Compact Accelerators for 99mTc Production

Hywel Owen

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of Accelerator Science and Technology

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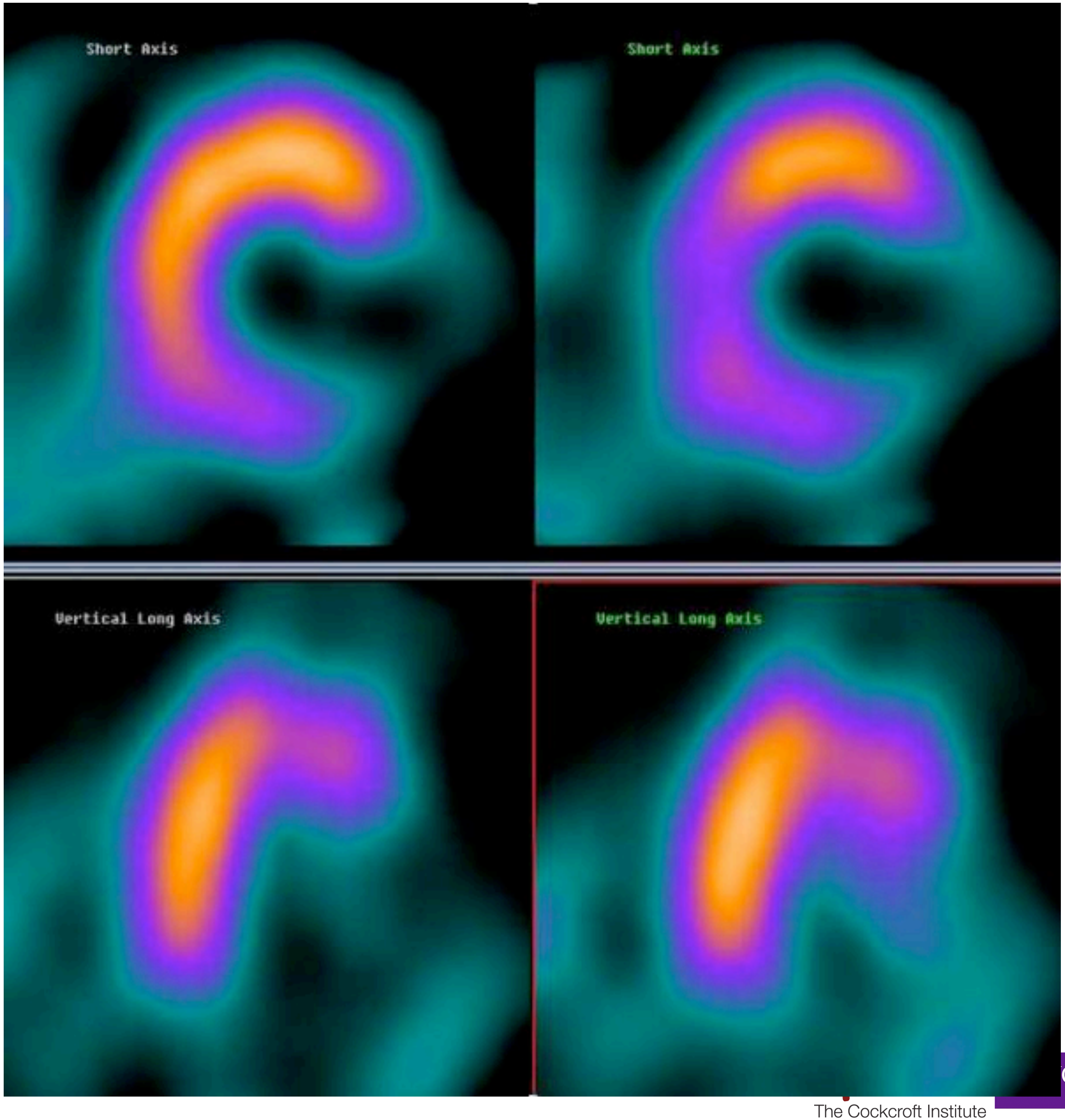
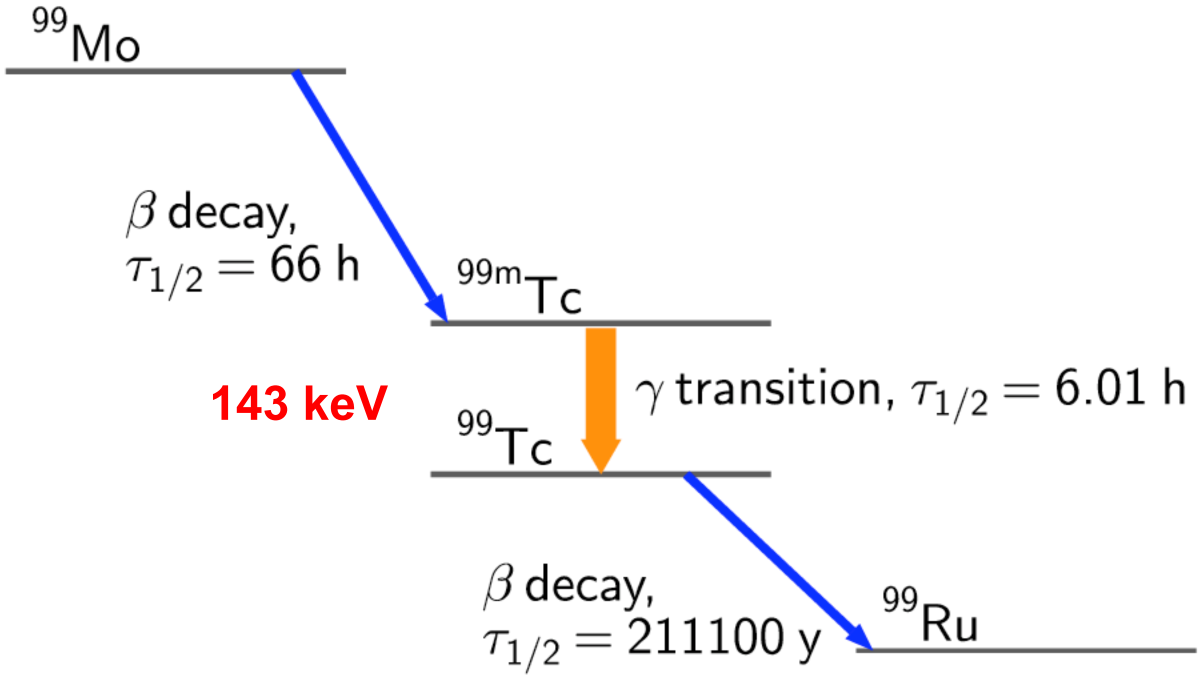
Cardiac Imaging



Mo-99/Tc-99m/Tc-99



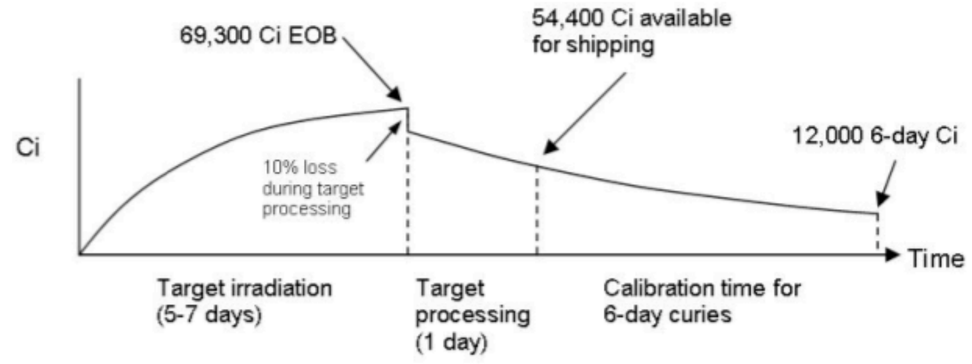
Tc-99m isomerism
Seaborg and Segrè, Phys. Rev. 54(9), 772
Seaborg and Segrè, Phys. Rev. 55(9), 808

Tl-201 (made with a cyclotron, t1/2~3d) emits at 80 keV (through electron capture) which is not as good for imaging

Some facts about 99mTc

- Hospital imaging:
  1. Computed Tomography
  2. Nuclear Medicine
     (85% Tc-99m)
  3. MRI

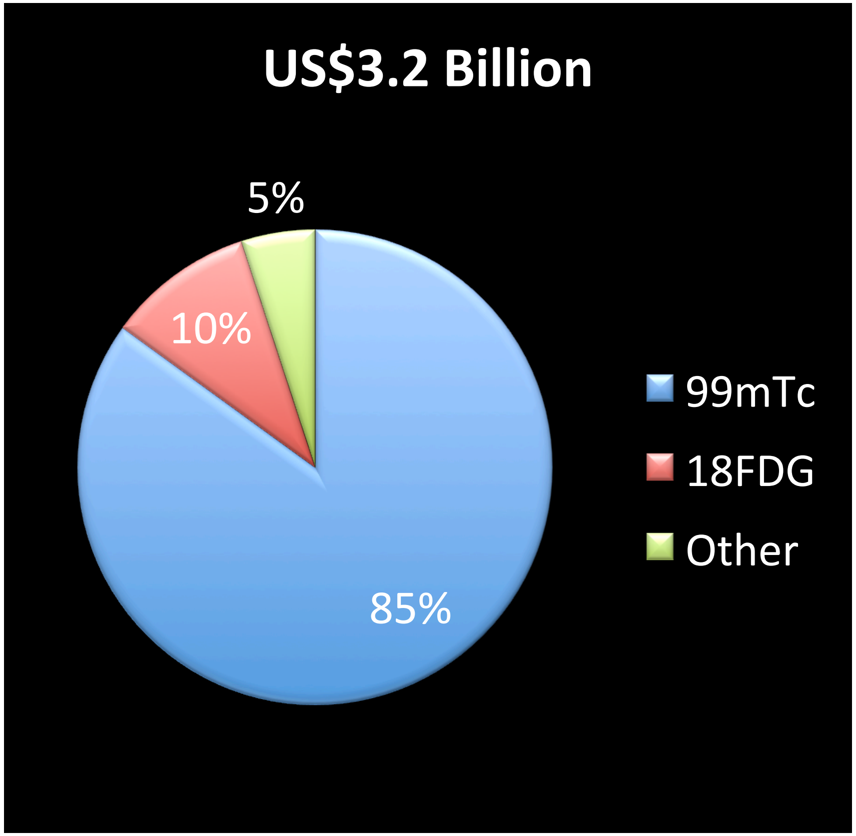
- Global demand: 60M/yr
  - 19M USA
  - 21M Europe
  - 20M Rest of World



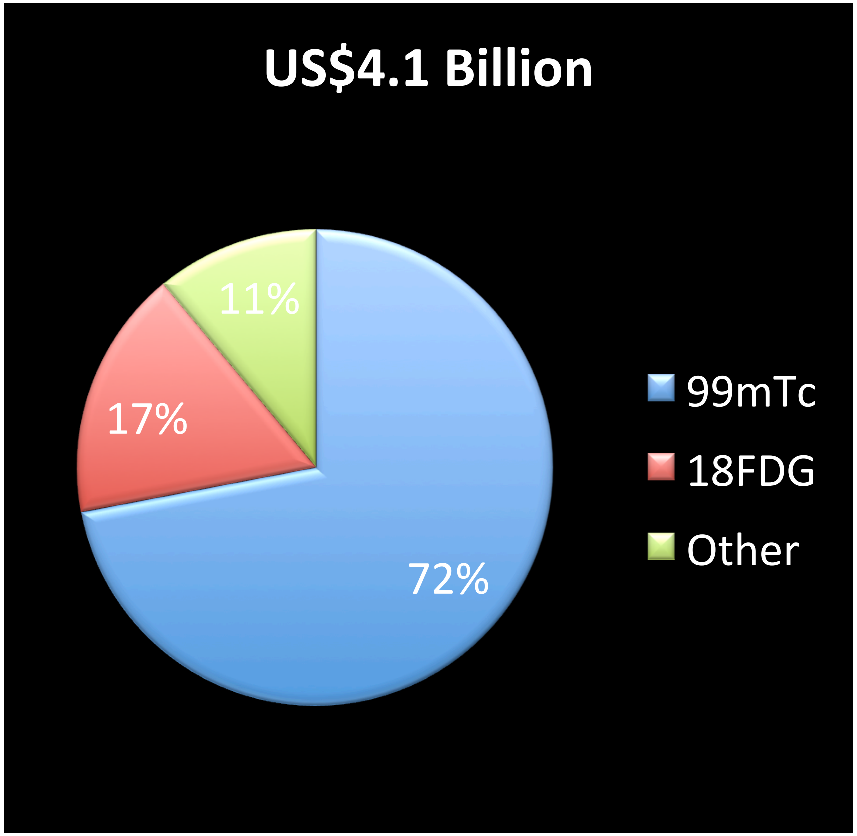
World weekly supply: 2g of 235U used, 0.11g Mo-99 provided
$140 M

Global Radiopharmaceutical Diagnostic Market (1,2,3)

2010



2017



1 Global Radiopharmaceuticals Market (PET/SPECT Imaging & Therapy) – Current Trends & Forecasts (2010 – 2015); MarketsandMarkets, August 2011
2 BMI - Business Monitor International Ltd, Molybdenum-99: Privatising Nuclear Medicine, Special Report 2011
3 Interim Report on the OECD/NEA High-Level Group on Security of Supply of Medical Radioisotopes, The Supply of Medical Radioisotopes, OECD 2012

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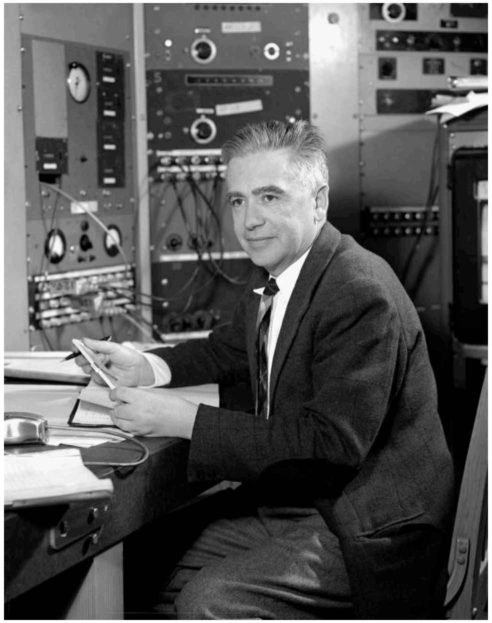
Isotope production

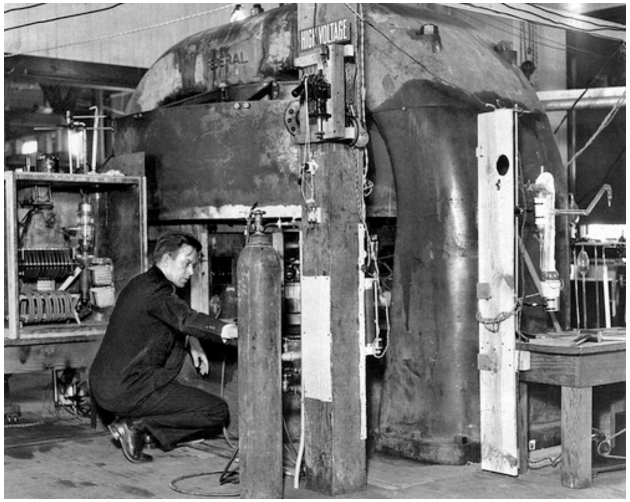
- Three main areas:
- Conventional short-lived isotopes:
  - F18, C11, N13
  - Hospital-based
  - Commercial solutions widespread
  - Compact low-cost accelerators
- Tc99m
  - Reactor-based production fragile
  - A number of accelerator methods exist
- Alpha-emitters, Ra223, At211, Bi213
  - Several methods and opportunities exist
  - CERN MEDICIS

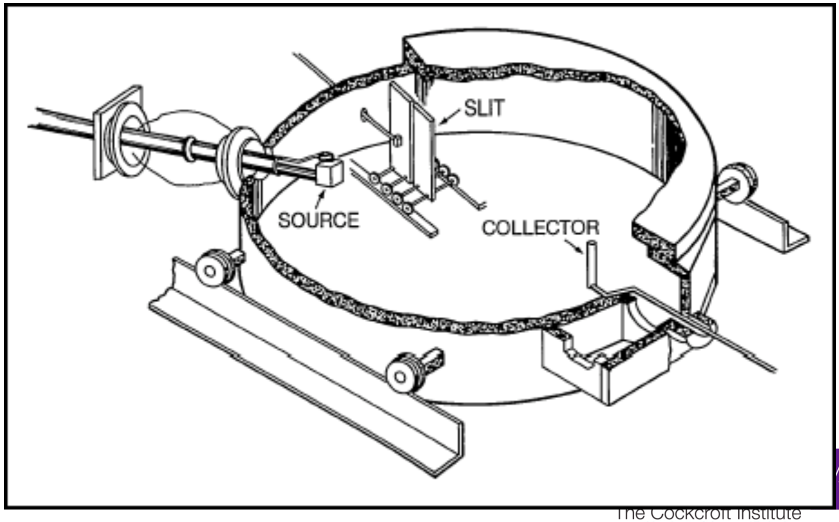
Nuclide	**F-18**	**C-11**	**N-13**	**O-15**	**Ge-68**
Half-Life	110min	20.5m	10m	2m	275d
Positron (keV)	630	960	1200	1730	1900
Gammas (keV)	511(2)	511	511	511	511

Emilio Segrè and the 37-inch cyclotron deflector foil

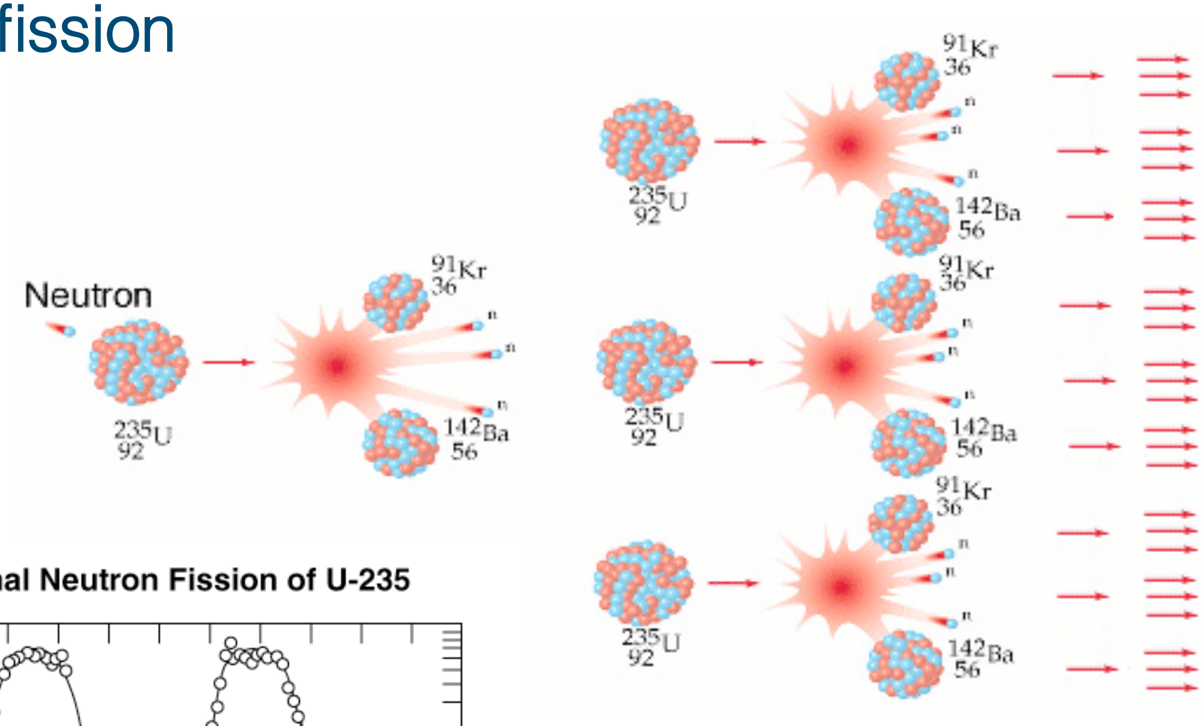


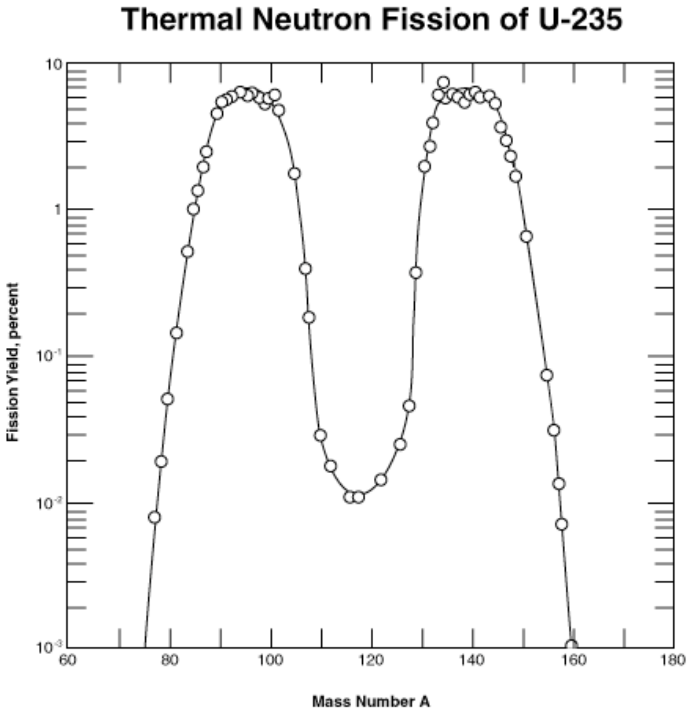
‘In February 1937 I received a letter from Lawrence containing more radioactive stuff. In particular, it contained a molybdenum foil that had been part of the cyclotron's deflector. I suspected at once that it might contain element 43. The simple reason was that deuteron bombardment of molybdenum should give isotopes of element 43 through well-established nuclear reactions. My sample, the molybdenum deflector lip, had certainly been intensely bombarded with deuterons, and I noted that one of its faces was much more radioactive than the other. I then dissolved only the material of the active face, in this way achieving a first important concentration of the activity. ‘





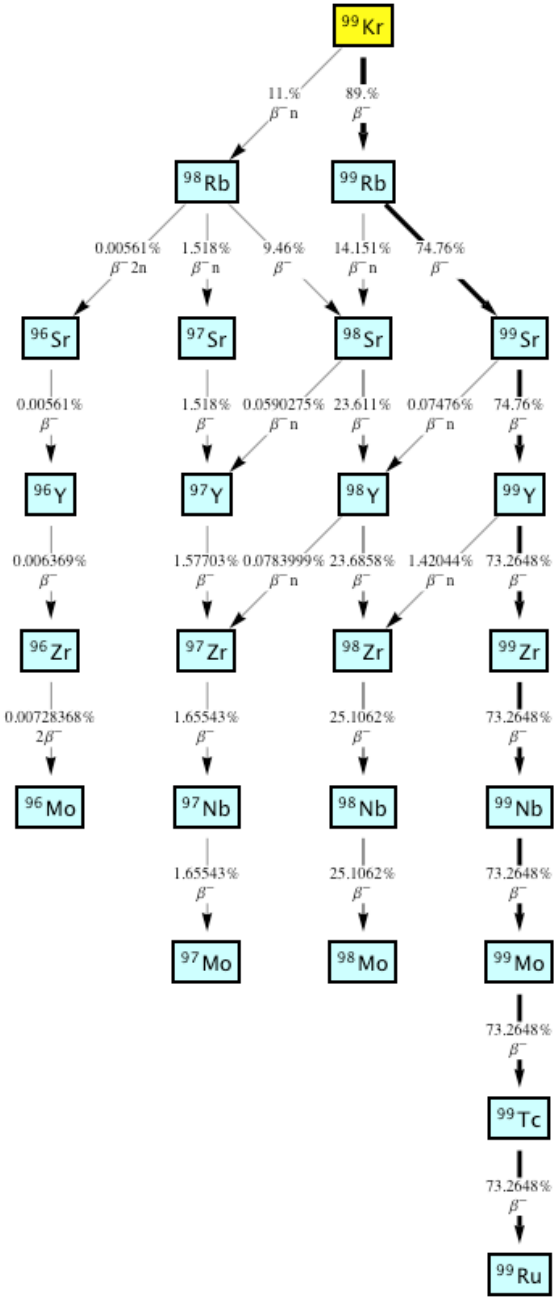
235U fission




Thermal Neutron Fission of U-235

99Kr Decay Chain

Nuclide	Halflife
99Y	1.470(7) s
99Zr	2.1(1) s
99Nb	15.0(2) s
99Mo	2.7489(6) d
99Tc	2.111(12)E+5 a
99Ru	Stable



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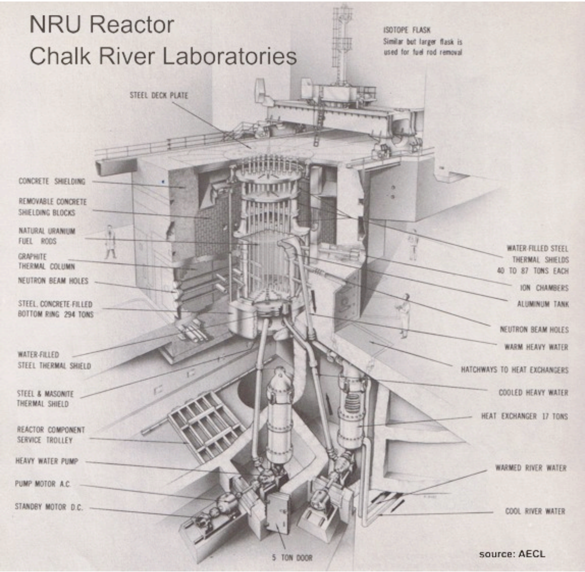
Research and Power Reactors

- Research reactors
  - Better neutronics, but need high power (>20 MW)
  - Easier fuel cycle: can extract targets out quickly and process them, needed to obtain Mo-99
  - Only a few reactors meet these requirements (not e.g. PWRs)


NRU Reactor
Chalk River Laboratories

source: AECL

Item	Reaction	Cycle time	T 1/2
^{99}Mo	**Fission, ^{235}U (n,Y)**	**8 days**	**66 hrs.**
^{131}I	Fission, ^{130}Te (n,Y)	21 days	8 days
^{133}Xe	Fission, ^{132}Xe (n,Y)	8 days	5.2 days
^{153}Sm	^{152}Sm (n,Y)	5 days	47 hrs.
^{89}Sr	^{90}Sr (daughter) ^{88}Sr (n,Y)	14 days	50.5 days
^{90}Y	^{89}Y (n,Y), ^{90}Sr (n,Y)	7 days	64 hrs.
^{32}P	^{31}S (n,Y)	28 days	14.3 days

Current Irradiators 2013

Reactor	Targets	Normal operating days	Available weekly capacity (6-day Ci)	Potential annual production (6-day Ci)[1]	Estimated stop production date
BR-2	HEU	140	7 800	156 000	2026
HFR	HEU	280	4 680	187 200	2024
LVR-15	HEU	210	2 800	84 000	2028
MARIA	HEU	180	1 400	36 000	2030
NRU	HEU	280	4 680	187 200	2016
OPAL	LEU	290	1 000	42 900	2055
OSIRIS	HEU	182	1 200	31 200	2015
RA-3	LEU	336	400	19 200	2027
SAFARI-1	HEU[2]/LEU	305	3 000	130 700	2030

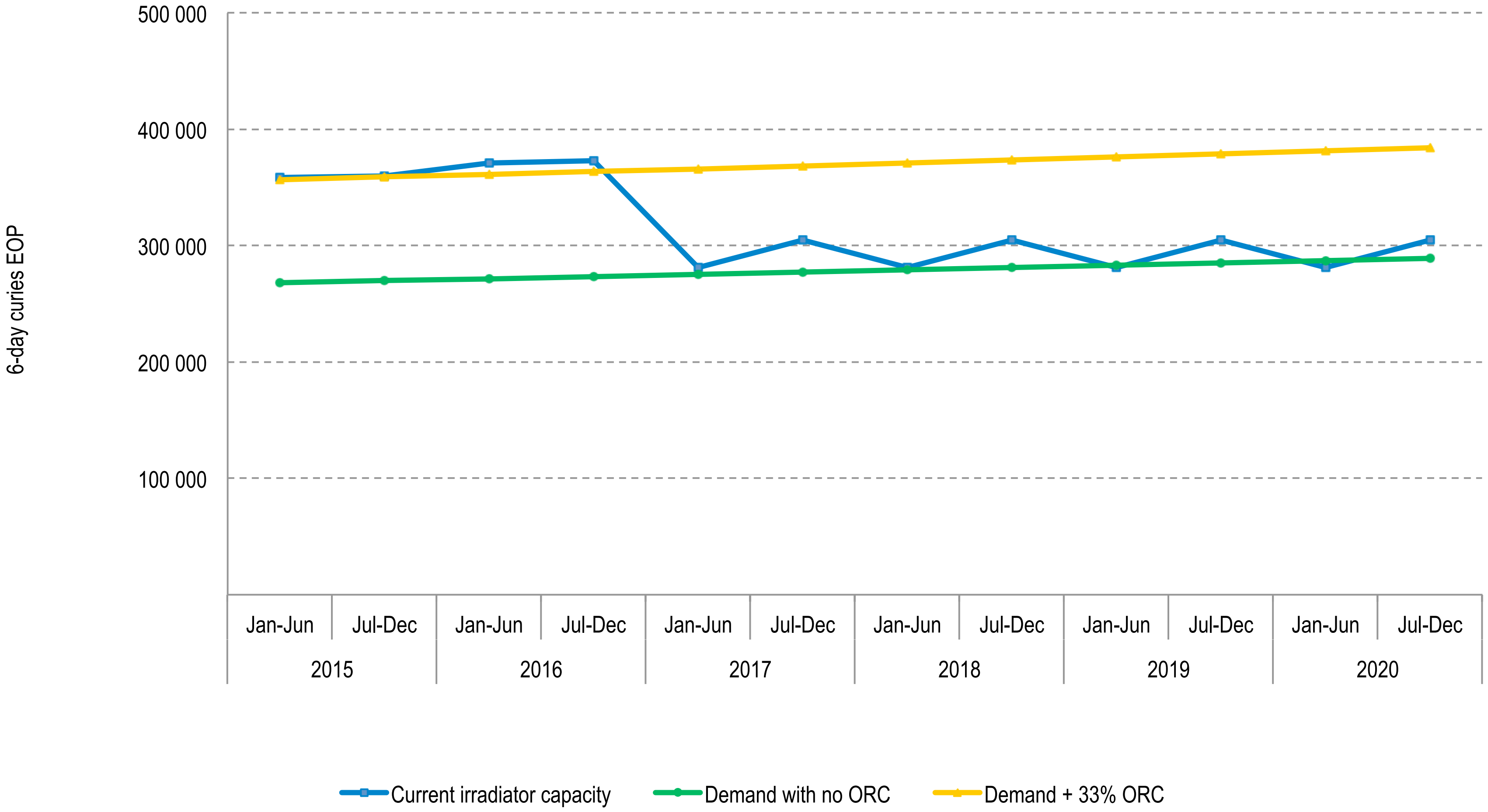
OECD January 2014
HLG-MR Report

Current Processors

Processor	Targets	Capacity per week (6-d Ci)	Available annual capacity (6-d Ci)[1]	Expected date of conversion to LEU targets
AECL/NORDION	HEU	7 200	374 400	Not expected
ANSTO HEALTH	LEU	1 000	52 000	Started as LEU
CNEA	LEU	900	46 800	Converted
MALLINCKRODT	HEU	3 500	182 000	2016
IRE	HEU	2 500	130 000	2016
NTP	HEU[3]/LEU	3 500	182 000	2014[4]

OECD January 2014
HLG-MR Report

Irradiation capacity and projected future demand, Global, 2015-2020



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Technetium Generators

Typical Mo-99 specific activity 3000 Ci/gm (0.6%)

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Typical price UKP 400-600, gives ~100 doses (depending on modality), 100-250 GBq (3-7 Ci)

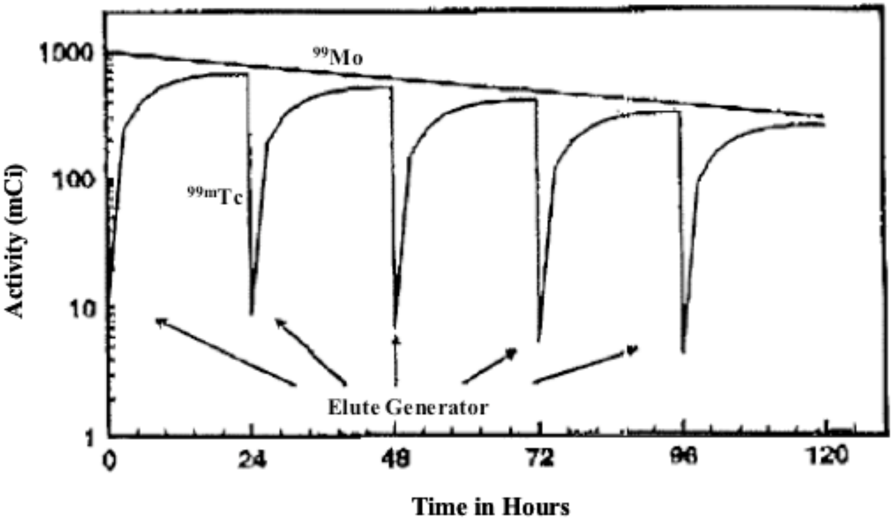
92,000 sold in USA in 2005

Total market around 600 MEuro, but this is artificially cheap because of effective state cross-subsidy

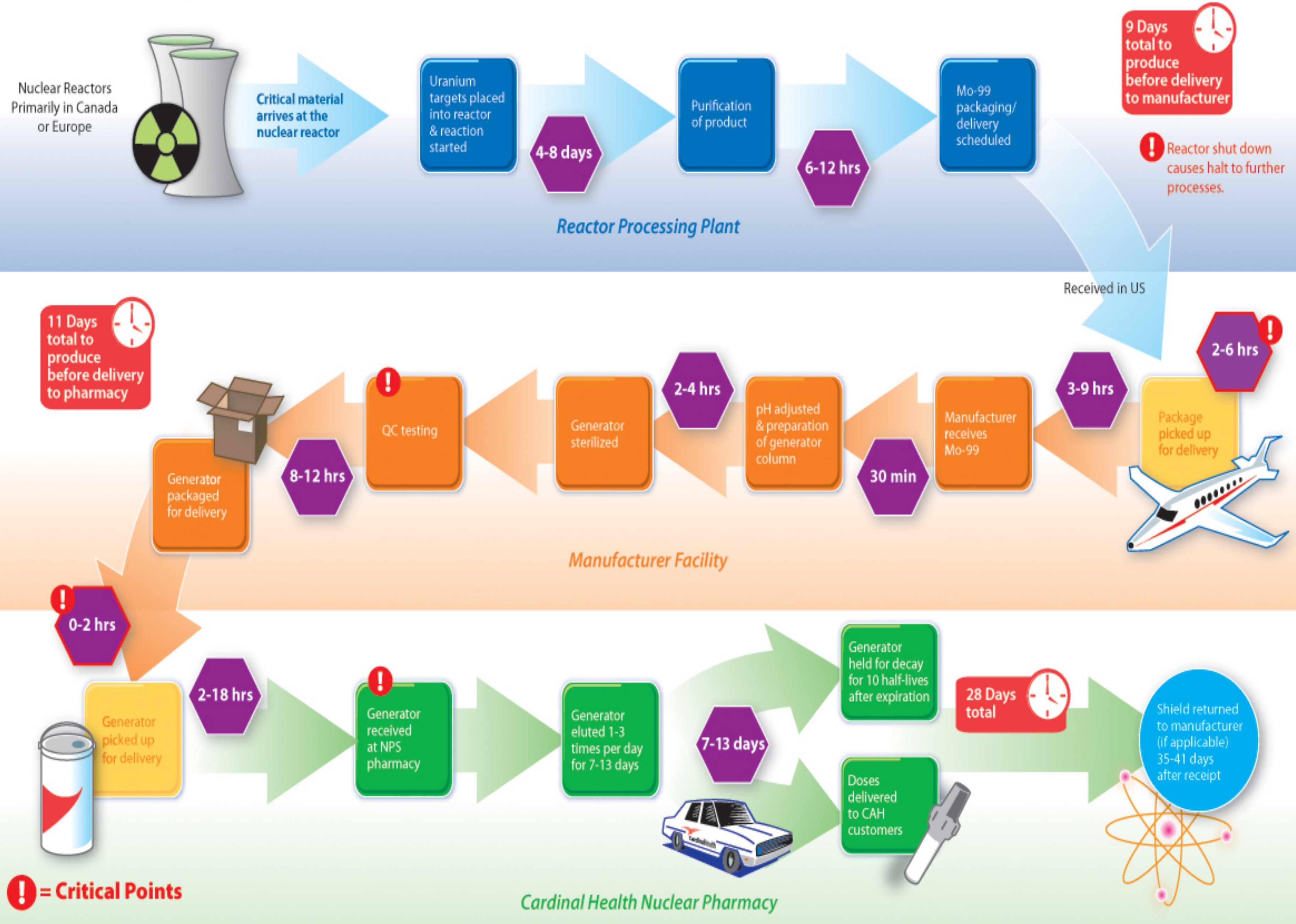
Only few companies worldwide doing either processing or packaging:

General Electric (50%), MDS Nordion,
Covidien (25%), Mallinckrodt, NTP

'Demand is 200% of supply' (Alan Perkins, BNMS)



Mo-99 supply chain



Nuclear Reactors
Primarily in Canada
or Europe

Critical material arrives at the nuclear reactor

Uranium targets placed into reactor & reaction started

4-8 days

Purification of product

6-12 hrs

Mo-99 packaging/ delivery scheduled

9 Days total to produce before delivery to manufacturer

! Reactor shut down causes halt to further processes.

Reactor Processing Plant

Received in US

! 2-6 hrs

Package picked up for delivery

3-9 hrs

Manufacturer receives Mo-99

30 min

pH adjusted & preparation of generator column

2-4 hrs

Generator sterilized

! QC testing

8-12 hrs

Generator packaged for delivery

11 Days total to produce before delivery to pharmacy

Manufacturer Facility

! 0-2 hrs

Generator picked up for delivery

2-18 hrs

! Generator received at NPS pharmacy

Generator eluted 1-3 times per day for 7-13 days

7-13 days

Generator held for decay for 10 half-lives after expiration

Doses delivered to CAH customers

28 Days total

Shield returned to manufacturer (if applicable) 35-41 days after receipt

Cardinal Health Nuclear Pharmacy

! = Critical Points

Potential New Irradiators 2013

Reactor	Targets	Operating days (Number)	Available weekly capacity (6-day Ci)	Potential annual production (6-day Ci)[1]	Estimated stop production date	Status
RIAR (Russia)	HEU in CRR	350	1200	60000	2015	Started
Karpov Institute	HEU in CRR	345	300	14800	2015	Started
NORTHSTAR/ MURR (USA)	Non-fissile in CRR	365	2750/ 3000	39100/ 156400	2015/17	Phase 1
FRM-II (Germany)	LEU in CRR	240	1 600	54300	2017	Infrastructure in place
MORGRIDGE/ SHINE (US)	LEU solution with DTA	300	3000	144000	2017	NYS
OPAL	LEU in CRR	300	2600	111400	2017	NYS
KOREA	LEU in CRR	300	2000	85700	2018	Concept
NORTHSTAR (USA)	Non-fissile from LINAC	336	3000	144000	2018	NYS
CHINA Advanced RR	LEU in CRR	350	1000	50000	2019	Modification
Brazil MR	LEU in CRR	290	1000	41400	2019	Preliminary
RA-10 (Argentina)	LEU in CRR	336	2500	120000	2019	Preliminary
Jules HOROWITZ RR (France)	LEU in CRR	220	3200	100600	2020	Under Construction

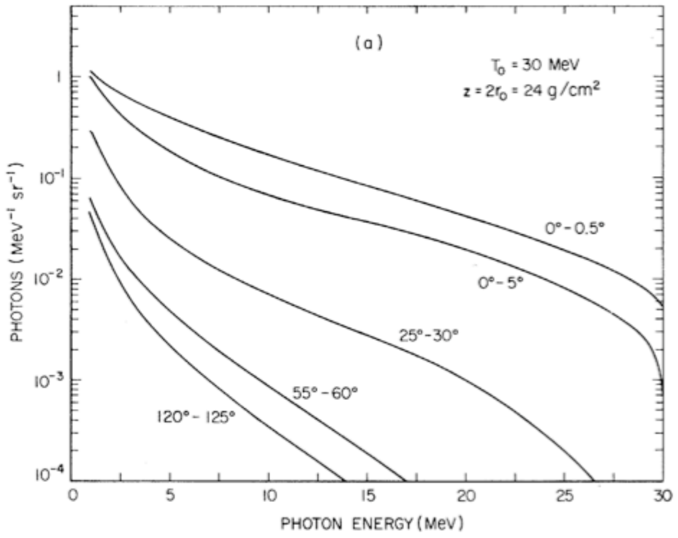
OECD January 2014
HLG-MR Report

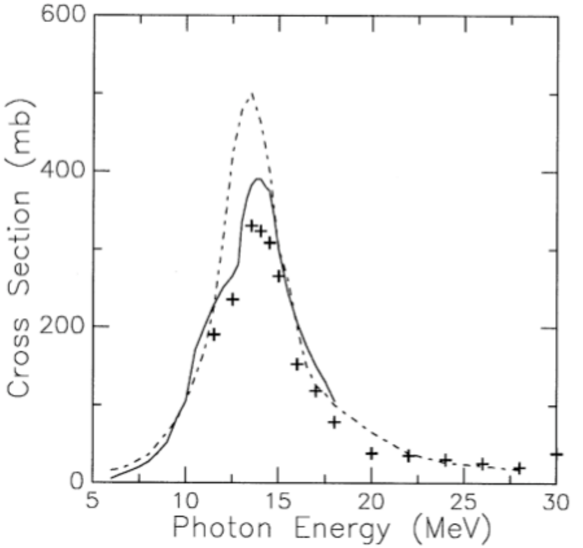
Mo-99 Candidate Production Methods

Accelerated	Incident	Reaction	Comments	Reference
Deuteron	Deuteron	98Mo(d,p)99Mo		Segre and Lawrence
Proton	Neutron	100Mo(n,2n)99Mo		Nagai & Hatsuwaka, JPSJ 78, 033201 (2009)
Proton	Proton	100Mo(p,2p)99,99mNb(β-)99Mo		
N/A	Neutron	98Mo(n,γ)99Mo	Reactor Mo	W.Diamond, AECL Oct 2008 Ryabchikov et al., NIM B 213, 364 (2004)
Proton	Neutron	98Mo(n,γ)99Mo	Be/Pb target	Froment al., NIM A 493, 165 (2002)
N/A	Neutron	235U(n,f)99Mo	Reactor method	
Proton	Neutron	235U(n,f)99Mo	~1 GeV	
Proton	Proton	238U(p,f)99Mo		Lagunas-Solar, Trans.Amer.Nucl.Soc. 74, 134 (1996)
Electron	Gamma	100Mo(γ,n)99Mo	30 MeV	Dikiy et al., Nuclear Physics Investigations (42), p.191-193 (2004)
Electron	Gamma	235/238U(γ,f)99Mo	Photofission/RIB	Coceva et al., NIM 211, 459 (1983)

Tungsten Target, Gamma Production, then Photofission

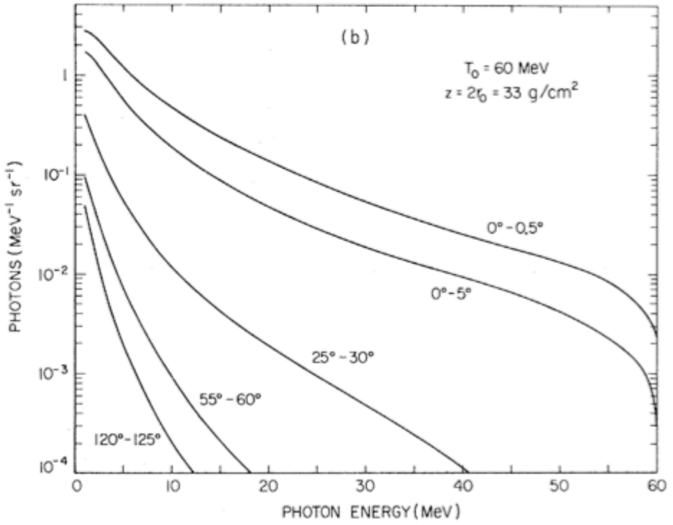
Haxby et al., Phys. Rev. 58(1), 92 (1940)

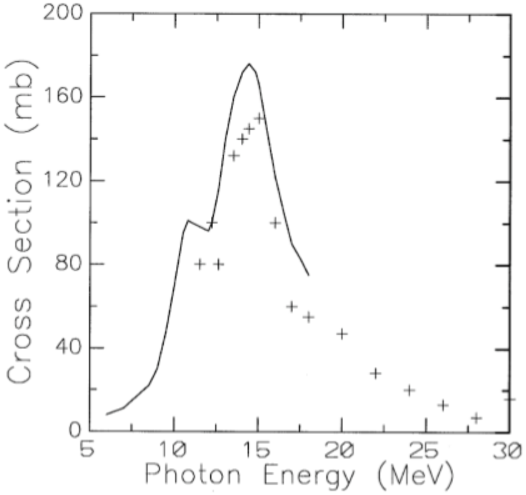




235U

(also benefits from neutron reflection and fission cascade)





238U

Berger and Seltzer, Phys Rev C 2, 621 (1970)

Diamond, NIM A 432, 471 (1999)

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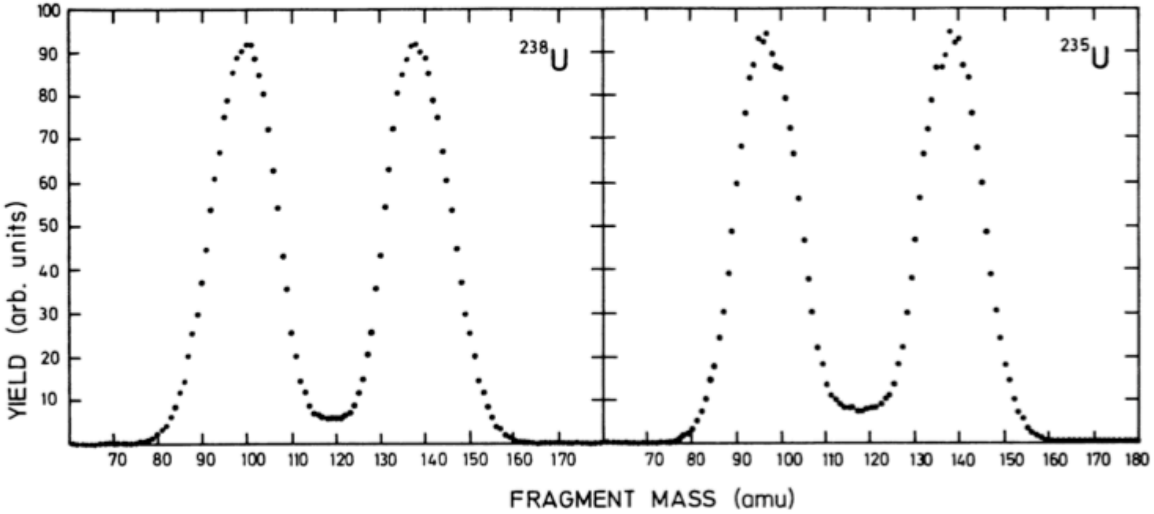
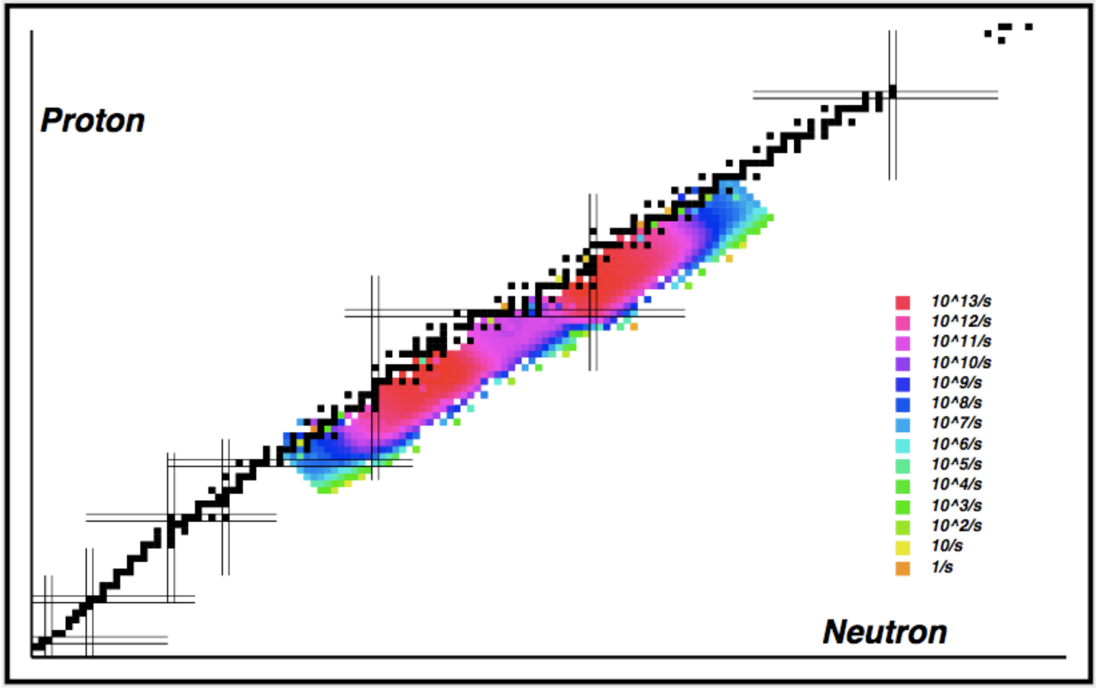
Photofission Yields



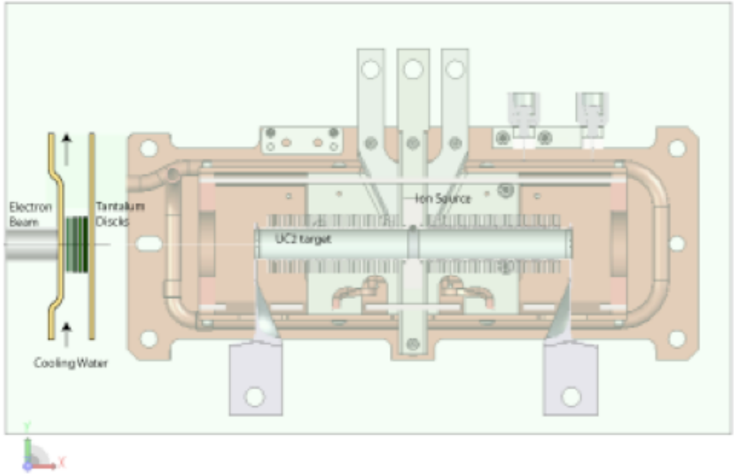
De Clerq et al., Phys Rev C 13 (4), 1536 (1976)



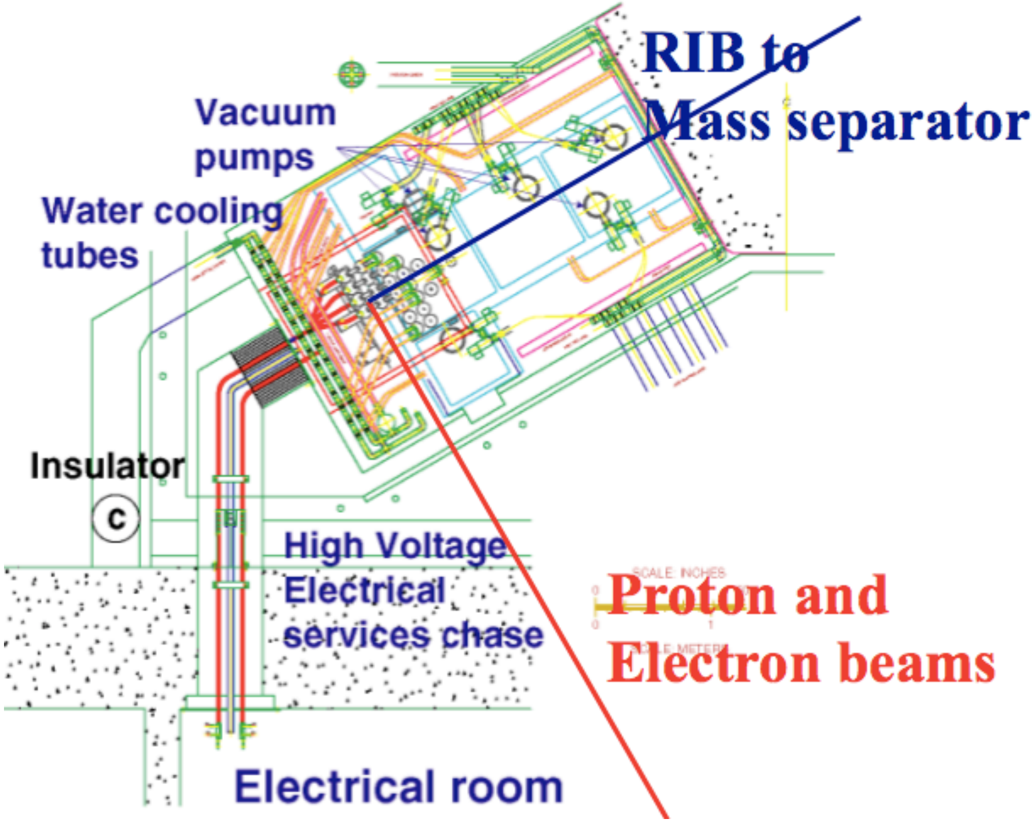
P. Bricault, TRIUMF

Diamond, NIM A 432, 471 (1999)
‘A radioactive ion beam facility using photofission’

Related target geometry (RIB)

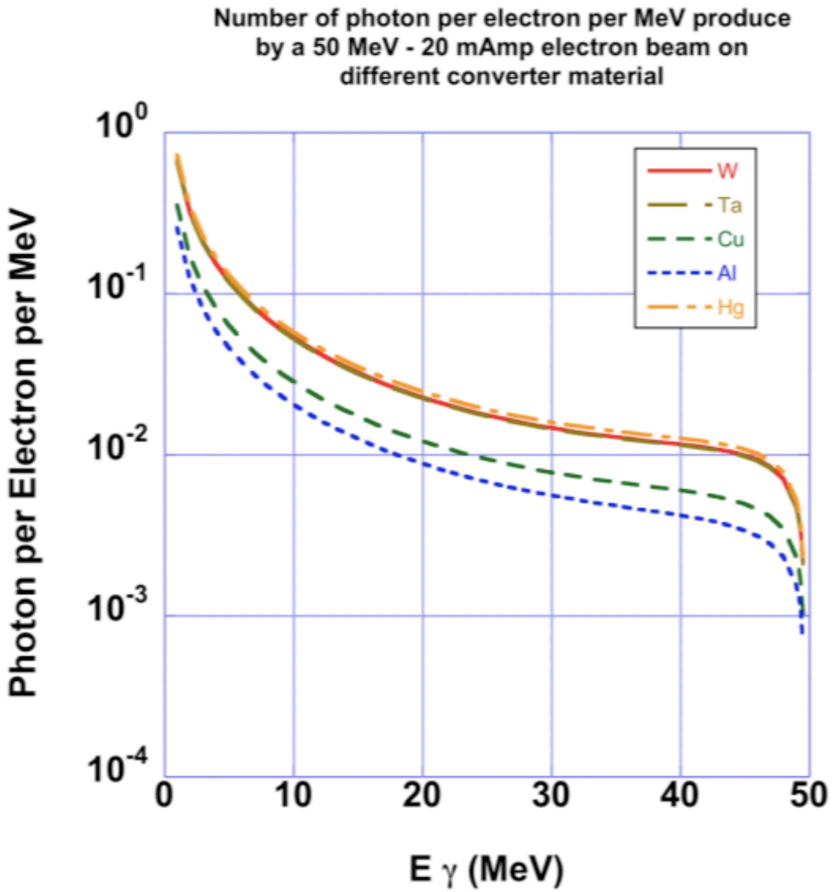


Target station plan view



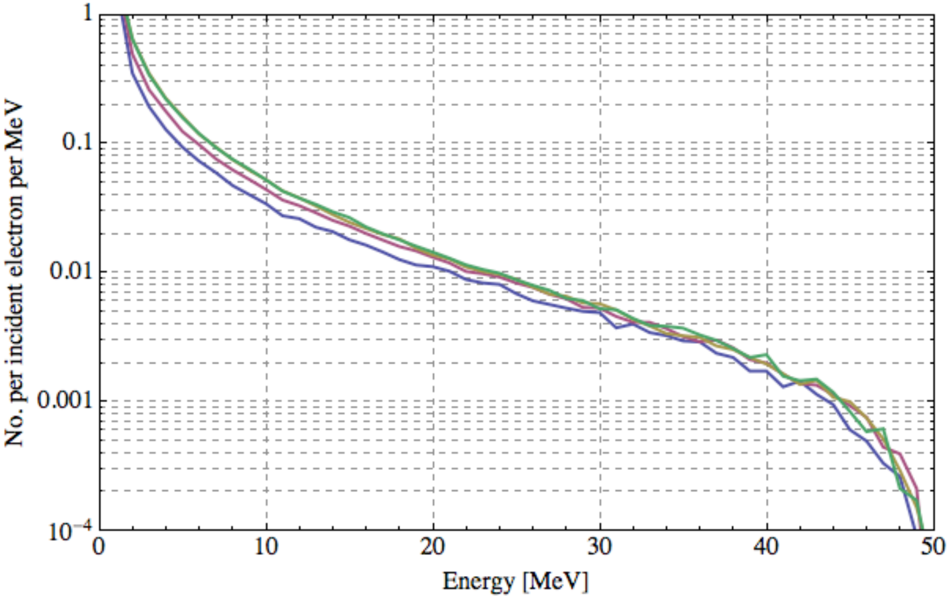
P. Bricault, TRIUMF

Bremsstrahlung spectrum

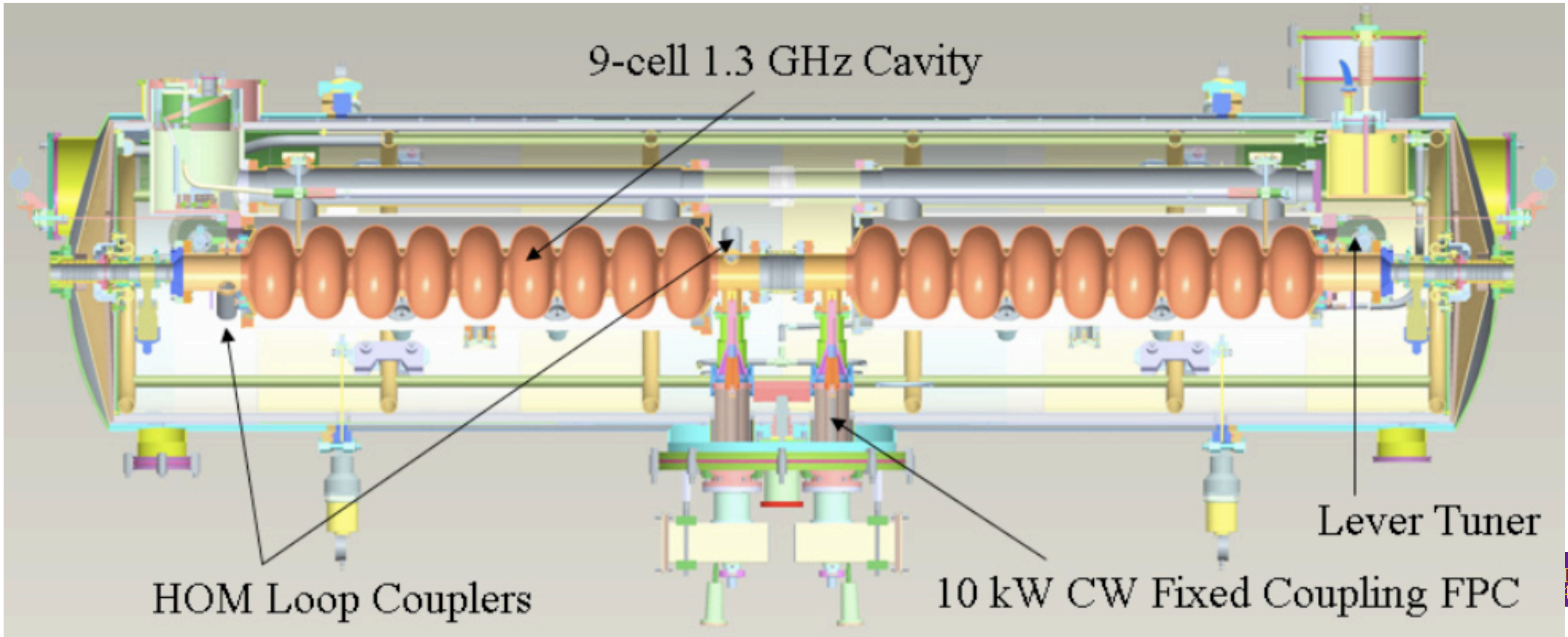


Number of photon per electron per MeV produce by a 50 MeV - 20 mAmp electron beam on different converter material

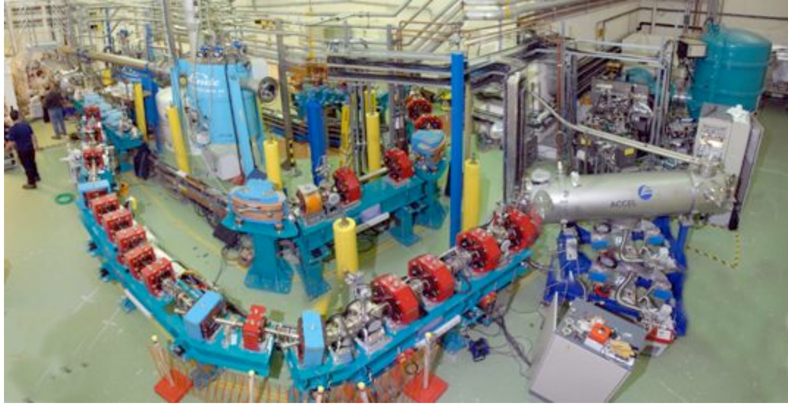
Bremsstrahlung yield from GEANT4 different geometry
(W at the top, Al at the bottom)



ALICE Cavity Development

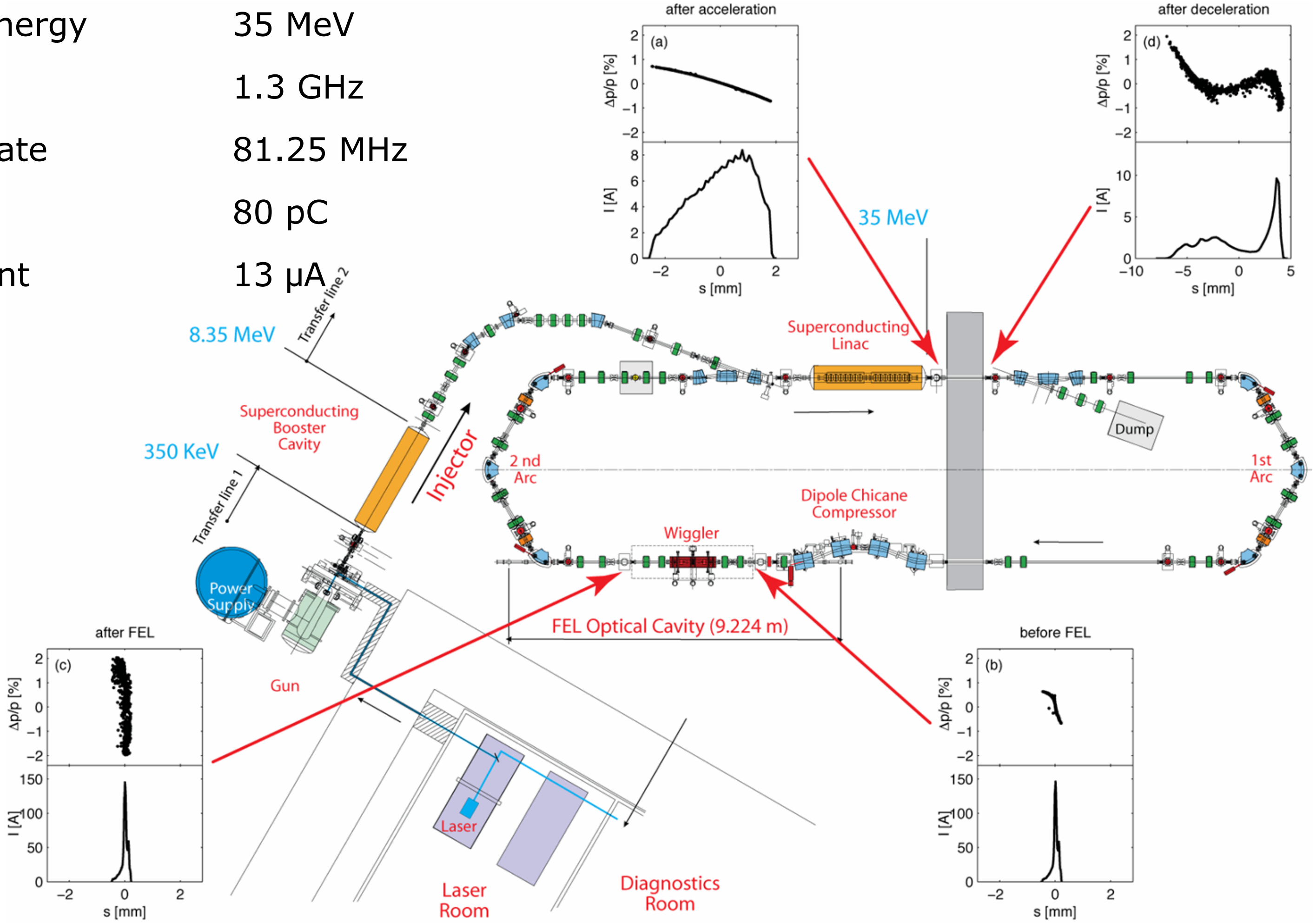


ALICE Accelerator Test Facility



Nominal Gun Energy	350 keV
Injector Energy	8.35 MeV
Circulating Beam Energy	35 MeV
Linac RF Frequency	1.3 GHz
Bunch Repetition Rate	81.25 MHz
Max Bunch Charge	80 pC
Max Average Current	13 µA

Alice
Accelerators and Lasers
In Combined Experiments

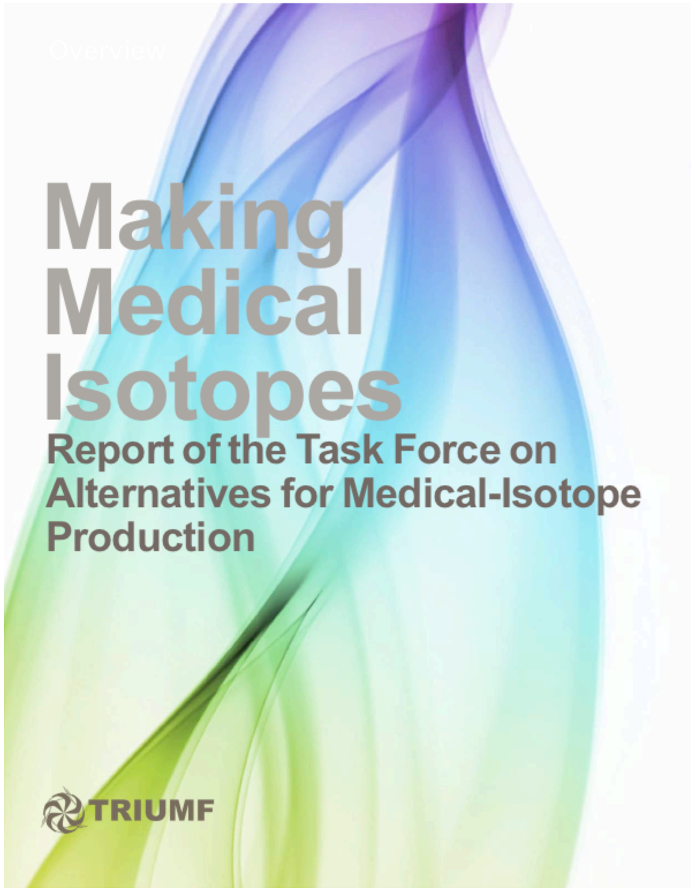


of Accelerator Science and Technology

1-8125 bunches @ 1-20 Hz

TRIUMF Plans

- TRIUMF have long-standing involvement with MDS-Nordion on medical isotope production using ~30 MeV proton cyclotrons
- Recent report is a response to Canadian isotope crisis
  - Propose high power e- linac and photofission



Overview

Making Medical Isotopes

Report of the Task Force on Alternatives for Medical-Isotope Production

TRIUMF

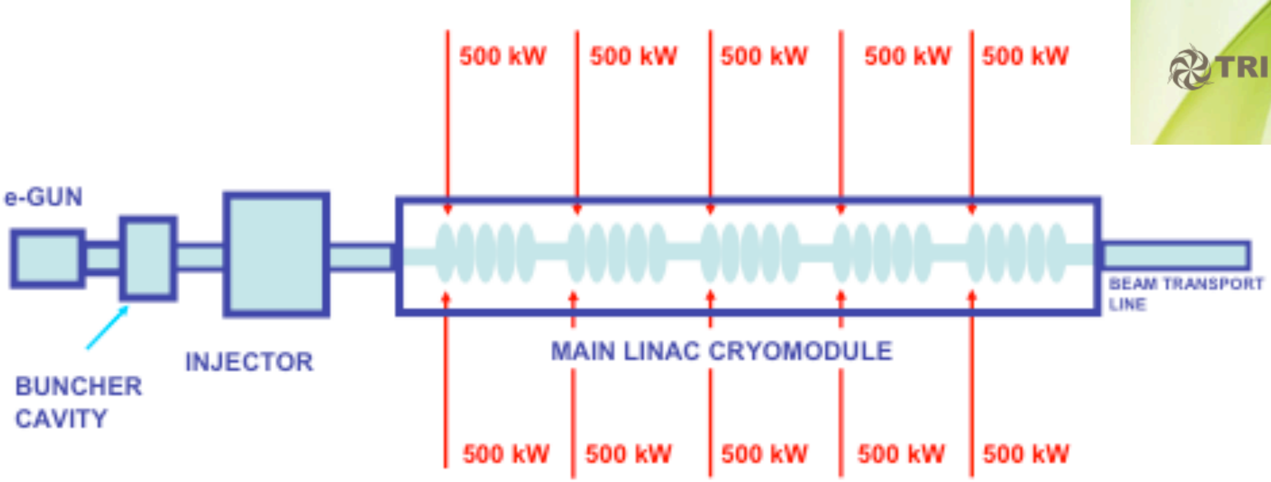
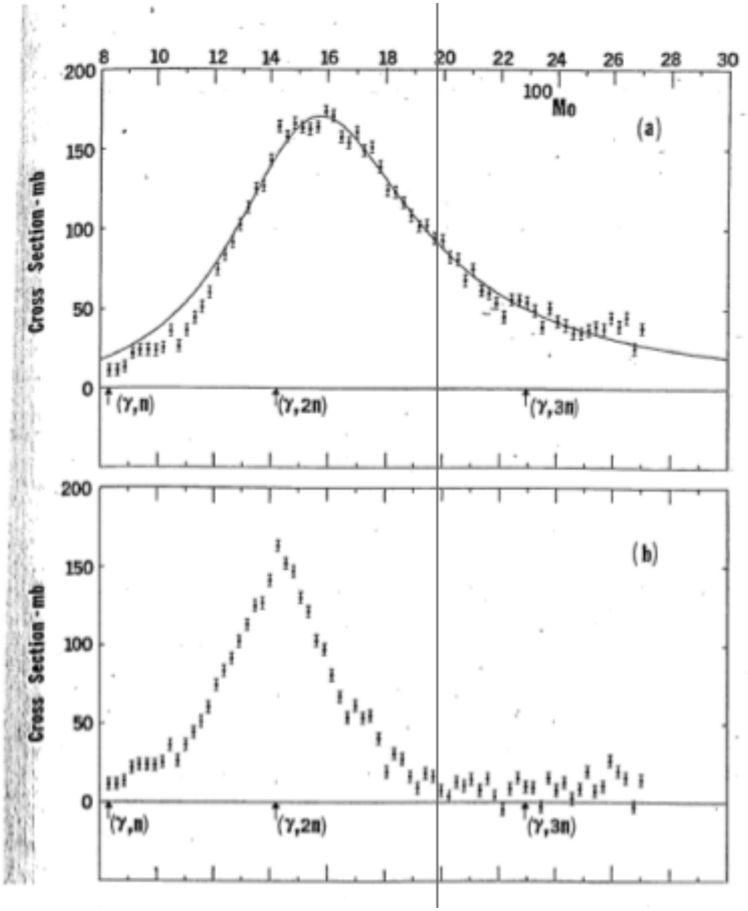


Figure 3.3: Schematic layout of 5 MW e-linac based on 704 MHz SCRF technology.

Photonuclear Cross-Section in 100Mo



W.Diamond, AECL, Oct 2008

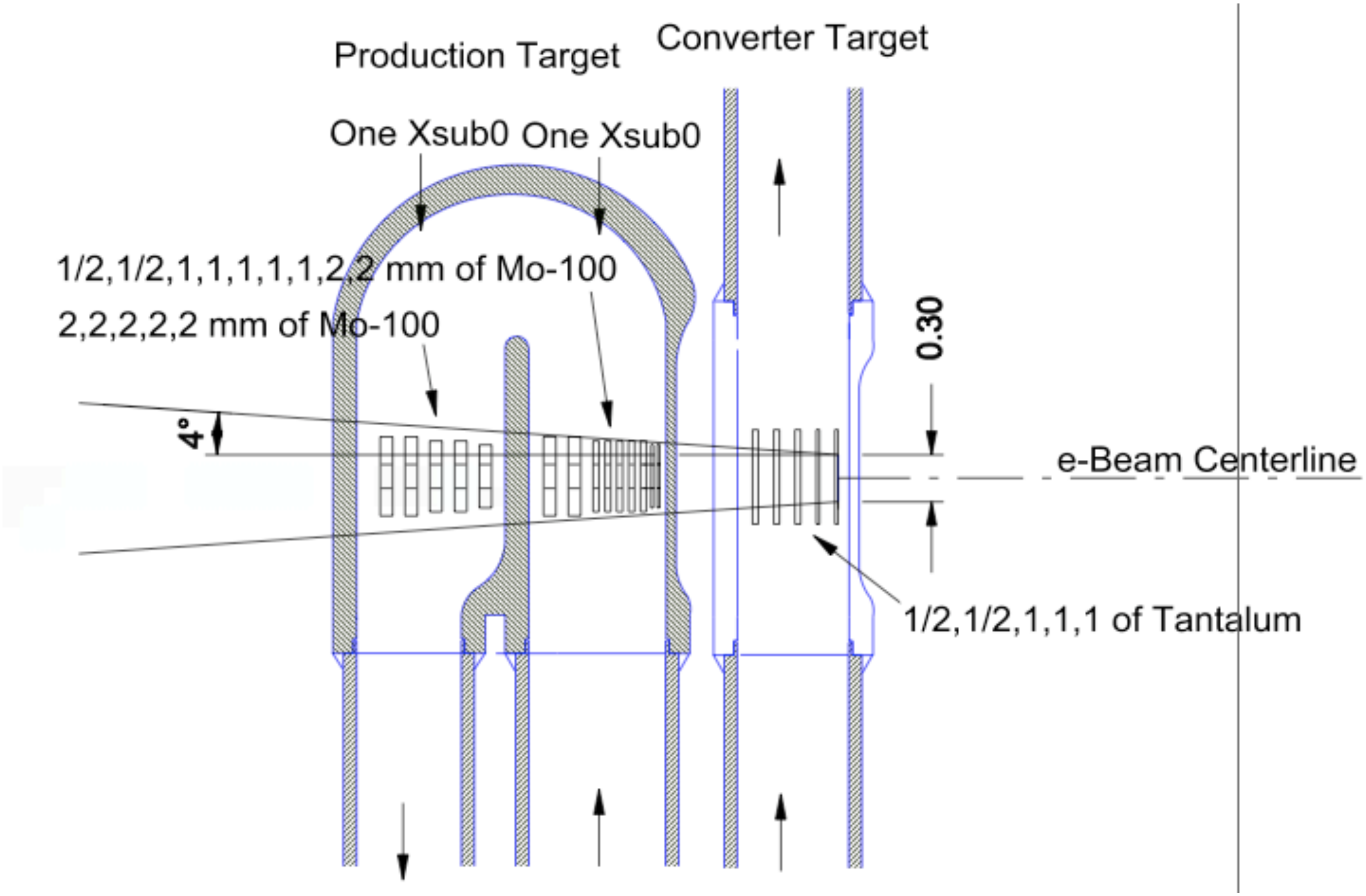
Around 100 Ci/g with 100kW/50MeV electrons into W
About 2 atoms in 10,000
(cf ~10% in fission products)
- this requires a different (bigger?) generator
- normal generator 60 in 10000

$$m = \frac{t_{1/2} R A}{N_A \ln 2}$$

Target design is crucial
‘Photofission is likely not practical’

Sabelnikov et al., Radiochemistry 48(2), 191 (2006)
- report 390 mb with direct irradiation with 25 MeV electrons

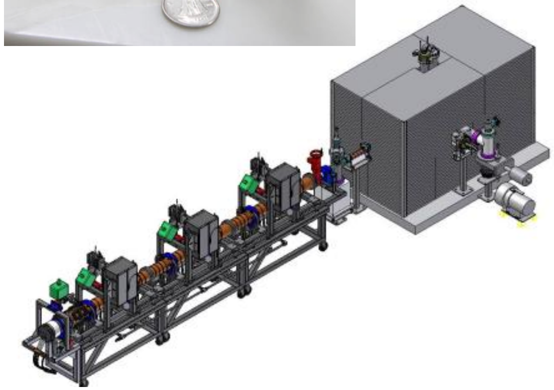
ORNL ORELA Neutron target design (Diamond/Beene)

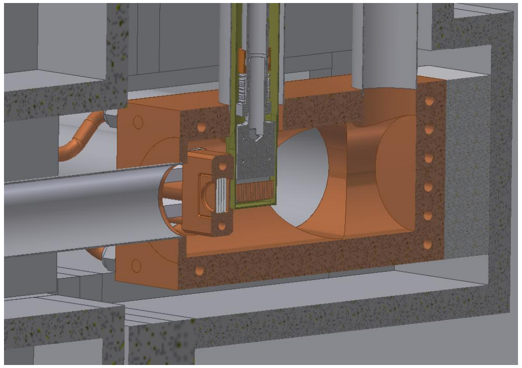


- Photo-nuclear reaction on ^{100}Mo:
  - $^{100}\text{Mo}(\gamma, n)\,^{99}\text{Mo}$

- Natural Mo about 10 % ^{100}Mo
- Available at enrichments of > 95 %
- Known for more than 40 years
- Photons produced via Bremsstrahlung using high-energy electrons from linear accelerator ⇨ high-energy X-rays

100Mo target (CLS)



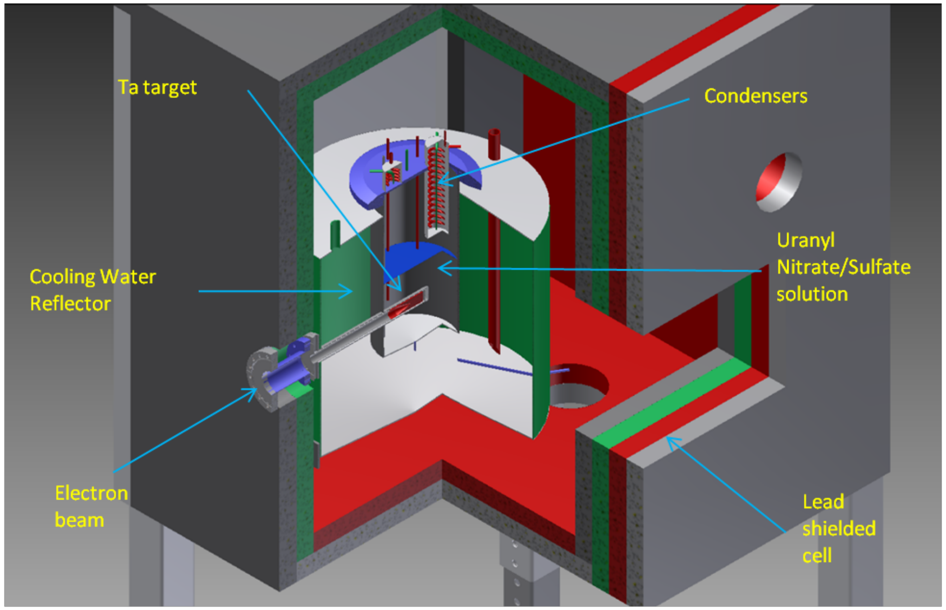


NRC INMS Proof-of-concept (Ottawa)

Courtesy M. de Jong, CLS

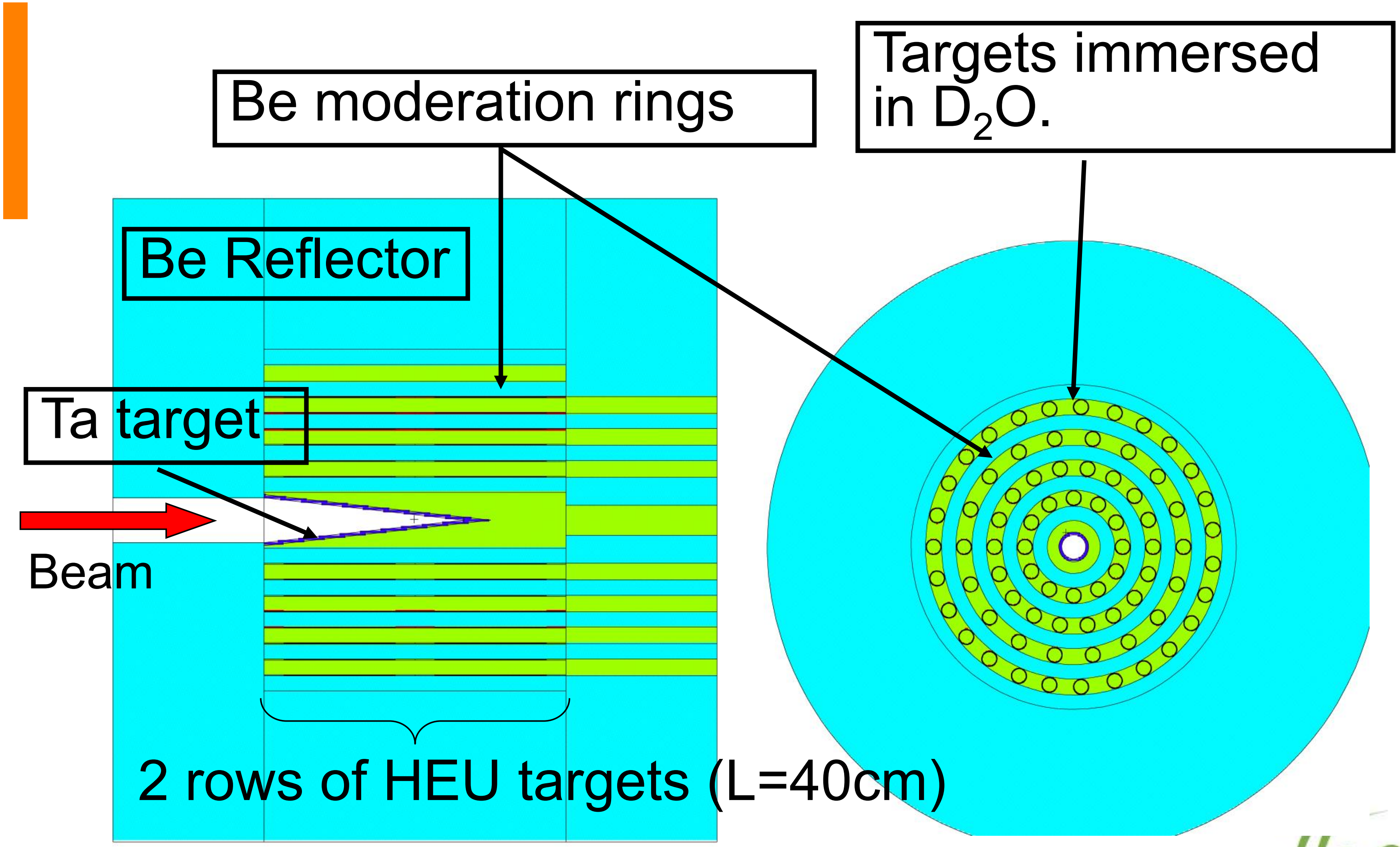
Other electron-based methods

- Electron linacs also useable in other methods
- Subcritical aqueous LEU solution
  - SHINE
- 100Mo(g,n)99Mo production
  - Ottawa, Saskatechewan
- Typical energy: 50 MeV
- Typical beam power: 10-100 kW



Target Layout of SHINE

Subcritical assembly – IBA Adonis Concept (150 MeV, 2mA p cyclotron)



Be moderation rings

Targets immersed in D_2O.

Be Reflector

Ta target

Beam

2 rows of HEU targets (L=40cm)

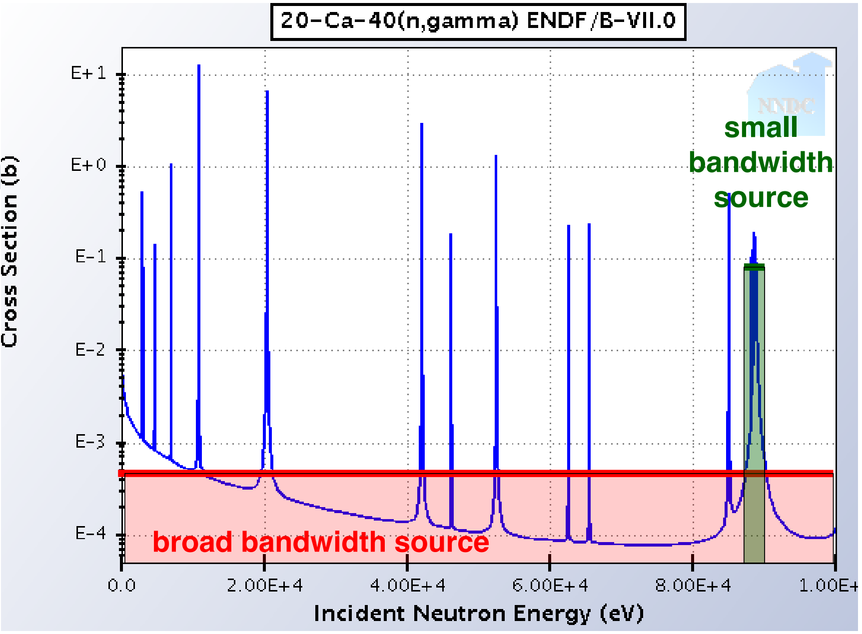
c. 50-100 Ci/g, 5000 Ci/week

Courtesy F. Stichelbaut, IBA

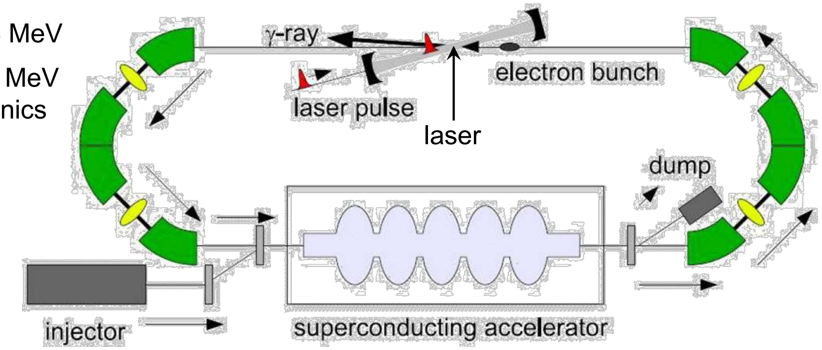
Resonant gamma production

- Energy recovery linac gives small electron beam size at high repetition rate
- Compton scattered photons give narrow, tuneable gamma ray energy

- Technically very difficult at present



Energy recovery linac (ERL)



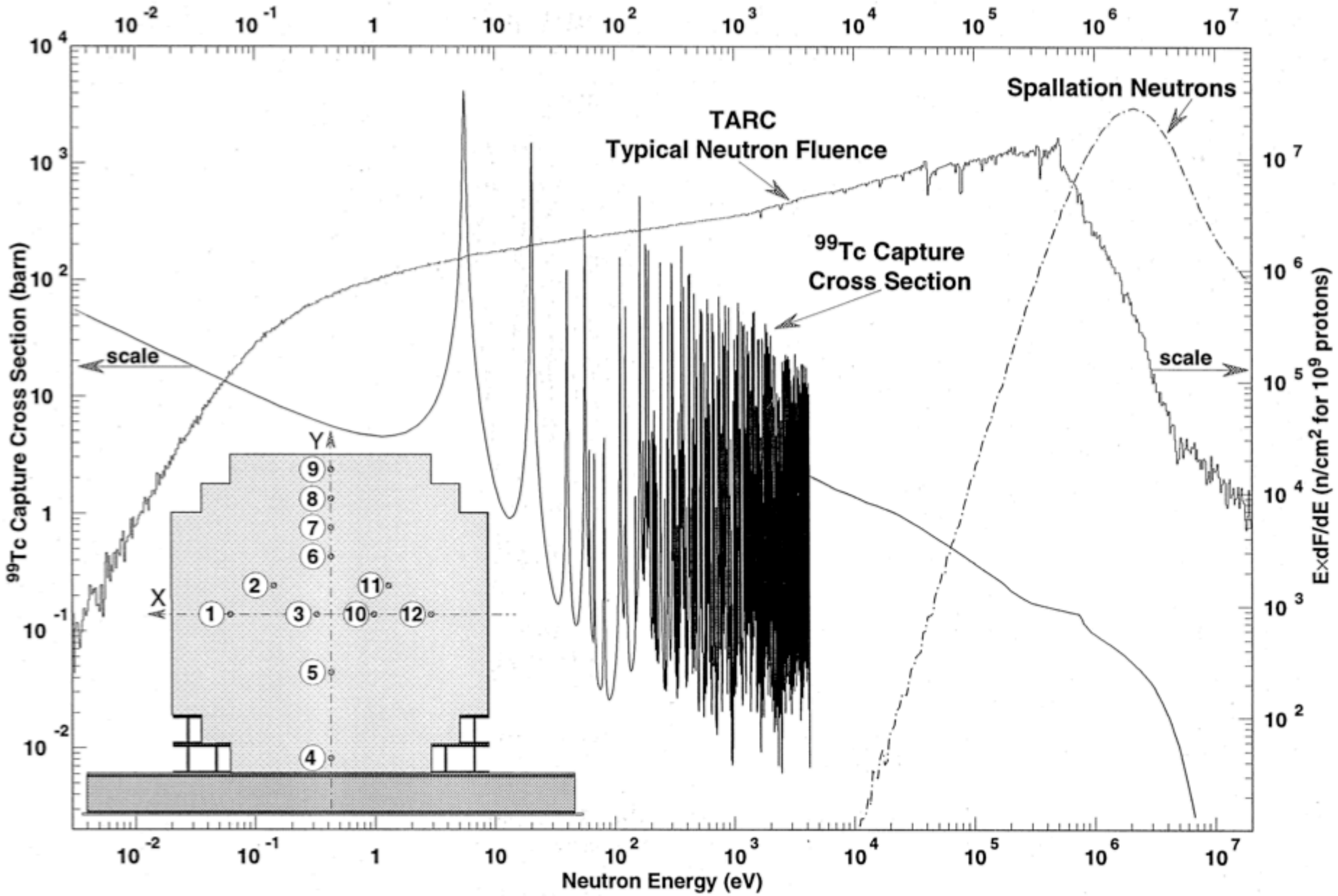
E_γ = 0.2 – 14 MeV

E_γ = 1 – 100 MeV
high harmonics

	high flux mode	**high brilliance mode**	**ultra-fast mode**
	80 pC, 130 MHz	8 pC, 1.3 GHz	100 fs
peak brilliance (s mm^2 mrad^2 0.1%BW)$^{-1}$	8·10^{21}	6·10^{22}	
flux	5·10^{15} s^{-1}	1·10^{15} s^{-1}	
spot	15 μm	10 μm	15 μm

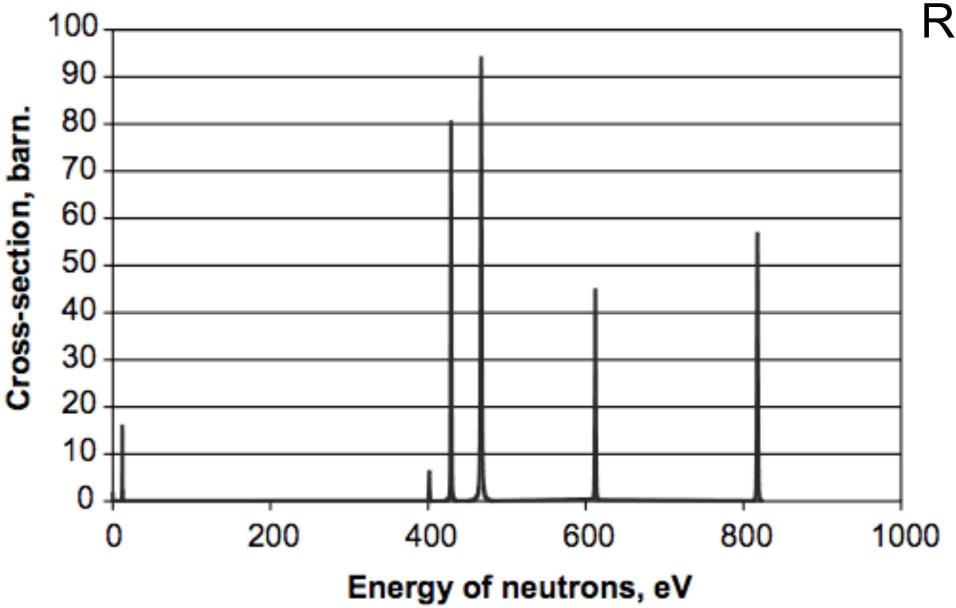
20% energy spread accepted for recovery; 1 GeV · 0.1 A = 100 MW

Adiabatic Resonance Crossing (Rubbia)

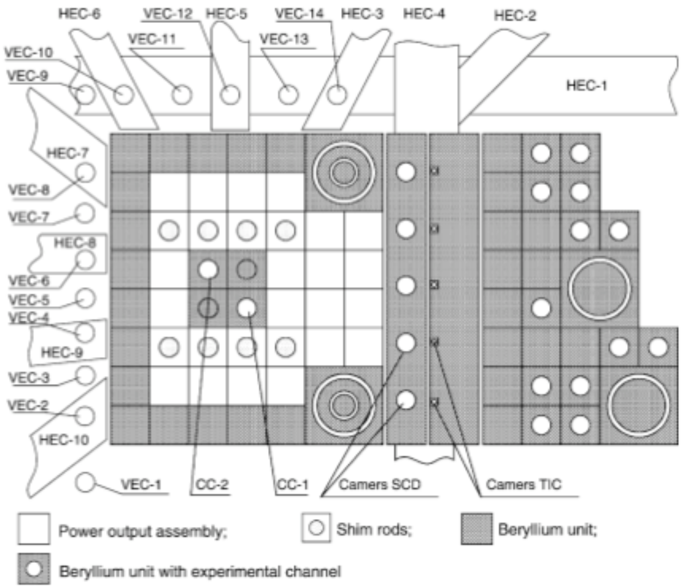


Rubbia, CERN/LHC/97-04
Arnould et al., Phys. Lett. B 458, 167 (1999)

Epithermal neutron capture in 98Mo



Ryabchikov et al., NIM B 213, 364 (2004)



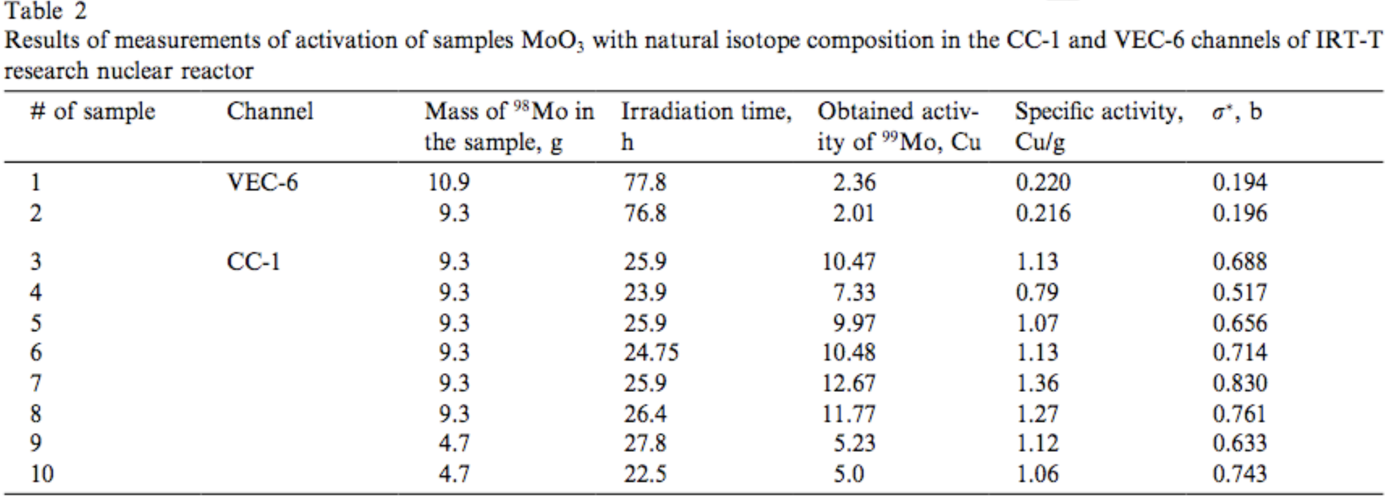


Table 2

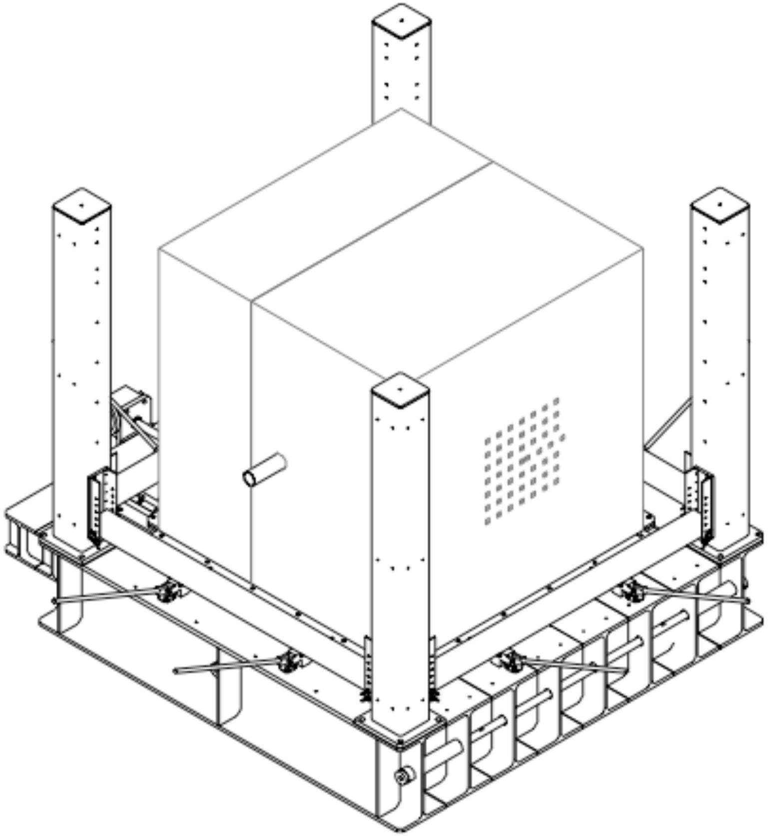
Results of measurements of activation of samples MoO_3 with natural isotope composition in the CC-1 and VEC-6 channels of IRT-T research nuclear reactor

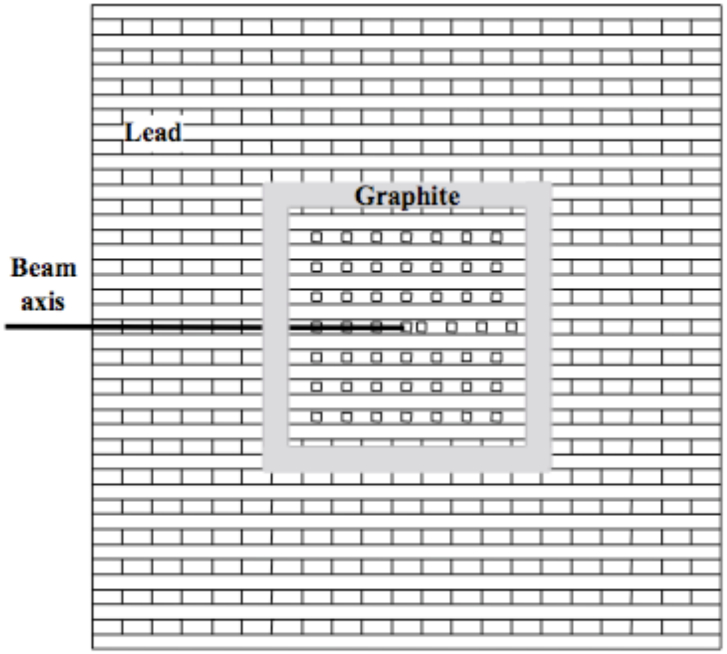
# of sample	Channel	Mass of ^{98}Mo in the sample, g	Irradiation time, h	Obtained activity of ^{99}Mo, Cu	Specific activity, Cu/g	σ^*, b
1	VEC-6	10.9	77.8	2.36	0.220	0.194
2		9.3	76.8	2.01	0.216	0.196
3	CC-1	9.3	25.9	10.47	1.13	0.688
4		9.3	23.9	7.33	0.79	0.517
5		9.3	25.9	9.97	1.07	0.656
6		9.3	24.75	10.48	1.13	0.714
7		9.3	25.9	12.67	1.36	0.830
8		9.3	26.4	11.77	1.27	0.761
9		4.7	27.8	5.23	1.12	0.633
10		4.7	22.5	5.0	1.06	0.743

Resonant Neutron Capture

Isotope	Abundance	Abs (barn)
Pb	---	0.171
204Pb	1.4	0.65
206Pb	24.1	0.03
207Pb	22.1	0.699
208Pb	52.4	0.00048

Lethargy $\xi = 1 + \frac{(A-1)^2}{2A} \ln(\frac{A-1}{A+1})$





Froment al., NIM A 493, 165 (2002)

van Do et al., NIM B 267, 462 (2009)

65 MeV Protons into Be target (7 hour exposure)

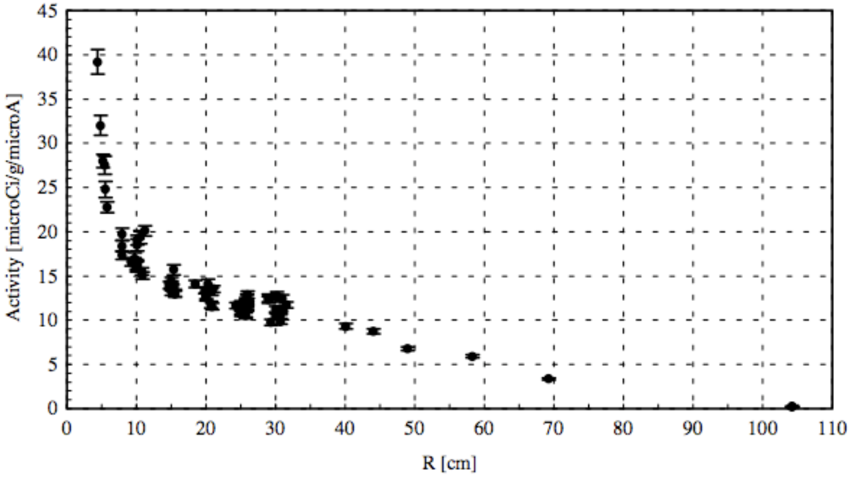
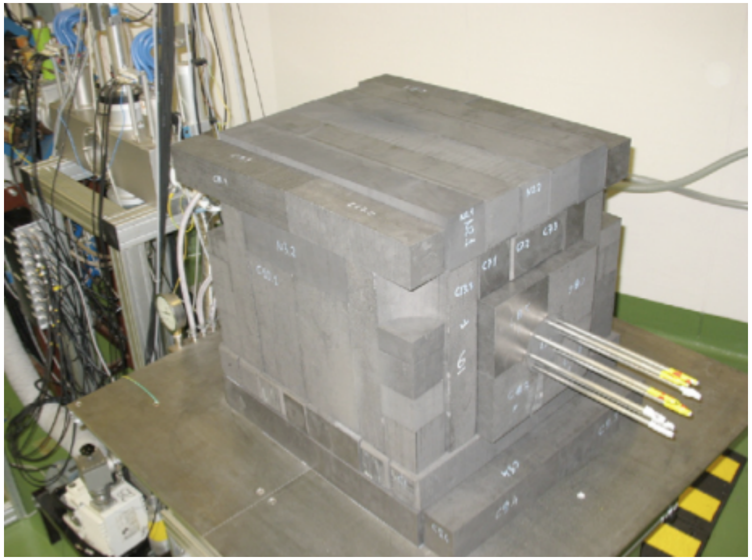


Fig. 3. ^{99}Mo activity generated by irradiation of metallic Mo foils with neutrons produced by bombarding the Be target with a 65 MeV proton beam. The results are presented as a function of the distance (*R*) between the sample and the Be target.



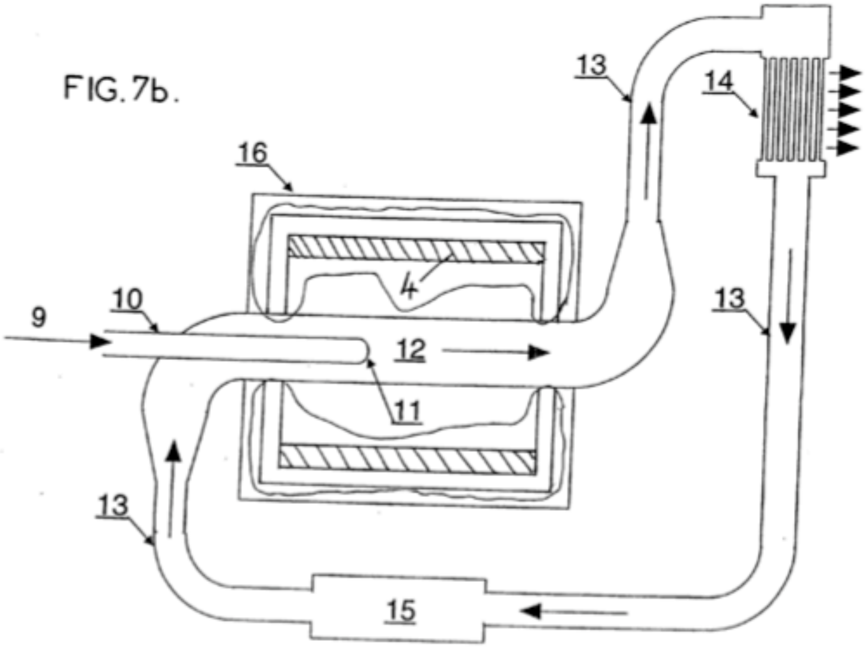
Froment et al., NIM A 493, 165 (2002)
Abbas et al. 601, 223 (2009)

About 1 neutron per 8 protons

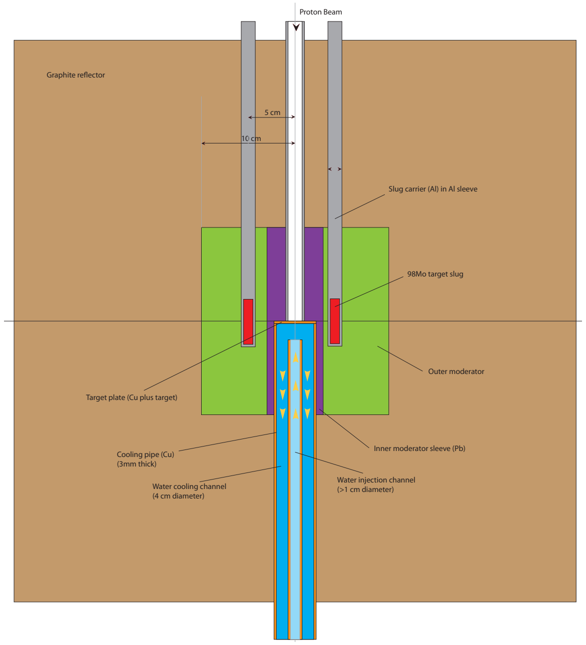
Carlo Rubbia patent

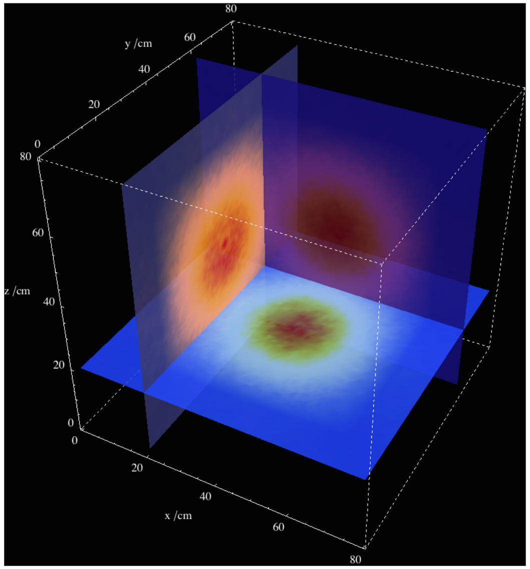
- Patent 2005/0082469 (2005)
- Resonant neutron capture in Mo, possibly Na2MoO4 solution

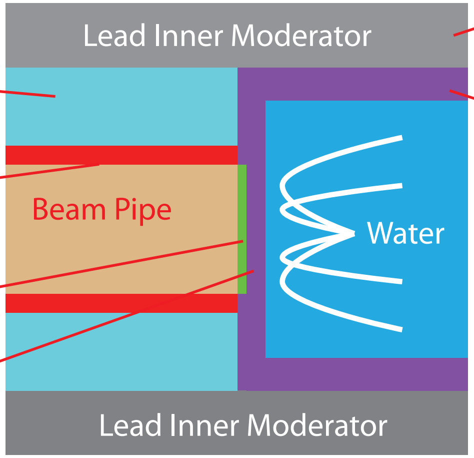
FIG. 7b.



Moderated Neutron Capture for 99mTc (Manchester)







Inner Moderator Cylinder (Pb)
ID 50 mm, OD 70mm

Graphite
Reflector

Cu Cooling Pipe
(5mm thick, 50 mm OD)

Aluminium Beam Pipe
(3mm thick, 26 mm OD)

Li/Water Target
(Be Foil Cover)

Cu Backing
(or hole to face of target)
3.5 mm thick

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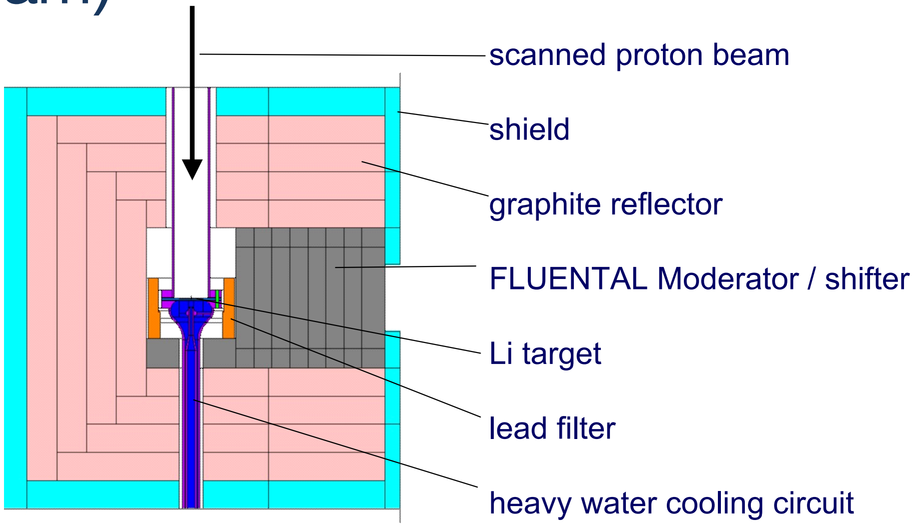
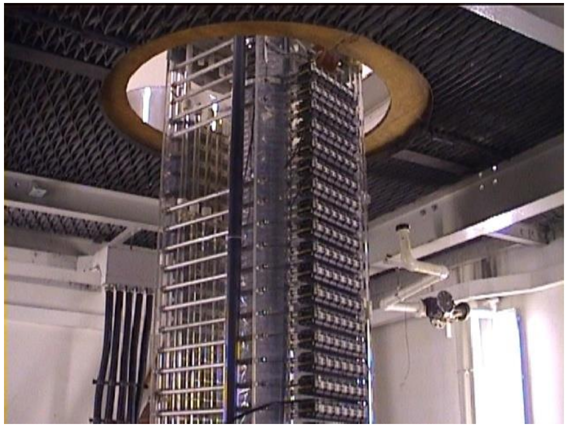
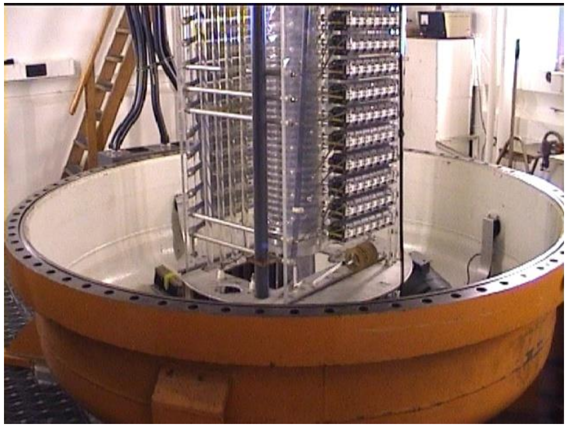
1824

Moderator for BNCT (Birmingham)

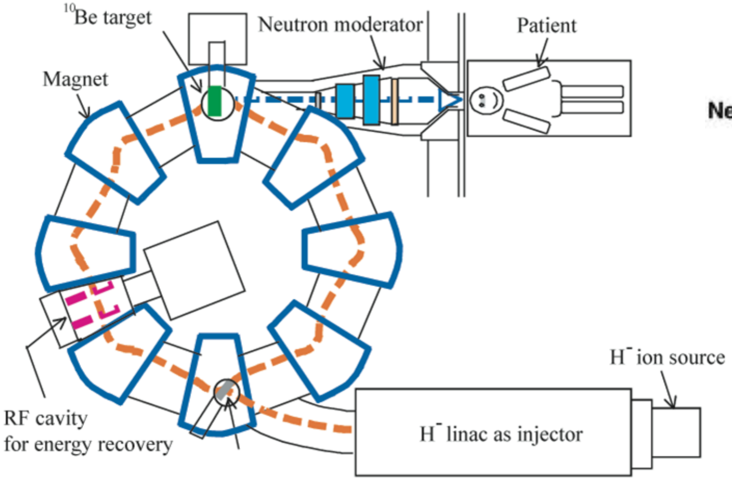
- 1.7 MeV reaction threshold
- Solid or liquid lithium target
- Useful flux of neutrons requires large currents
  - 10^12 n/s requires 1 mA

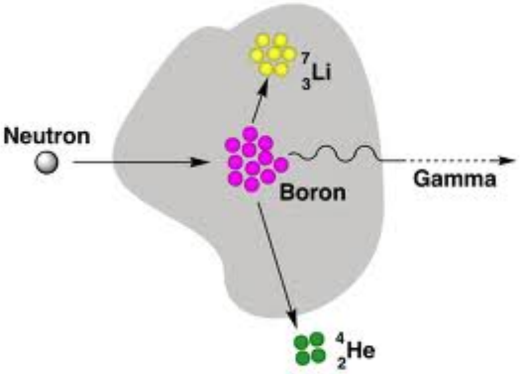






courtesy S. Green, UHB



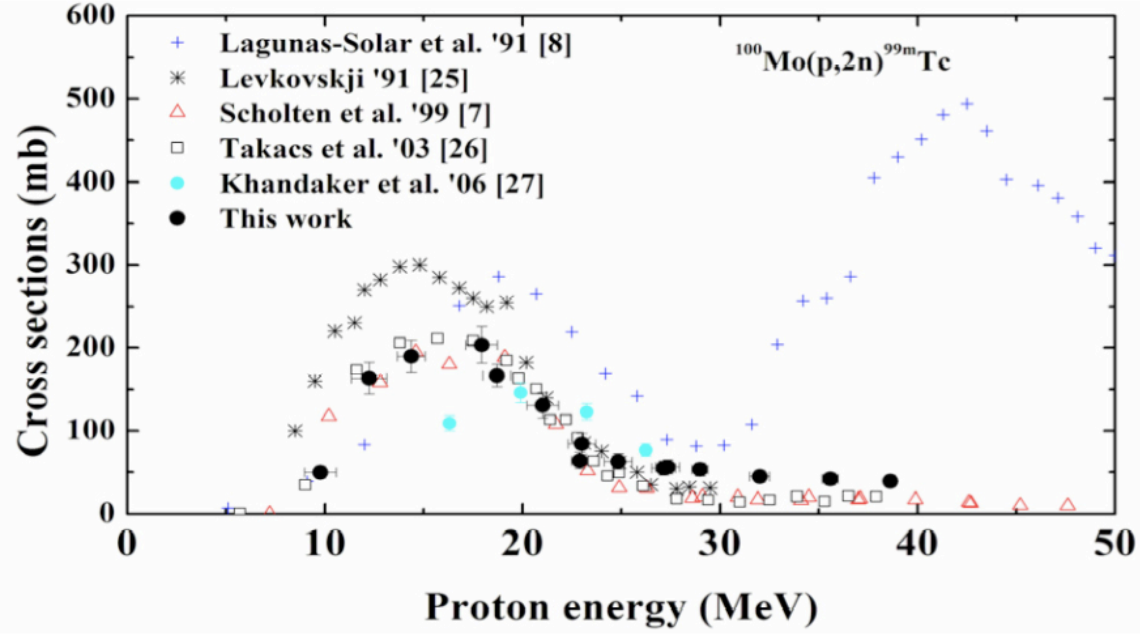


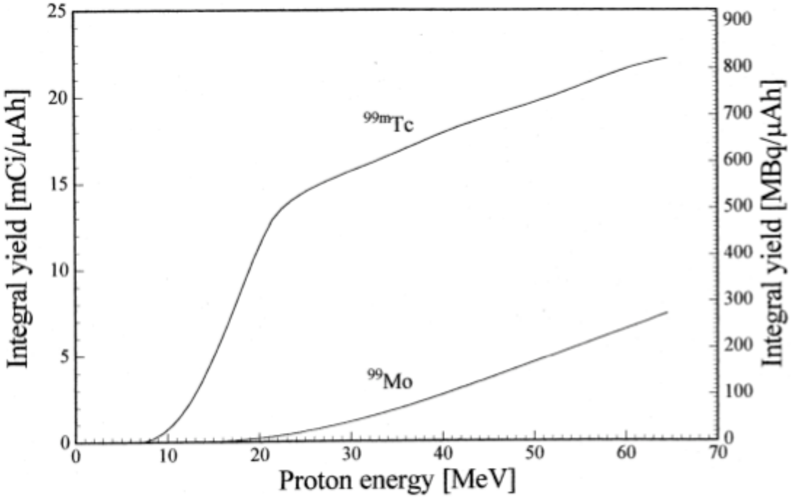
Direct Proton Reactions

100Mo(p,pn)99Mo
100Mo(p,2n)99mTc
98Mo(p,γ)99mTc

Kim et al., IEEE Nuclear Science Symposium Conference Record, 2007. NSS'07, N15-307

Scholten et al., Applied Radiation and Isotopes 51, 69 (1999)





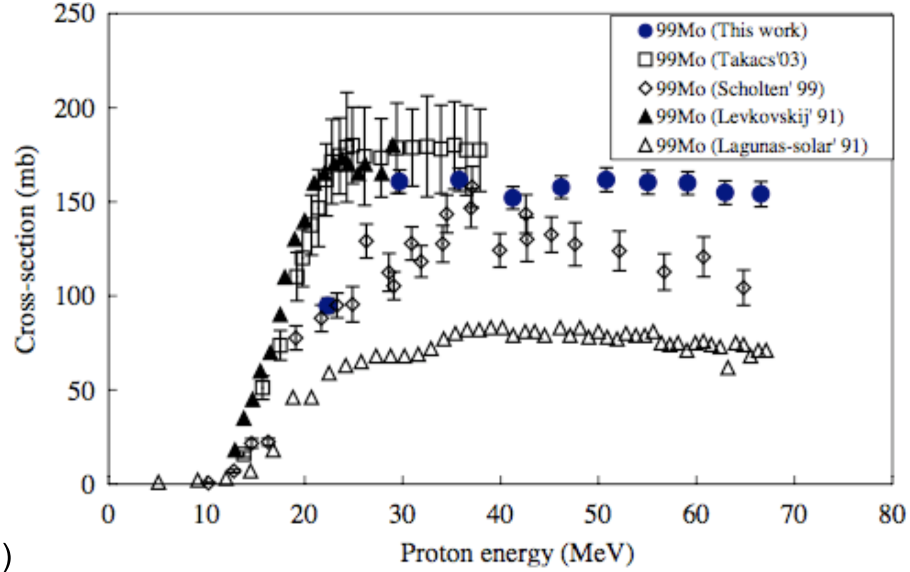
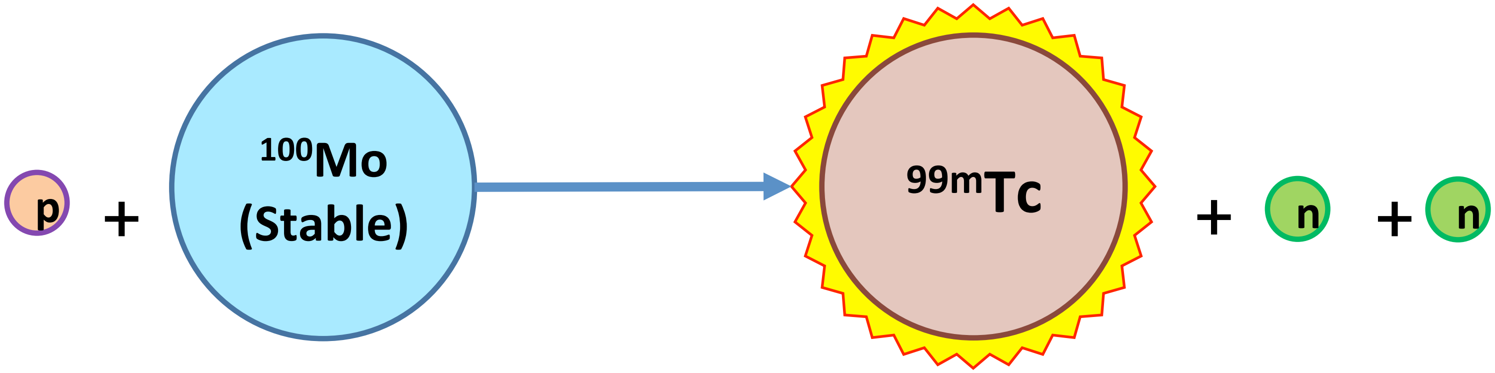


Fig. 3. Excitation functions of the ^{100}Mo(p,x)^{99}Mo reaction.

Uddin et al., Applied Radiation and Isotopes 60, 911 (2004)
M. Challan et al., J. Nucl.Rad.Phys. 2(1), 1 (2007)

Alternative ^{99m}Tc Production Method

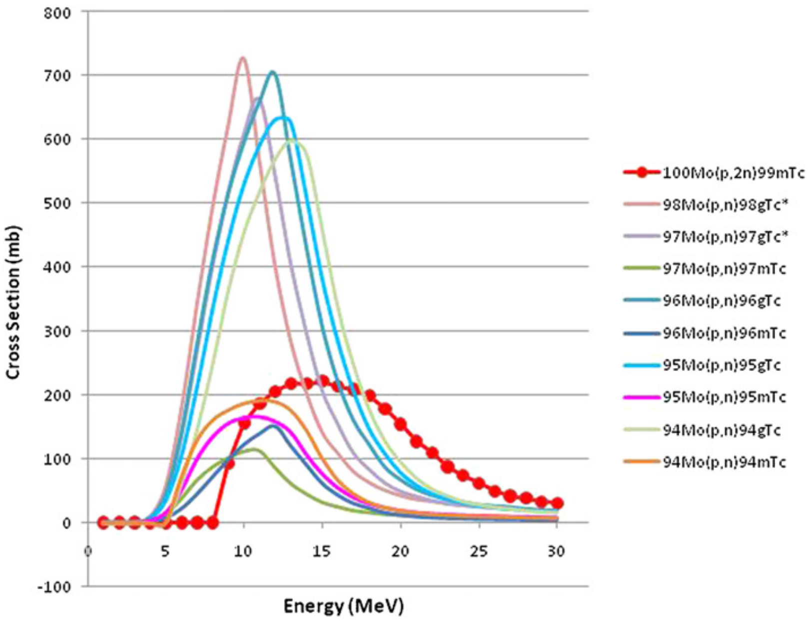
- One possible alternative is to make ^{99m}Tc directly on a cyclotron.
- This entails the proton irradiation of a target made of enriched molybdenum-100 (^{100}Mo).

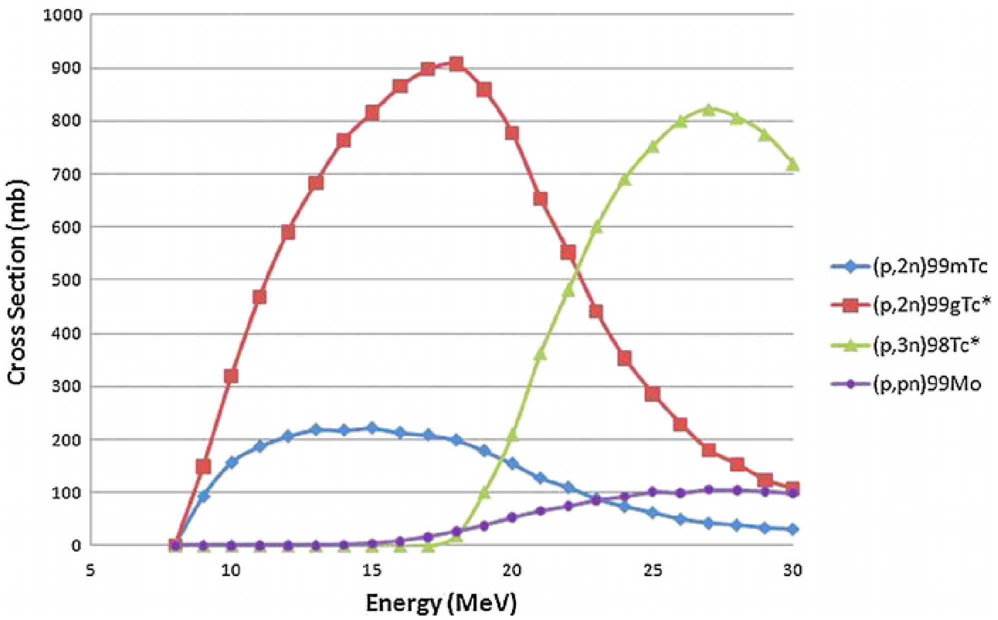


- New research, regulatory, and distribution challenges are noted with the cyclotron scheme.
- The cyclotron scheme however offers low radioactive waste, it eliminates the for ^{235}U, a network of cyclotrons would lead to redundancy in the ^{99m}Tc supply chain, and the cyclotrons could also be used to make other medical isotopes.

Cyclotron Production of Tc-99m

$^{98}\text{Mo}(p,\gamma)^{99m}\text{Tc}$
$^{100}\text{Mo}(p,2n)^{99m}\text{Tc}$
$^{100}\text{Mo}(p,pn)^{99}\text{Mo} \rightarrow {}^{99m}\text{Tc}$





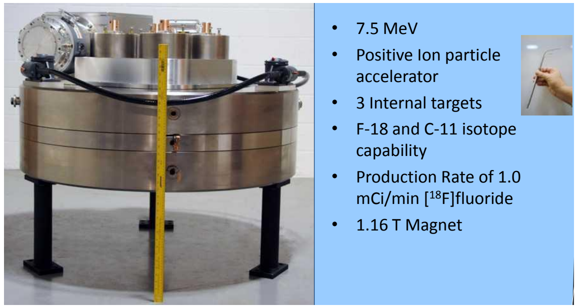
Celler et al., PMB 56, 5469 (2011)

University of Alberta Cyclotron

- TR 19/9 operational in 2002
- Produce 3-4 batches of ~300 GBq $[^{18}F]F^-$, ~4.5 days/week
- Routine production of ^{11}C
- Have produced ^{124}I, $[^{18}F]F_2$
- Interested in large-scale cyclotron production of ^{99m}Tc
- Currently developing a new cyclotron facility (for a TR24)
- TR24 commissioning currently underway
- Ongoing research and development activities 2013 - 2016

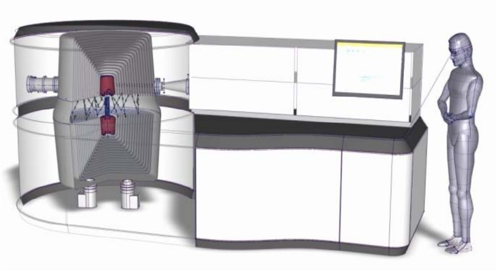
Comparing proton technical solutions

- Cyclotrons
  - Well-established, mature
  - Some difficulty in obtaining higher powers
  - Compact lower-energy cyclotrons trend for 18F

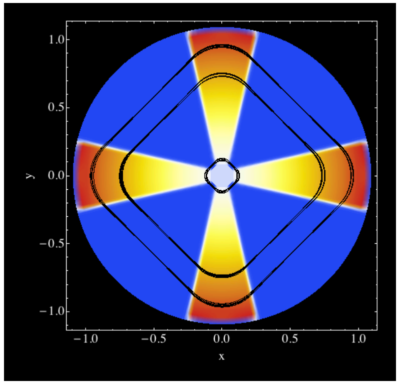


- 7.5 MeV
- Positive Ion particle accelerator
- 3 Internal targets
- F-18 and C-11 isotope capability
- Production Rate of 1.0 mCi/min [^{18}F]fluoride
- 1.16 T Magnet

- Oniac (RAL/Siemens)
  - New DC technology (no magnet), intended for PET production
  - Could be cheaper
  - Probably limited < 10 MeV (too low)
  - Progress in demonstration appears to have stalled



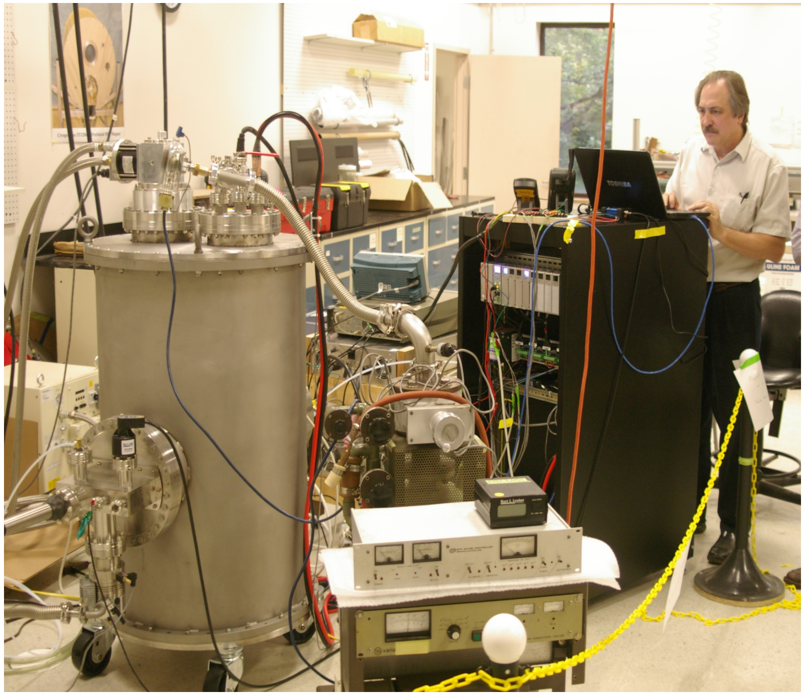
- FFAGs for p/d isotope production (Huddersfield)
  - Designs underway; internal target
  - Belief that stronger focusing allows higher current, but not published yet
  - Larger and more complex than equivalent cyclotrons

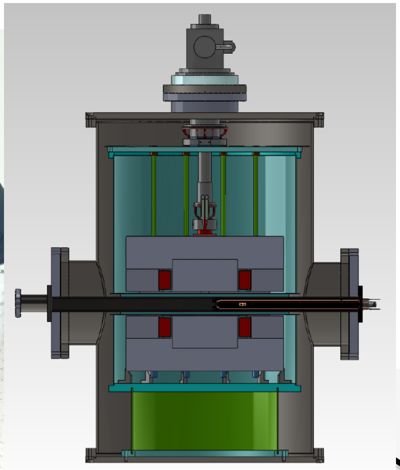


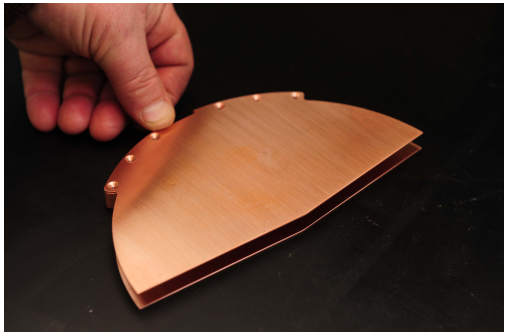
Example pFFAG design (H Owen)

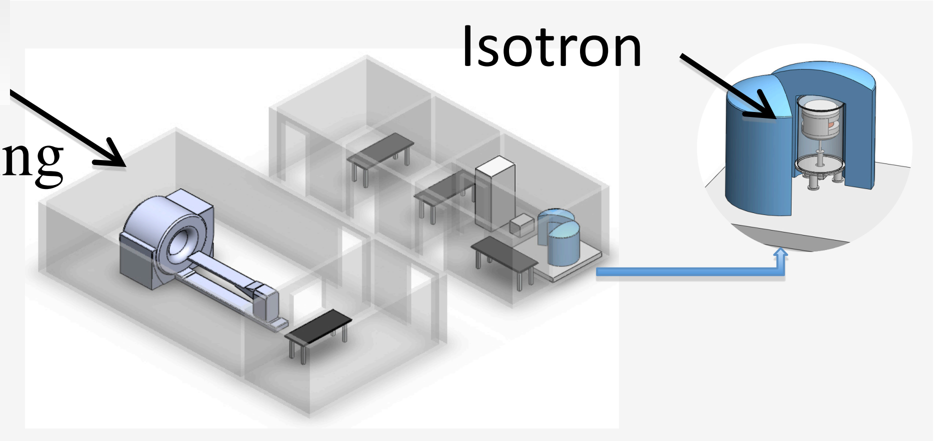
Superconducting cyclotrons

- Lower energy allows higher current
- Ionetix Isotron:
  - 12.5 MeV/~6 T/35 kW
  - 13N production ($t_{1/2}$=10 minutes)
- No particular barrier to higher energies







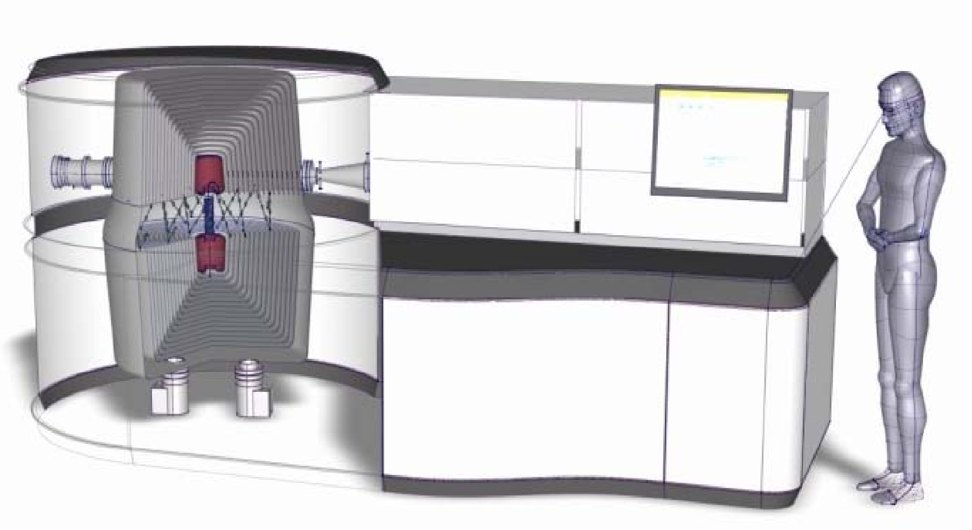


Mevion Monarch 250

- 250 MeV proton cyclotron
  - ‘about the size and cost of a modern 18 MeV PET cyclotron’ (T Antaya)

- Operational and treating patients (Barnes Jewish Hospital)

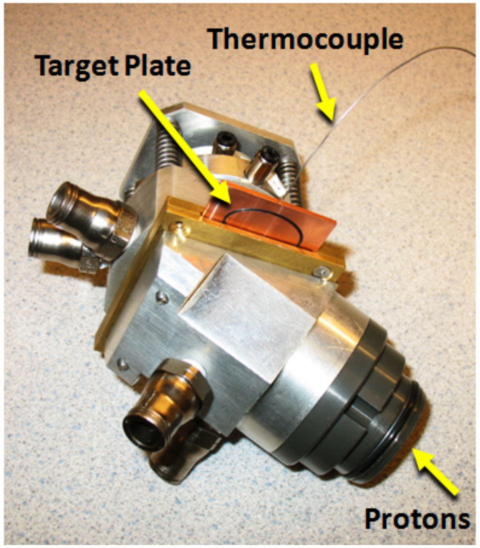
Siemens Oniac

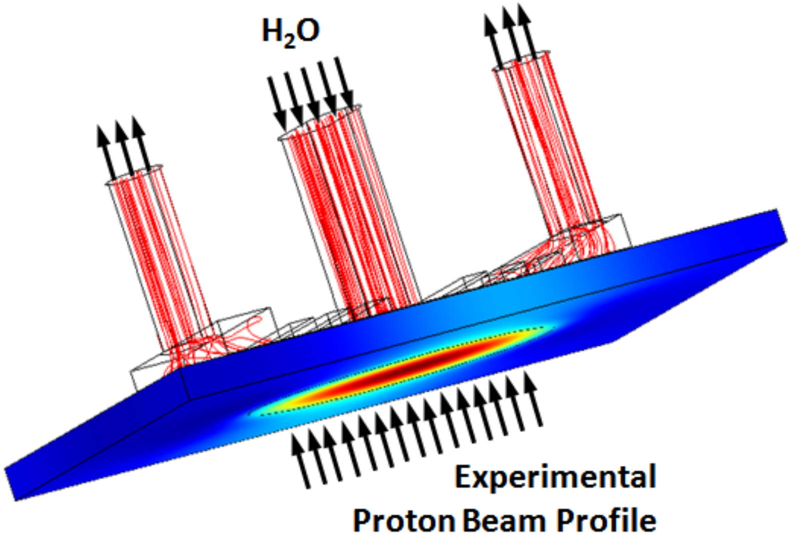


- ‘Magnet free’
- Single stage only, perhaps up to 10 MV
- 5-stage Greinacher cascade, H$^-$ n , stripped to H+ at centre
- Demonstrator installed at RAL – results to come!

High-current target design: thermal modelling

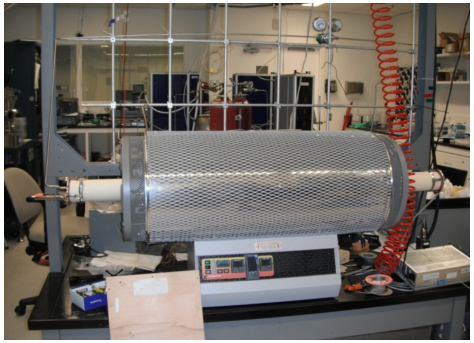
- Although yields may be increased by increasing the beam current, production is often limited by thermal performance of the target.
- Use computer simulation (Comsol Multiphysics) and experimental validation to model thermal performance of target based on geometry, material selection, cooling flow/temperature, heat transfer coefficient, proton current, etc.

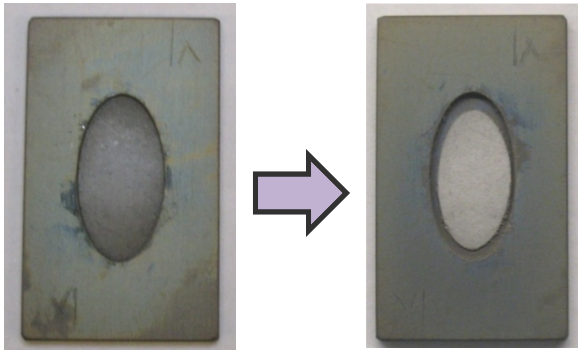




Critical component

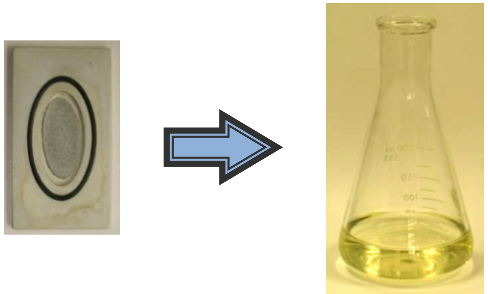
Results:

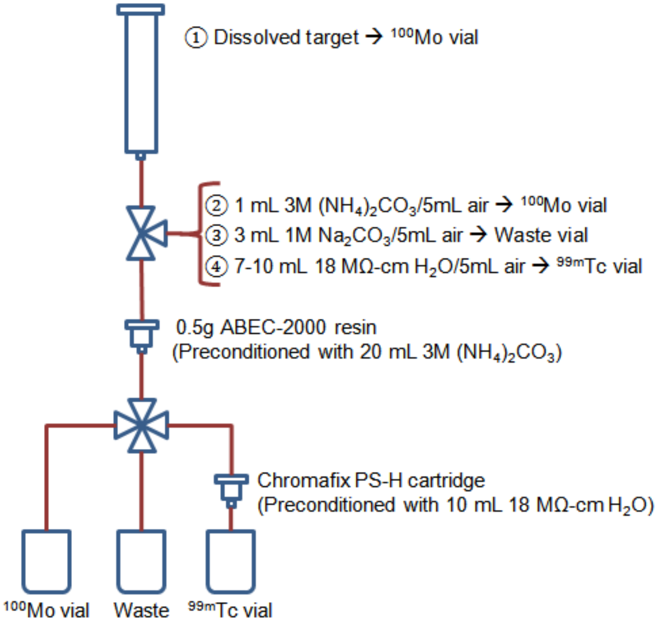




- Typical mass losses of ^{100}Mo <2% during target preparation
- Can sinter many plates at once
- Non-sticking of pellet to Ta is beneficial
- Improved strength (e.g. for target transfer)
- Increased density → improved thermal performance
- Tested to 17.5 MeV @ 80 μA (1.4 kW)
- Successful extraction of Curie quantities of ^{99m}Tc

Radiochemical Separation





① Dissolved target → ^{100}Mo vial

② 1 mL 3M $(NH_4)_2CO_3$/5mL air → ^{100}Mo vial

③ 3 mL 1M Na_2CO_3/5mL air → Waste vial

④ 7-10 mL 18 MΩ-cm H_2O/5mL air → ^{99m}Tc vial

0.5g ABEC-2000 resin
(Preconditioned with 20 mL 3M $(NH_4)_2CO_3$)

Chromafix PS-H cartridge
(Preconditioned with 10 mL 18 MΩ-cm H_2O)

^{100}Mo vial

Waste

^{99m}Tc vial

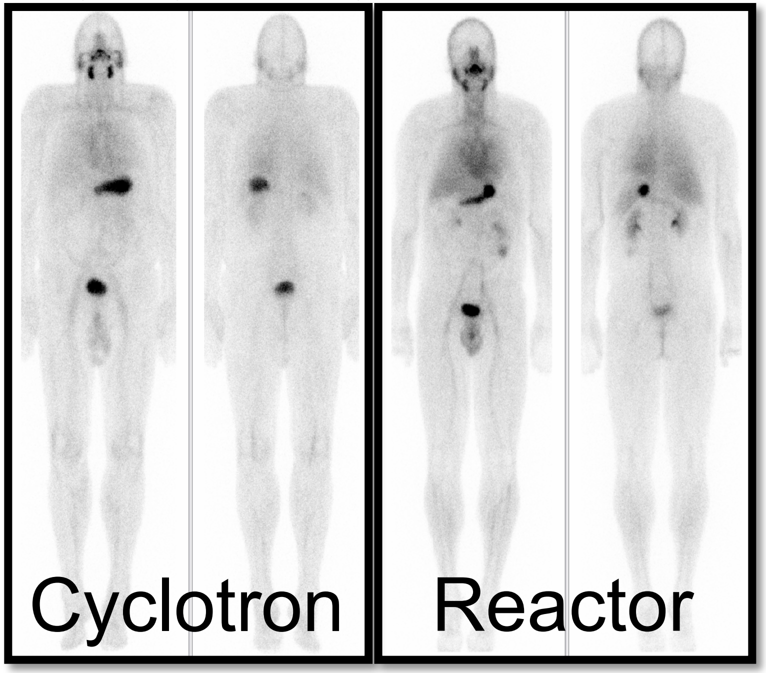
- Successful dissolution of target material with 30% hydrogen peroxide (H_2O_2)
- Molybdenum target dissolved in < 5 min at 50 C.
- Our extraction studies have been primarily focussed on aqueous biphasic extraction chromatography (ABEC™) [Appl Radiat Isot 67(2009) 1985].
- Elution with 18 MΩ-cm H_2O water.
- The process has been automated to produce $[^{99m}Tc]TcO_4$ within ~30 minutes.

Where are Alberta now?

- Target design validated
  - Sintering methodology
- GBq yields at 18 MeV and 100μA
- Extraction validated
  - Radiochemical purity meets generator USP
- Recycling validated
- Radiopharmaceuticals labeled successfully
- Animal biodistribution studies
- cGCP clinical Phase 1 study completed

First clinical CPERT images

- First two patients in cyclotron arm of trial imaged 12 Oct 2011.
  - Images were first presented at the Annual Congress of the European Association of Nuclear Medicine, Birmingham, UK, Oct 2011.
- Phase 1 trial; completed March 2012.
  - Abstract presented at the Society of Nuclear Medicine Meeting, Miami, June 2012 (J Nucl Med, 53 (2012) S1: 1487).



Workflow: ~2hr

EOB

^{99m}Tc Extraction

Delivery to Central Radiopharmacy

Dispensing/QA/QC

Delivery to NM Dept.

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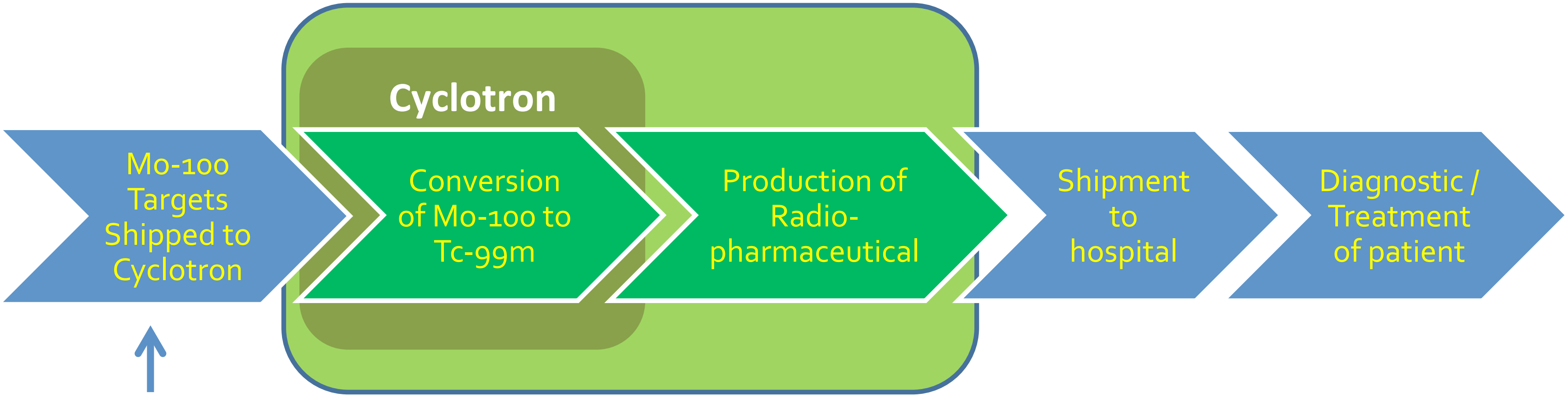
Cost Analysis – Preliminary Overview – Tc-99m Manufacturing Facility

- Annual Amortization Costs (20y): $1,000,000
  - Construction: $9,000,000
  - Equipment: $6,000,000
- Annual Regulatory Costs: $750,000
- Annual Consumable Costs: $550,000
- Personnel Costs: $850,000
- Facility Costs: $450,000
- Maintenance Contracts: $400,000
- Total: $4,000,000
- Assume 200,000 doses per year:

$20.00/Dose

Proposed Tc-99m Supply Chain (Cyclotron)



Cyclotron

Mo-100 Targets Shipped to Cyclotron

Conversion of Mo-100 to Tc-99m

Production of Radio-pharmaceutical

Shipment to hospital

Diagnostic / Treatment of patient

Non-HEU/LEU

- No radioactive material crossing borders
- No time sensitive material crossing borders
- No fissile waste
- Produce when you want as you want
- Evolutionary path to new molecular imaging techniques