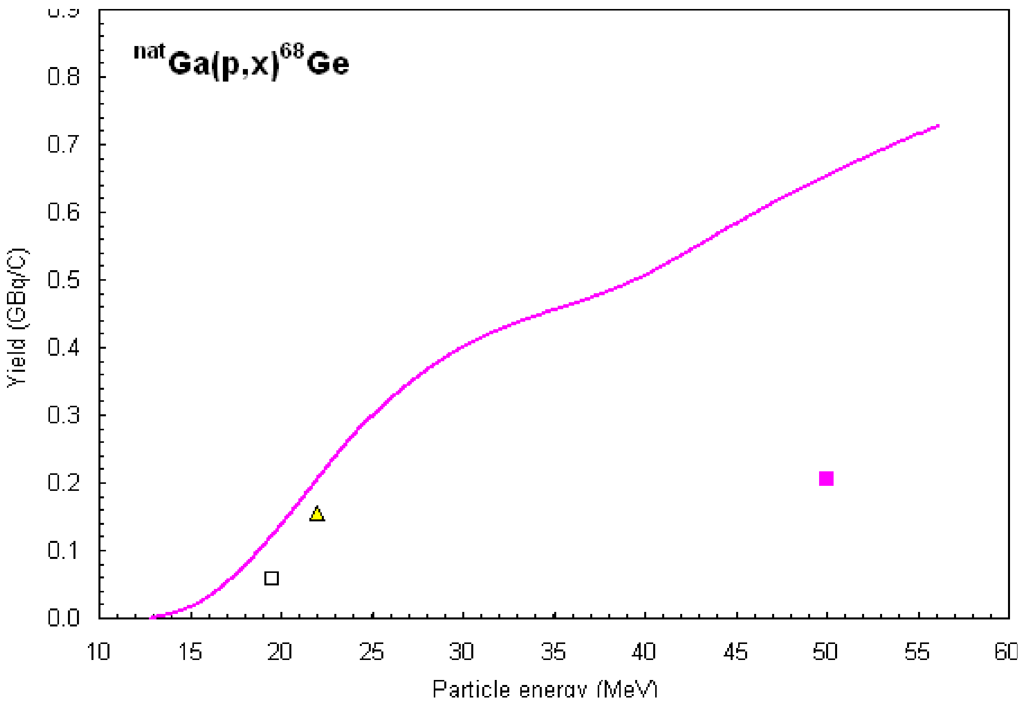


Yield at 25 MeV is 5 MBq/uAhr

IAEA medical portal



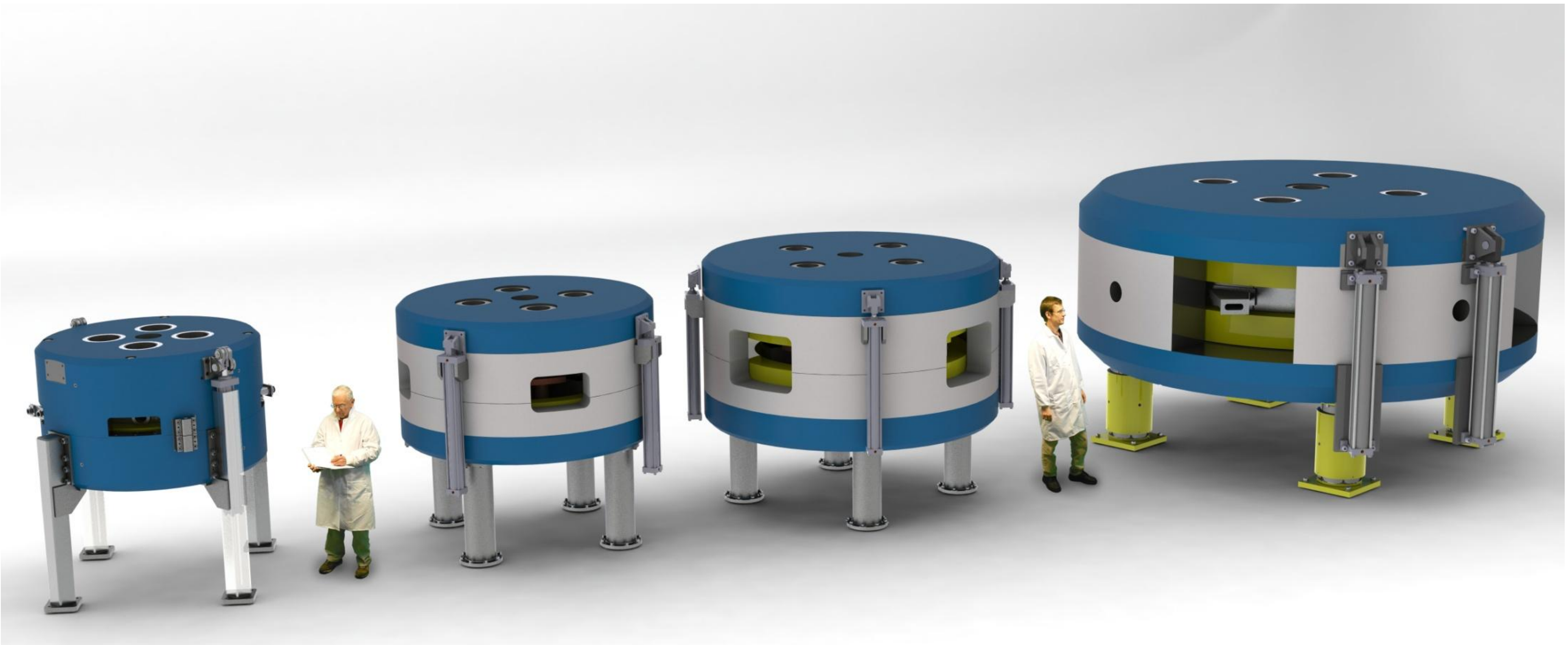
Yield at 40 MeV is 1.8 MBq/uAhr



IAEA medical portal

Key features for Medical Radioisotope Production with compact cyclotrons

Energy, intensity, targets



B15 PET
15 MeV
1000 (200} uA +
Targets Radiochem

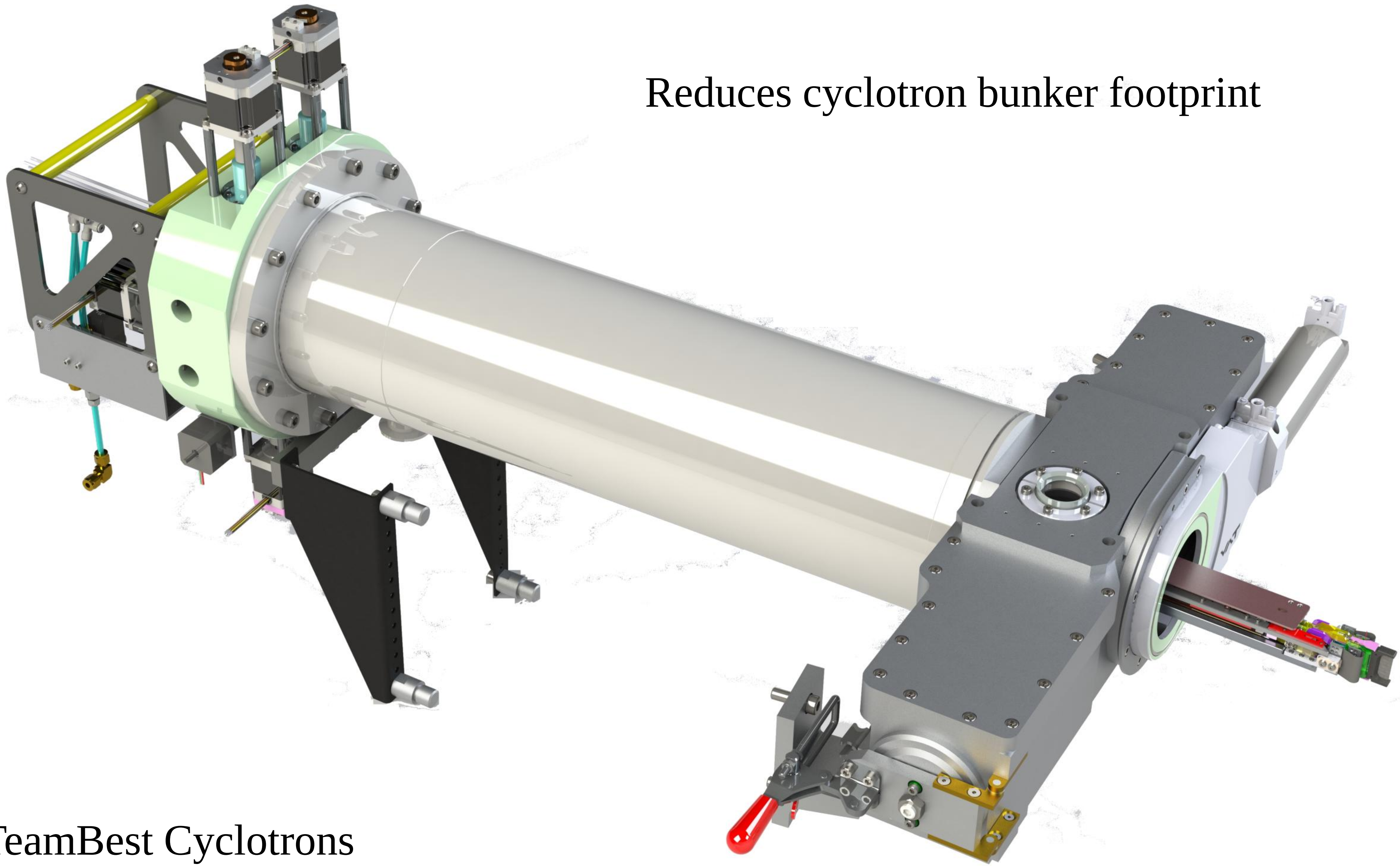
B25
20-25 MeV
1000 (400)uA +
Targets Radiochem

B35 (28)
15-35(28) MeV
1000(400) uA
Targets Radiochem

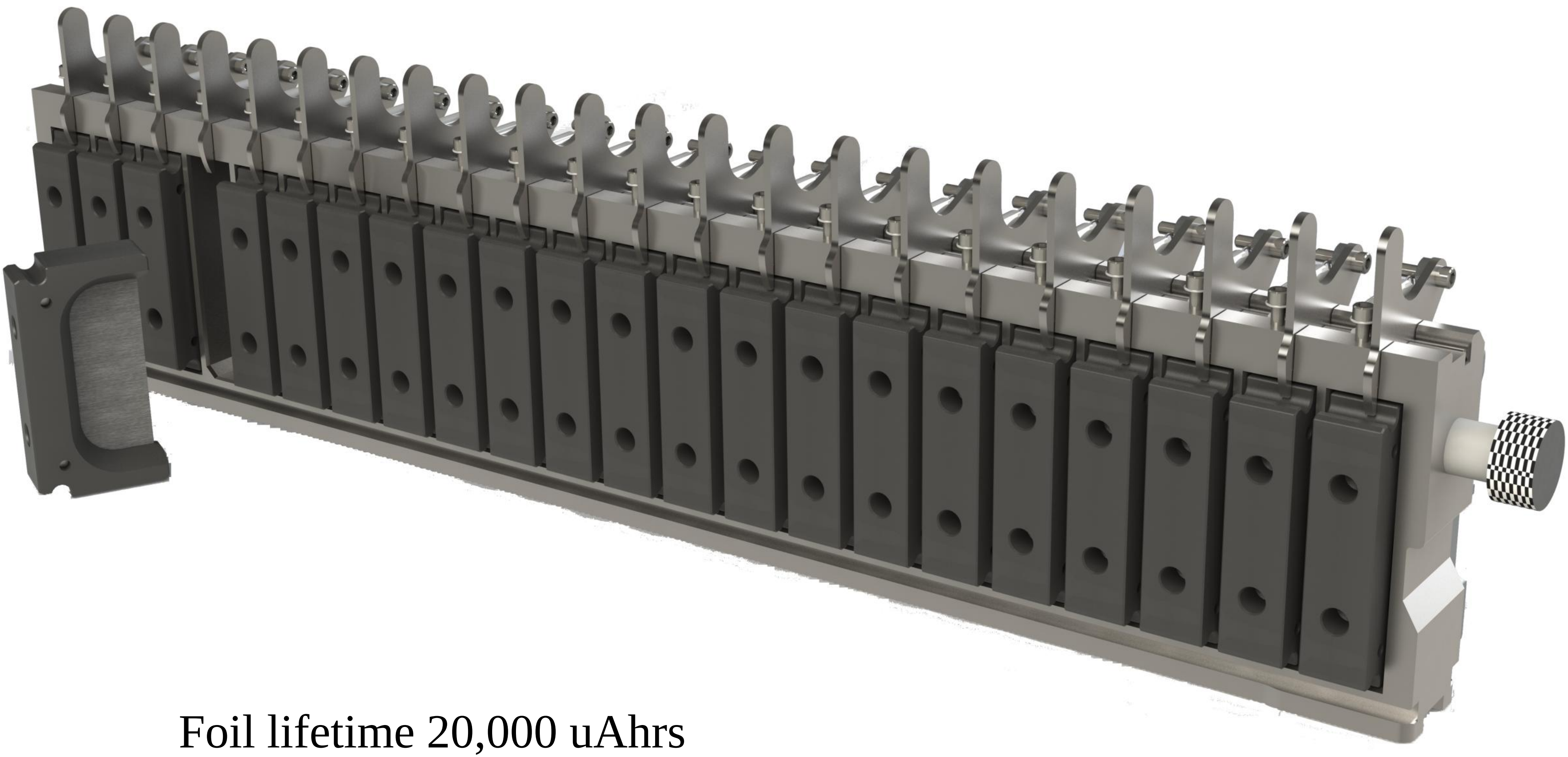
B70
35-70 MeV
1000 uA
Targets Radiochem

Extractor for high current operation

Reduces cyclotron bunker footprint



Extractor mechanism holds 21 foils

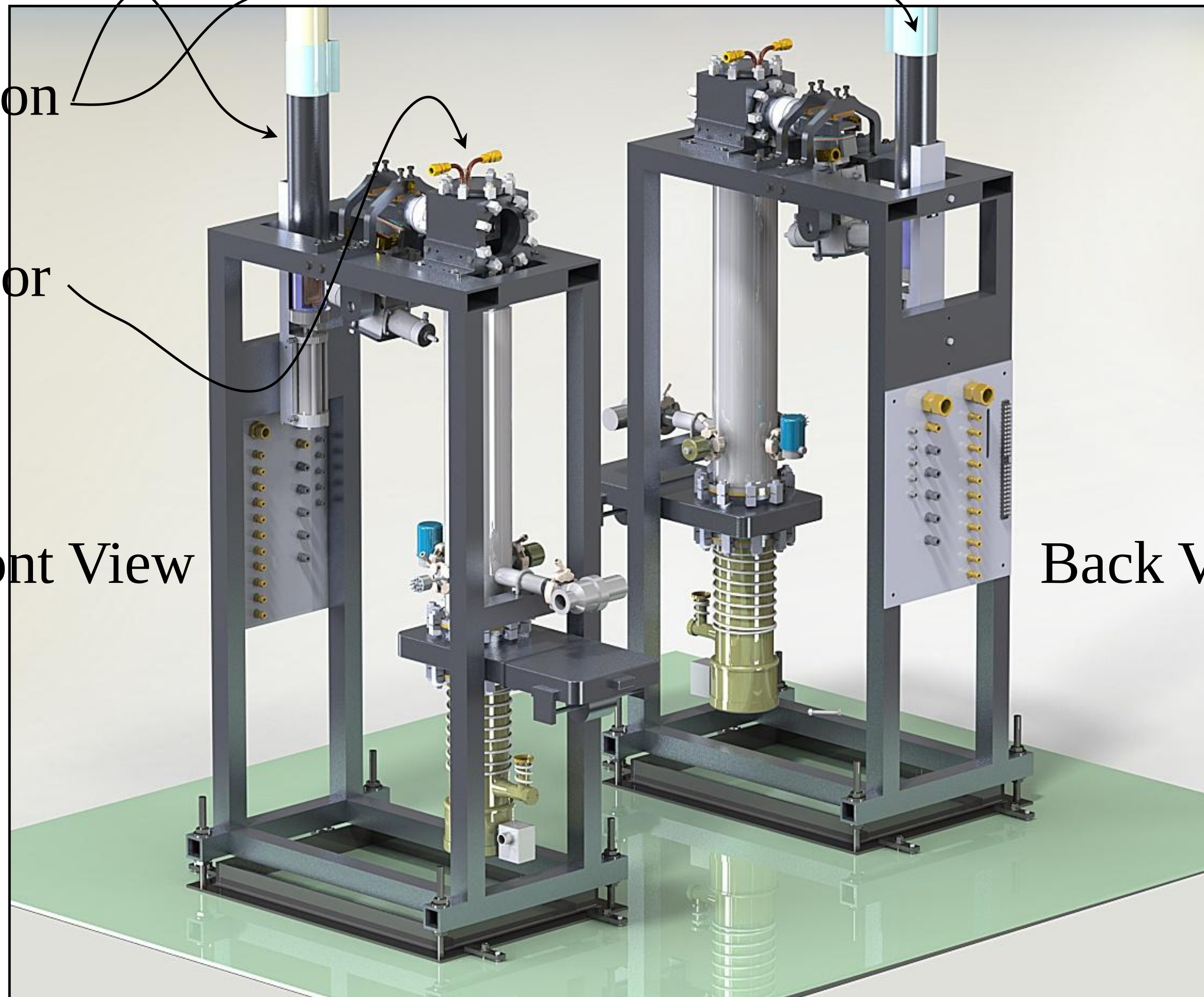


Foil lifetime 20,000 uAhrs
@1000uA is 20 hours.

Solid Target Station … **50 kW**

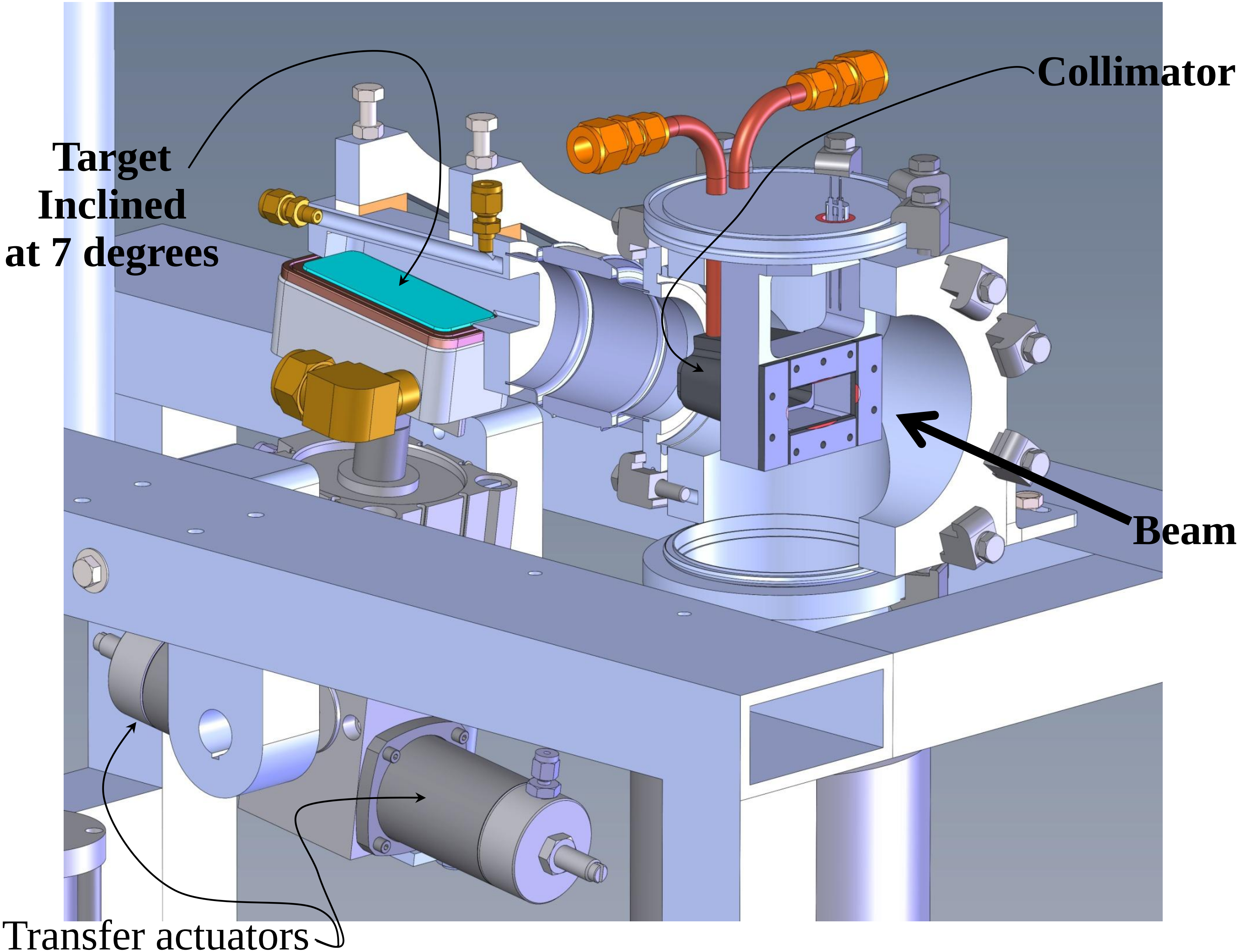
Send receive station

collimator

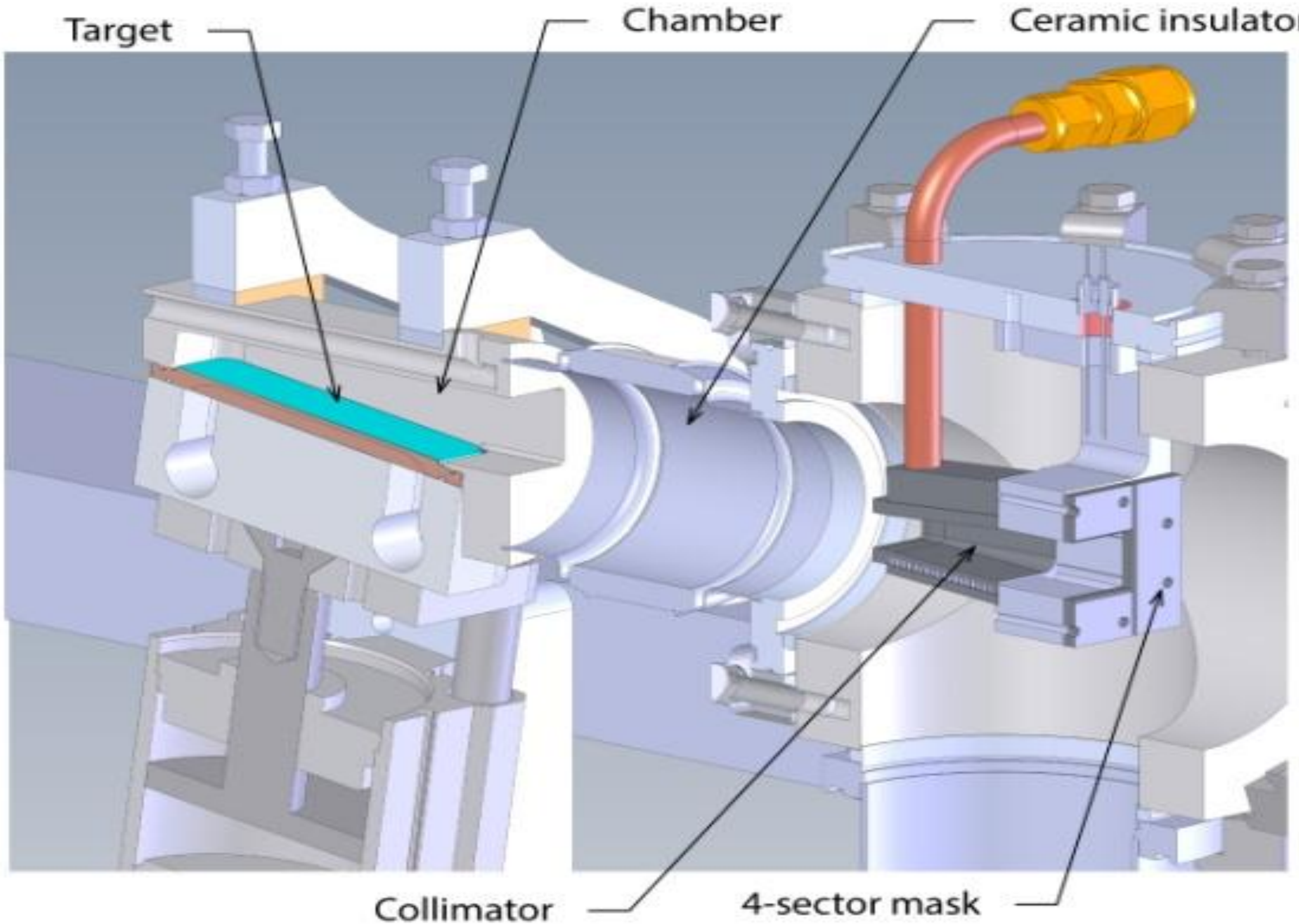


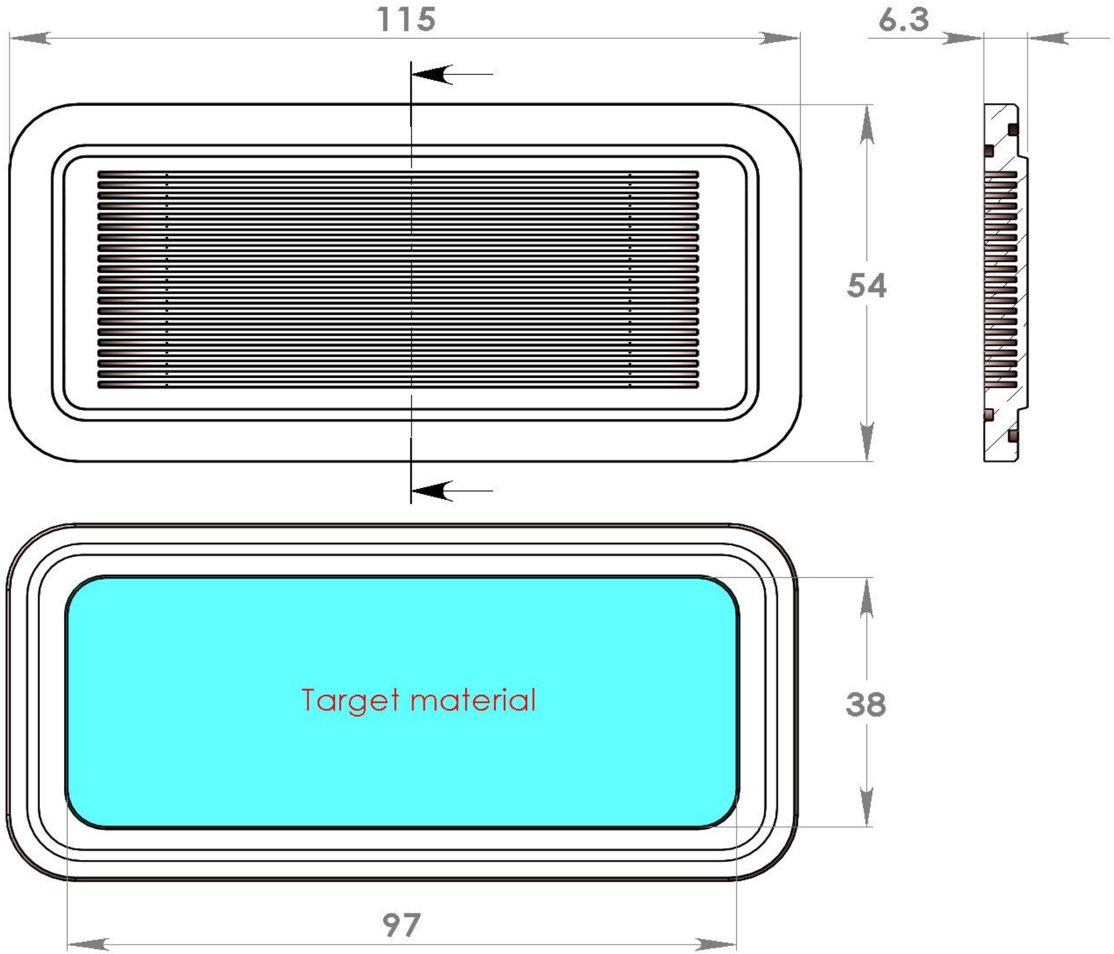
Front View

Back View

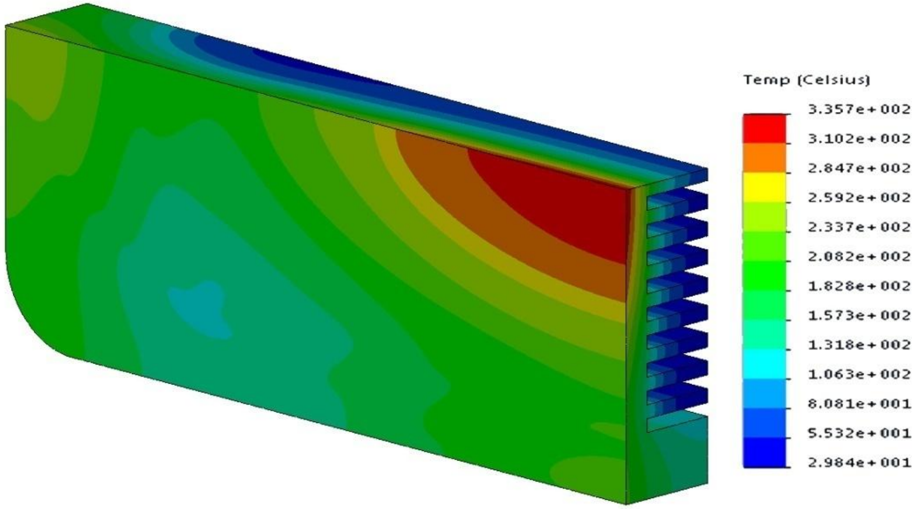


Target station details


Target
Chamber
Ceramic insulator
Collimator
4-sector mask



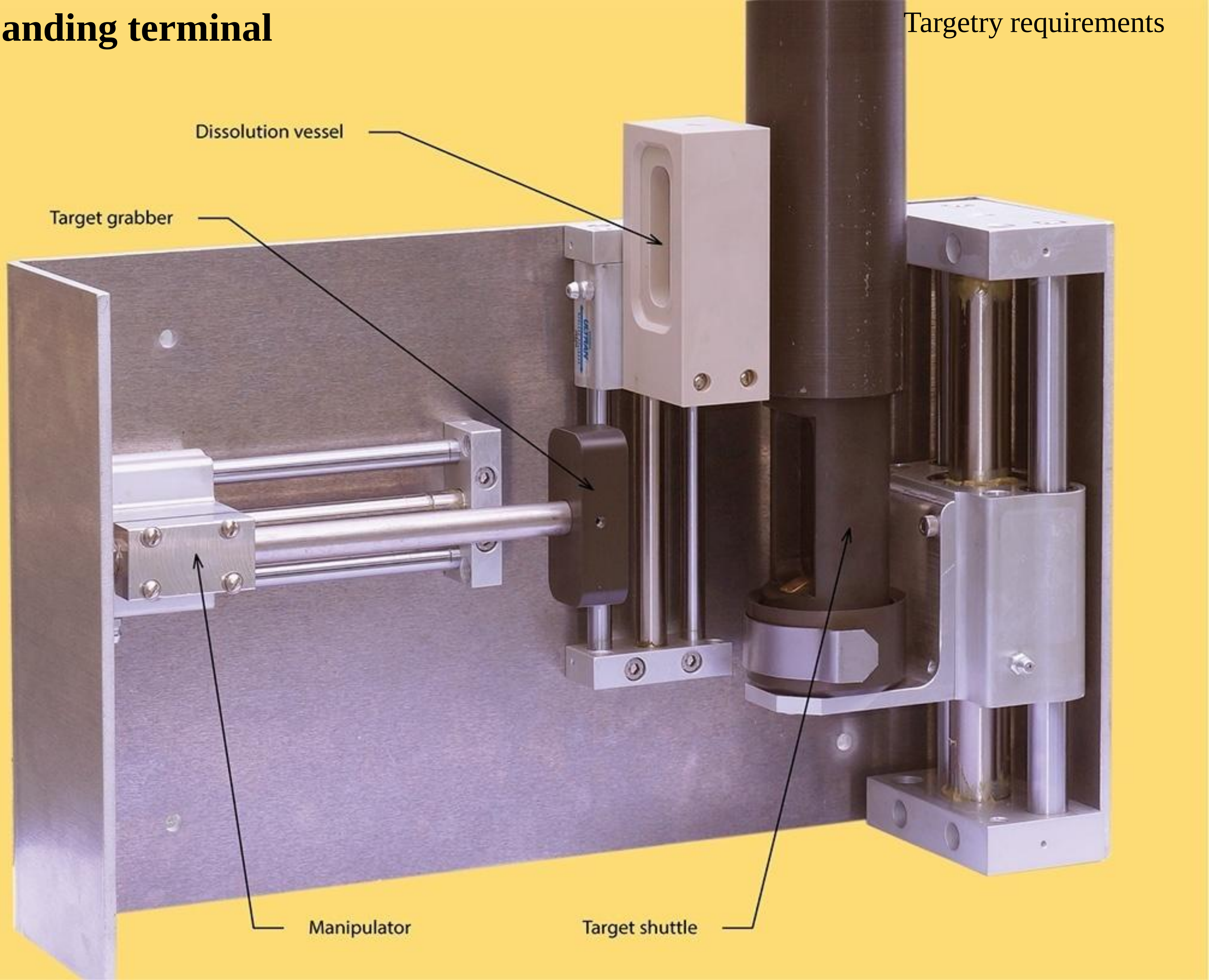
Target Substrate
copper

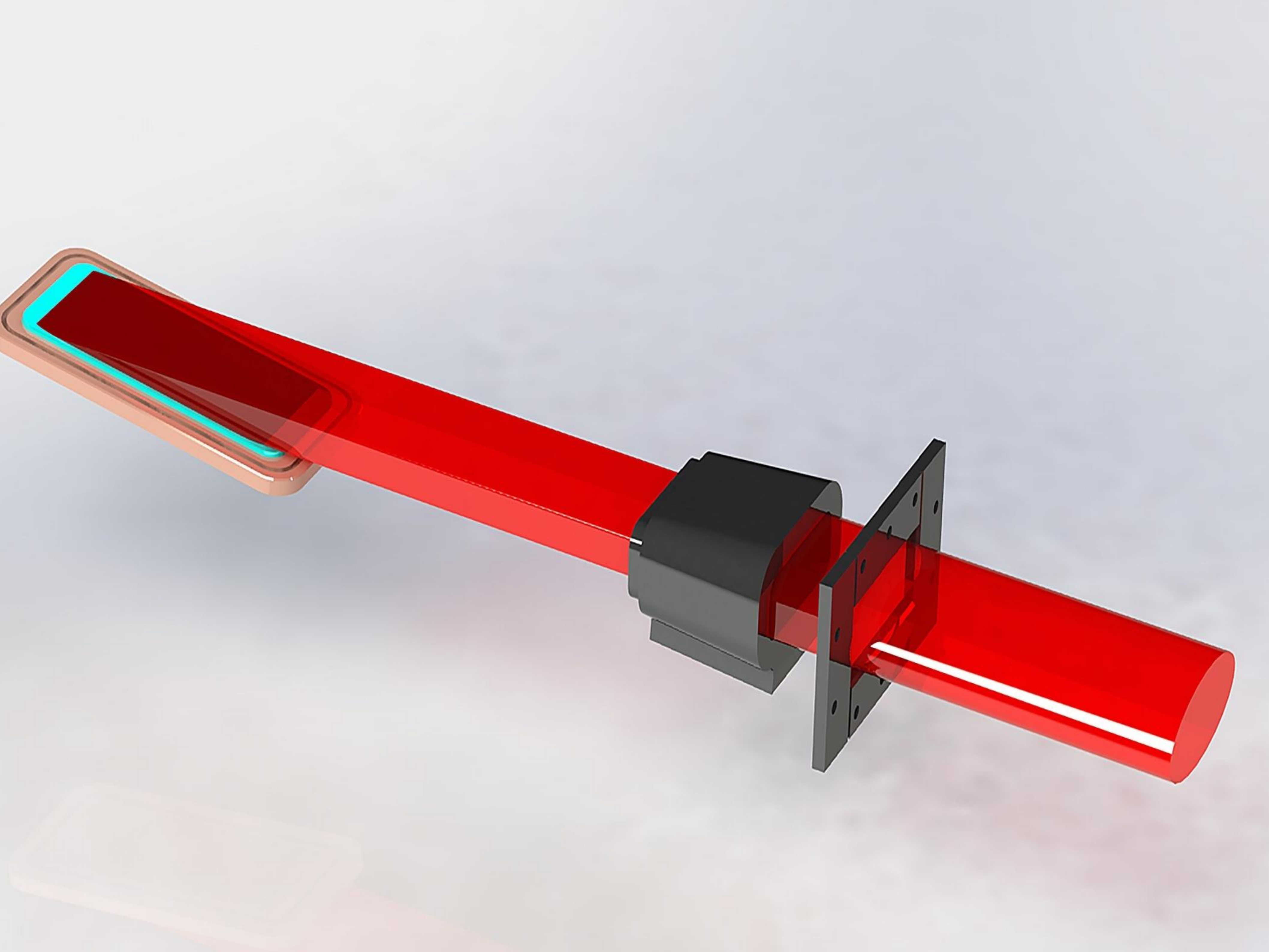


Temperature distribution on target with 42.5 kW on target and 7.5 kW on collimator

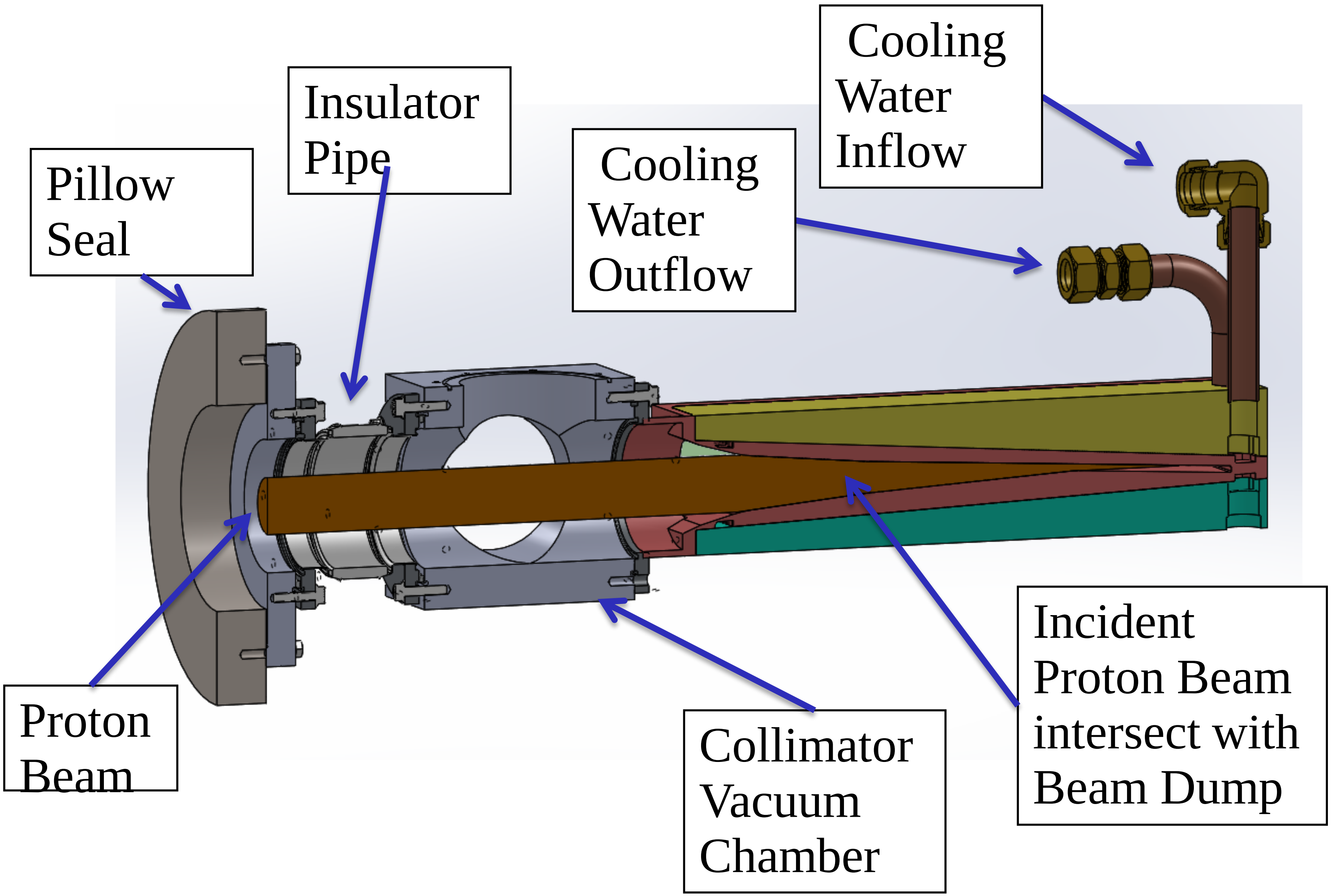
40 L/min water flow

Landing terminal





50 kW Beam Dump Assembly – Cut Through Vertical Symmetry Axis



Lesson

Target station and Beam stop tolerate 1 mA operation
and are engineered for remote repair and access

Applications

Use direct reaction when possible

Example Y^{177} production

Apply neutron production when needed

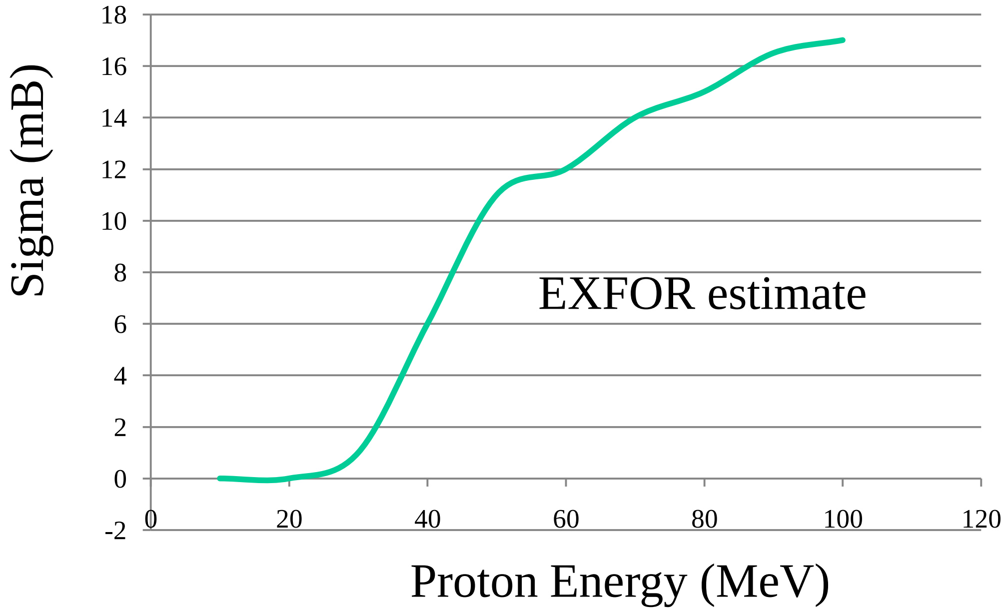
Example BNCT

Case Study Lu^{177}

Y^{177} production estimate

Hf^{178} (p,2p) Lu^{177}

Thick target yield estimate
Yield = 7 MBq/uA hr



Production yield estimate ~ 100GB /day = 2.6 Ci/day
(700uA, 20 hrs)

Recall unit therapy dose is 200 mCi or 13 therapy doses

Reactor estimate is ~ 500 GB/day/mg
Dash etal.,Nucl Med Mol Imaging (2015) 49

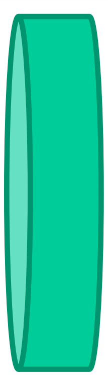
To Do for cyclotrons: Cross section, Contaminants, Specific Activity
Etc, etc,etc

Case Study

Boron Neutron Capture Therapy

Neutron production Target: Material selection

Target	Melting Point (°C)	Boiling Point (°C)	Thermal conductivity (W/mK)	Neutron yield (n/s mA)	Gamma-ray per neutron
Li	180	1340	84.7	1.14e14	0.09
W	3422	5555	174	9.63e14	1.39
Ta	3017	5448	57.5	1.25e14	0.93
Be	1278	2974	201	1.90e14	0.02



Lower Gamma production

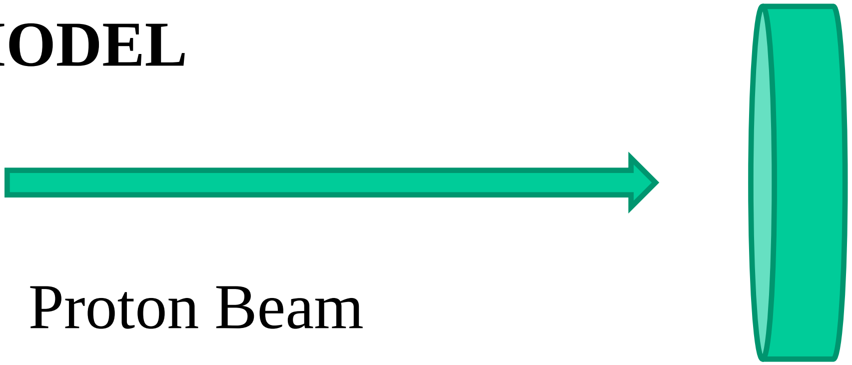
Better Thermal conductivity

Higher Melting point

Beryllium is our preferred target

Neutron production Target

MODEL



Simulations with MCNP6

↓

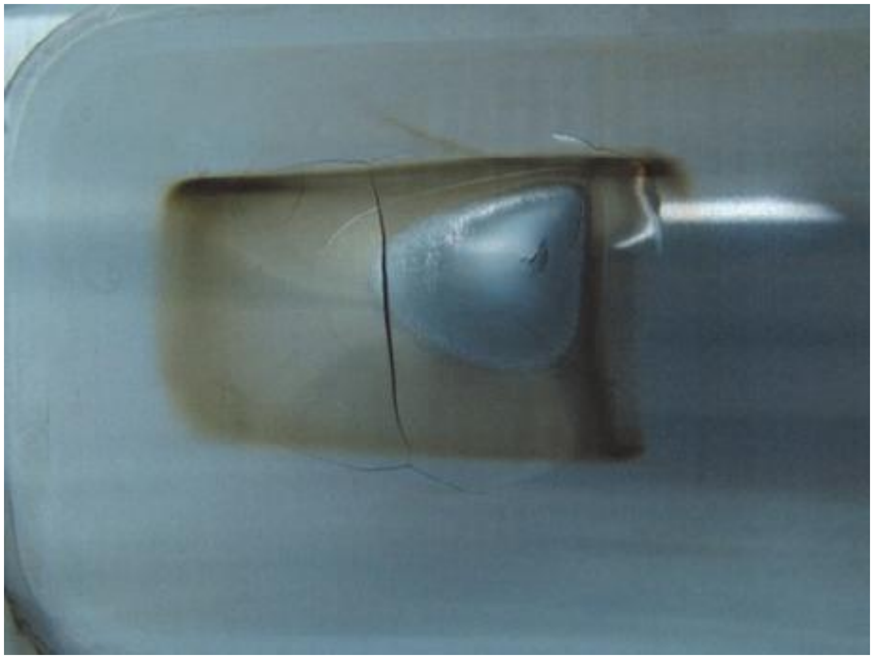
1.90e14 n/s at 30 MeV, 1mA

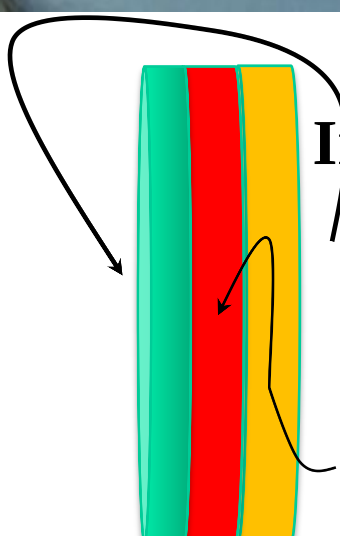
Over the whole
solid angle

Be9(p,n)B9

Beryllium Target inconvenients

Beryllium has low hydrogen solubility





Insert layer of Palladium to adsorb the hydrogen!

Beryllium

Palladium

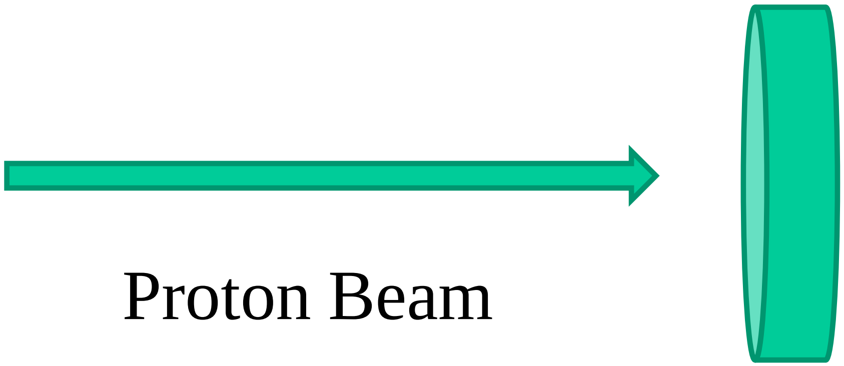
Union of Compact Accelerator-Driven Neutron Sources I & II

Target Performance at the Low Energy Neutron Source

T. Rinckel*[a], D. V. Baxter[a], J. Doskow[a], P. E. Sokol[a], and T.Todd[a]

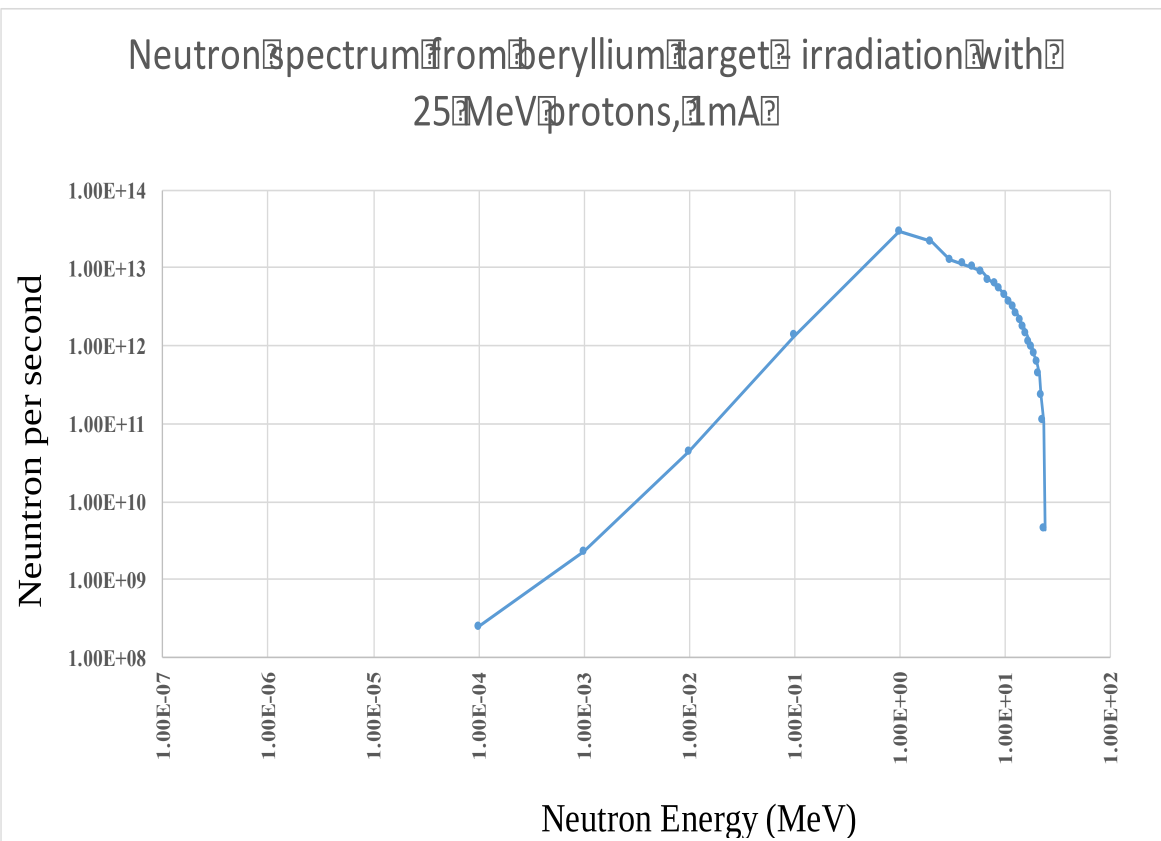
[a]*Indiana University Center for Exploration of Energy and Matter, 2401 Milo B. Sampson Lane, Bloomington, IN 47408, USA*

Irradiation at 25 MeV

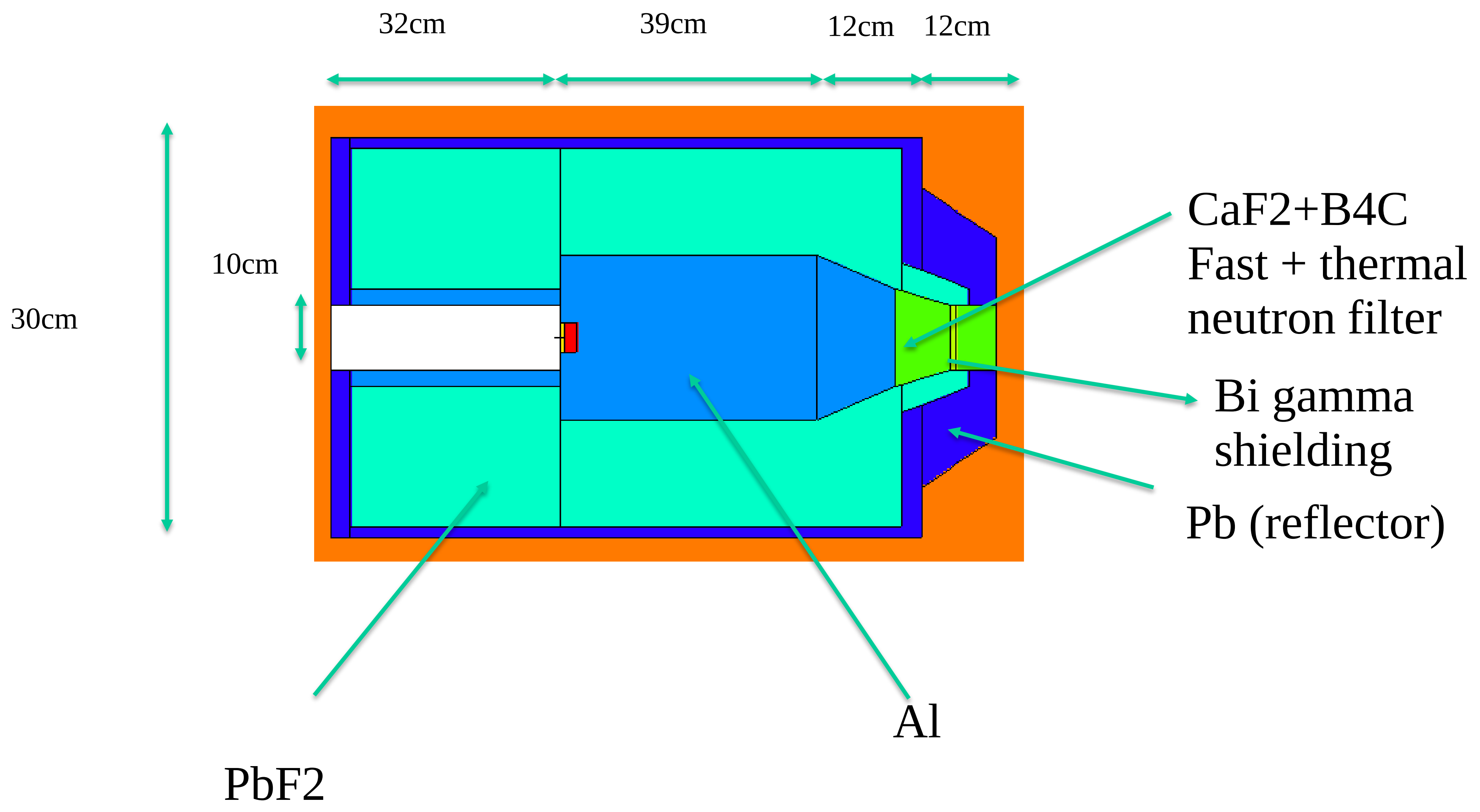


Simulations performed by MCNP6

Proton beam energy 25MeV
Target thickness: 3.97mm
Target radius: 2.5cm
Pd Layer: 200 um
Cu cooling bulk: 2cm

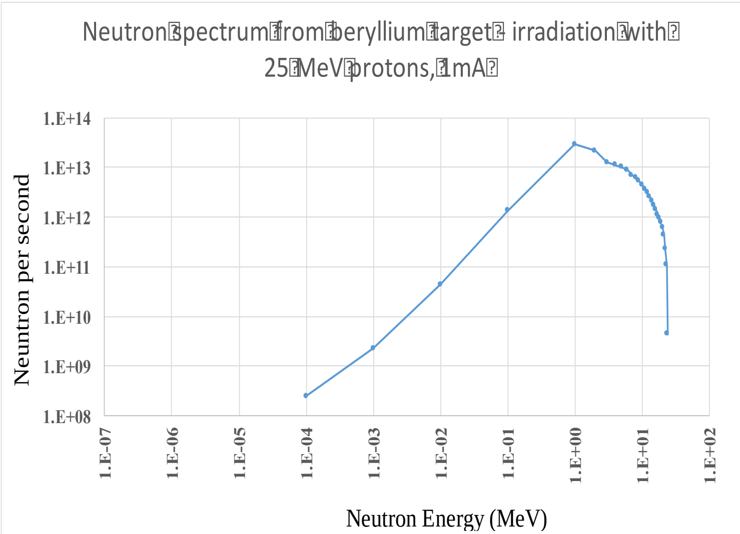


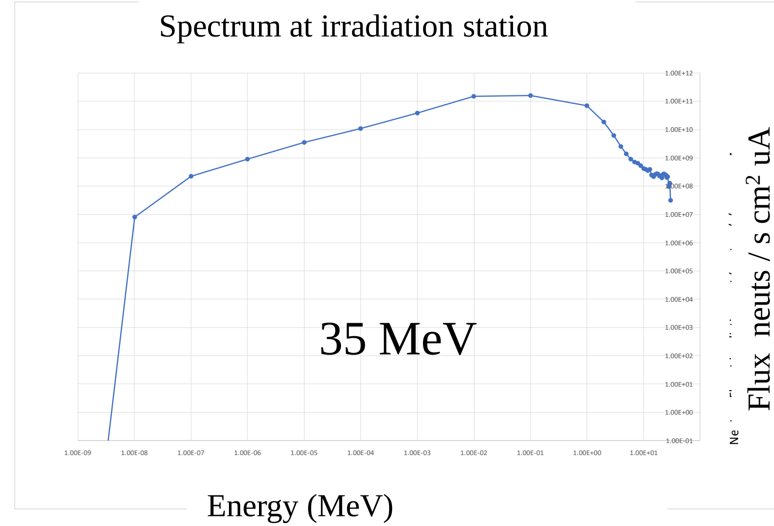
Neutron beam shaper for BNCT

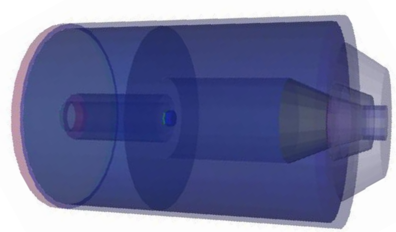


Similar to I.M. Ardana J. Tek. Reaktor. Nukl. 19 ,3 2017

Adjust beam shaper material and geometry to obtain legitimate spectrum



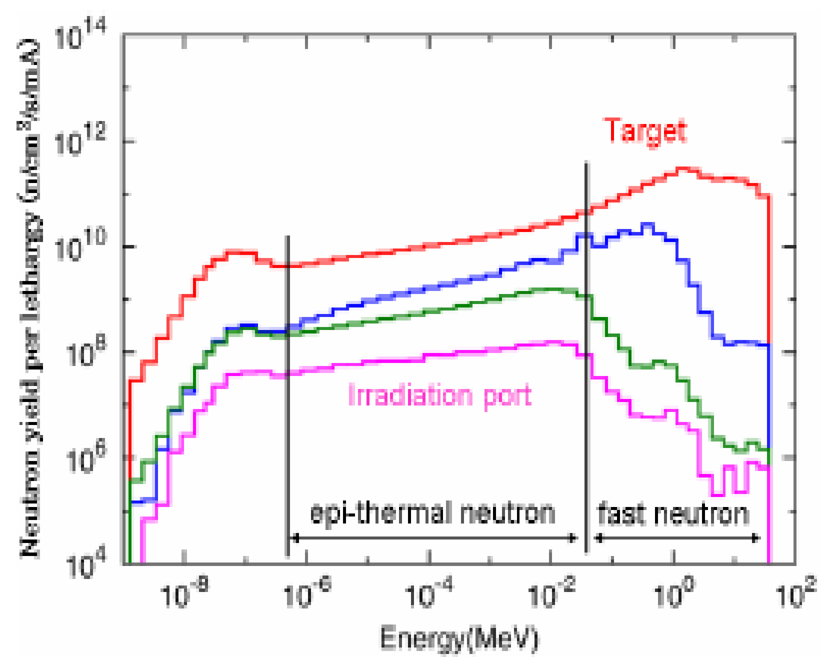




Simulations by MCNP6

A 25 MeV cyclotron may be enough

Still working on it TBA



[T. Mutsimoto et al 2010]

BNCT

Summary

Theranostics are giving results but there must be care

Cyclotrons and their targets now have high current capability and there is **engineering for high activity** handling.

Two case studies

Lu^{177} may be competitive with reactor production. Depends on real cross section and specific activity

BNCT there needs more beam shaping development.

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