# Medical Isotope Production by Electron Accelerators

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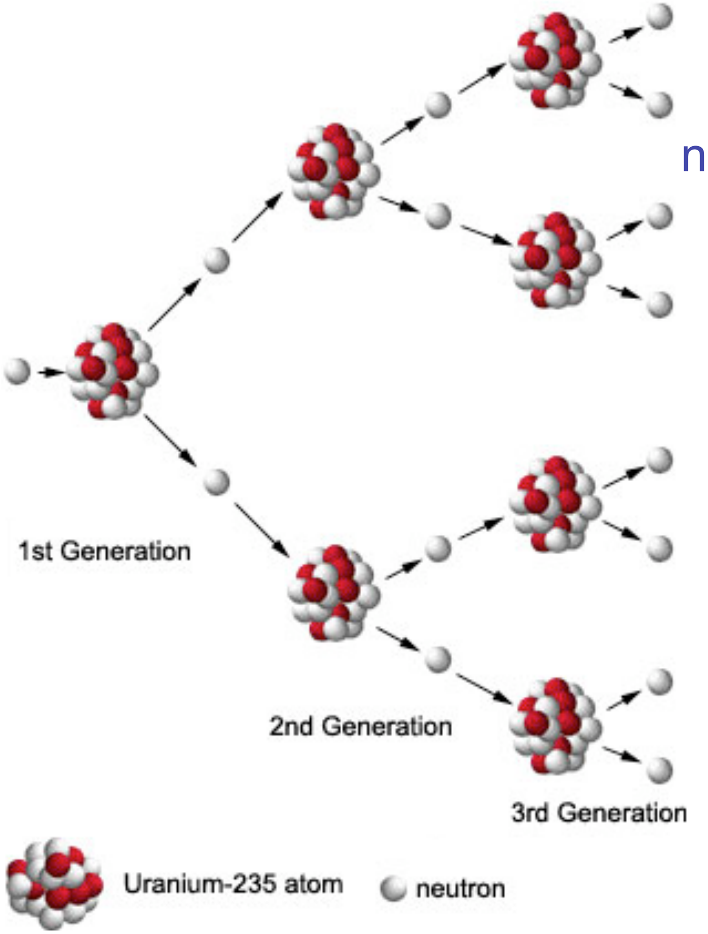
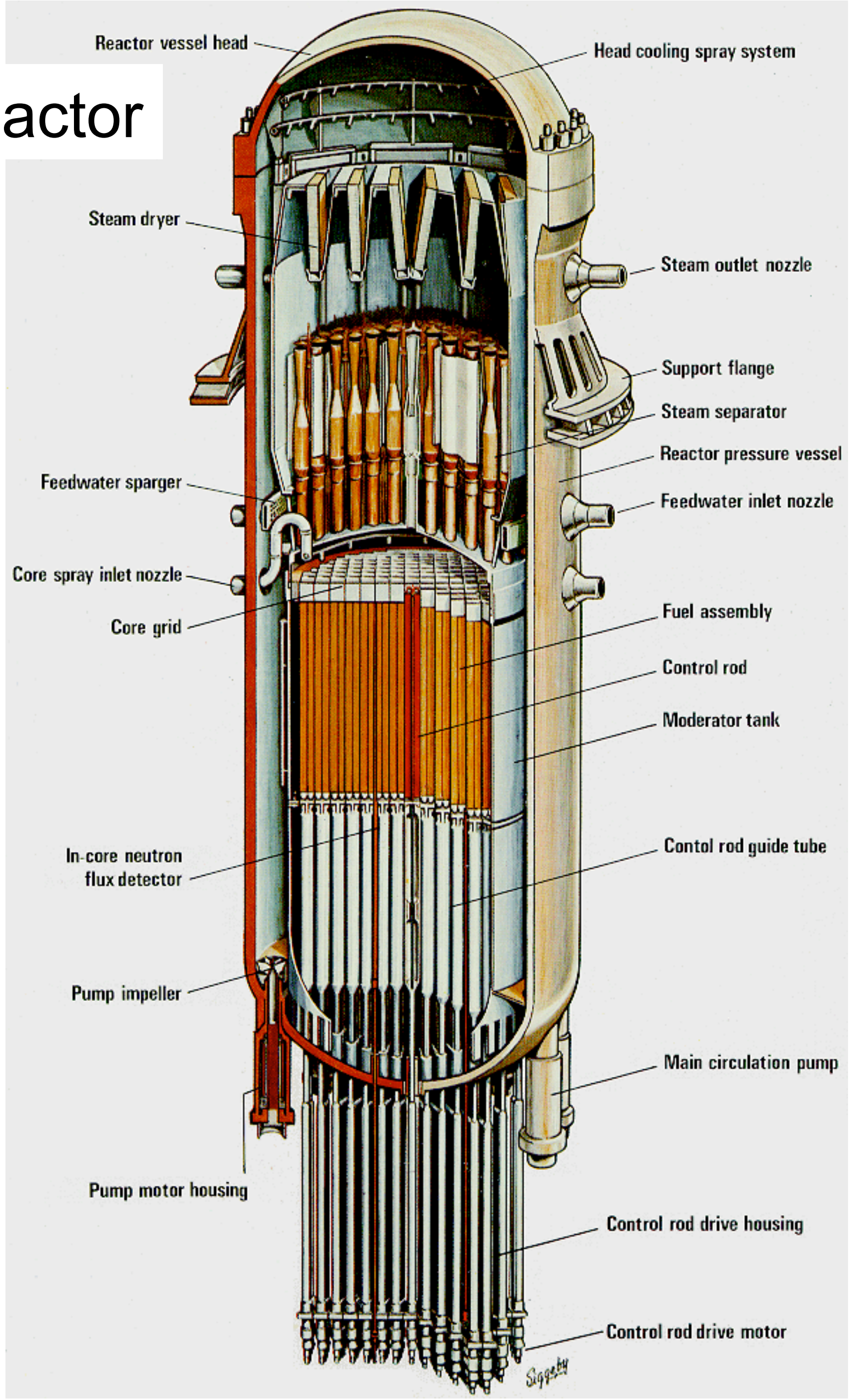
# Power Reactor

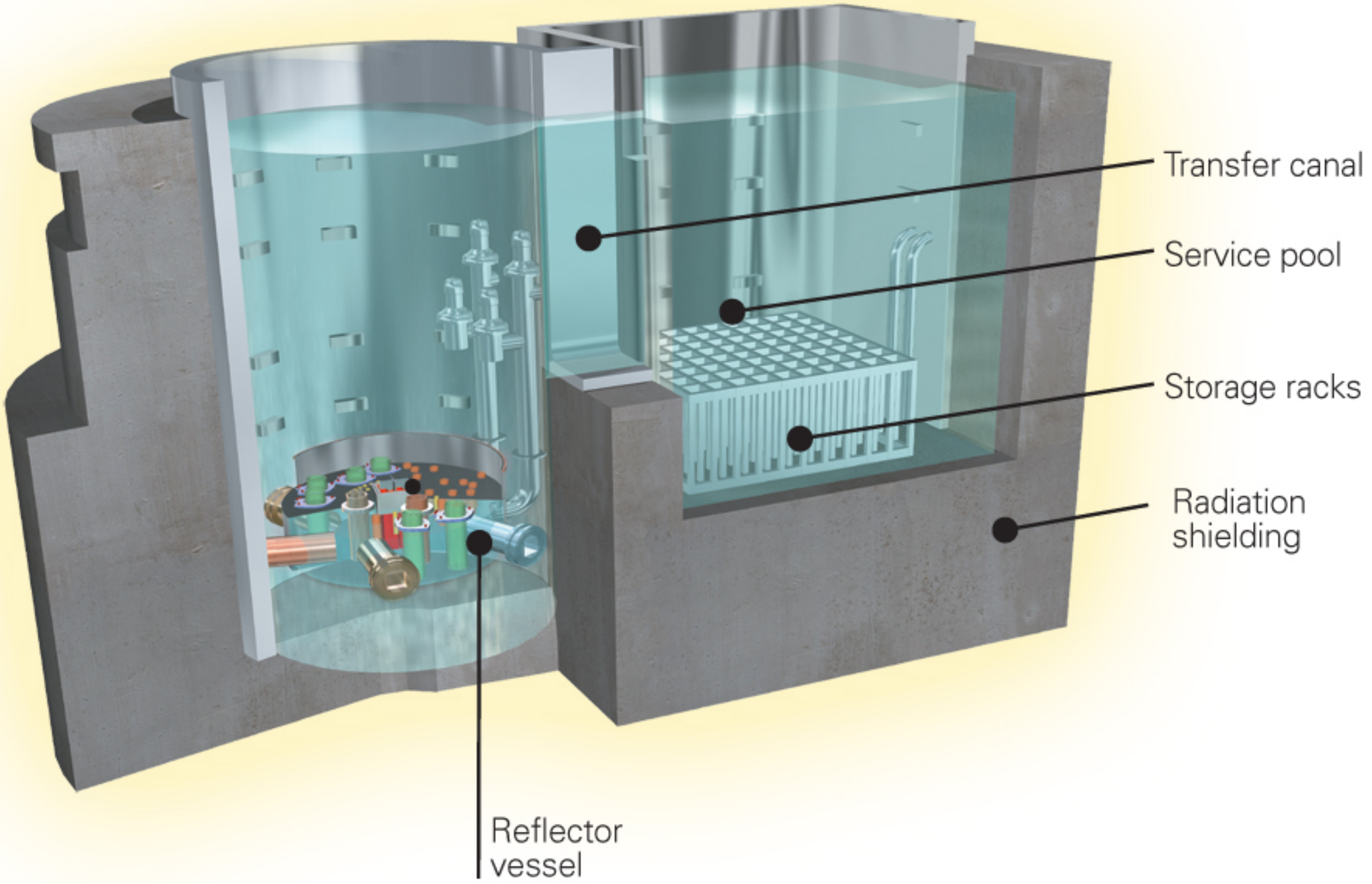
# Uranium Fission Chain reaction

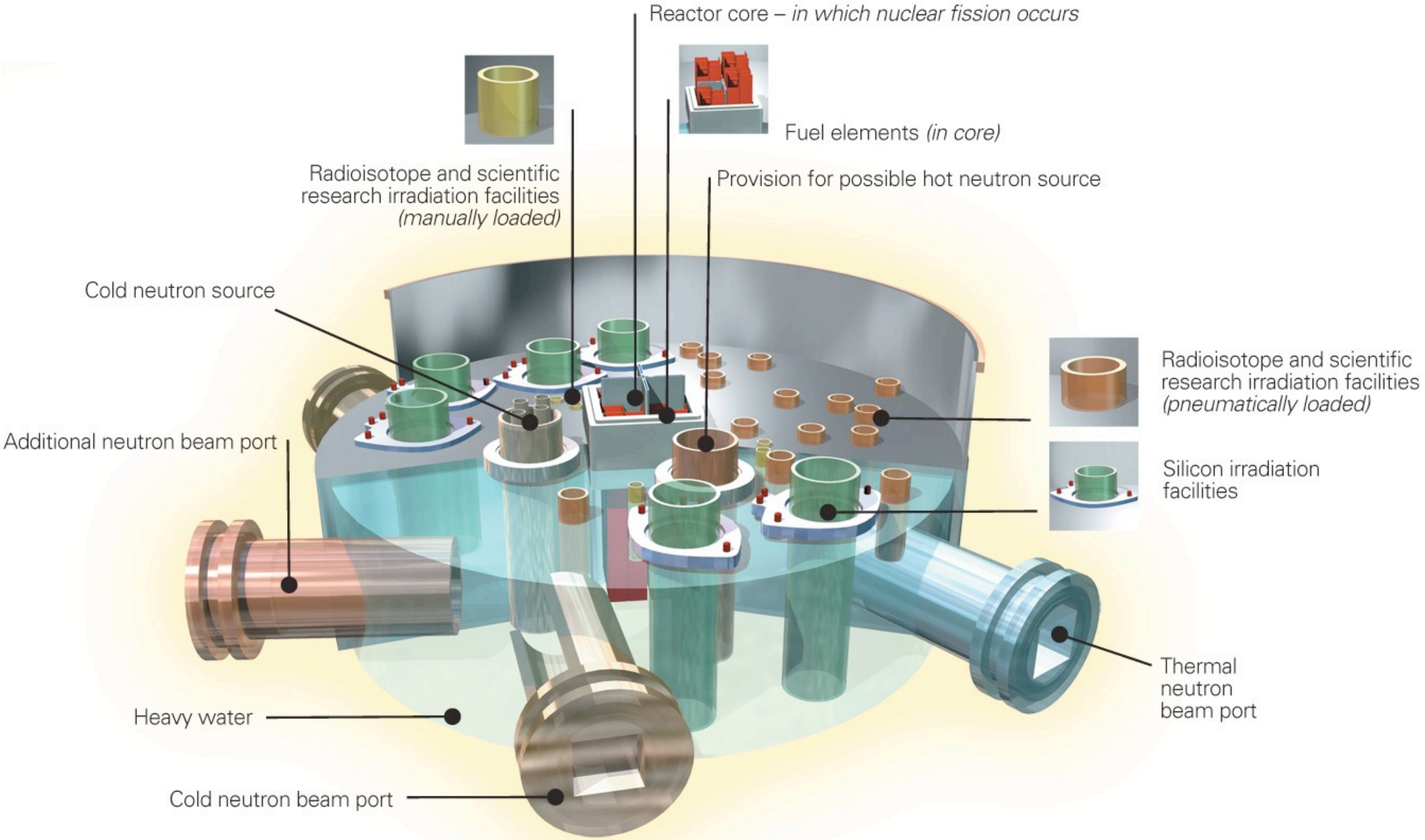


neutrons

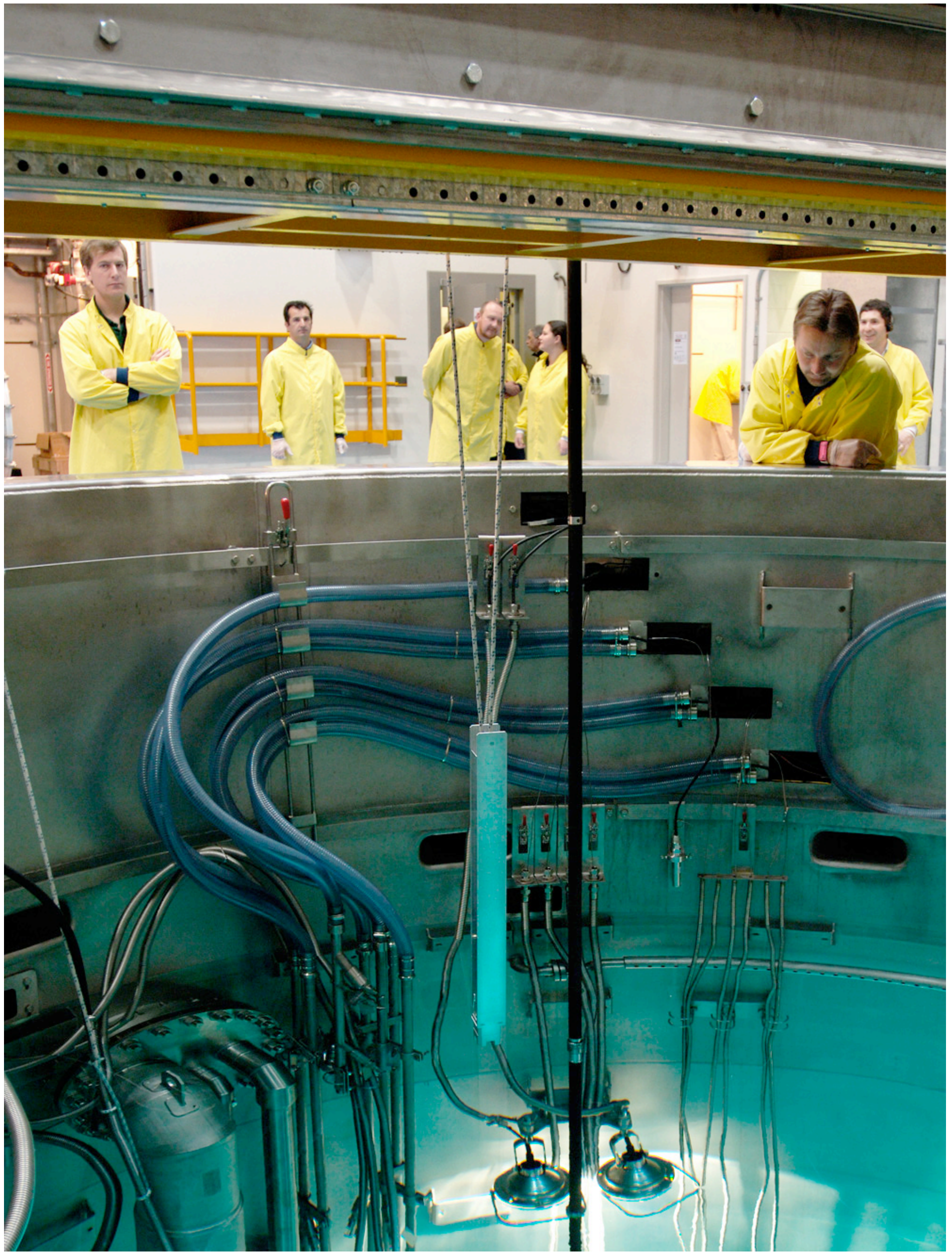


**ANSTO's Open Pool Australian Lightwater (OPAL)**
Reactor is a state-of-the-art 20 Megawatt reactor
that uses low enriched uranium fuel
and is cooled by water.

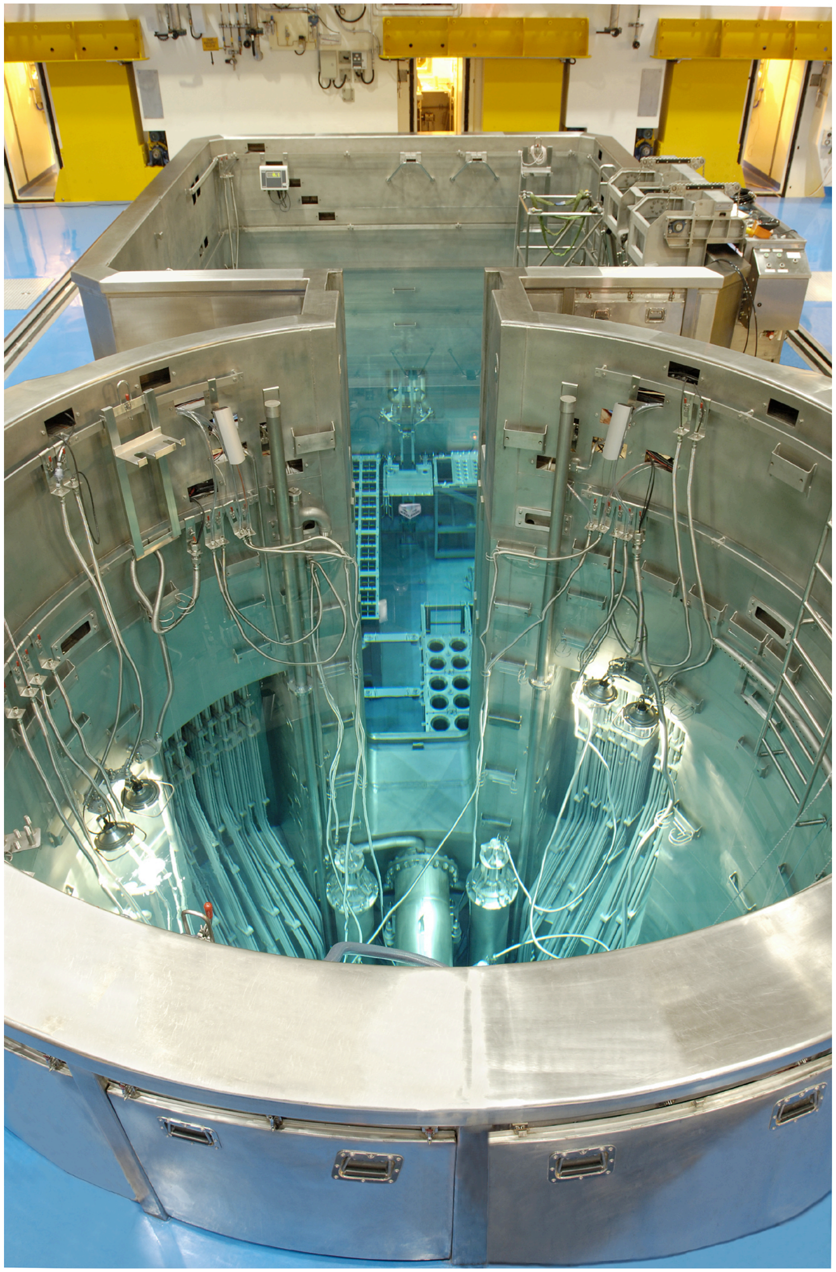



Reactor core – *in which nuclear fission occurs*
Fuel elements *(in core)*
Radioisotope and scientific research irradiation facilities *(manually loaded)*
Provision for possible hot neutron source
Cold neutron source
Radioisotope and scientific research irradiation facilities *(pneumatically loaded)*
Additional neutron beam port
Silicon irradiation facilities
Thermal neutron beam port
Heavy water
Cold neutron beam port

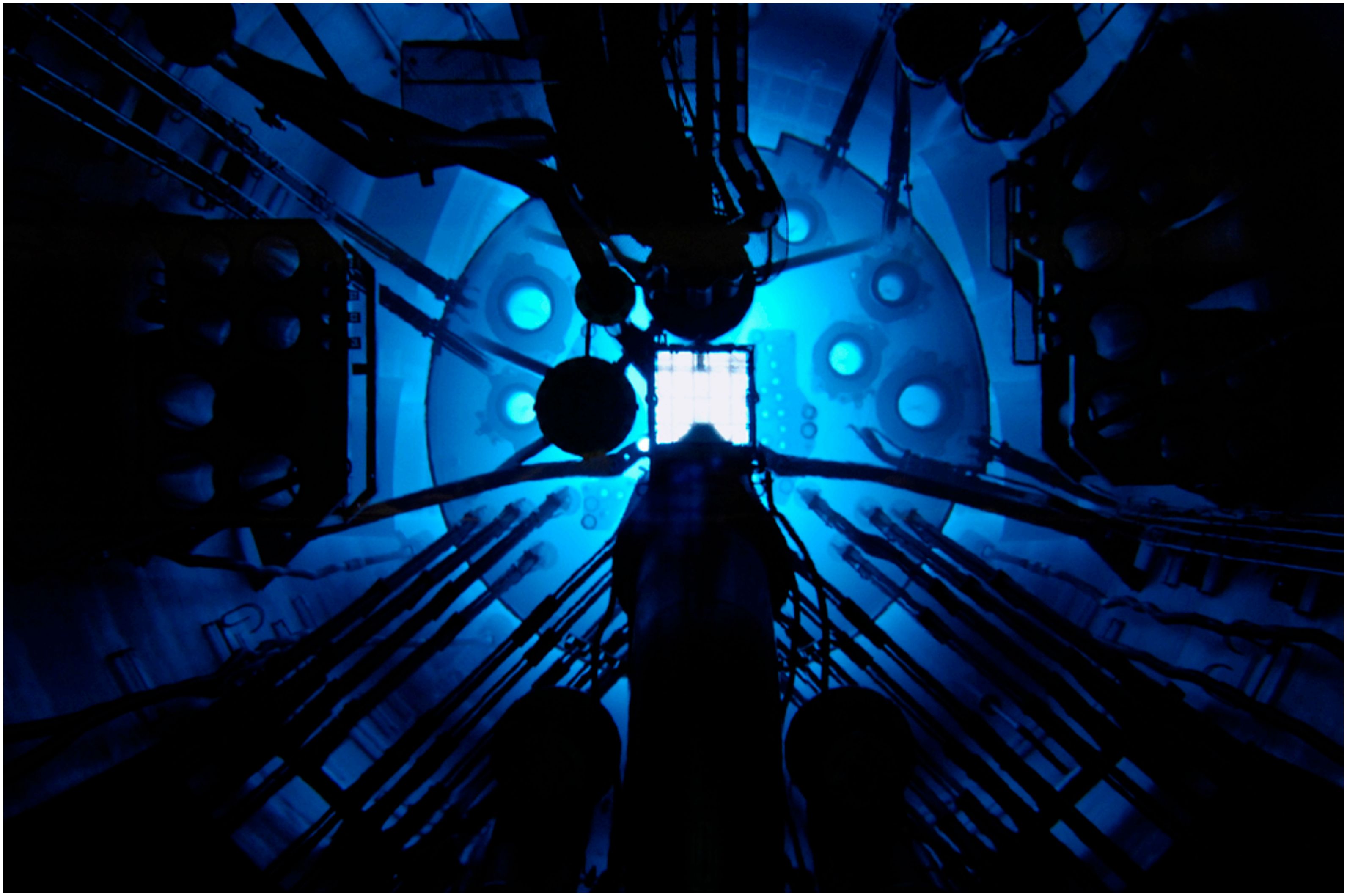
## First Fuel Rod



## View into Reactor Pool



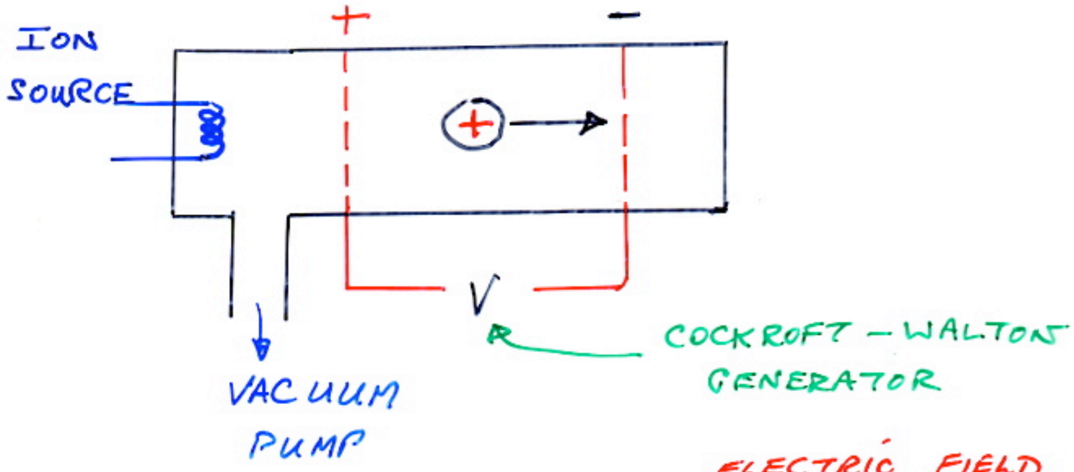
# Cherenkov Radiation from reactor under power



# NU Reactor at Chalk River

# SIMPLE ELECTROSTATIC ACCELERATOR

USED BY COCKROFT & WALTON TO DISCOVER ARTIFICIAL RADIOACTIVITY



$$\vec{F} = q\vec{E}$$

ELECTRIC FIELD

CHARGE ON PARTICLE

$$|\vec{E}| = V/d$$

AVERAGE FIELD

ENERGY GAINED BY CHARGED PARTICLE

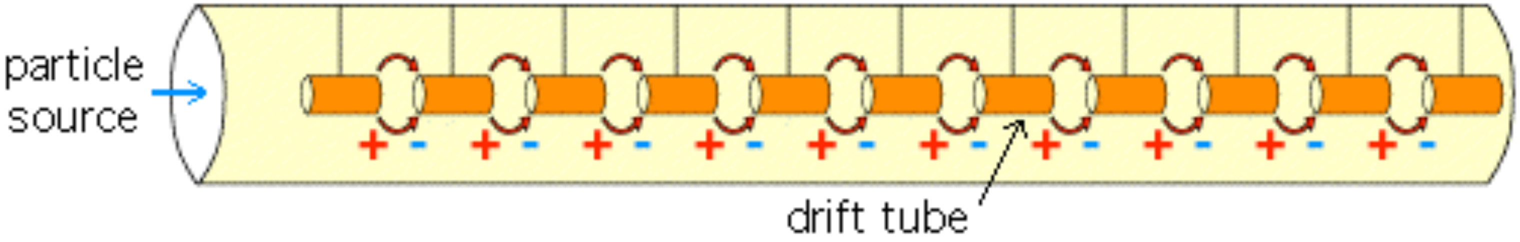
$$E_n = Fd = qV$$

TWO PROBLEMS

- GENERATING HIGH VOLTAGE
- INSULATING BEYOND $\sim 100\,KV$ $\left(100\,\frac{KeV}{c}\right)$

# Resonant Accelerator Concept

Ising - 1924 , Wideroe - 1928



**Alternating (radio frequency) fields allow higher voltages**

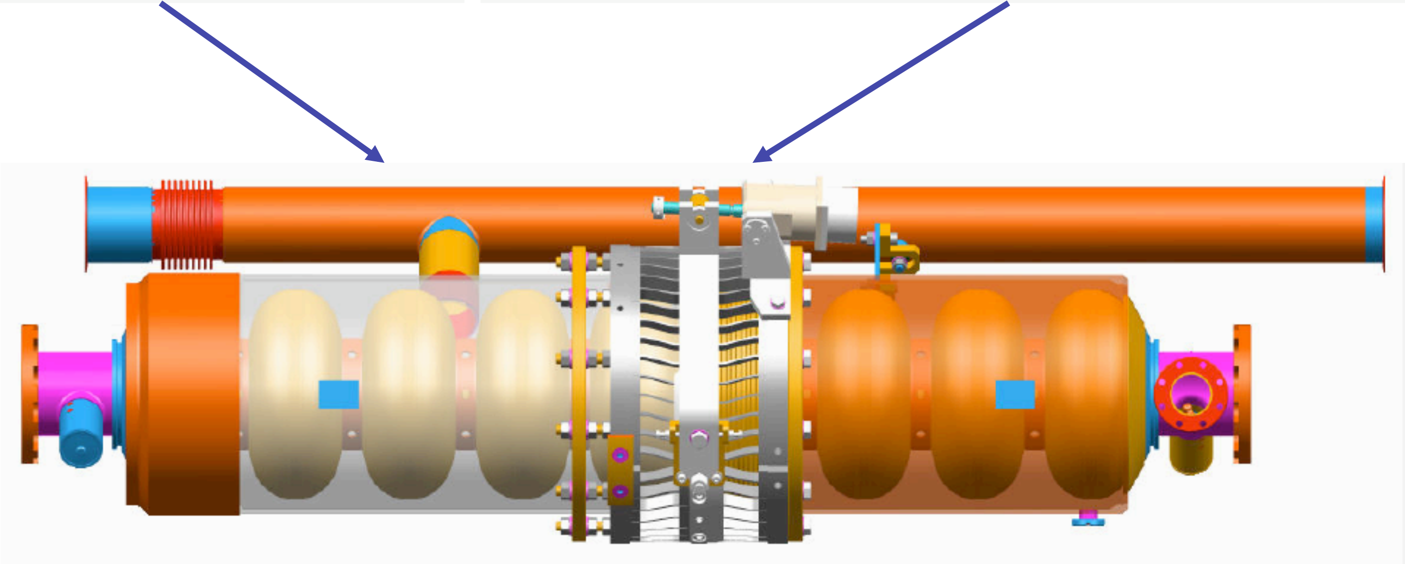
- The acceleration occurs in the electric field between cylindrical *drift tubes*.
- The RF power must be *synchronised* with the motion of the electrons, so that acceleration occurs in every gap.

Linear Accelerator = LINAC

# TRIUMF eLINAC 1.3 GHz ILC Technology

Cornell/Orsay (DC) Coupler

TESLA/ILC 9-Cell Cavity

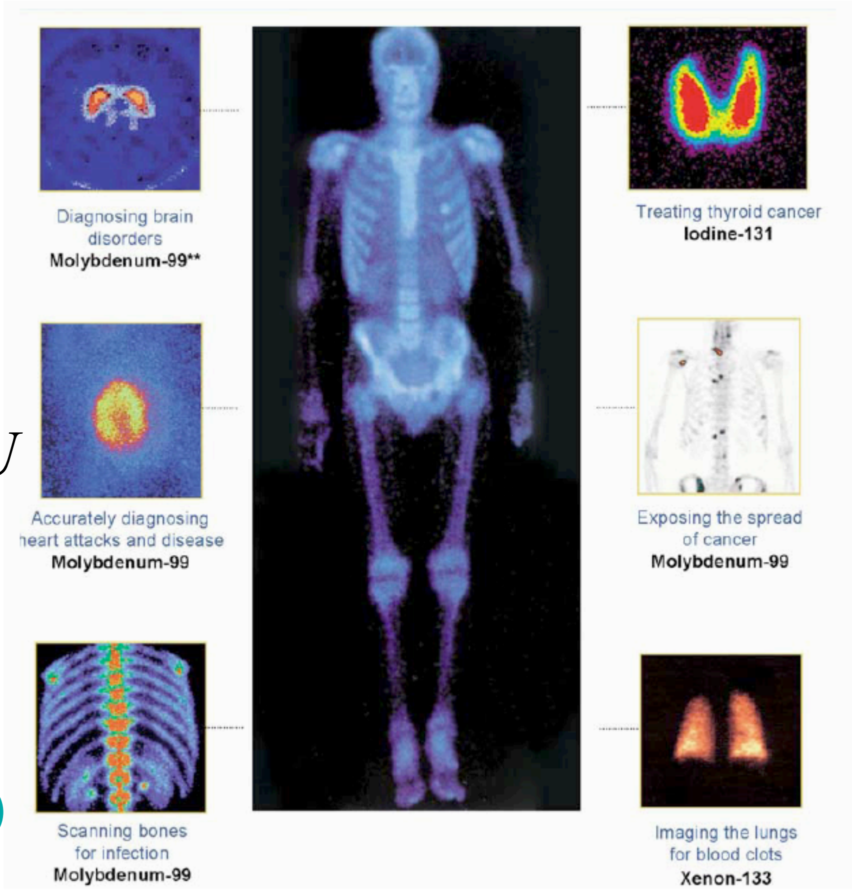


ILC Main LINAC Cryomodule


HITACHI
HITACHI
STF-Cryom
le 1

# Current Issues in Isotope Production

- $^{99m}Tc$ used in 80% of all nuclear medicine procedures.
- $^{99m}Tc$ is supplied via $^{99}Mo$ generator.
- $^{99}Mo$ is produced by fission of $^{235}U$
- Two major producers
  - AECL NRU reactor (Canada)
  - Covidien HFR reactor (Netherlands)



# Current Demand

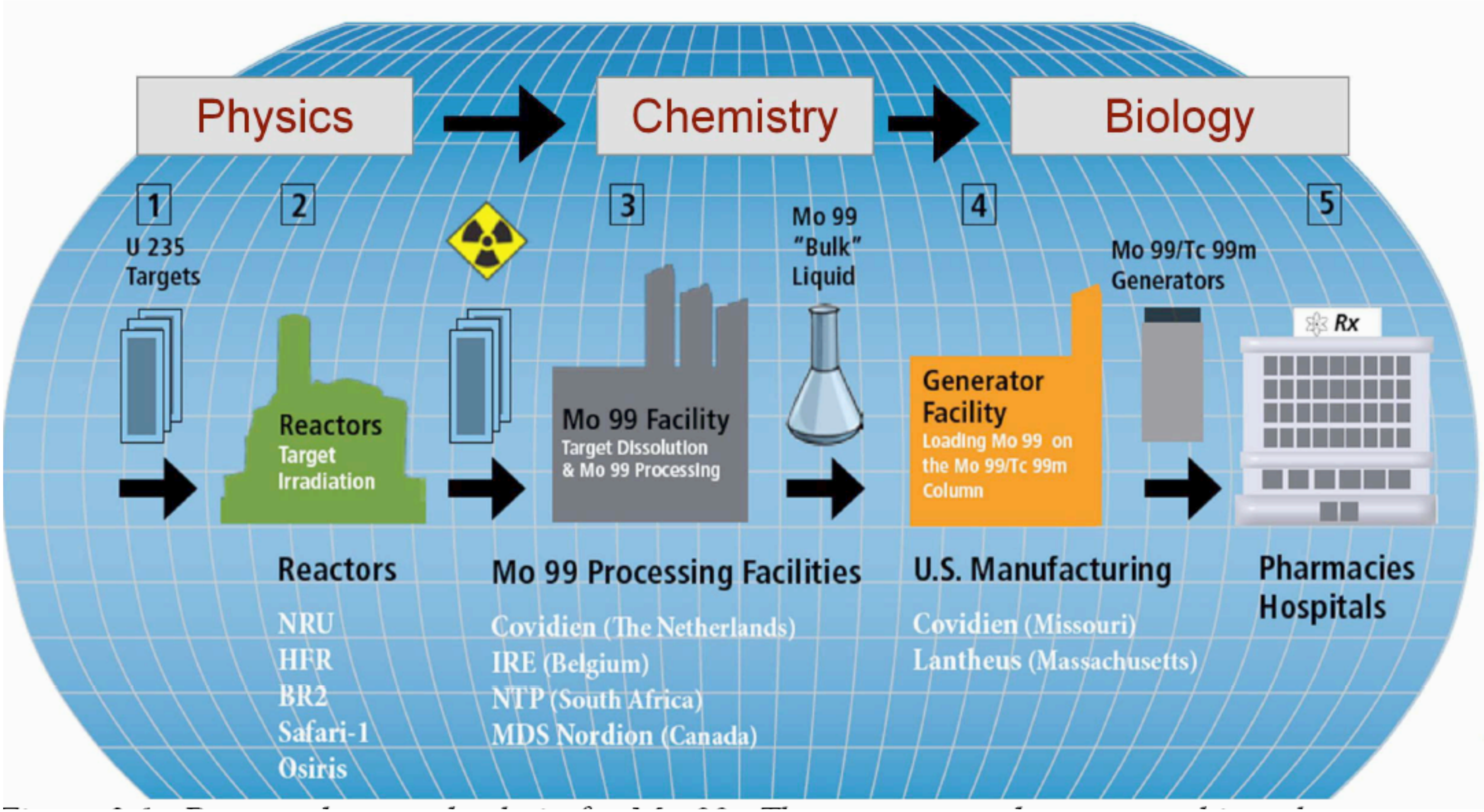
- In North America
  - US - ~70,000 procedures daily using $^{99m}Tc$
  - Canada about 7% of this
- Half life of $^{99}Mo$ is 66 hours , 20% decays each day
- “6-day” curie is unit of measurement
  - Amount available for use after 6 days
- North America uses ~7,000 6-day-Ci per week
- World demand is ~ 12,000 6-day-Ci

# Current Production Process

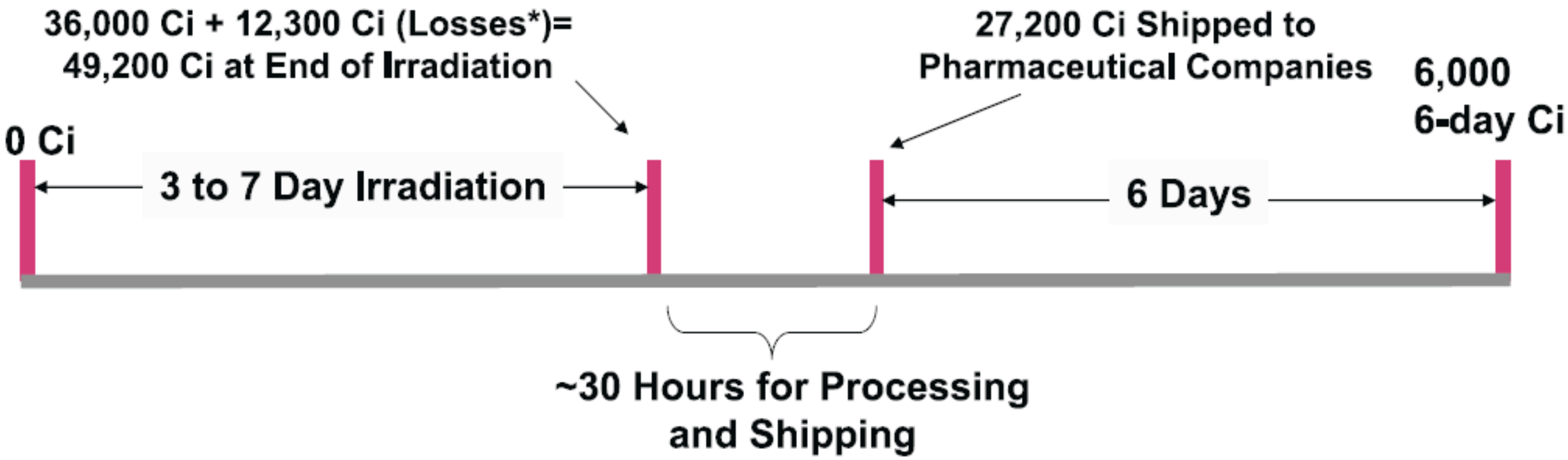
- Reactor used to irradiate Highly Enriched Uranium (HEU) target with neutrons

- Reactor downside
  - HEU – weapons proliferation issue
  - Target waste stream
  - Reactor safety issues
  - Reactor licensing
  - Reactor decommissioning

# Overview of Production Chain



# Estimated 2009 U.S. Mo-99 Demand
# at least 6,000 6-day Curies/Week



36,000 Ci + 12,300 Ci (Losses*)=
49,200 Ci at End of Irradiation

27,200 Ci Shipped to
Pharmaceutical Companies

6,000
6-day Ci

0 Ci

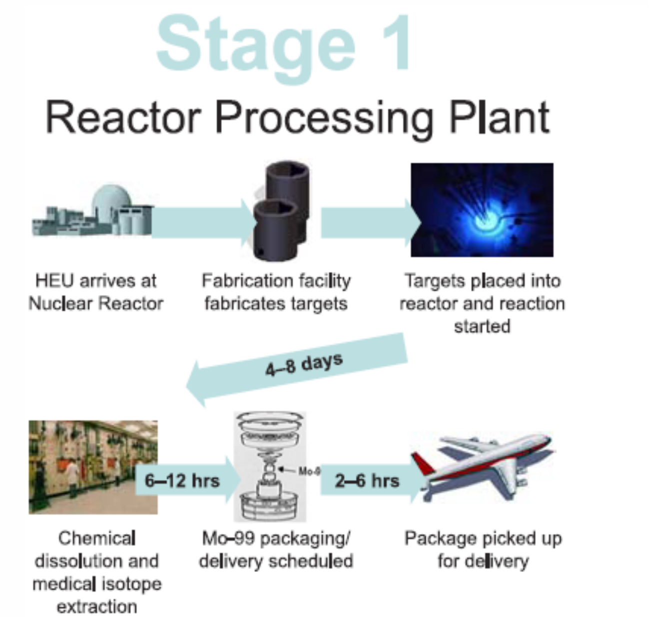
3 to 7 Day Irradiation

6 Days

~30 Hours for Processing
and Shipping

*Assumes 75% Mo-99 Recovery During Processing

# Time Critical Process



## Stage 1

### Reactor Processing Plant

HEU arrives at Nuclear Reactor

Fabrication facility fabricates targets

Targets placed into reactor and reaction started

4–8 days

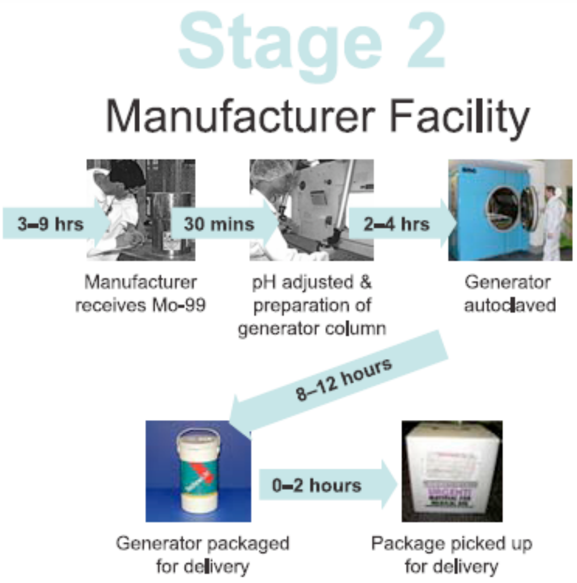
Chemical dissolution and medical isotope extraction

6–12 hrs

Mo-99 packaging/ delivery scheduled

2–6 hrs

Package picked up for delivery



## Stage 2

### Manufacturer Facility

3–9 hrs

Manufacturer receives Mo-99

30 mins

pH adjusted & preparation of generator column

2–4 hrs

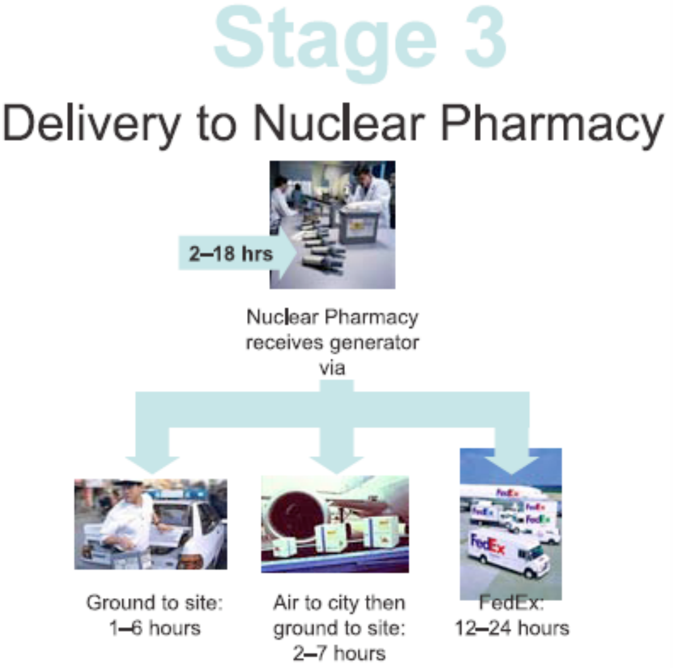
Generator autoclaved

8–12 hours

Generator packaged for delivery

0–2 hours

Package picked up for delivery



## Stage 3

### Delivery to Nuclear Pharmacy

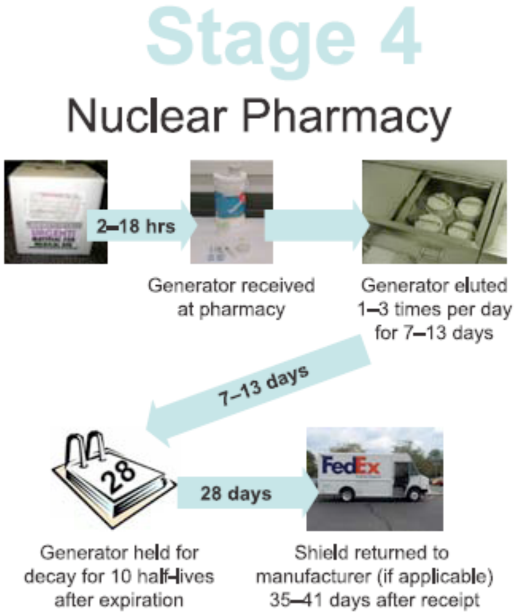
2–18 hrs

Nuclear Pharmacy receives generator via

Ground to site: 1–6 hours

Air to city then ground to site: 2–7 hours

FedEx: 12–24 hours



## Stage 4

### Nuclear Pharmacy

2–18 hrs

Generator received at 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

28 days

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

# ${}^{99}Mo$ Major Producers and Suppliers

- MDS Nordion (AECL, Canada) – 40% (60%)
- Covidien (Netherlands) – 25% (40%)
- Institut National des Radioélements (Belgium) – 20% (0%)
- Nuclear Technology Products (South Africa) – 10% (0%)
- Australian Nuclear Science & Technology Organization 0 (0)

# Reactors

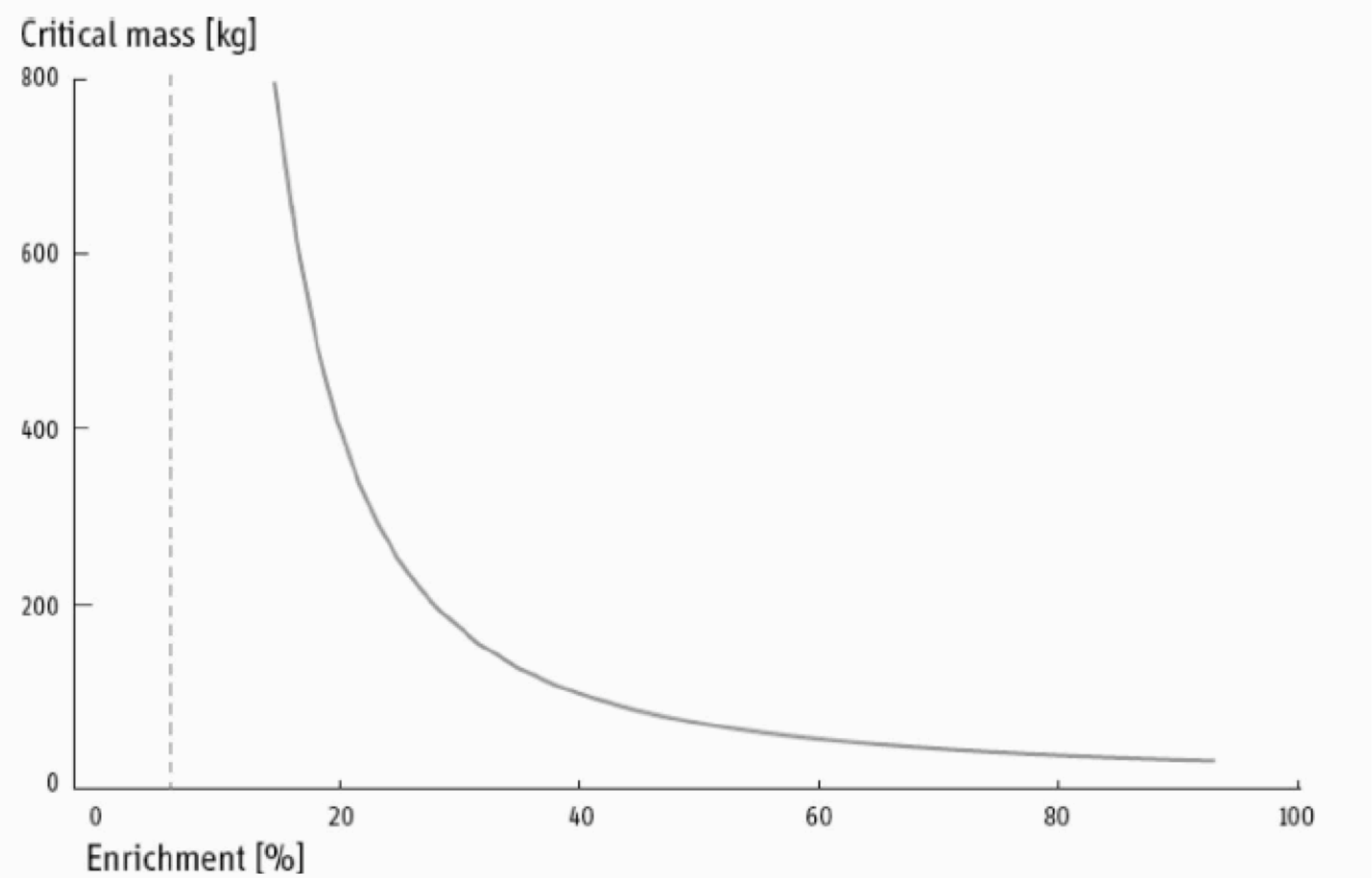
- NRU (Canada) – 135 MW, started 1957
- HFR (Netherlands) – 45 MW, started in 1961
- BR2 (Belgium) – 100 MW, started 1961
- SAFARI (South Afrika) – 20MW, started in 1965
- Osiris (France) – 70 MW, started in 1966
- OPAL (Australia) – 20 MW , started in 2007

# Some Facts

- Most reactors mentioned use Highly Enriched Uranium
- OPAL uses 25% $^{235}U$
- North American Production need 6000 6-day curies/ week 50% of global demand
- Most reactors are aging
- OPAL cannot supply North American needs

| *Reactor* | *In-service date* | *Target uranium enrichment type* |
|---|---|---|
| NRU (Canada) | 1957 | HEU |
| BR2 (Belgium) | 1961 | HEU |
| HFR (Netherlands) | 1963 | HEU |
| SAFARI (South Africa) | 1965 | HEU |

# Critical Mass of $^{235}U$ vs Enrichment Level



*Williams & Ruff, Medicine, Conflict and Survivial (2007)*

# Reactor Reliability Issues

- NRU – shutdown for 3 weeks late 2007.
    - May 2008 – Heavy water leak
    - return to service 1st quarter 2010
    - Canadian government "get out of isotope business"
- HFR – technical problems in 2008 – back in 2009.
    - Replacement due 2015++
- BR2 – shut down in Fall 20008 due to $^{131}I$ release.
- OPAL – startup delayed to 2008 – on power.
- Osiris – replaced by "Jules Horowitz" 2014
    - at most 25% of world supply
- Near term solution is supplying local needs from cyclotrons

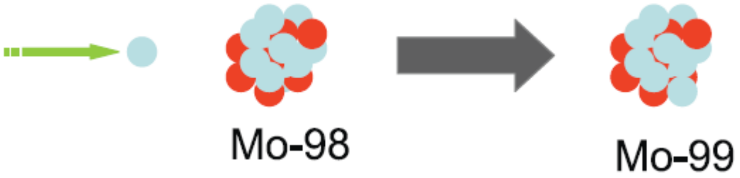
# Canadian “Solution”

- MDS-Nordion contracted AECL to construct two reactors.
- 10 MW HEU – principally $^{99}Mo$
- MAPLE 1 – 2000
- MAPLE 2 – 2003
- Simulations showed power coefficient reactivity – 0.12mk/MW
- Measurement +0.28mk/MW
- Not understood – problem for license
- Cancelled May 2008
- $Millions down the drain…..

# Non HEU Alternatives

- Present Process -Reactor

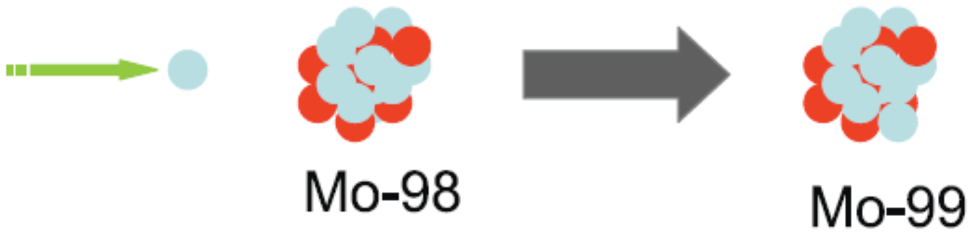
- $^{98}Mo(n,\gamma)^{99}Mo$ Reactor



- $^{100}Mo(\gamma,n)^{99}Mo$ Electron Accelerator

- $^{238}U(\gamma,F)^{99}Mo$ Electron Accelerator

# Neutron Capture $^{98}Mo(n,\gamma)^{99}Mo$

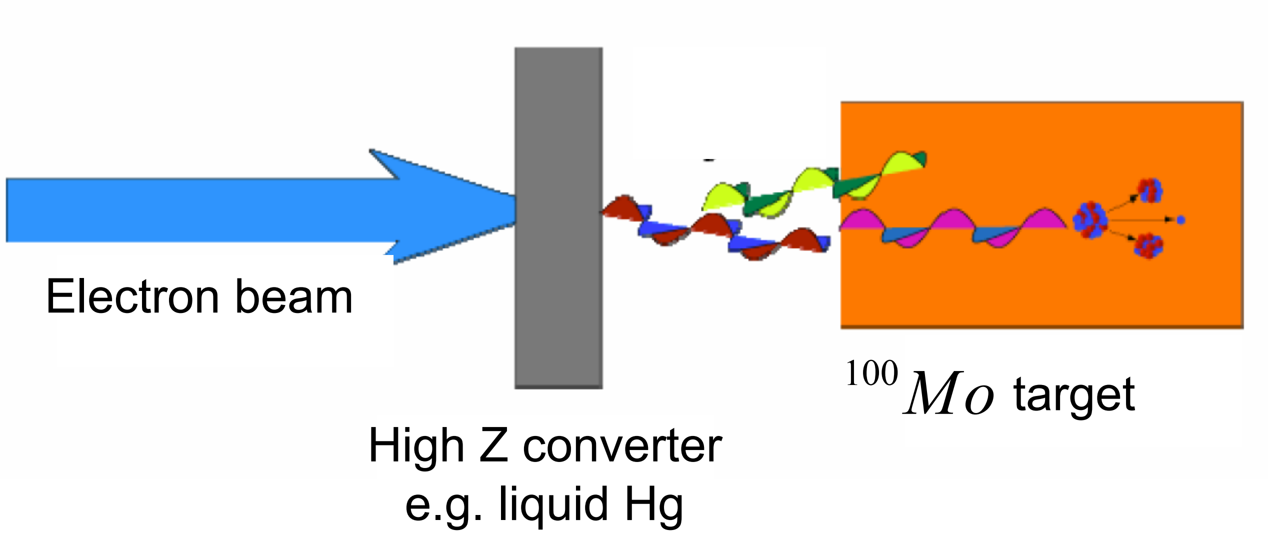


- For a reactor flux of $3\times10^{14} n/s/cm^2$
  - Secular equilibrium after 14 days – 2.6 six-day-Ci per gm.
    - Low activity cf. 150 6-day-Ci for HEU reactor process

- Advantage
  - No target waste stream.
- Disadvantages
  - Major change in technology of separation of two Mo isotopes for generator + low activity
  - High Flux reactor based technique

# Photo-neutron $^{100}Mo(\gamma, n)^{99}Mo$

- 50 MeV, 500 kW electron accelerator – Bremsstrahlung irradiator



# Photo-neutron $^{100}Mo(\gamma, n)^{99}Mo$

| Target mass (g of Mo-100) | Ci/100kW at saturation | Spec. Activity (Ci Mo-99/g of Mo) | Power deposited in target (kW) |
|---|---|---|---|
| 0.29 | 100. | 360. | 2.2 |
| 1.0 | 210. | 208. | 4.8 |
| 2.3 | 300. | 147. | 11.4 |
| 9.1 | 518. | 57. | 16.4 |
| 70.6 | 900. | 12.8 | 29.0 |

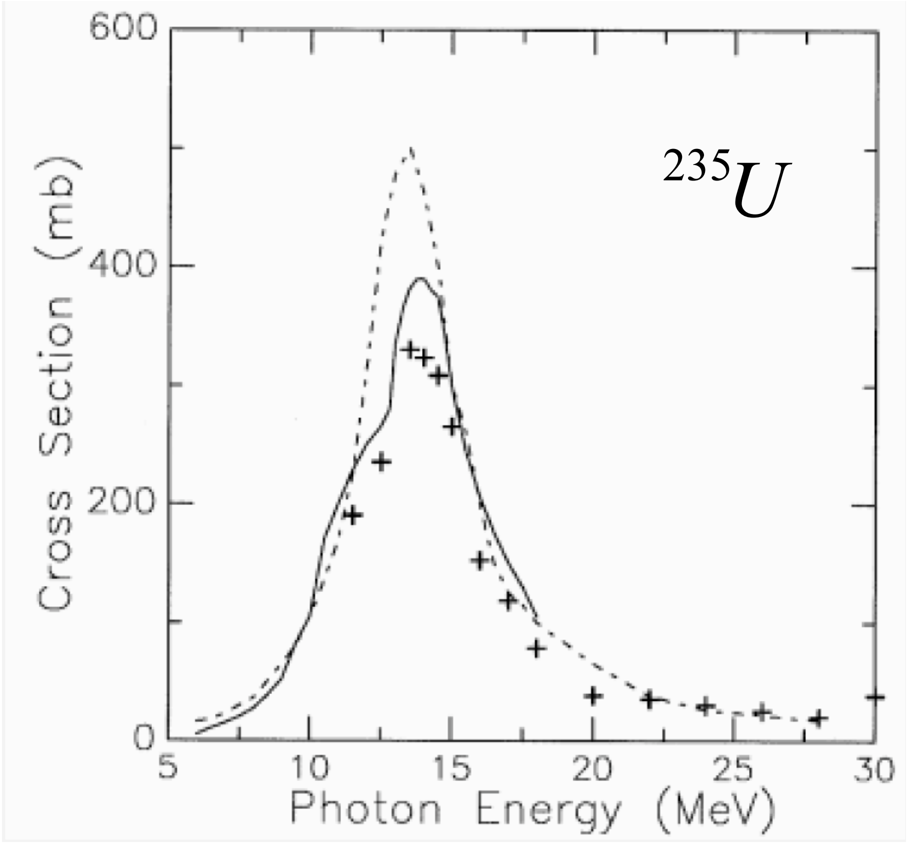
- 500 kW accelerator
  - After 14 days – 21 six-day-Ci per gm.
    - High activity

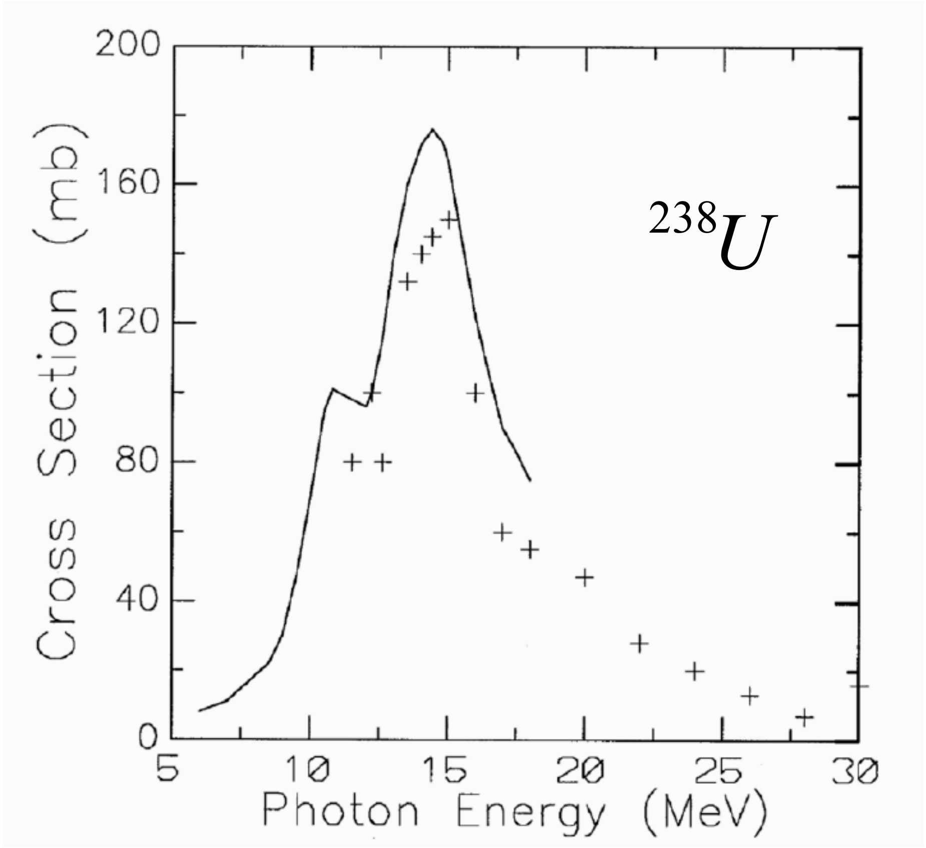
# Photo-neutron $^{100}Mo(\gamma, n)^{99}Mo$

- Advantages
  - No target waste stream.
  - Ease of licensing.
  - Cost and scheduling more predictable for accelerator.

- Disadvantages
  - Major change in generator technology because of different target.
  - Clinical testing/approval for new product.
  - Cost of target – 10% isotope.

# Giant Dipole Resonance & Photo-fission

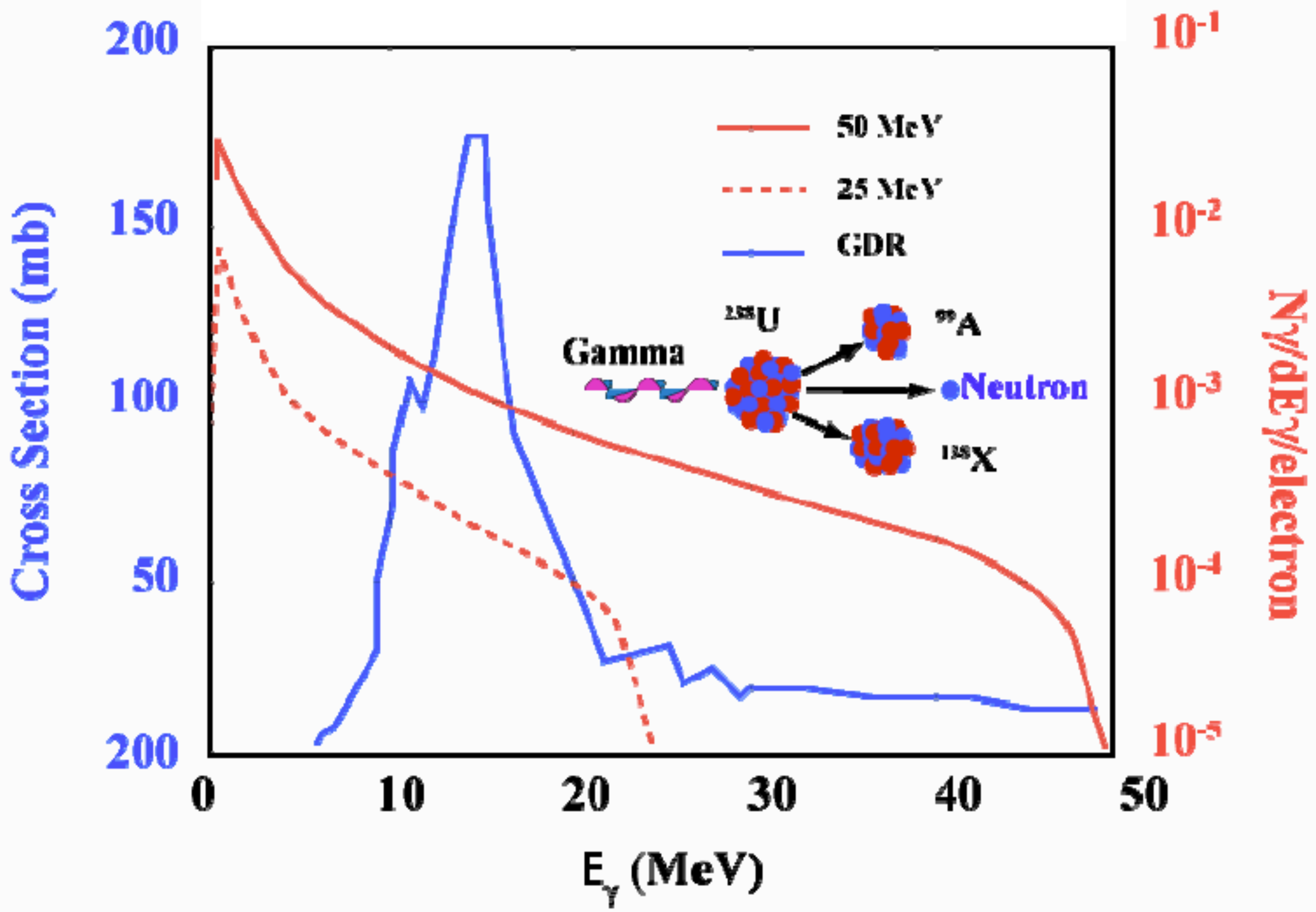




*W.T. Diamond / Nuclear Instruments and Methods in Physics Research A 432 (1999) 471}482*

# Giant Dipole Resonance (GDR)

Bremstrahlung and $^{238}U$ Photofission

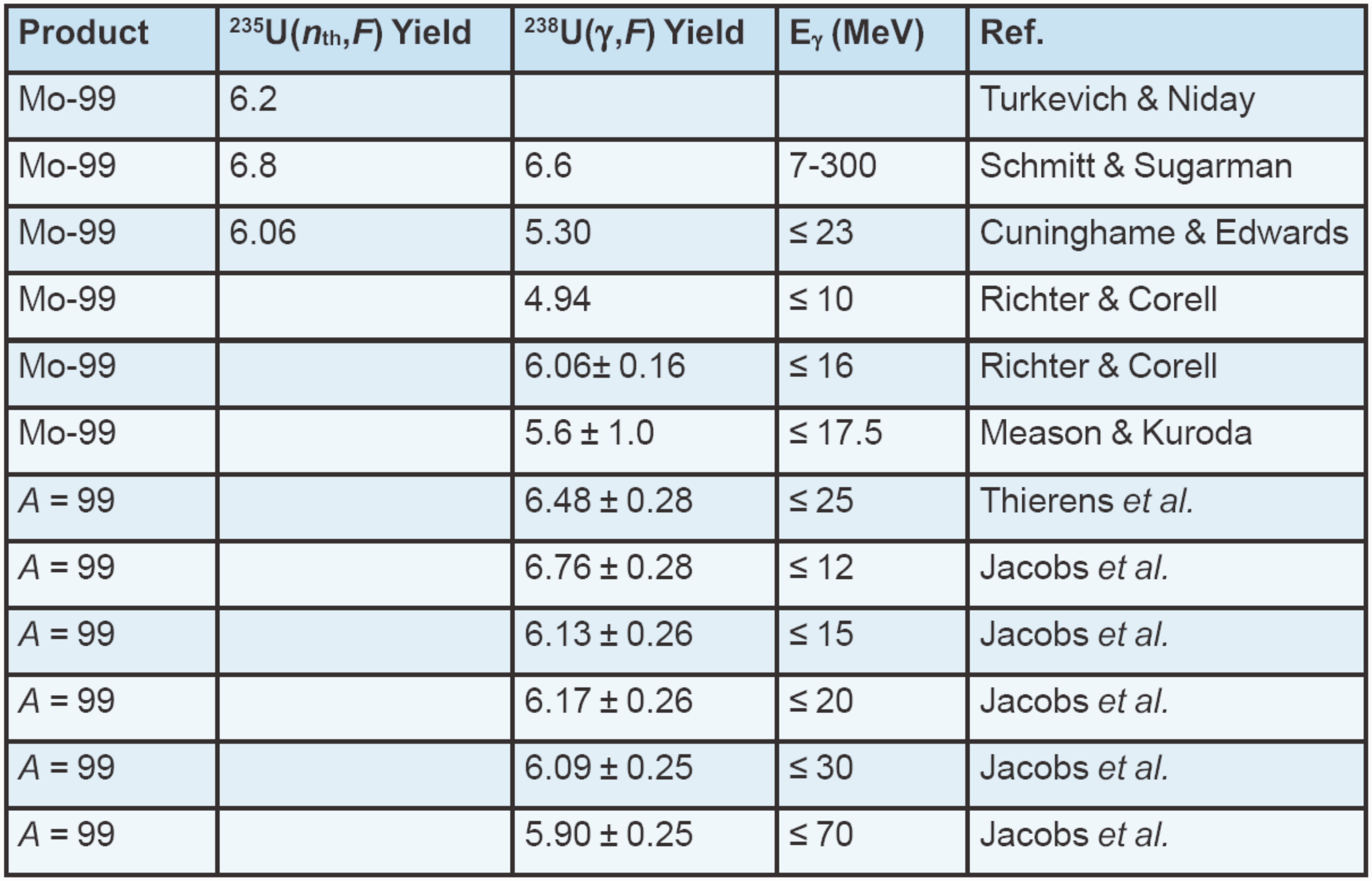


# Yield Comparison

- Neutron induced $^{235}U$ fission in reactor:
  - Flux of $3\times10^{14}\, n/s/cm^2$ gives $4.6\times10^{14}\, f/s/gm$
  - 15kW/gm – Aluminum matrix to absorb power.
  - At 6% $^{99}Mo$ yield – 150 6-day-Ci per gram.

- Photo-fission of $^{238}U$ in an electron accelerator:
  - Assume 50% of energy of 50 MeV machine into photons 0-50MeV.
  - 45% overlap with GDR (10 – 20 MeV ) concentrated at 15 MeV.
  - 11.25kW of photons at 15MeV per mA of beam current.
  - $\gamma$ fission rate/gm of $^{238}U$ in 50 kW beam is $1.44\times10^{11}$
  - At 6% $^{99}Mo$ yield – 0.86 6-day-Ci per gram.
  - Need about 200 times target material - $^{238}U$ is cheap.

# Can We Really Get 6% Yield?



| Product | $^{235}U(n_{th},F)$ Yield | $^{238}U(\gamma,F)$ Yield | $E_\gamma$ (MeV) | Ref. |
|---|---|---|---|---|
| Mo-99 | 6.2 | | | Turkevich & Niday |
| Mo-99 | 6.8 | 6.6 | 7-300 | Schmitt & Sugarman |
| Mo-99 | 6.06 | 5.30 | ≤ 23 | Cuninghame & Edwards |
| Mo-99 | | 4.94 | ≤ 10 | Richter & Corell |
| Mo-99 | | 6.06± 0.16 | ≤ 16 | Richter & Corell |
| Mo-99 | | 5.6 ± 1.0 | ≤ 17.5 | Meason & Kuroda |
| $A = 99$ | | 6.48 ± 0.28 | ≤ 25 | Thierens *et al.* |
| $A = 99$ | | 6.76 ± 0.28 | ≤ 12 | Jacobs *et al.* |
| $A = 99$ | | 6.13 ± 0.26 | ≤ 15 | Jacobs *et al.* |
| $A = 99$ | | 6.17 ± 0.26 | ≤ 20 | Jacobs *et al.* |
| $A = 99$ | | 6.09 ± 0.25 | ≤ 30 | Jacobs *et al.* |
| $A = 99$ | | 5.90 ± 0.25 | ≤ 70 | Jacobs *et al.* |

# Advantages of Accelerator over Reactor

- Can be quickly turned on and off – no consequences.
- Does not produce radioactive waste from operation.
  - Target waste is similar to reactor solution.
- Yield is not sensitive to use of LEU or HEU.
  - Proliferation issue.
- Scalable technology.
  - Additional accelerators can be turned on/off to meet demand.
- Licensing & decommissioning straightforward.

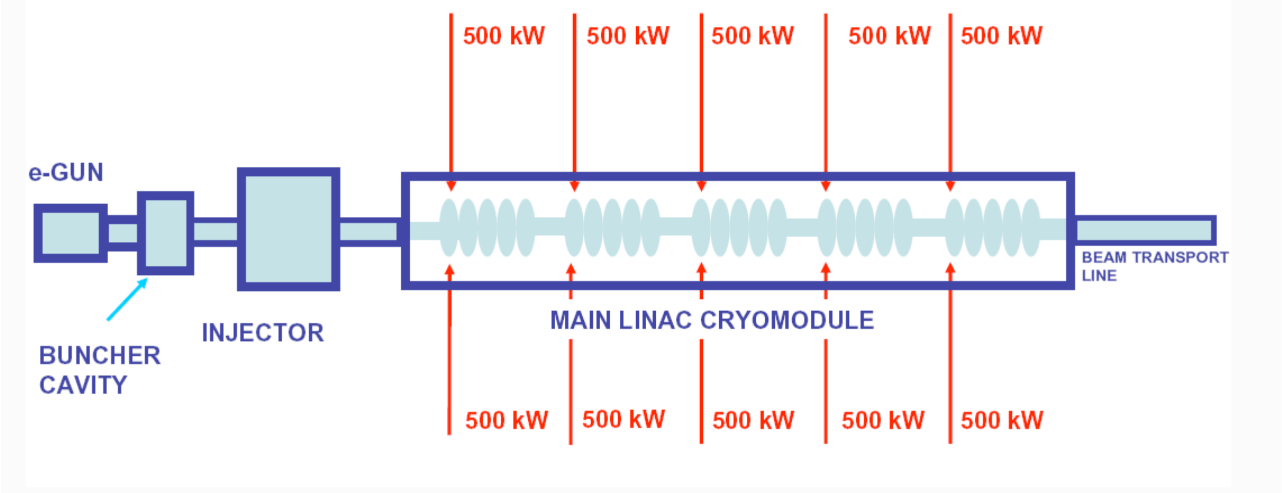
# Caveats on Accelerator

- New technology – intrinsically unproven.
  - Substantial R&D – e.g. high power target.
- Irradiated material may not be compatible with existing HEU recover and refinement facilities.
- Remains to be seen if it is economically competitive.

# Accelerator Requirements

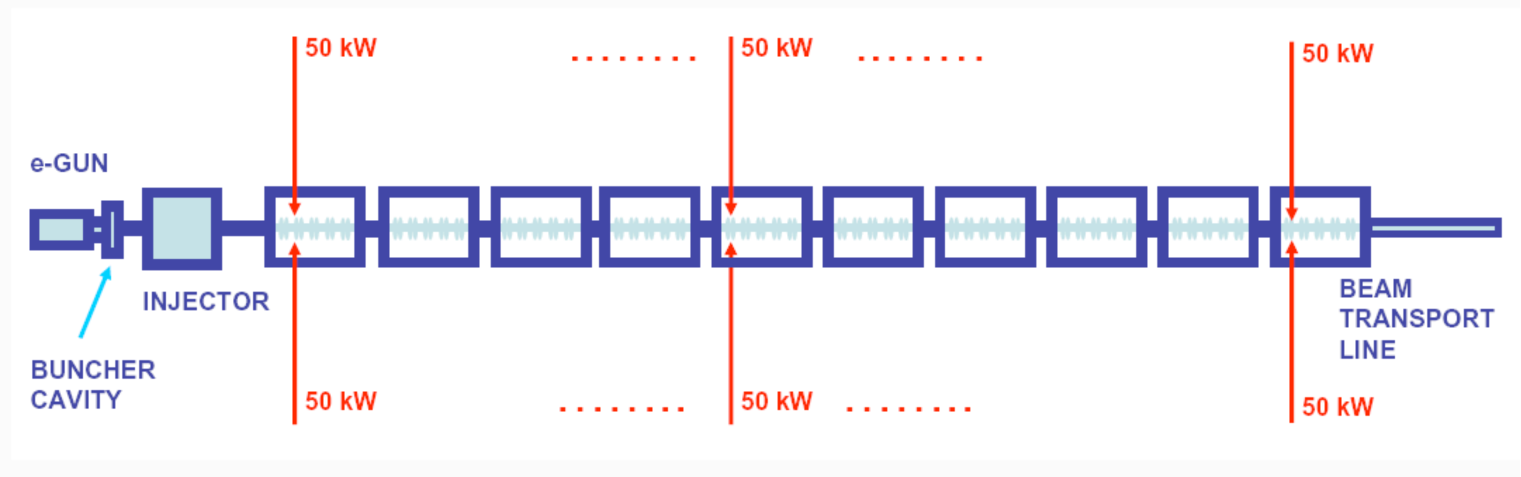
- Progress in technology has made high power electron accelerators an economic proposition.
  - Notably super conducting radio frequency cavities.
    - Power efficiency.
    - Compactness.
    - High accelerating gradient.
- Need several MegaWatts at 100% duty factor.
- 50 MeV at 100 mA – 5 MWatt machine
- Two frequencies have commercial klystrons etc.
  - 704 MHz
  - 1.3 GHz

# 704MHz Option



- Based on Brookhaven Energy Recovery LINAC.
  - 100 mA, 704MHz, 140 pC per bunch.
  - Single cryomodule housing 5x5-cell superconducting RF cavities.
  - 10 MeV per cavity – 100 mA => 1MW per cavity – 2x500kW klystrons.
  - Wall-plug efficiency 40% (klystrons 60%) => 12MW for 2K cavities.
  - 704MHz allows 4K operation of cavities – several advantages
    - Reduced complexity, lower operating and capiotal costs.
  - C$60 Million.

# 1.3 GHz Option



- Scaled version of Cornell 0.5 MW 1.3GHz LINAC.
  - 50x 2-cell cavities driven by 50 klystrons – 5 MW
  - 5 cells per cryostat
  - C$125 Million

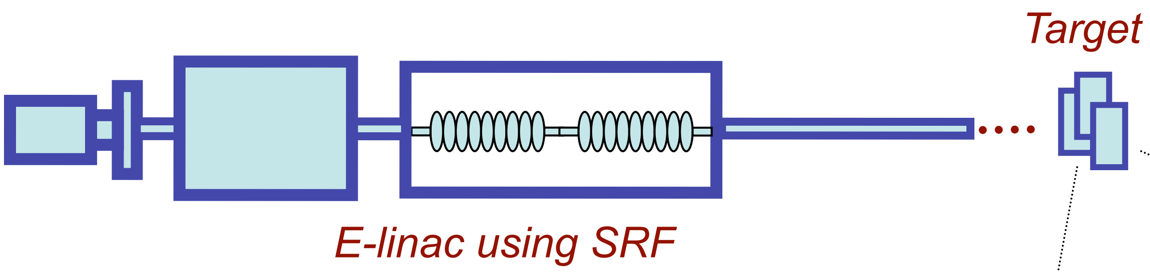
# 704MHz versus 1.3GHz

- 704MHz
  - Frequency is in TV broadcast range.
    - Klystrons less specialized than 1.3G Hz.
  - RF structures have large apertures.
    - Reduces wake-field problems.
  - RF input couplers can operate at higher power levels than 1.3 GHz.
    - Fewer components- lower cost + reliability.
  - 4 K operation.

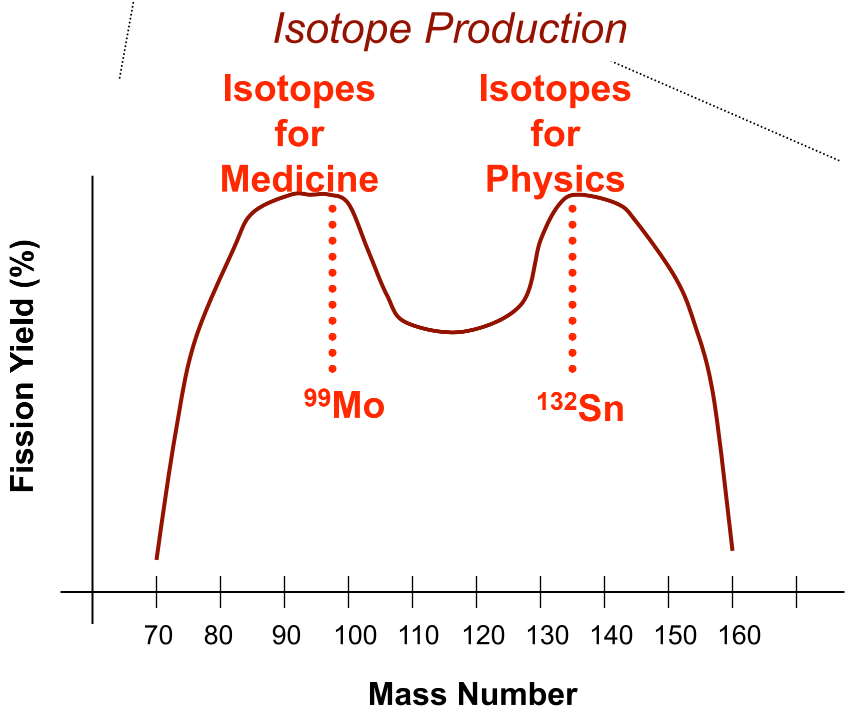
- 1.3 GHz
  - Synergy with other projects in many Labs.
    - International Linear Collider.
    - Free electron lasers.
    - 3rd generation light sources.

TRIUMF

# Plans



New 50 MeV electron LINAC funded
By Canada Foundation for Innovation



- Develop, deploy, & transfer SRF technology to Canadian industry
- Produce novel isotope beams for nuclear physics and materials science
- Demonstrate a transformative approach for producing medical isotopes

# TRIUMF eLINAC

7kV, NC

500 keV acceleration & bunching

Four 9-cell cavities, 10 MV/m, Q=$10^{10}$

Length, 13 m

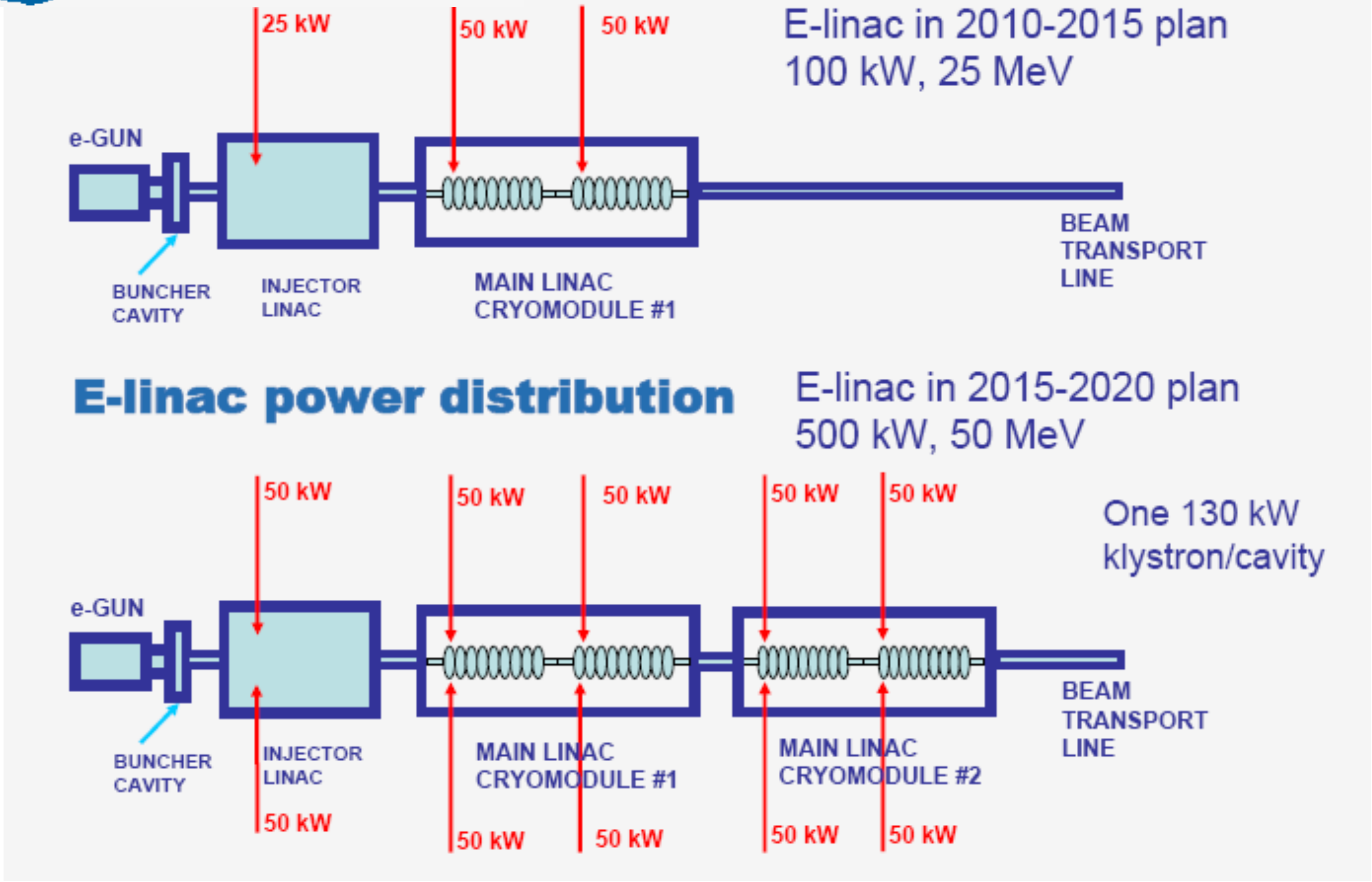
Thermionic gun: triode; 100 keV; 1.3 GHz

9-cell cavity; 10 MV/m
Doubles as H test cryostat

Focusing & diagnostic packages

| **Injector linac** | **Main linac** | |
|---|---|---|
| 10 mA, 10 MeV<br>100 kW beam pwr | 10 mA, 40 MeV<br>400 kW beam power | **Fission driver** |
| Single 9-cell cavity | 4 cavities; 9 cell/cavity | All K.E. dumped in target |
| Two 50 kW input coupler;10 MV/m | Two 50 kW coupler/cavity; 10 MV/m gradient | |
| Single HOM absorber | 1 HOM absorber/cavity | 500 kW |

# eLINAC Time Evolution



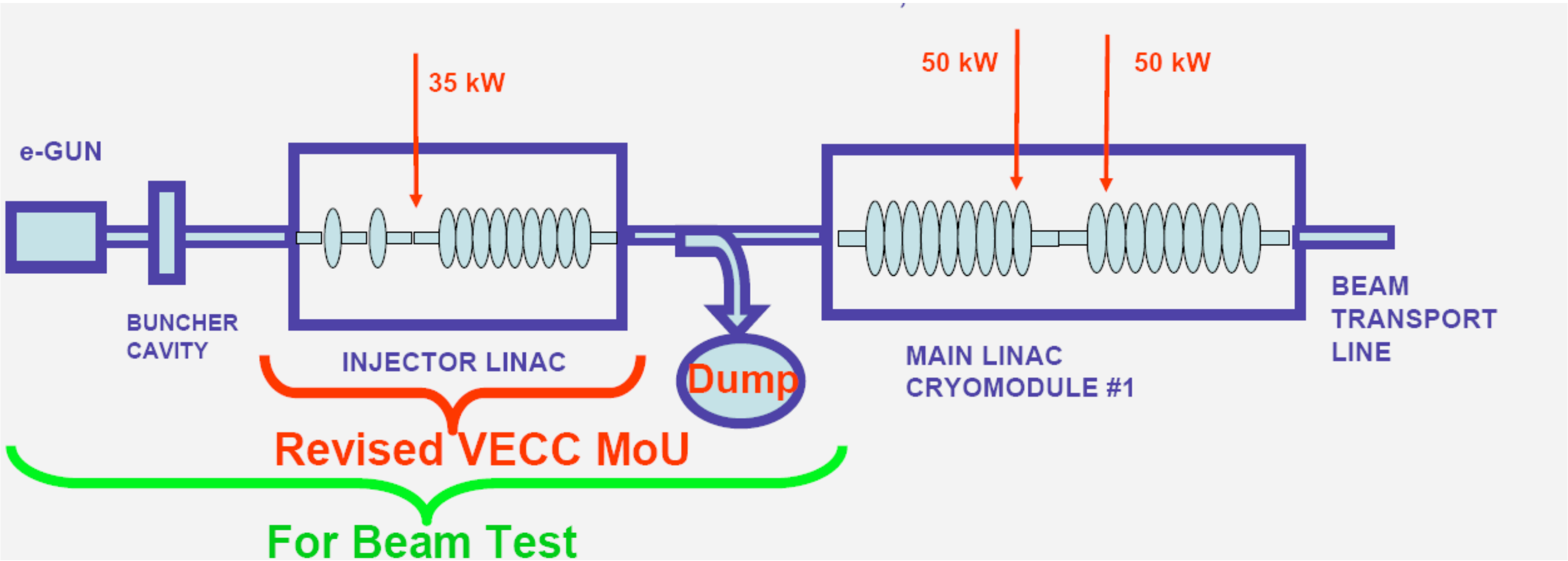
E-linac in 2010-2015 plan
100 kW, 25 MeV

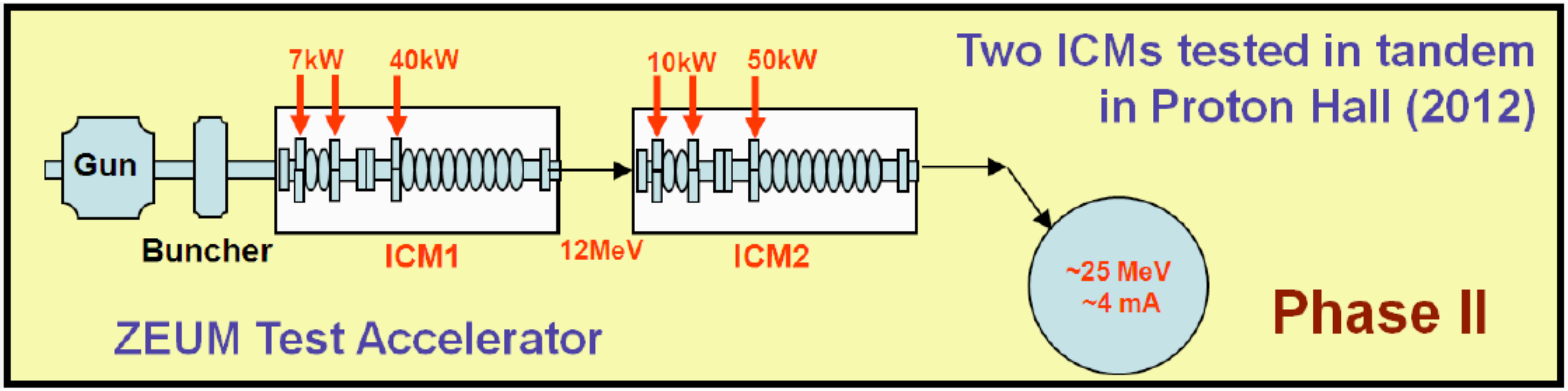
**E-linac power distribution**

E-linac in 2015-2020 plan
500 kW, 50 MeV

One 130 kW klystron/cavity

# TRIUMF Proof of Principle (2010-2012)





Two ICMs tested in tandem
in Proton Hall (2012)

ZEUM Test Accelerator

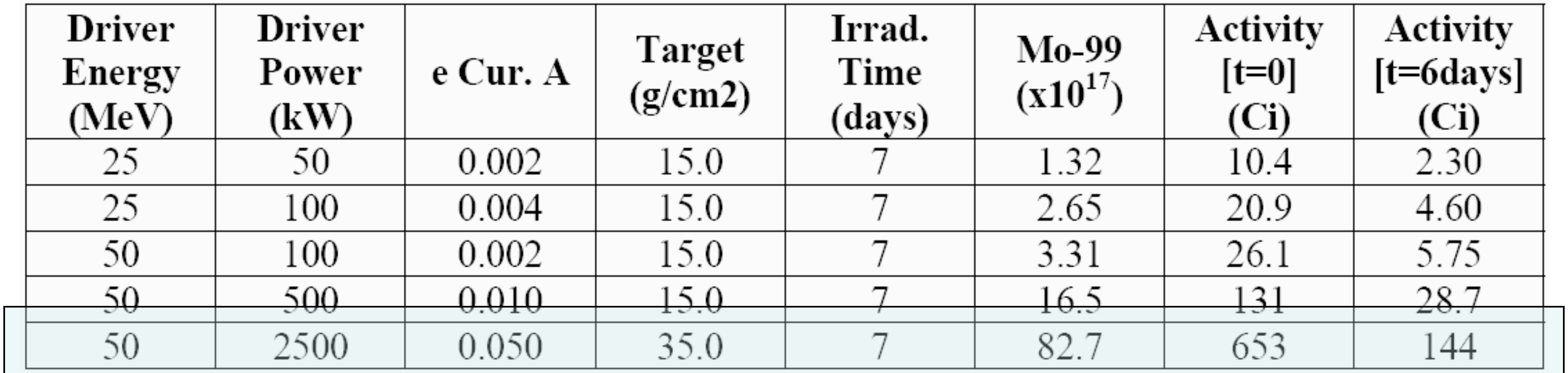
**Phase II**

# TRIUMF Proof of Principle (2010-2012)

- Assemble test accelerator system.
  - Based on eLINAC injection cryomodule (ICM)
- Fabricate and commission targets with MDS Nordion.
- Transfer “hot” target to extraction system.
- Purify Mo-99
- Quality control

- ICM fabrication in Collaboration with Variable Energy Cyclotron Centre (VECC) in Kolkata

# Yield of 6-day-Ci vs Energy and Power

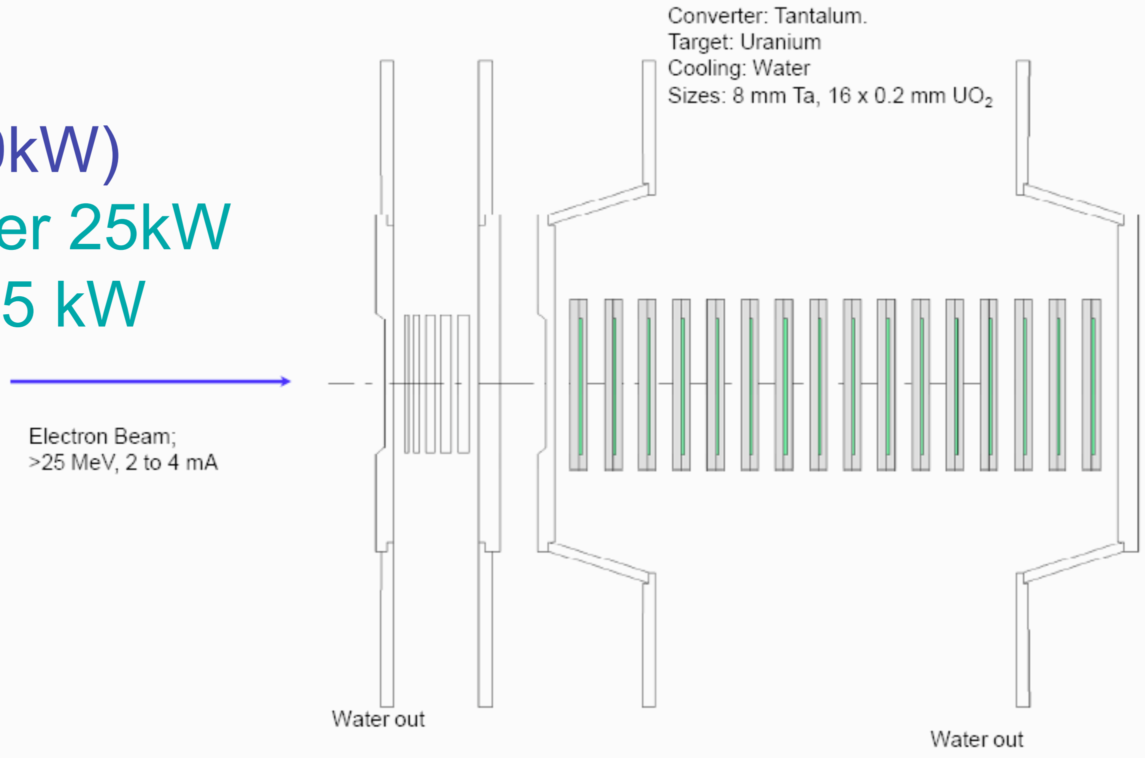


| Driver Energy (MeV) | Driver Power (kW) | e Cur. A | Target (g/cm2) | Irrad. Time (days) | Mo-99 ($x10^{17}$) | Activity [t=0] (Ci) | Activity [t=6days] (Ci) |
|---|---|---|---|---|---|---|---|
| 25 | 50 | 0.002 | 15.0 | 7 | 1.32 | 10.4 | 2.30 |
| 25 | 100 | 0.004 | 15.0 | 7 | 2.65 | 20.9 | 4.60 |
| 50 | 100 | 0.002 | 15.0 | 7 | 3.31 | 26.1 | 5.75 |
| 50 | 500 | 0.010 | 15.0 | 7 | 16.5 | 131 | 28.7 |
| 50 | 2500 | 0.050 | 35.0 | 7 | 82.7 | 653 | 144 |

# Target System

- Target system a challenge
  - Production system 750 kW of $\gamma$ and fission
    - 5 converters each followed by 10 targets
    - 15 kW per target
  - Liquid Hg or water cooled W

- Proof of Principle (50kW)
  - Power in converter 25kW
  - Power in target 15 kW



# Conclusion

High Power eLINACs can be a viable alternative to reactors for the production of

$$^{99}Mo$$