New Methods in the accelerator production of radioisotopes

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Introduction

- A major crisis has developed in the world of nuclear medicine: the production of Tc99m, the radioisotope most commonly used in nuclear medicine has seen severe interruptions. The problem is the end of life of nuclear reactors producing medical radioisotopes. The situation will further degrade in the coming years.
- We will show how cyclotrons or CW electron accelerators could be used to produce safely and economically the RI which are produced today in nuclear reactors

Plan of this presentation

- The Mo99 > Tc99m generator
- The present crisis
- Alternate methods of production
- ADONIS, a cyclotron driven subcritical reactor
- Direct proton induced fission of Uranium
- A subcritical reactor based on photo fission caused by high power electron beams

The importance of the Mo99 > Tc 99m generator

- We know very well the production of radioisotopes by cyclotrons
- But 80% of the RI used in nuclear medicine are produced in nuclear reactors
- Among these reactor produced RI, the Technetium 99m (6 hrs), a decay product of Molybdenum 99 (66 hours) is the most commonly used RI in nuclear medicine
- Every year, 36 million medical procedures based on Tc99m are conducted in the world. This not only is critical for the timely diagnostic of patients, but also represents more than 20 Billion $ in medical fees

The production of Mo99 today

- Mo 99 can be produced by neutron capture on natural Mo (Mo 98 = 24%). The process is simple and inexpensive, but yields a very low specific activity
- High specific activity Mo 99 can be obtained by U235 fission. 6% of the U235 fission events produce a Mo99 nucleus as a fission product. Targets are made highly enriched Uranium (HEU), with a progressive shift toward Low Enrichment Uranium (20% U 235) (LEU)
- Typically, in today's production, aluminum targets containing 4 gm of HEU powder are irradiated for a week in high flux research reactors
- After irradiation, the highly radioactive target is allowed to decay for one day, then is sent to the processing facility

iba Particle Therapy

Mo 99 processing

- The irradiated HEU targets (40,000 Ci !!!) are transported to the Mo99 processing facility (Fleurus, Petten, Chalk River, Pelindaba)
- The targets are dissolved, and the selected fission products are chemically separated. Each target gives around 800 Ci of Mo99 EOI, or 135 Ci post-calibrated 6 days
- The world weekly production is 8,000 to 10,000 Ci, p.c. 6 days. USA and Western Europe use most of this.
- So each week, about 60 targets are irradiated worldwide
- The purified Mo99 is sent in bulk form to the producers of generators

The Mo99 > Tc 99m generator

- For the distribution to the final customer, the Mo99 solution is fixed on a small ion exchange alumina column
- The Mo99 (66 hours) decays continuously into Tc99m. Because of it's different chemical properties, the Tc99m is not stably fixed on the alumina column
- When needed, the user washes the Tc99m out of the ion exchange column with a sterile saline solution
- The Tc99m is used to label a molecule which will target the body site to be studied
- Mo99 > Tc99m generators are produced by radiopharmaceutical companies and distributed to hospitals or radio-pharmacies on a weekly basis

Some economic data

- A nuclear medicine or PET examination is generally charged 500 to 1500€ to the patient or to the social security
- A patient dose of cyclotron produced RI is generally sold to the hospital 150 to 300€
- In contrast, the cost to the hospital of a patient dose of Tc99m is generally less than 15€ (but this cost is rising). In this price, the cost of the neutron irradiation of the target is today less than 1€
- Reactor produced isotopes, such as Tc99m are therefore much less expensive than cyclotron produced RI

The present crisis (1)

- The neutron irradiation of HEU targets for the production of fission products for medical application is made in a small number of aging research reactors
- All the production for North America is done on NRU a very old research reactor in Chalk River (Canada). NRU was put in operation in the early 50's!
- In Europe, the production is done on a small number of aging research reactors: HFR (Petten), BR2 (Mol), Osiris (Marcoule)
- More recent production reactors are also found in South Africa (SAFARI) and Australia (OPAL)

The present crisis (2)

- The present reactors used for medical RI production are research reactors, paid by public money to do research on nuclear technology
- RI production is not their primary mission, and is charged at marginal (minimal) cost. The cost paid today for irradiation in state-sponsored reactors is so low that the construction of new reactors for medical RI production cannot be financed
- These research reactors are characterized by cycles of operation of a few months, separated by maintenance periods
- Most of these reactors have vastly exceeded their design lifetime
- Construction of new research reactors is unpopular. Only the Jules Horowitz reactor is being built by the CEA. It is expected for 2015…2017

The present crisis (3)

- 10 years ago, Nordion, the world largest Mo99 producer, ordered from AECL the construction of two new reactors for the production of medical RI: the Maple-X reactors
- But the design of the Maple-X reactor was flawed, and at the first tests, the new reactors exhibited a positive temperature coefficient for the reactivity. They were never allowed to operate
- After 10 years of efforts, and more than 600 Mcan$ spent, the Canadian government decided to abandon the Maple X reactors?

The present crisis (4)

- In 2009, both HFR (Petten) and NRU were closed after leaks were discovered in the primary loop of the reactor
- Both reactors were restarted in 2010 after extensive repairs. However how much longer they will be able to operate remains a question
- Osiris will be definitely reach the end of its life in the coming years, and will be closed at the start of the JHR
- As a result, the distribution of Mo99 > Tc99m generators was seriously disturbed in 2009-2010.
- With the restart of NRU and HFR, the situation is improving, but the world supply remains fragile

The situation of USA

- While USA is the world single largest user of Mo-Tc generators, there is today no large scale domestic supply of Mo99 in USA
- USA would like to curb the use of HEU, but is in a difficult position to impose unilaterally this policy while all the production is abroad, in countries which are allies of USA, but are independent countries.
- Today, most of the world supply of Mo99 is made by irradiating HEU targets.
- Converting a production site from HEU to LEU requires a complete redesign of the production targets, and of the chemical separation chain. The required investment exceeds 100 M$/production site. However, the neutron source does not generally require extensive modifications.

What can we do?

- What do you do when Mo99 from reactors becomes unavailable?
- You ration the use of generators between your customers (this was done during the crisis)
- You can substitute cyclotron produced RI (like NaF18 for bone scans) at a much higher cost (done during the crisis)
- You can produce directly Tc99m from a p-2n reaction on Mo100 with a PET or SPECT cyclotron (M. Lagunas Solar, UC Davis). The yield is OK (10 Ci/hour at 21 MeV, 500 µA) but logistics and costs are similar to F18 production
- You could also (theoretically only) produce Mo99 by a p-p,n reaction on Mo100, but the yield is terrible (ibidem)
- You can think to alternates to nuclear reactors

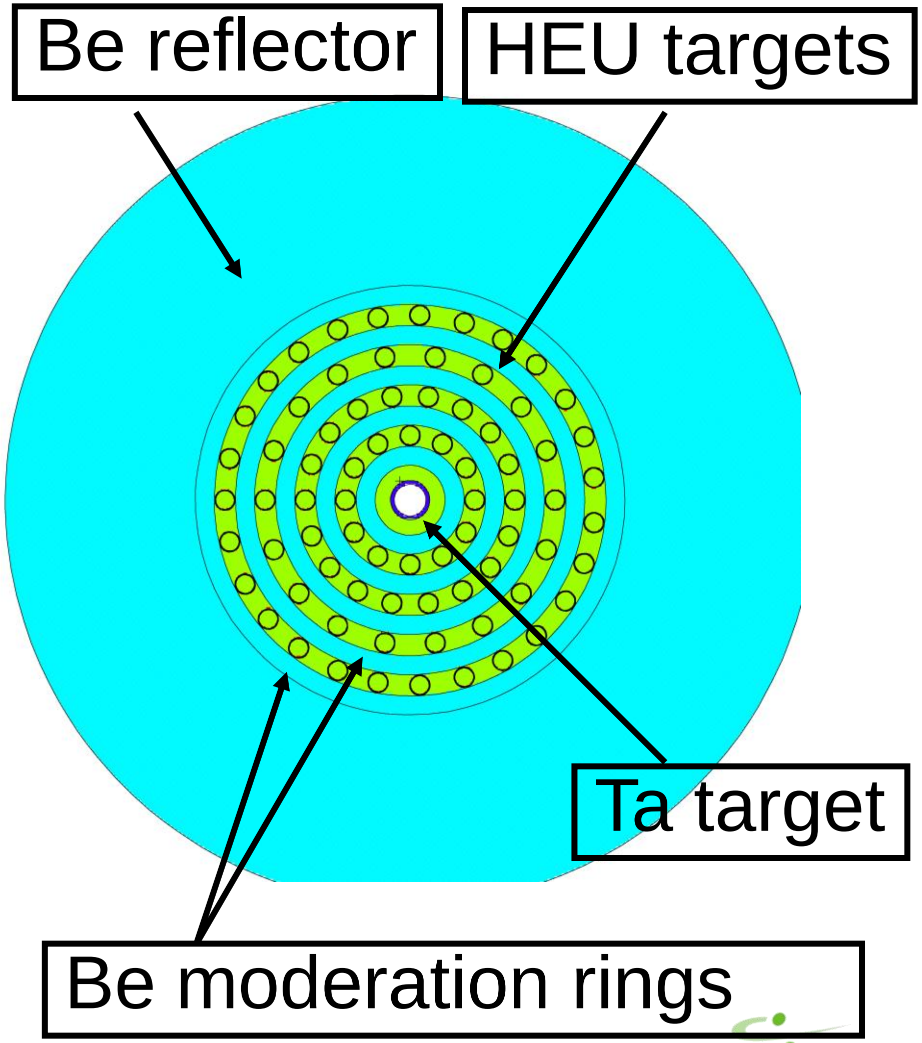
#1: ADONIS
a cyclotron driven subcritical reactor

Design #1: ADONIS

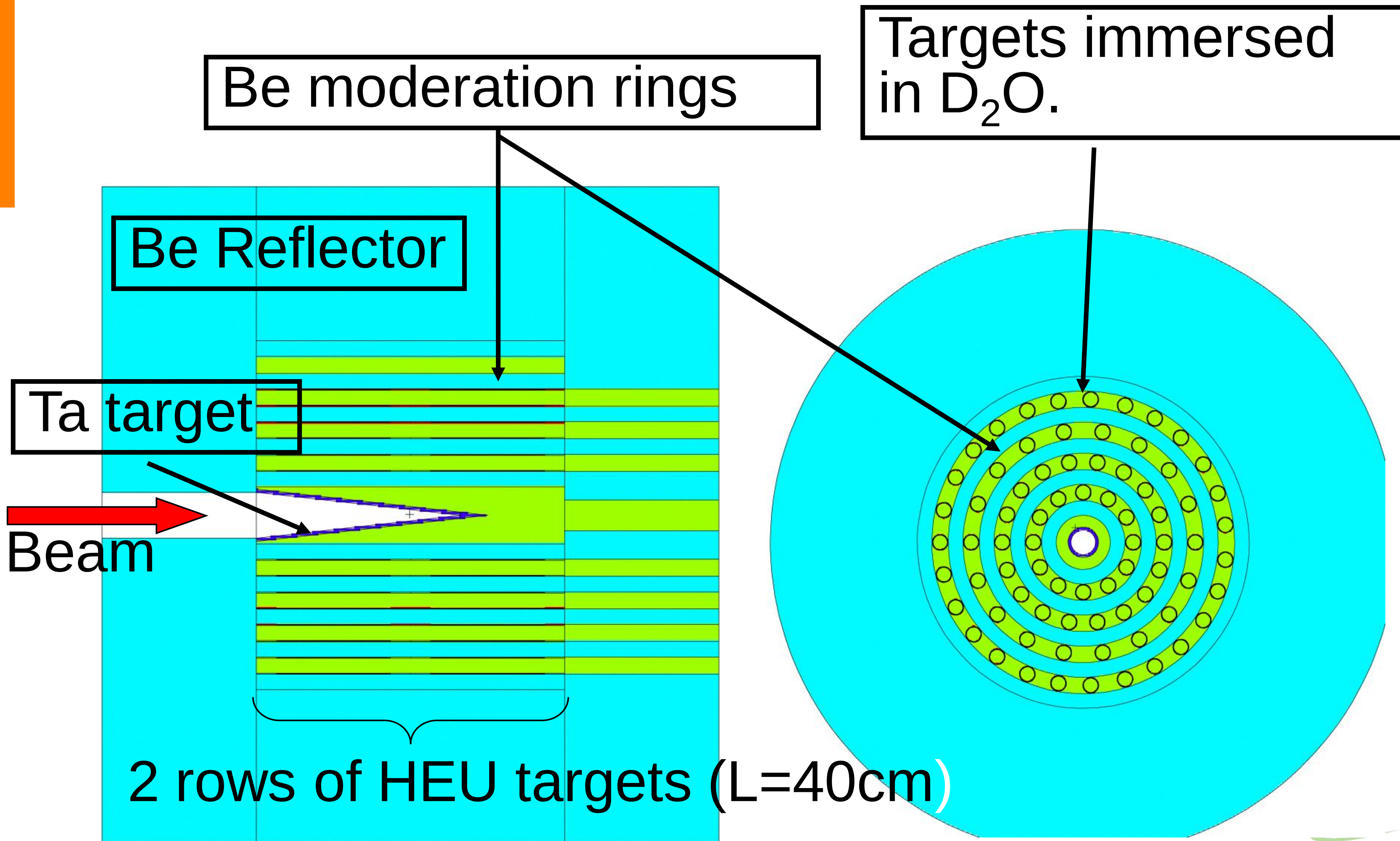
- In 1995, IBA started to think about new ways to produce ^{99}Mo based upon cyclotrons instead of nuclear reactors.
- The proposed ADONIS (Accelerator Driven Optimized Nuclear Irradiation System) was based on a 150 MeV / 2 mA H^- cyclotron.
- With the revival of a ^{99}Mo crisis, this concept was revisited this year and new neutron calculations were performed by IBA and SCK-CEN in Belgium.
- ADONIS concept based upon neutron-induced fissions:
  - neutrons produced by a Tantalum spallation target
  - Spallation target surrounded by HEU targets
  - Sub-critical reactor with K_{eff} ~ 0.9
  - Goal is to reach a weekly production of 5000 Ci of ^{99}Mo (post-calibrated 6 days after EOI).

Sub-critical Assembly Design (1)

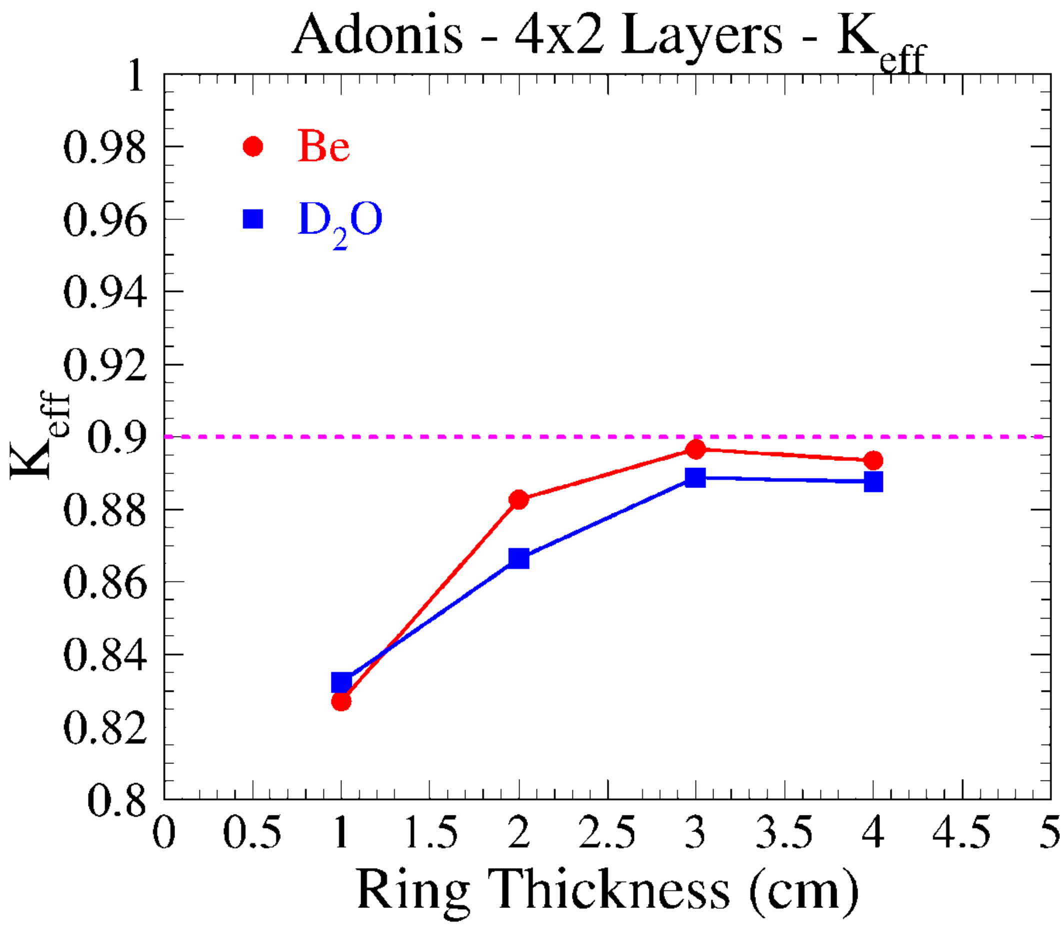
- Conical Tantalum spallation target.
- Design based on cylindrical targets as used today.
- Beryllium moderation rings between target layers.
- HEU targets (4g ^{235}U) immersed into D_2O.
- Be reflector (20 cm thick).
- Targets disposed on 4 cylindrical layers, each layer being made of 2 rows of targets ➔ total of 150 targets
- Modeling done with MCNPX 2.5.0



Sub-critical Assembly Design (2)

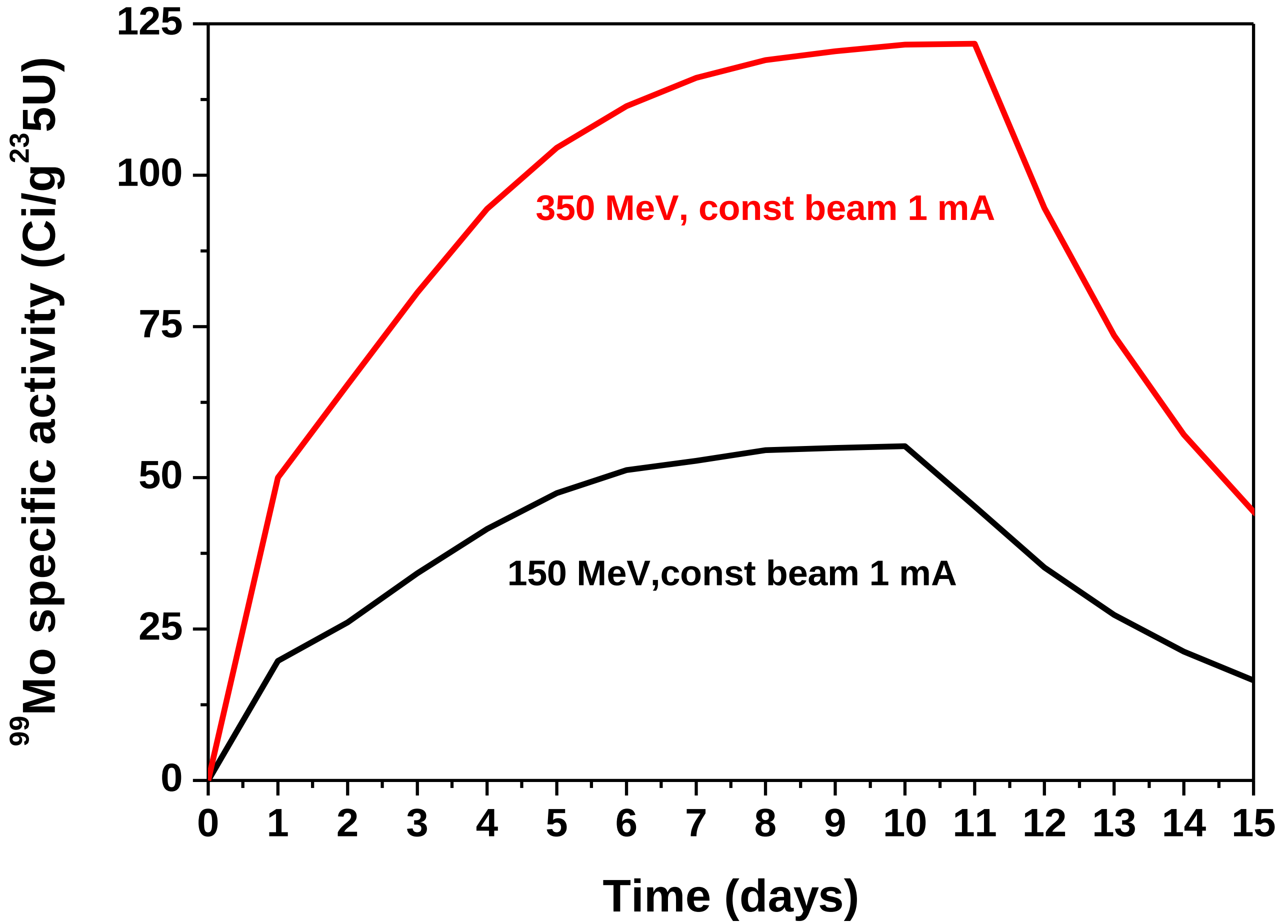


Criticality Calculations



➔ K_{eff} remains below 0.9

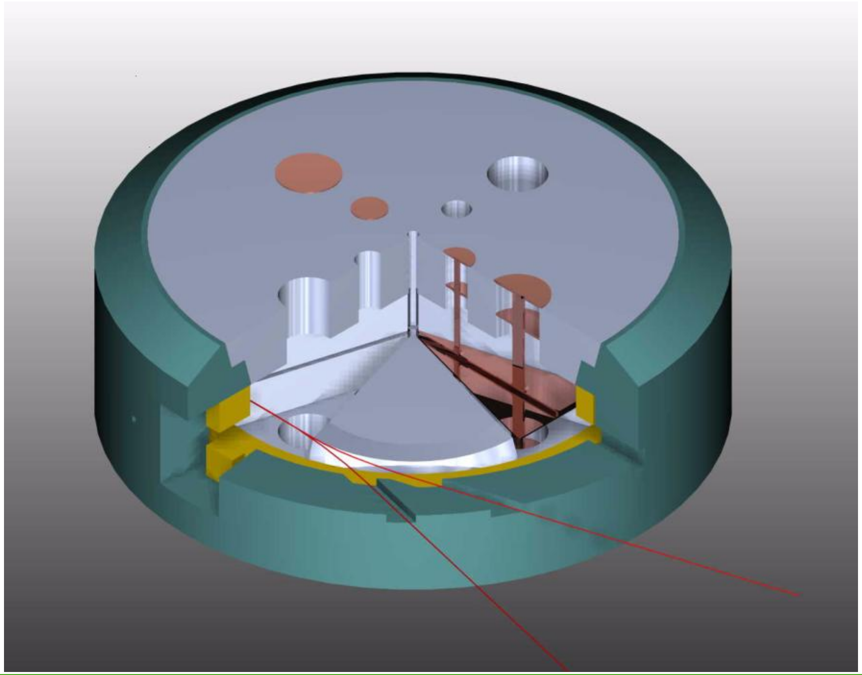
Comparing the ^{99}Mo Activity at 350 vs. 150 MeV

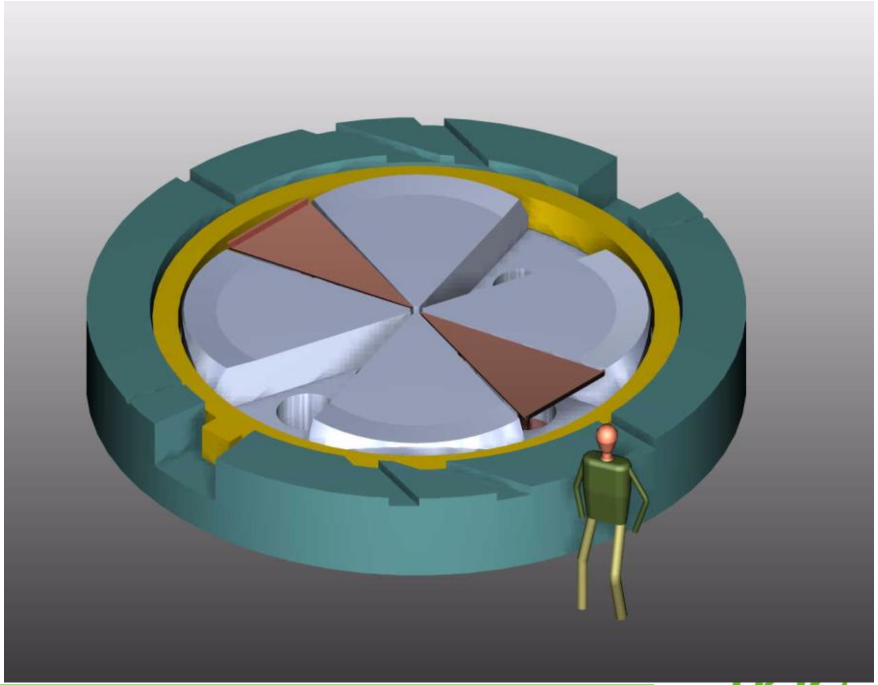


➔ 350 MeV / 1 mA beam needed to produce 5000 Ci/week
➔ Need HEU targets or LEU targets containing 4 g ^{235}U each

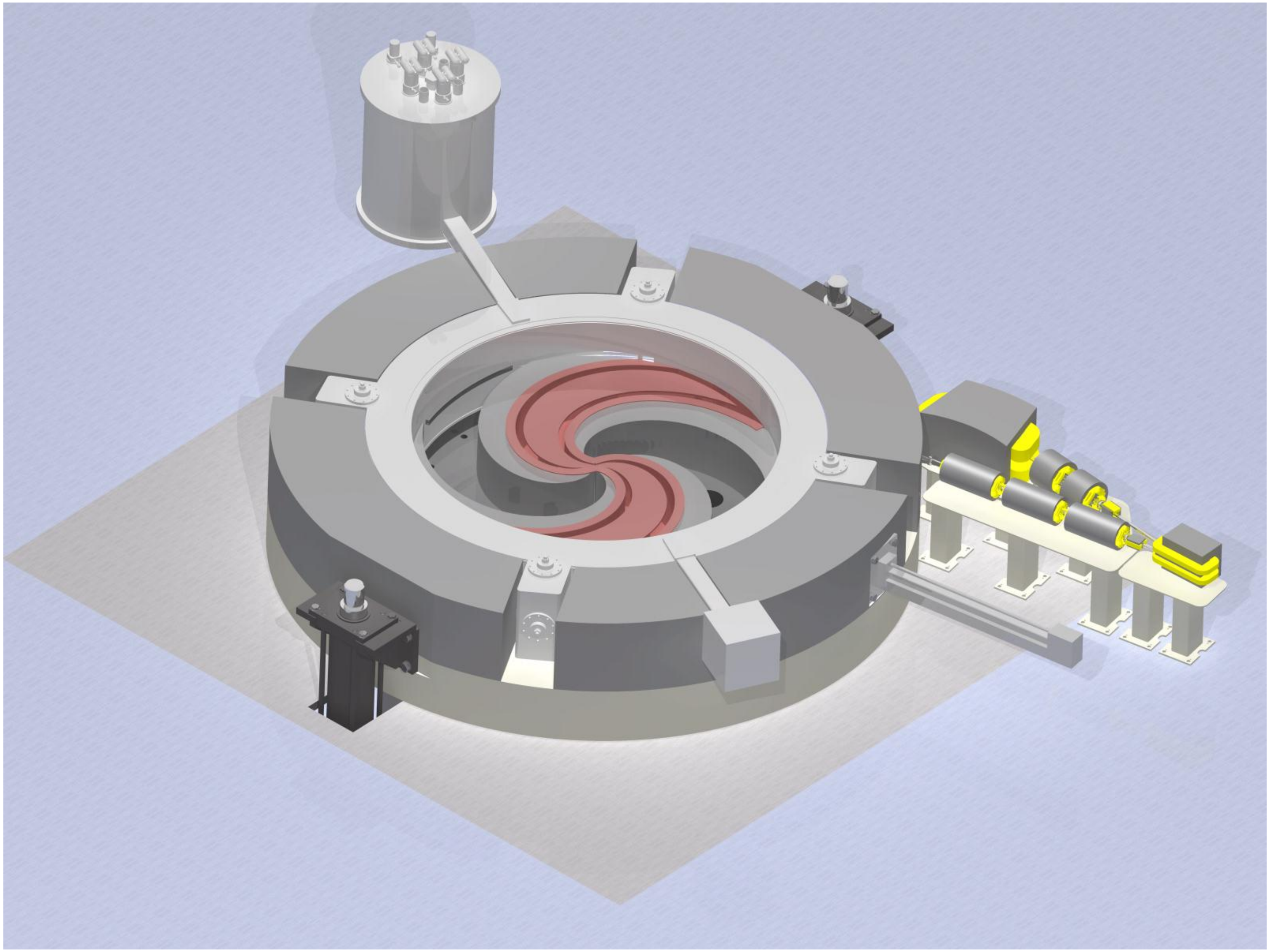
Basic design of the 200 MeV cyclotron

- Cyclotron outside diameter: 6.42 m
- Cyclotron magnet vertical size: 2.16 m
- Cyclotron magnet weight: 405 Tons
- Ampere-turn in main coils: 102 000 Aturn
- Total power in main coils: 92 kW





The 350 MeV H2+ superconducting cyclotron



Extraction trajectories

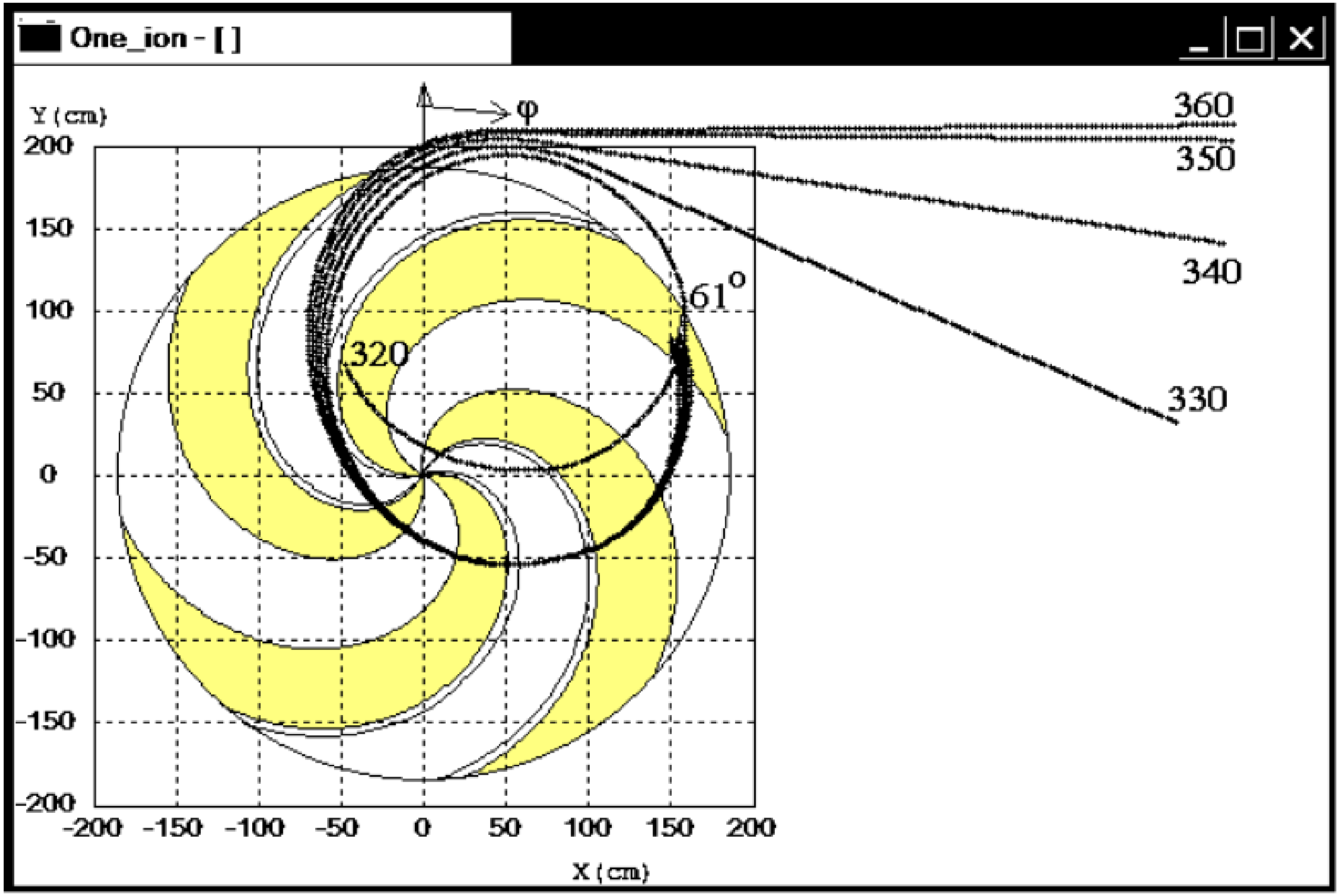
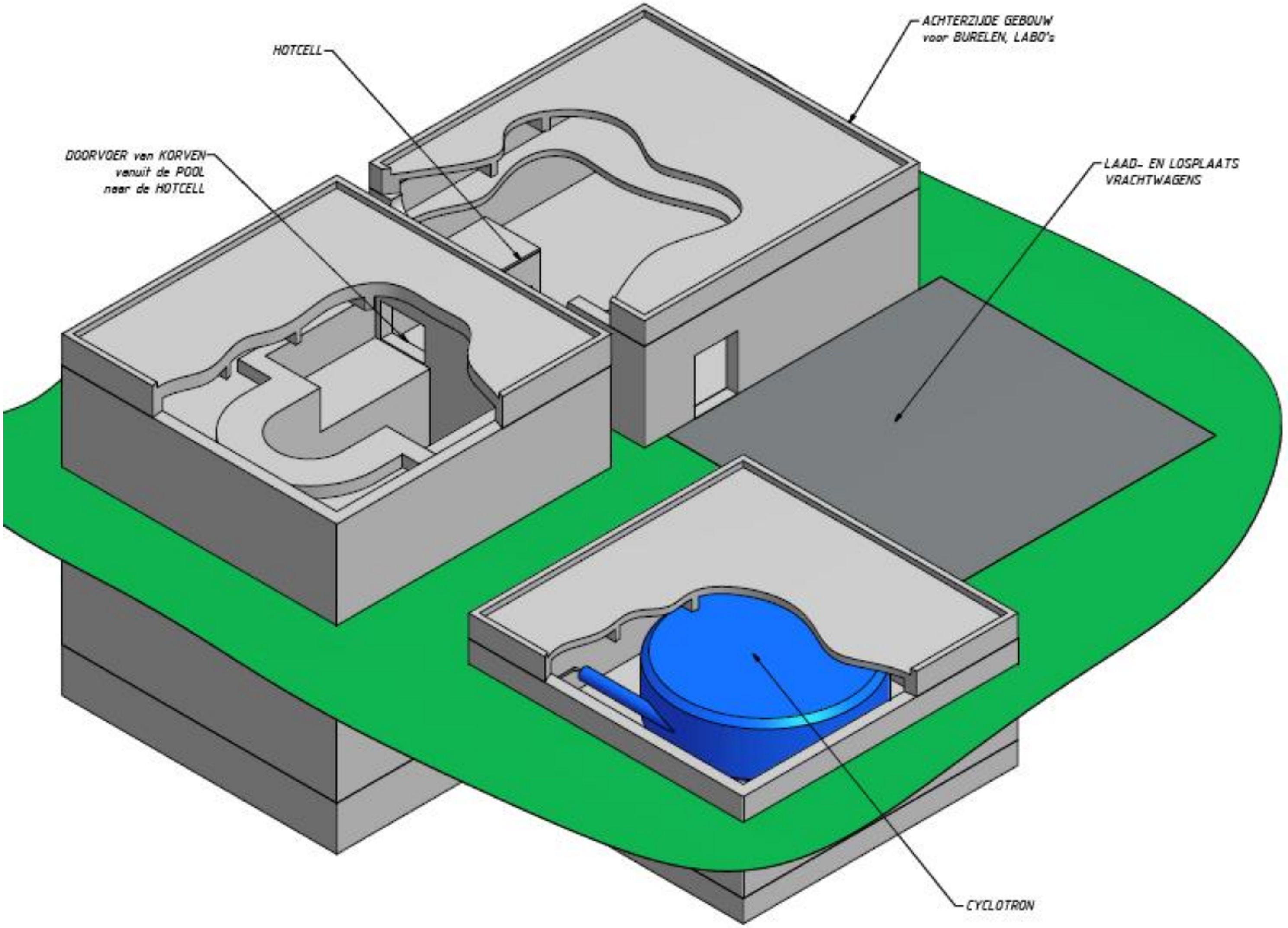


Fig. 6.1.3.4. Trajectories of protons with different energies (320-360 MeV) if the foil is located at azimuth 61°

Main cyclotron parameters

- Accelerated beam: 750 µA of H2+ up to 700 MeV
- Extraction by stripping of the H2+ into protons
- K bending 1600
- R extr. 187 cm, Hill field 4.5 T, Valley field 2.45 T, weight 650 T
- Design similar to IBA C400

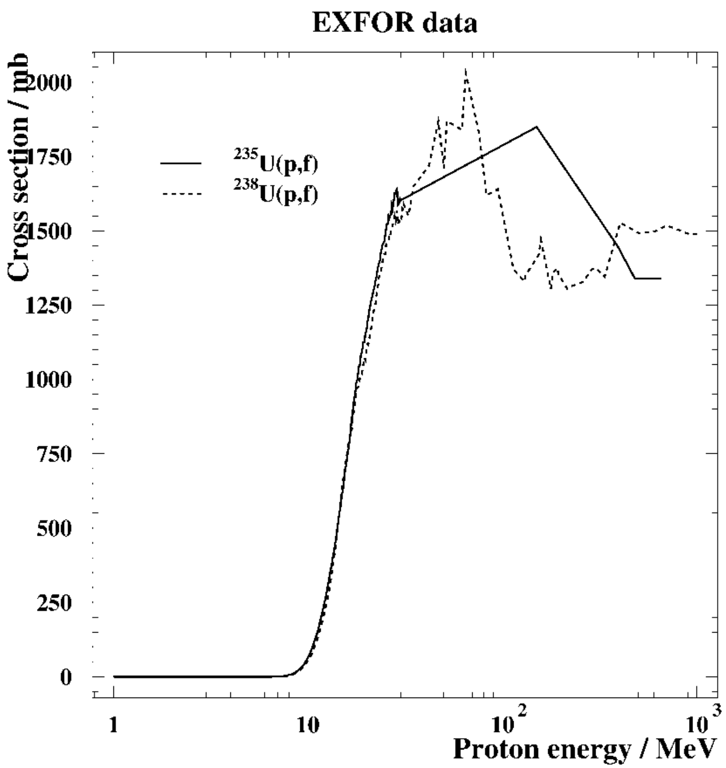
Conceptual design of ADONIS building (SCK-CEN)

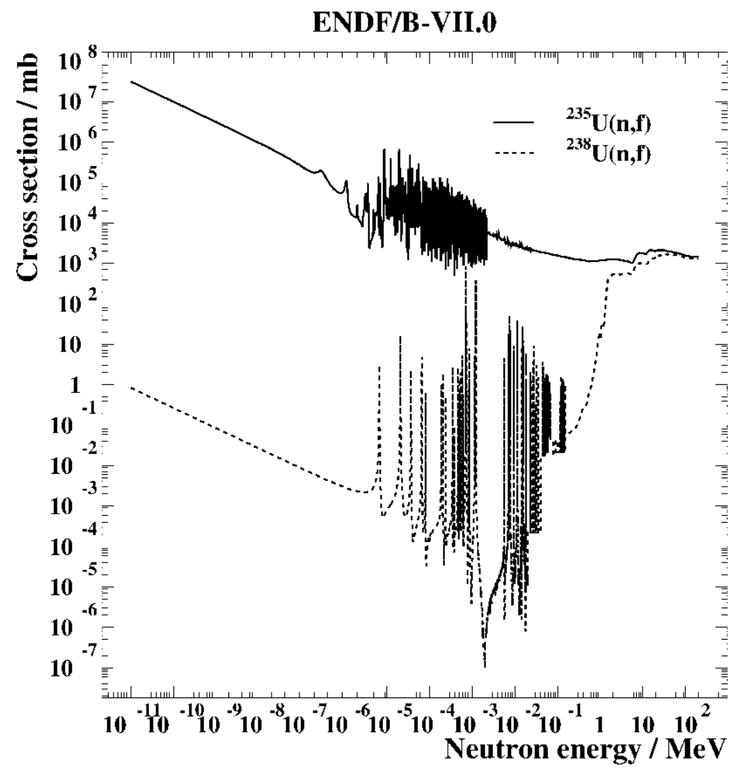


#2: Proton induced fission (let’s skip the primary spallation target)

Design #2: Proton-induced Fissions

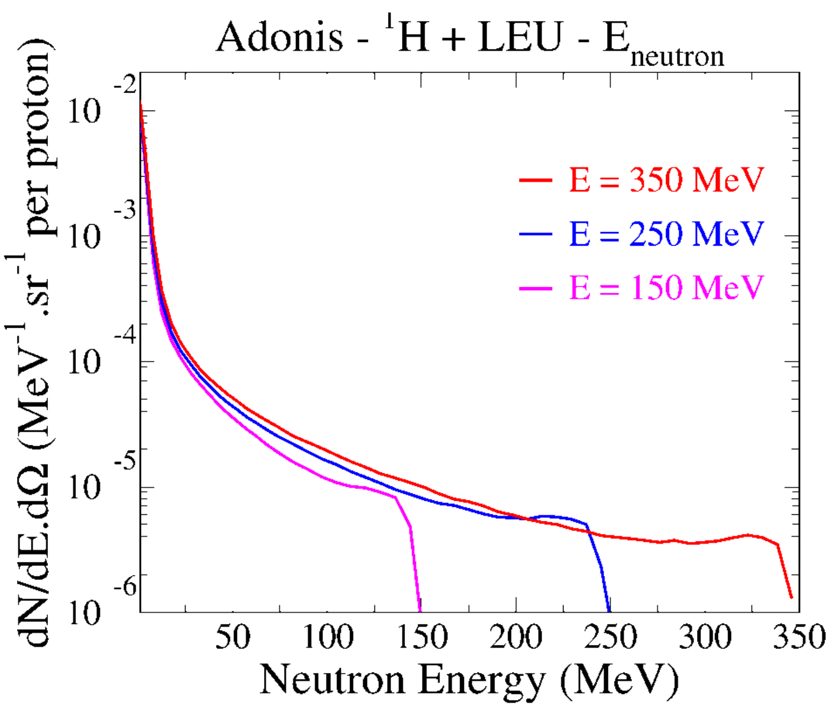
- **In addition to thermal neutrons, Uranium has significant fission cross section for**
  - Protons above 20 MeV ➔ σ(p,f) ~ 1.5 barn
  - Neutrons above 10 MeV ➔ σ(n,f) ~ 1.5 barn
- **For these particles, ^{235}U and ^{238}U exhibit very similar cross sections.**

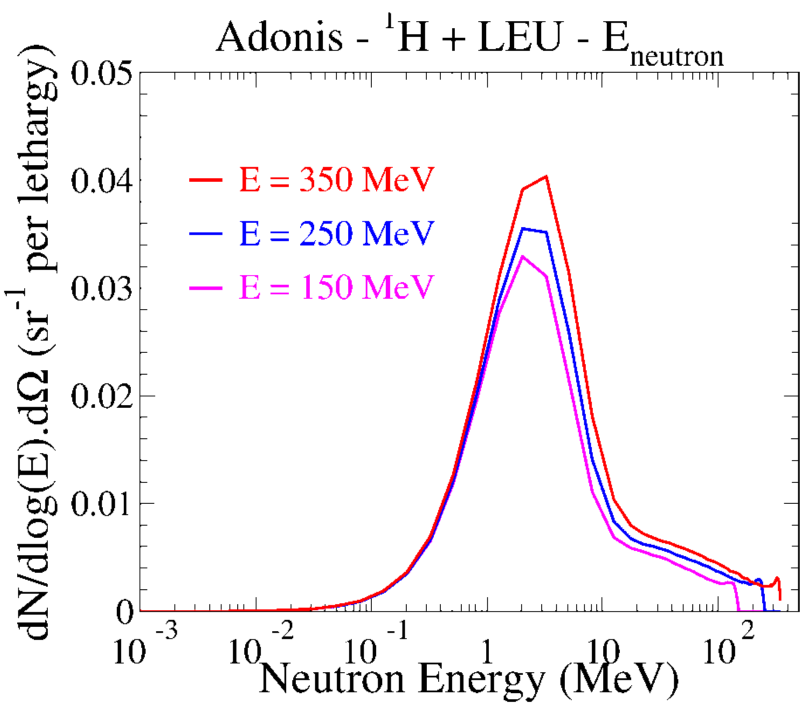




Secondary Neutrons from ^1H + U: Energy Spectra

- Secondary neutrons exhibit a broad energy spectrum, up to the proton energy.
- But most of these neutrons are evaporation neutrons and have energy around 2 MeV

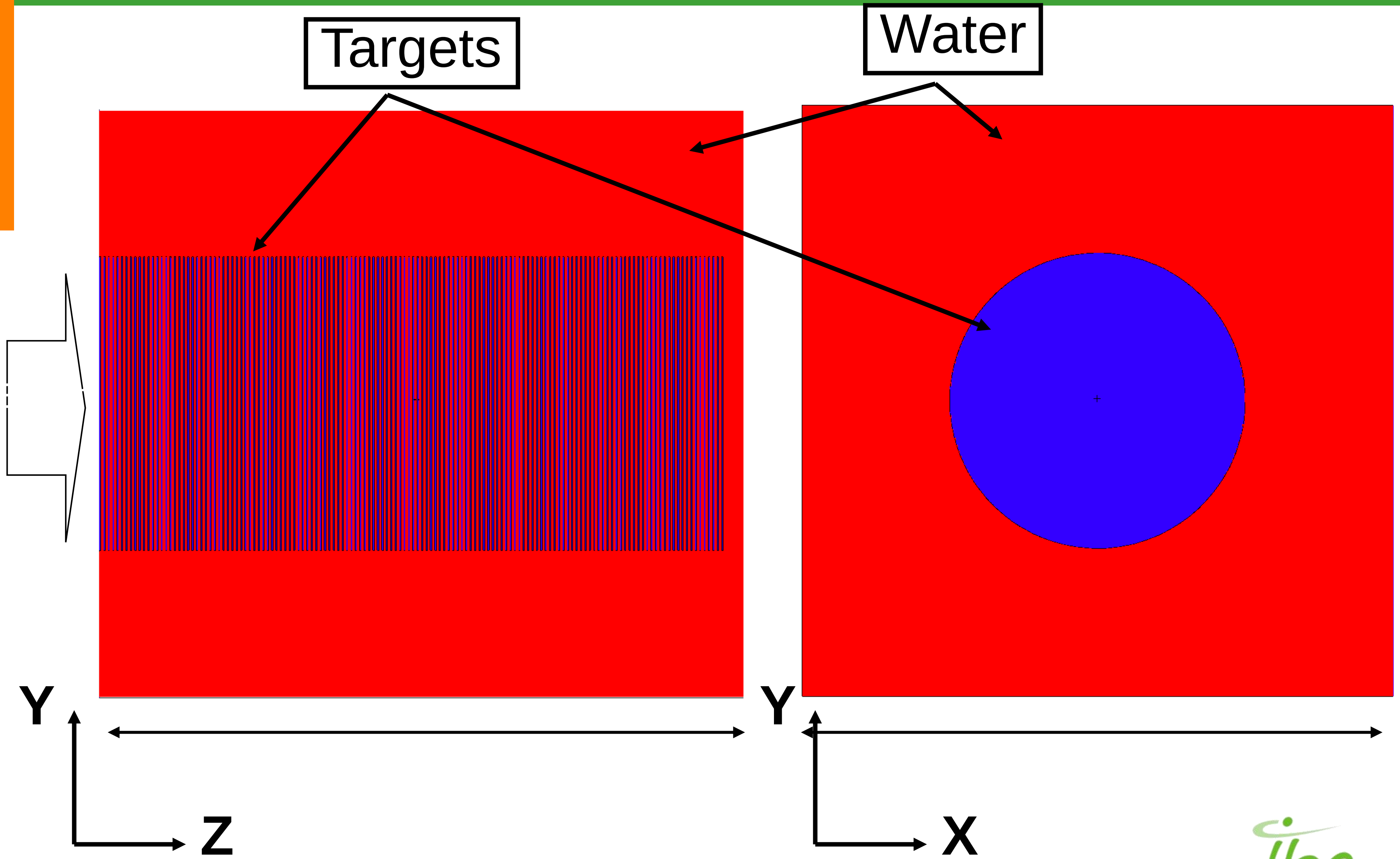




LEU Target Assembly (1)

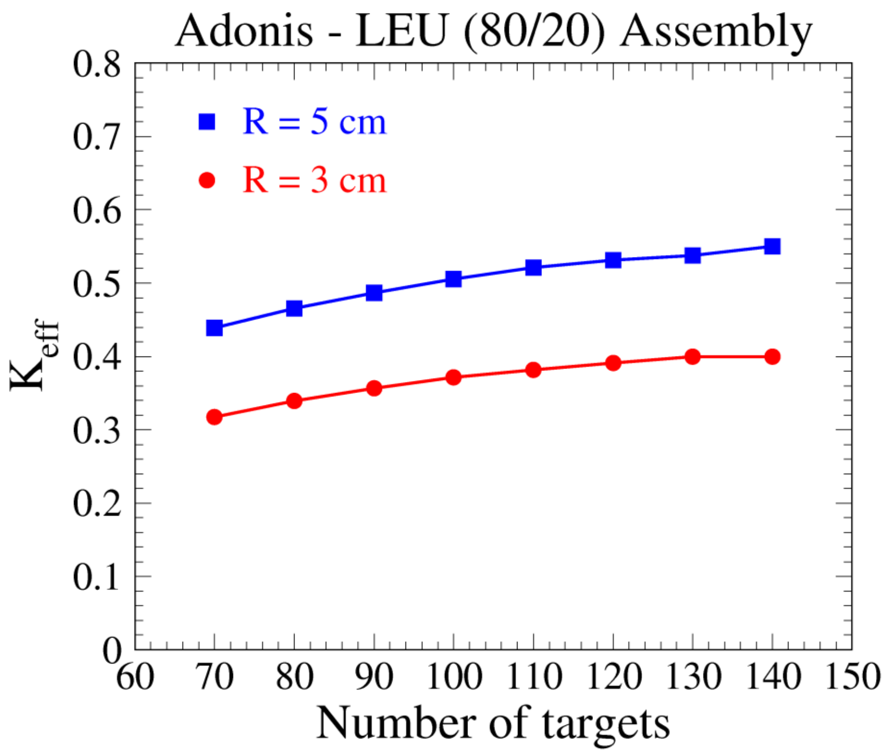
- Target made of 0.5 mm thick metallic Uranium foils. U foil radius = 3 cm or 5 cm.
- U foils separated by 1 mm thick water channels for cooling.
- Consider only Lowly-Enriched Uranium (LEU) with ^{235}U fraction below or equal to 20%.
- Proton beam = 200 MeV or 350 MeV with 1 mA.
- Beam radius = 2.8 or 4.8 cm
- For E_{beam} = 200 MeV, assembly limited to 80 foils.
- For E_{beam} = 350 MeV, assembly contains 142 foils.

LEU Target Assembly (2)



Target Assembly: Criticality Calculation

- Study the evolution of K_{eff} for the LEU target assembly as a function of target number and target radius R.
- ➔ The target assembly is very far from criticality.



Summary

6-day calibrated ^{99}Mo activity per week using a 1.0 mA proton beam.

Energy (MeV)	Radius (cm)	Total (Ci/week)
200	3	892
	5	1470
350	3	2530
	5	4940

→ Possibility to produce ~5000 6-day calibrated Ci/week using 350 MeV / 1 mA proton beam.

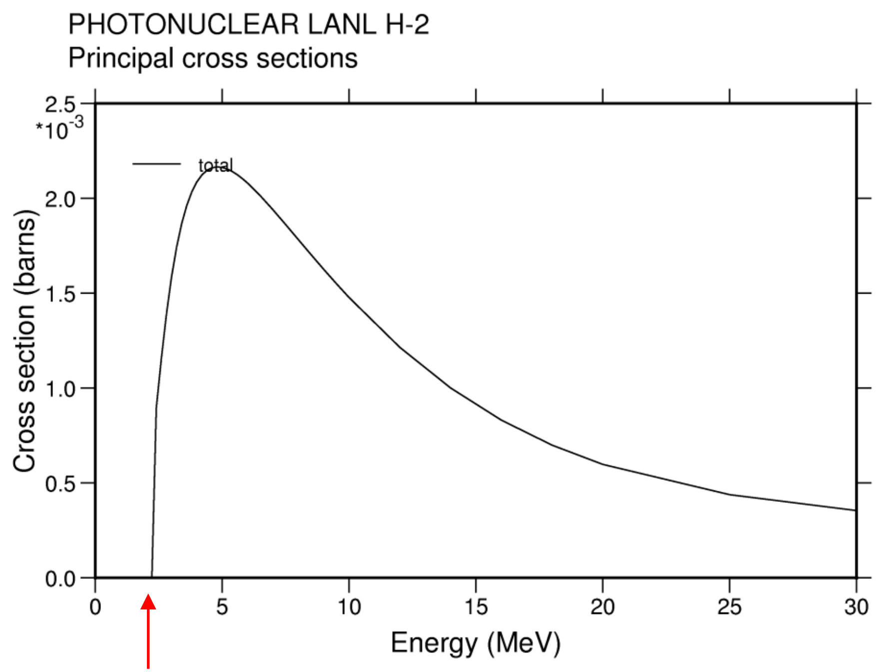
#3: Starting from Photo Fission

Design #3: Electron Accelerator-Based Solution

- <u>Basic idea</u>: Generate a large thermal neutron flux from an electron accelerator connected to a vessel containing a D_2O solution.

. Dhale and J.M. Gahl in Nucl. Sci. Eng. 149 (2005) 288)

$\boxed{^{2}H(\gamma,n)^{1}H}$

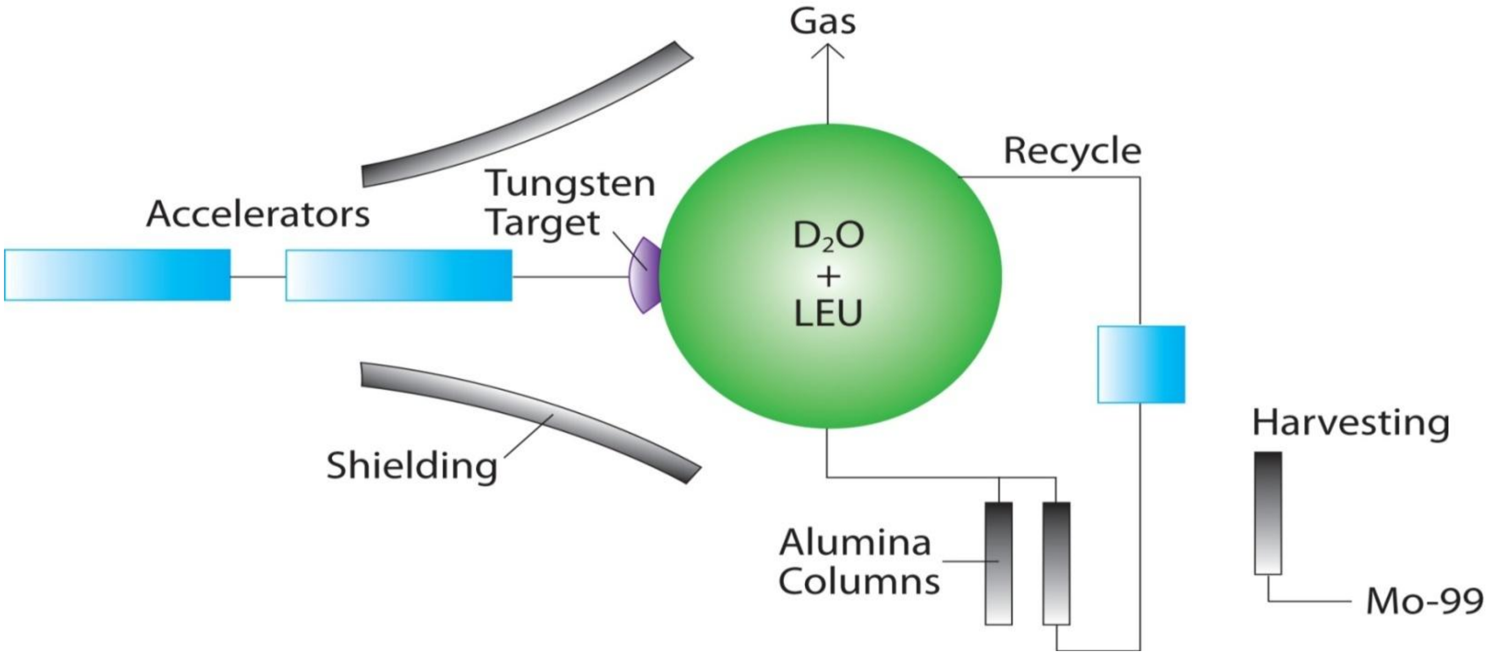


2.23 MeV

Particle Therapy

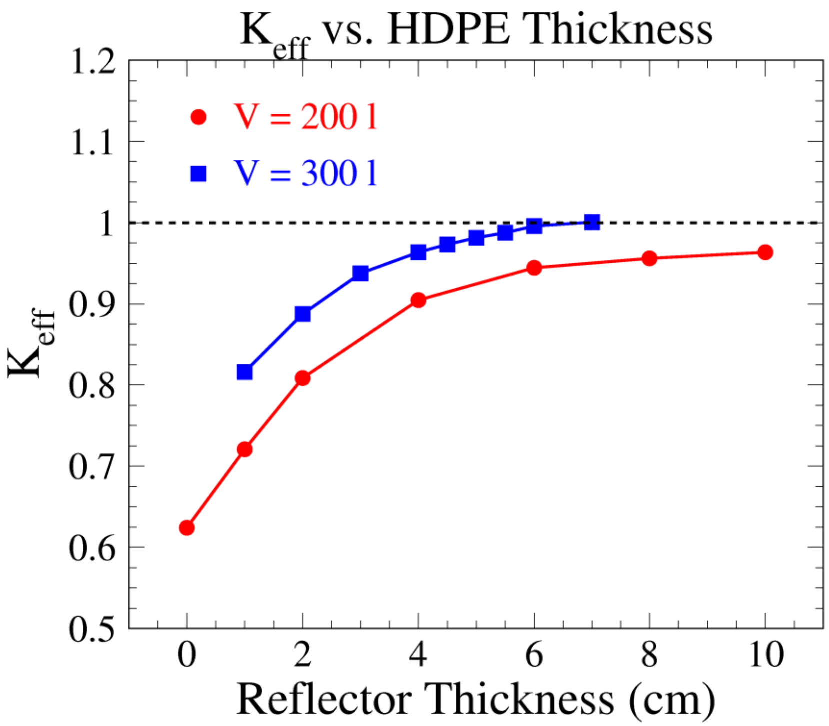
Production Hardware

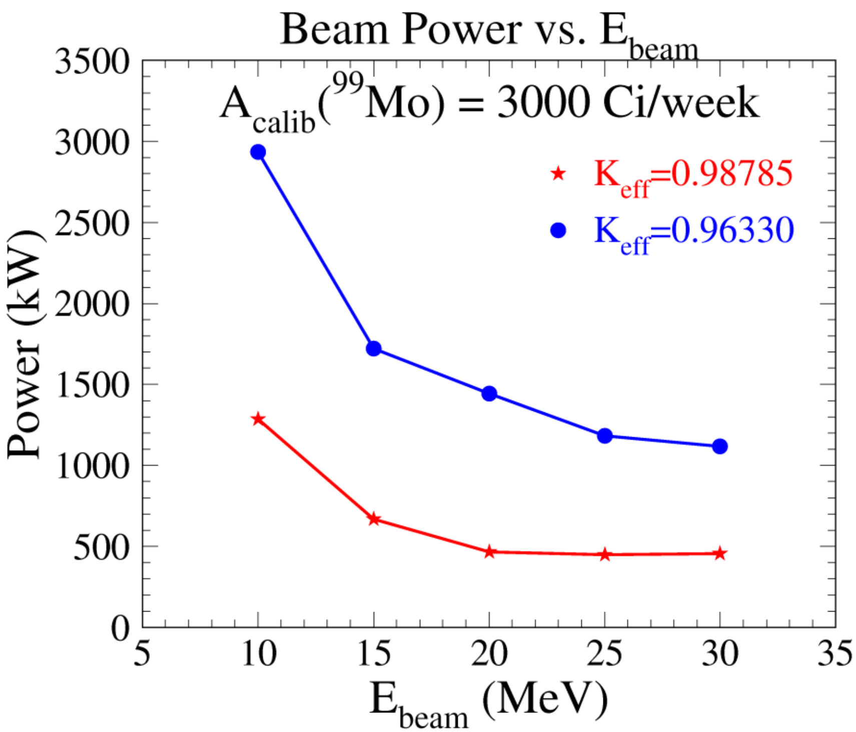
- Medium-energy electron beam: 10 – 30 MeV
- X-ray converter: Ta or W target
- Vessel containing D_2O + LEU salts (50 g/l, 20% ^{235}U)
- Thick reflector surrounding the vessel (HDPE or Be)



IBA Particle Therapy

MCNPX Simulations (1)





➔ Work with a k_{eff} ~ 0.99,
➔ Thermal flux amplification factor ~ 100

➔ With k_{eff} ~ 0.99, need 450 kW of beam power above 20 MeV to generate 3000 Ci/week of 6-day calib ^{99}Mo.

Particle Therapy

Accelerator solutions

- Parallel simulations done by Advanced Medical Isotope Corporation (AMIC) lead to very similar results with a 24 MeV / 380 kW electron beam to produce 3000 6-day calib. Ci/week.
- This electron beam can be produced using existing machines such as the Rhodotron.
- Rhodotrons are CW recirculating RF accelerators, accelerating electrons at 10…12 MeV, with average beam power ranging from 50 kW to 700 kW
- More than 20 Rhodotrons have been built by IBA, and have been operating very reliably in industrial environments
- Two Rhodotrons operated in series could provide in excess of 1 MW of electron beam at 24 MeV.
- One 700 kW industrial x-ray sterilization facility based on a high power Rhodotron is now operated in Switzerland.
- 200 kW to 400 kW of e-beam at 24 MeV, converted into x-ray is required here

Particle Therapy

Open Rhodotron

Conclusions

- The total US needs in Mo99 (around 5000 Ci/weel PC 6 days) could be provided by one relatively inexpensive system (~100 M$) based on existing accelerator technology
- If the proton route is selected, proton induced fission, enhanced by neutron multiplication seems the solution of choice:
  - 350 MeV, 1 mA cyclotron
  - Target made of thin circular foils of metallic LEU
  - Keff around 0.5
- If the photo fission route is selected
  - Higher Keff is needed: 0.99 (licensing issues ???)
  - Beam power can be provided by 2 Rhodotrons in series providing 400 kW of e-beam at 24 MeV
  - Liquid core reactor is used

Thank you…