Producing Medical Isotopes Using X-rays

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Canadian Light Source

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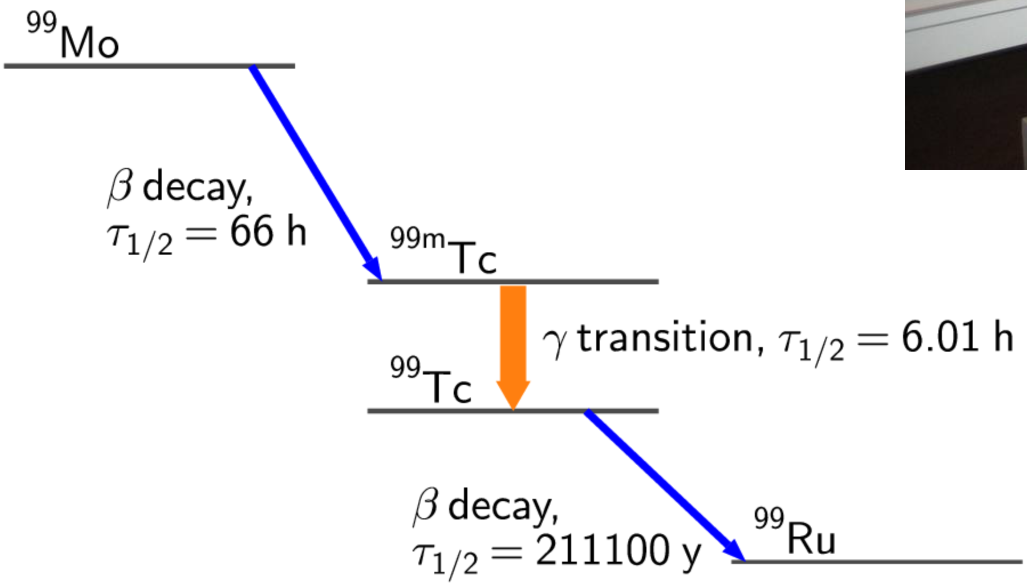
The Goal: ^{99m}Tc

^{99m}Tc:

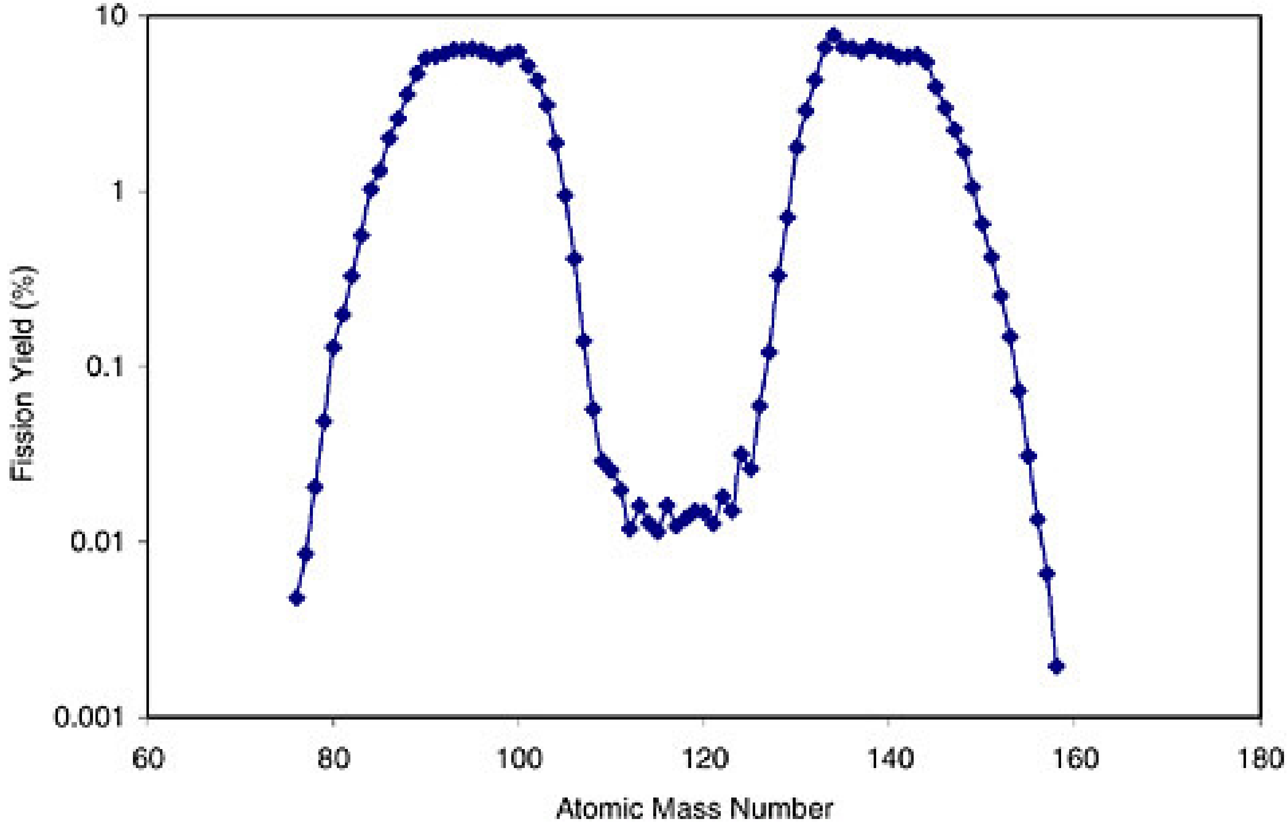
- 140 keV γ-ray, 6 hr half life
- Used for ~90 % of nuclear medicine diagnostic imaging
- Canada – about 5500 procedures per day



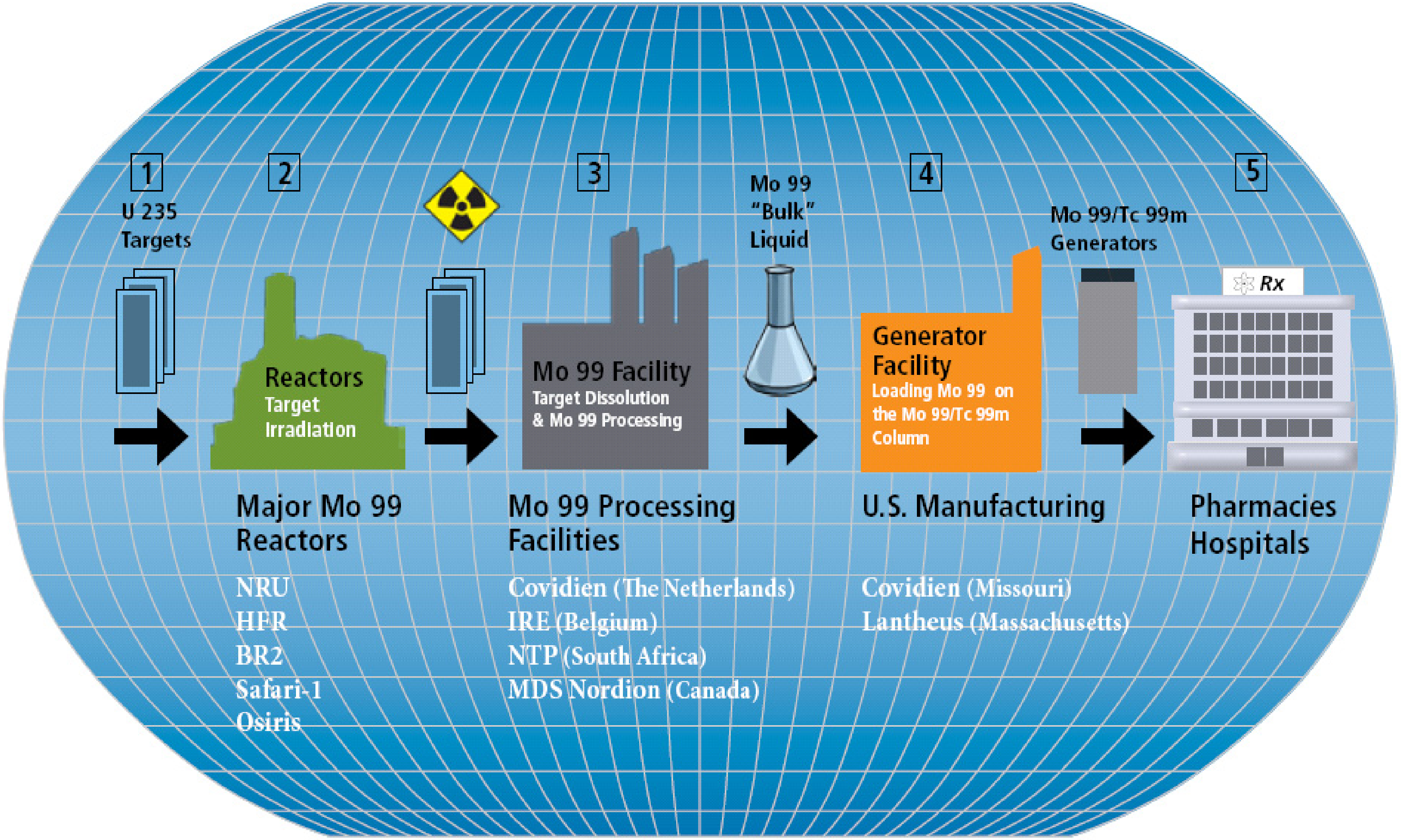
Current Production Method

Mo-99 via U-235 fission:

- Mo-99 at peak of fission mass distribution
- ~ 6 % of fissions yield Mo-99
- Half life of 66 hrs



Current Production Method



NRCan 2010 Call for Proposals for Accelerator Production ^{99m}Tc

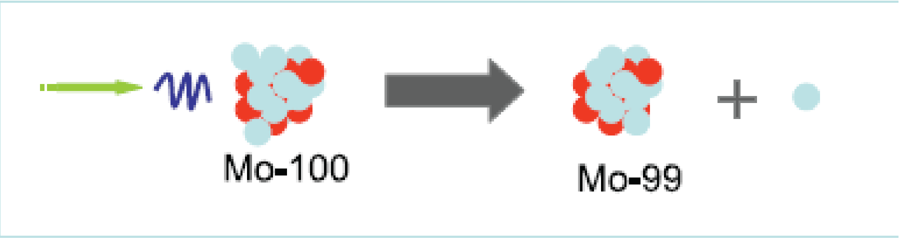
- Non-reactor-based Isotope Supply contribution Program (NISP – announced 2010 June 2)
  - $35M total funds available
  - Particle accelerator production of ^{99}Mo or ^{99m}Tc
  - Demonstrate “commercial-scale” production
  - Two approaches funded:
    - Electron linear accelerator (linac) production of ^{99}Mo
    - Proton cyclotron production of ^{99m}Tc
  - Covers a maximum of 90% of total costs
  - NRCan funding ended 2012 March 31

- Four projects funded:
  - two linac-based (CLSI and PIPE)
  - two cyclotron-based (ACSI and TRIUMF)

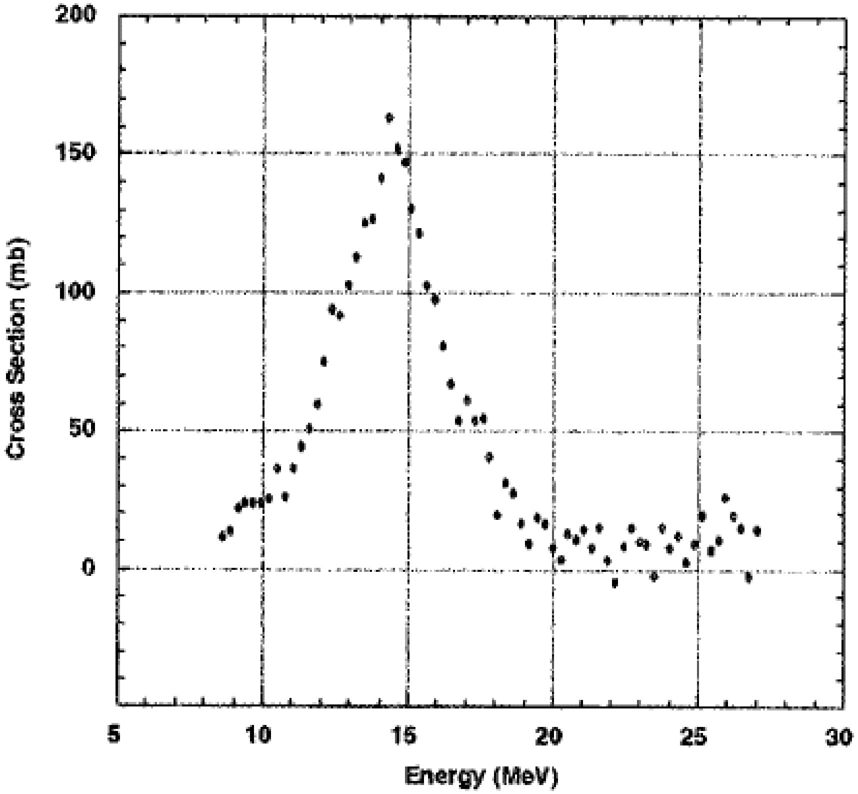
Linac Production of ^{99}Mo

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

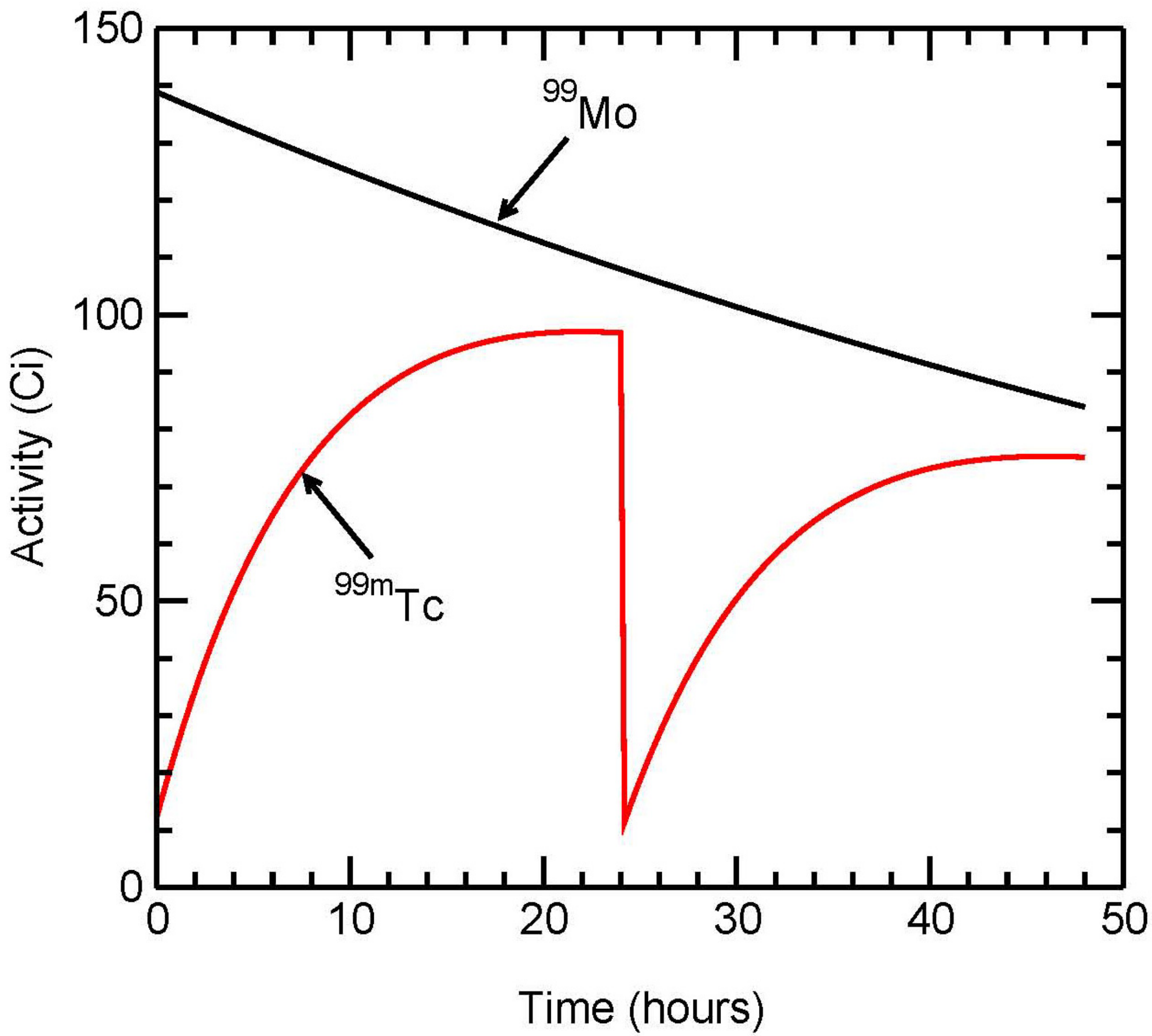
- Natural Mo about 10 % ^{100}Mo
- Available at enrichments of > 95 %
- Known for more than 40 years
- Photons produced via Bremsstrahlung using high-energy electrons from linear accelerator ⇨ high-energy X-rays



Exploit “giant dipole resonance” around 15 MeV in most heavy nuclei



Mo-99 decay and Tc-99m production



Production Capacity Needed

•For Canada, 5,500 Tc-99m procedures per day •Each procedure requires 10 - 30 mCi; thus 110 Ci/day of Tc-99m •Every 24 hrs, can elute ~100 % of remaining Mo-99 activity	•So need to replace 22 Ci/ day of Mo-99 •From EoB to delivery can be less than 1 $t_{1/2}$ (~ 3 days) •Conclude 44 Ci/day, EoB, should be adequate

- ***Certainly optimistic because of other losses***
- ***Mo-99 and Tc-99m decay whether it's used or not!***

Why Electron Linear Accelerators?

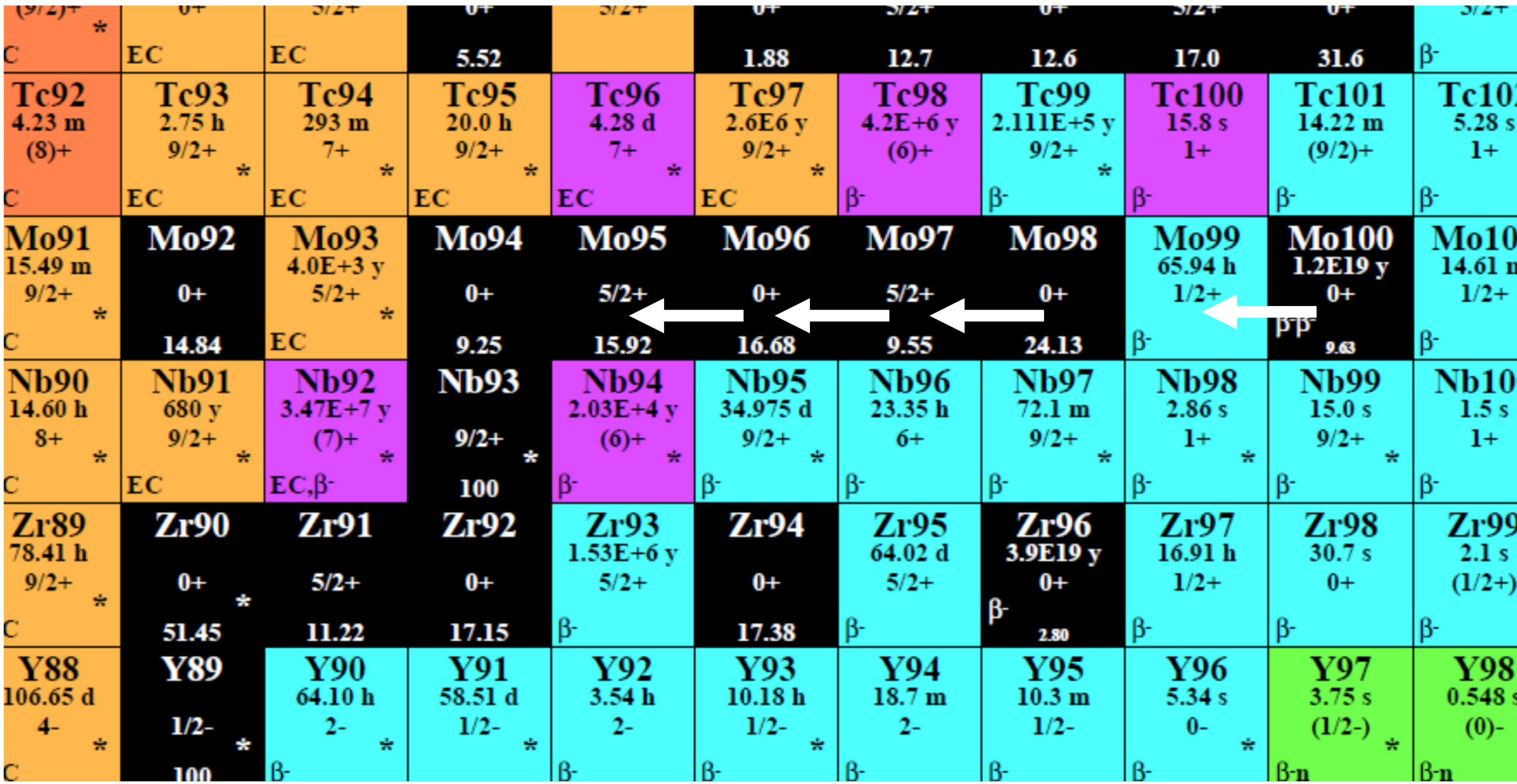
- Disadvantages:
  - Lower cross-sections (electromagnetic vs nuclear interactions)
  - Fewer reaction channels, especially for positron emitters

- Advantages:
  - Photons are more penetrating => thicker targets, windows
  - Photons are "cheap"
  - Electron linacs are generally simpler and more reliable
  - Fewer reaction channels
    - Fewer undesired isotopes
    - Less radioactive waste

- Relatively unexplored option!

Other Reaction Channels

- Arrows show (γ, n) reactions on Mo isotopes
- (γ, p) produces Nb isotopes which decay to Mo
- Trace amounts of ^{95}Nb and ^{94}Nb may arise in time

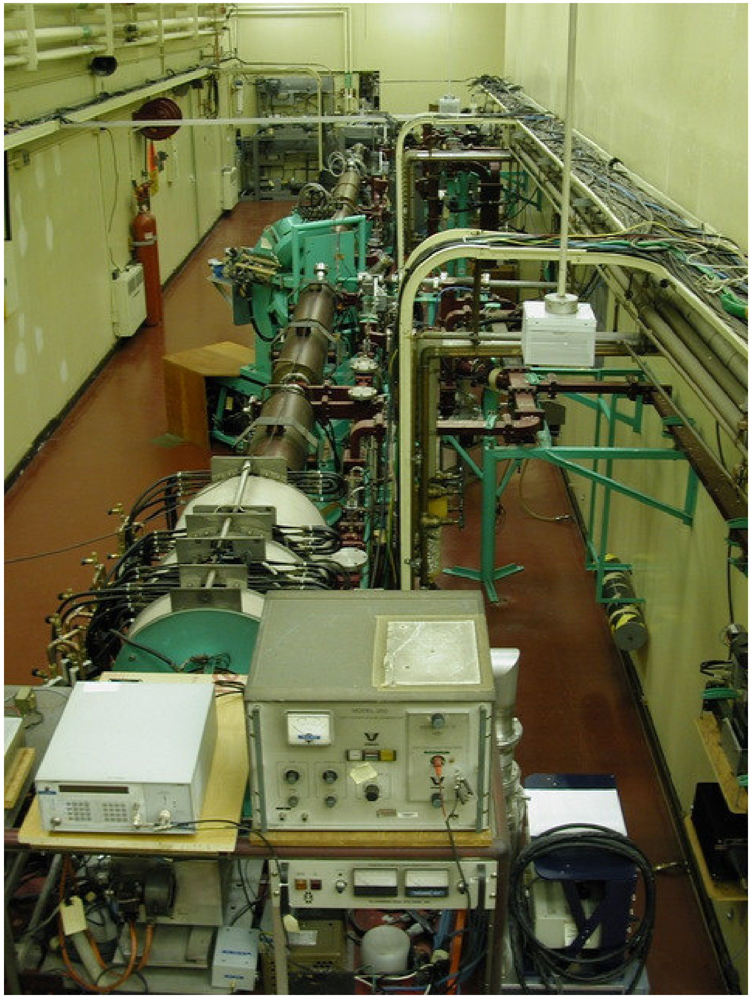


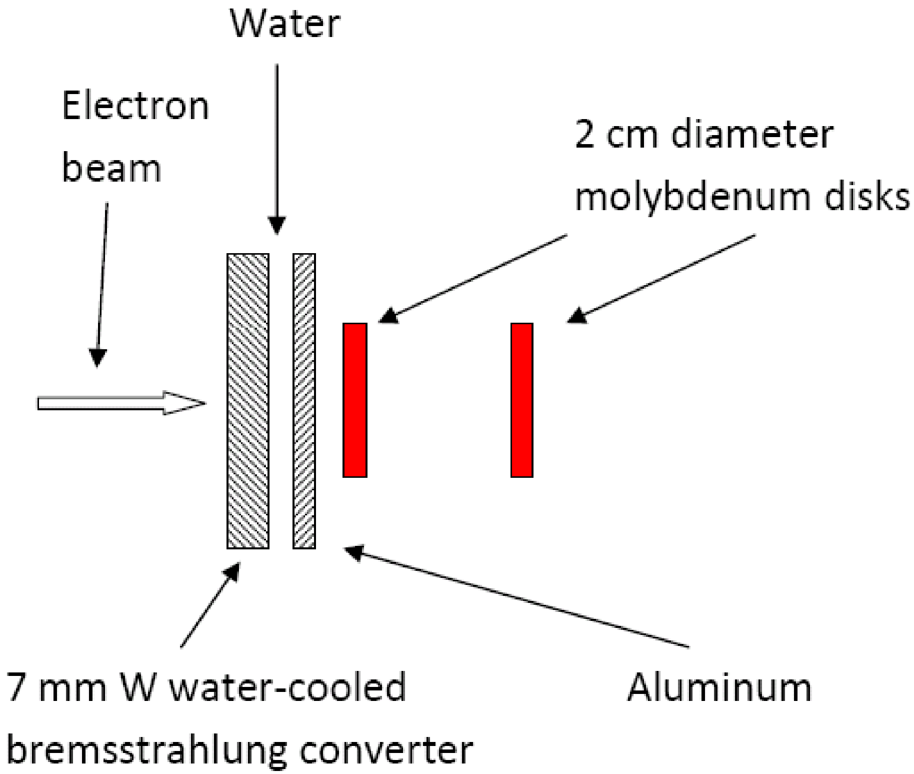
CLS Project Scope

- Fabrication methods for ^{100}Mo targets
- Low-power testing (< 3kW) of the bremsstrahlung converter and target design to validate production yield estimates
- Evaluation of the quality of the ^{99}Mo produced and the ^{99m}Tc separation process required for radio-pharmaceutical production
- Design and fabrication of high-power (>20 kW) converter and target assembly
- Installation of a high-power 35 MeV industrial electron linac at CLS
- Development of a suitable recycling process to recover the ^{100}Mo after irradiation and ^{99m}Tc separation for future targets

NRC (Ottawa) - INMS

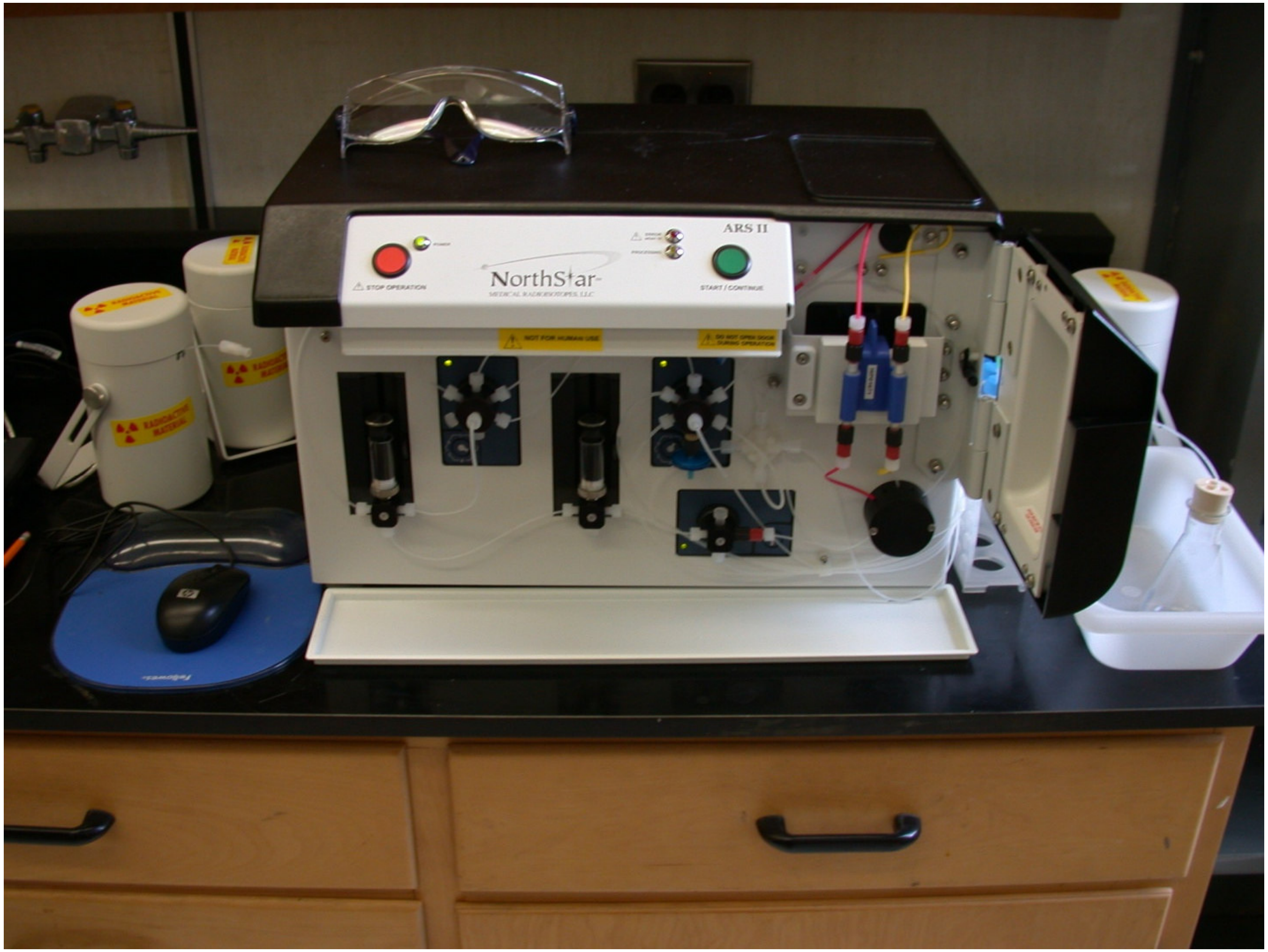
- Proof-of-concept work using 35 MeV, 2 kW linac at INMS





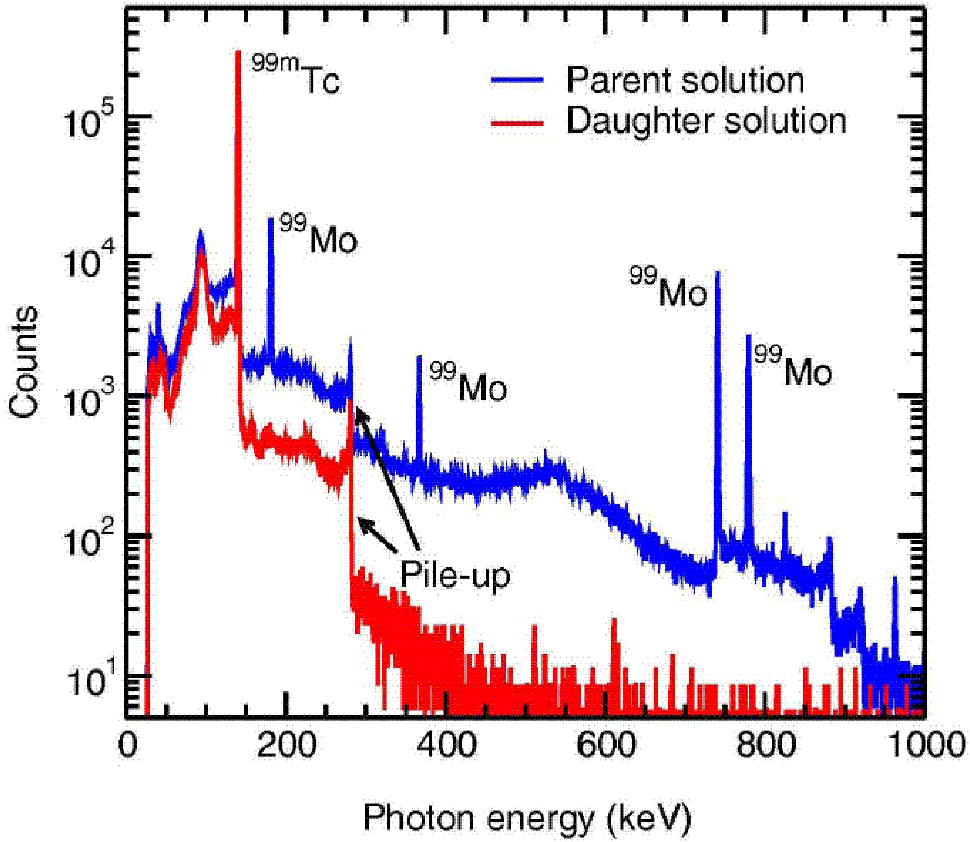
NRC (Ottawa) - INMS

Used automated separator to extract ^{99m}Tc from Na_2MoO_4 solution.



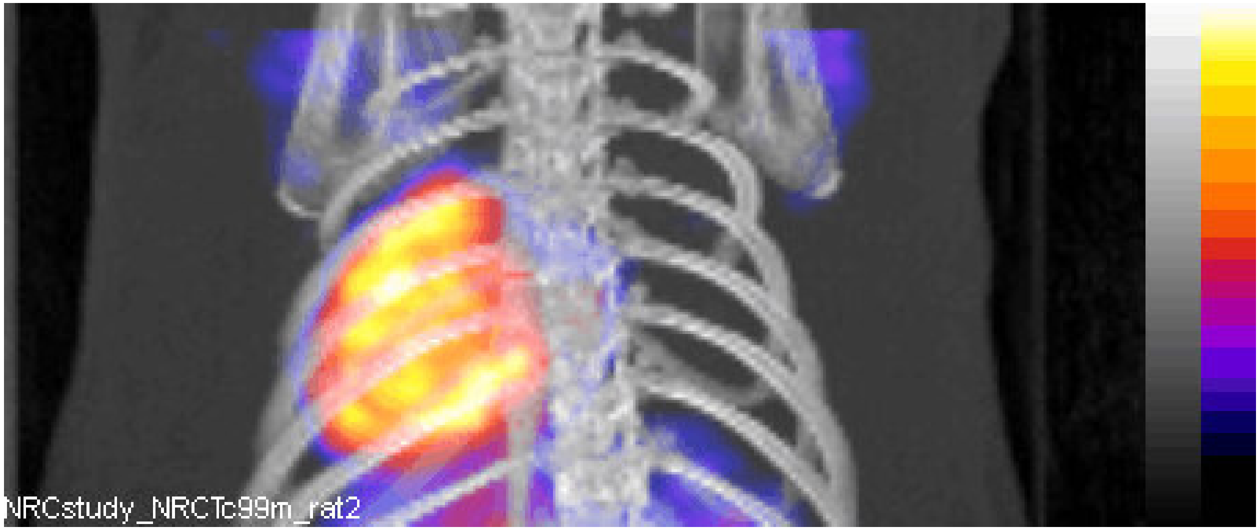
NRC (Ottawa) - INMS

- $Na[^{99m}TcO_4]$ is clinically equivalent in:
  - Radio-purity
  - No Al contamination
  - pH 5 – 9
  - Sterility
  - Radio-chemical purity
  - Pyrogen free
- Meets all USP tests



NRC + Ottawa Heart Institute

- Performed pre-clinical trial comparing linac ^{99m}Tc to standard Mo-generator
- Used heart scan comparison on three rats
  - Heart scans comparable
  - Detected more Tc in kidneys with linac-sourced ^{99m}Tc
  - Identified problem in pH adjustment process in separator



NRC + Winnipeg HSC

- Three ^{100}Mo irradiations each yielding ~6 GBq (~160 mCi) ^{99}Mo
  - Performed at NRC linac
  - ~12 hours at 3 kW, 35 MeV

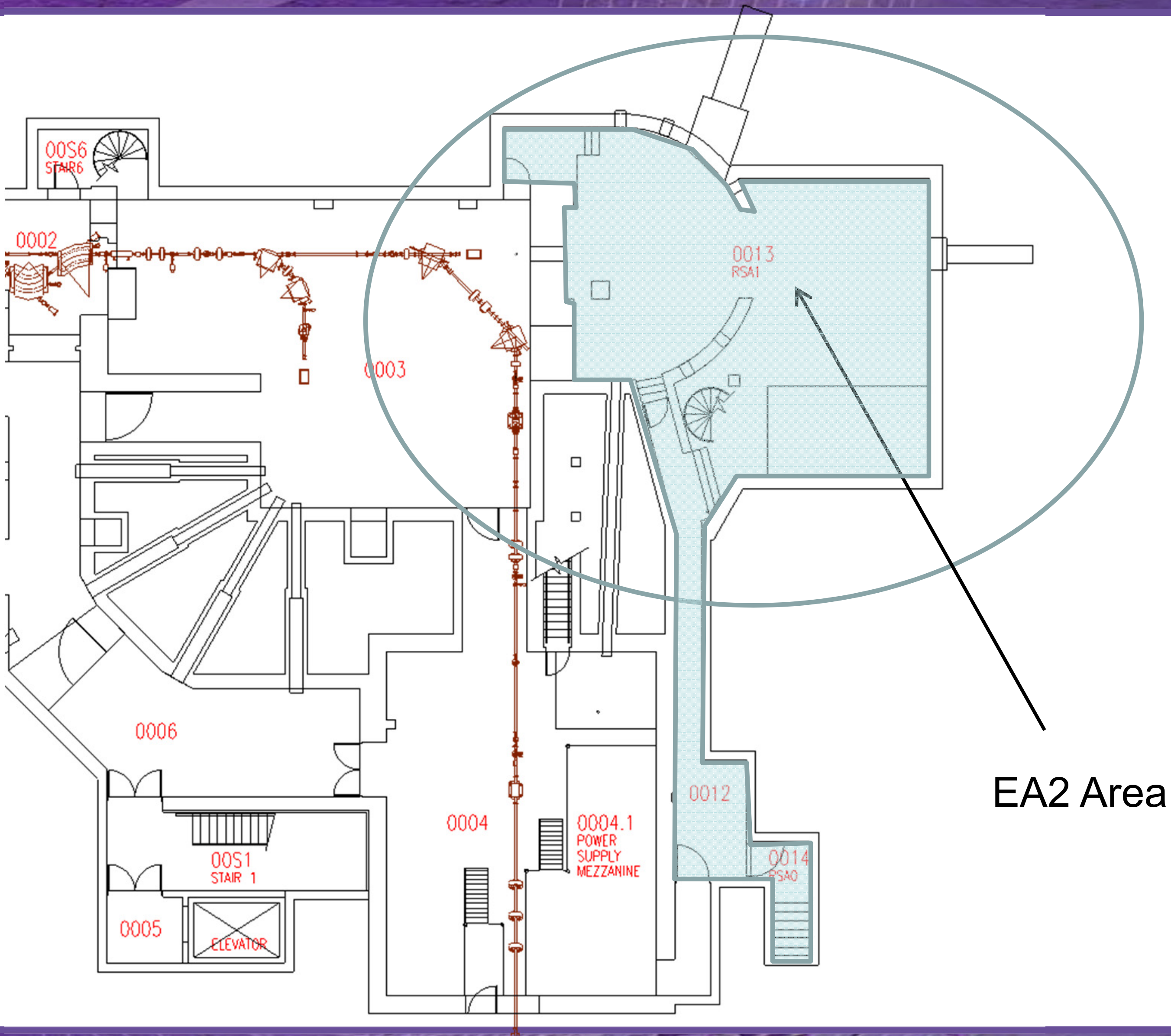
- Targets were shipped Winnipeg HSC Radiopharmaceutical Research Group for evaluation of ^{99}Mo and ^{99m}Tc

- ^{99}Mo targets were dissolved, and ^{99m}Tc extracted (~90% efficiency) using automated solvent-solvent extraction generator (developed at HSC/CCMB)
  - ^{99m}Tc-pertechnetate passed standard QC for Mo-breakthrough, alumina and pH up to 7 days after delivery
  - ^{99m}Tc-labelled MDP, DTPA, MIBI, and MAA were produced
  - MDP and DTPA consistently passed radiochemical purity, pH and stability tests
  - MIBI and MAA failed one or more tests, probably due to low level of activity at time of production

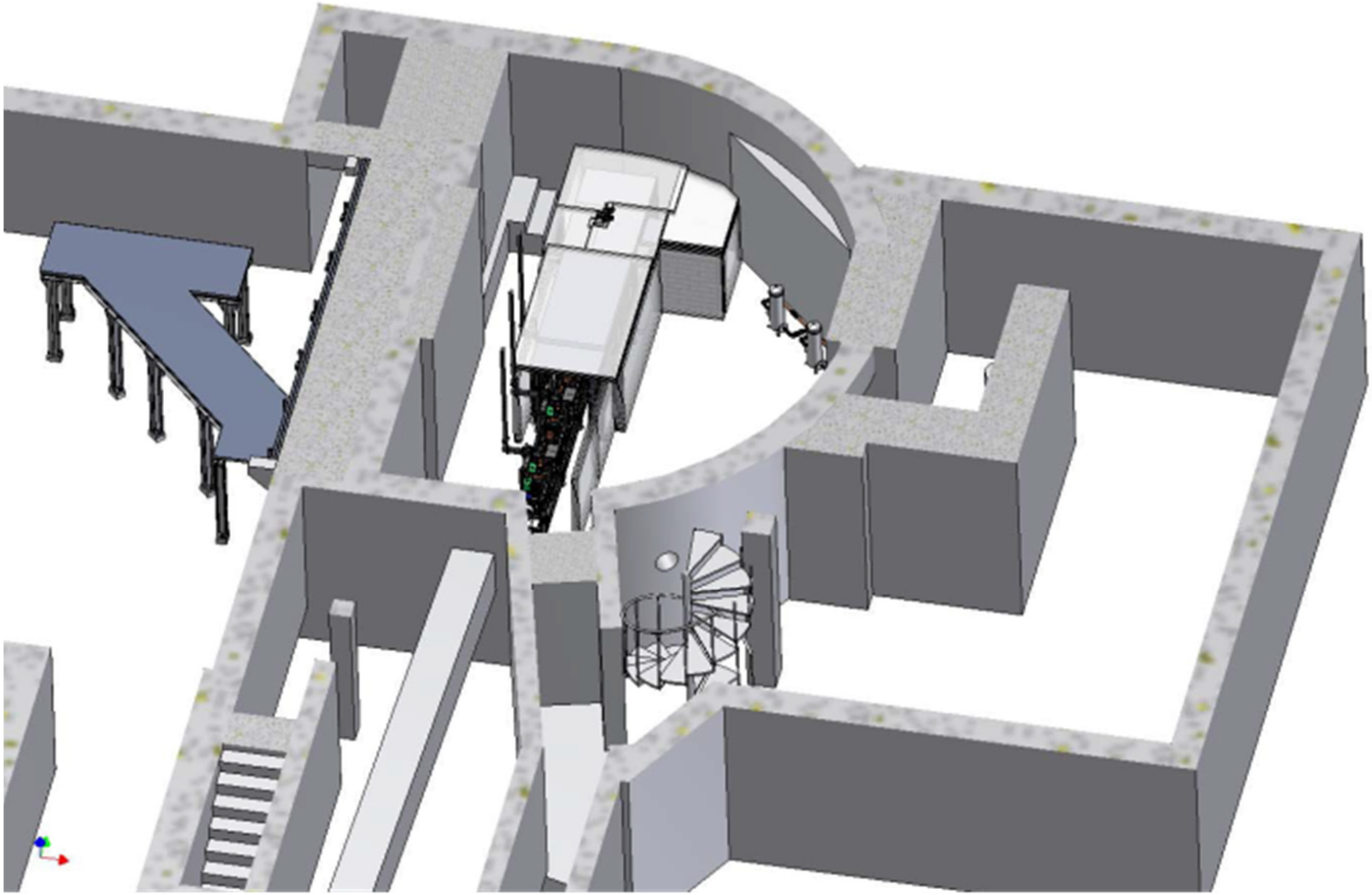
CLS Work

- Install 35 MeV, 40 kW, industrial linac in an existing underground experimental hall
  - Three 1.2m S-band on-axis coupled standing-wave sections
  - Three modulators + klystrons 5MW peak, high-duty factor
  - 60 kV thermionic gun
- Design & build bremsstrahlung converter and target holder
  - must handle > 20 kW beam power
  - modest remote handling requirements
  - evaluate maximum power handling of converter and Mo-100 targets
- Install nuclear substance laboratory to support target manufacture and recycling
- Develop plan to support post-project activities
- Winnipeg HSC to evaluate production of ^{99}Mo from CLS

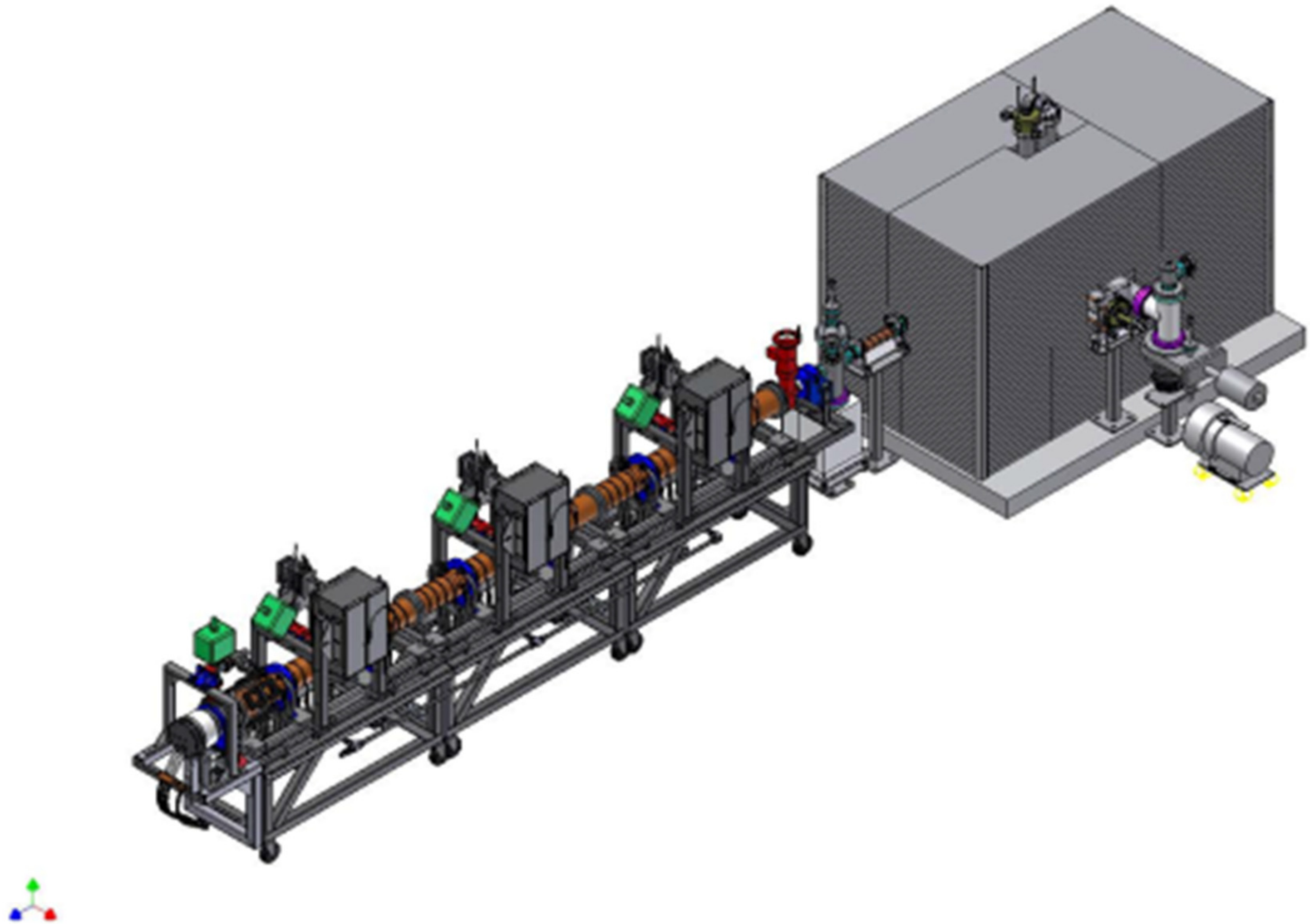
Location of Isotope Linac at CLS



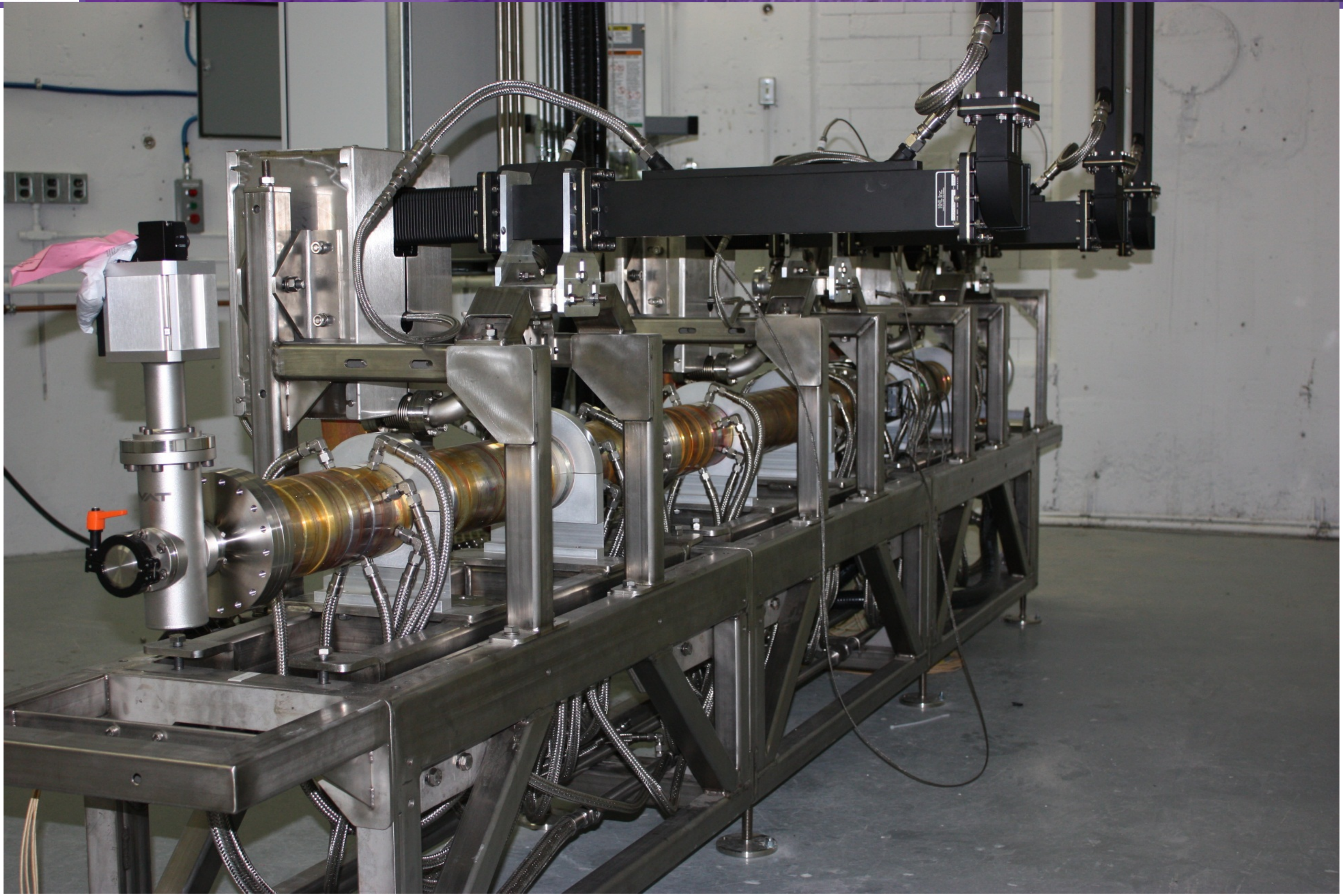
Layout of Isotope Production Facility



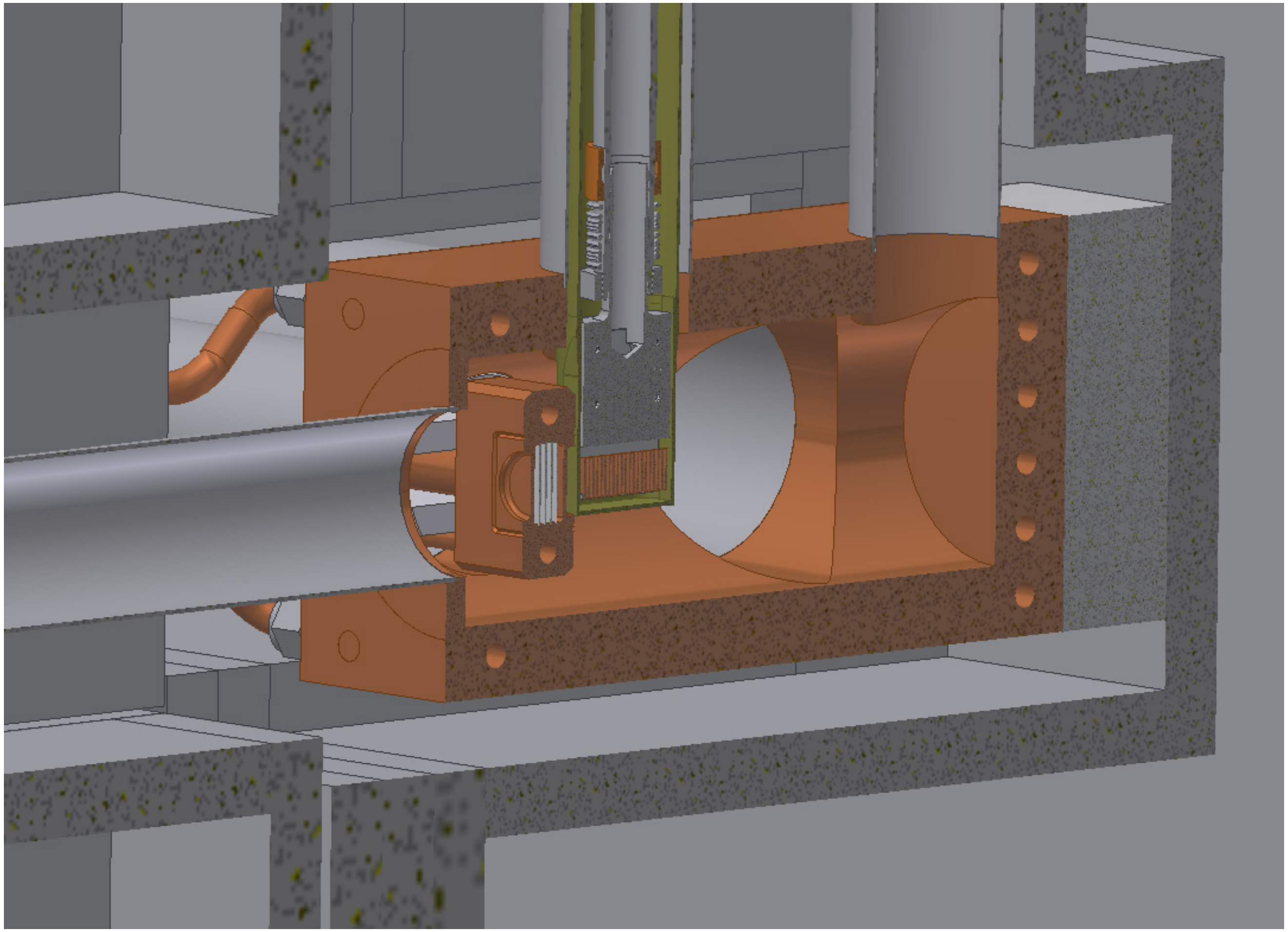
Isotope Linac and Target Assembly



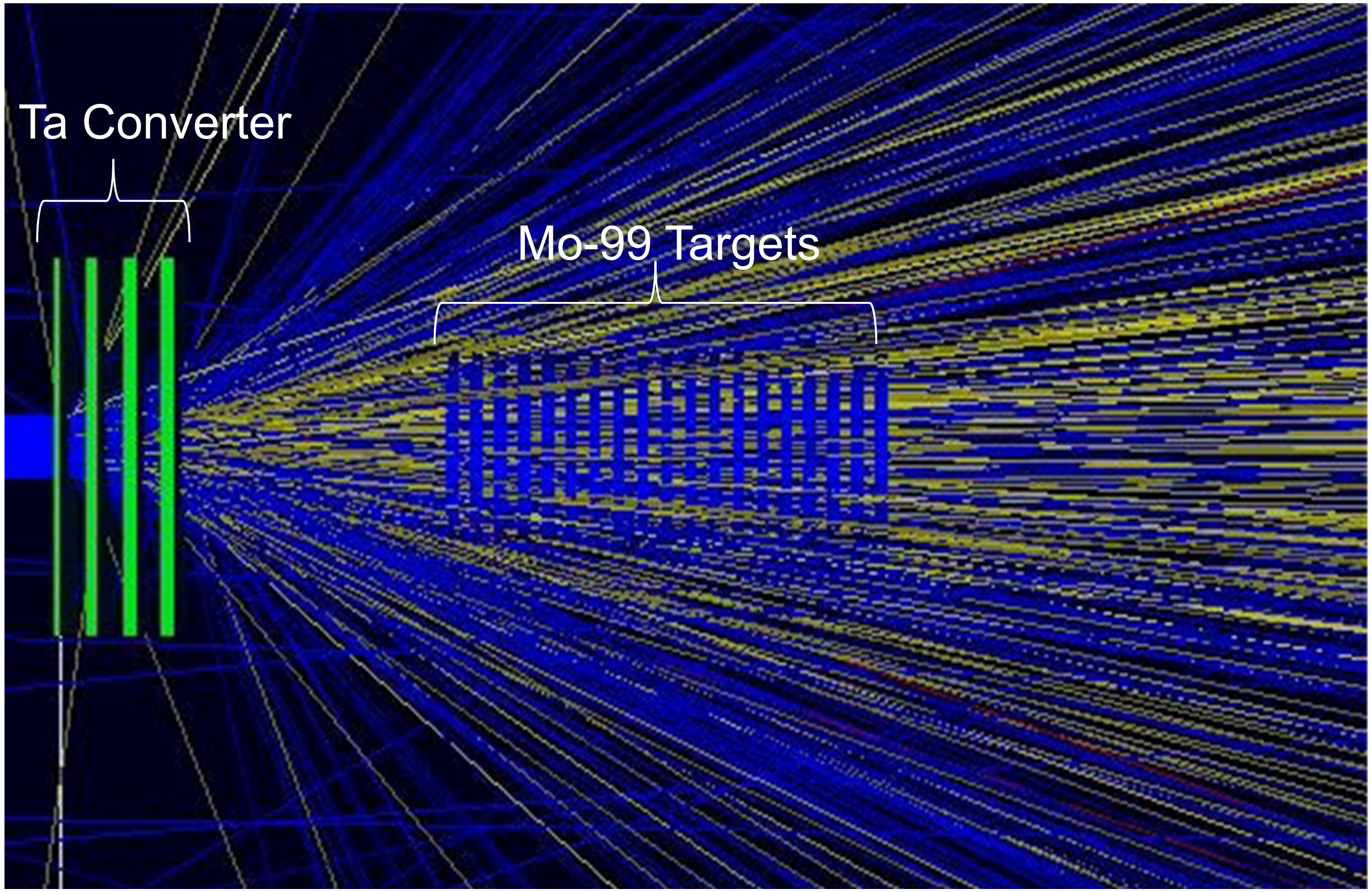
Isotope Production Electron Linac



Converter and Target Holder

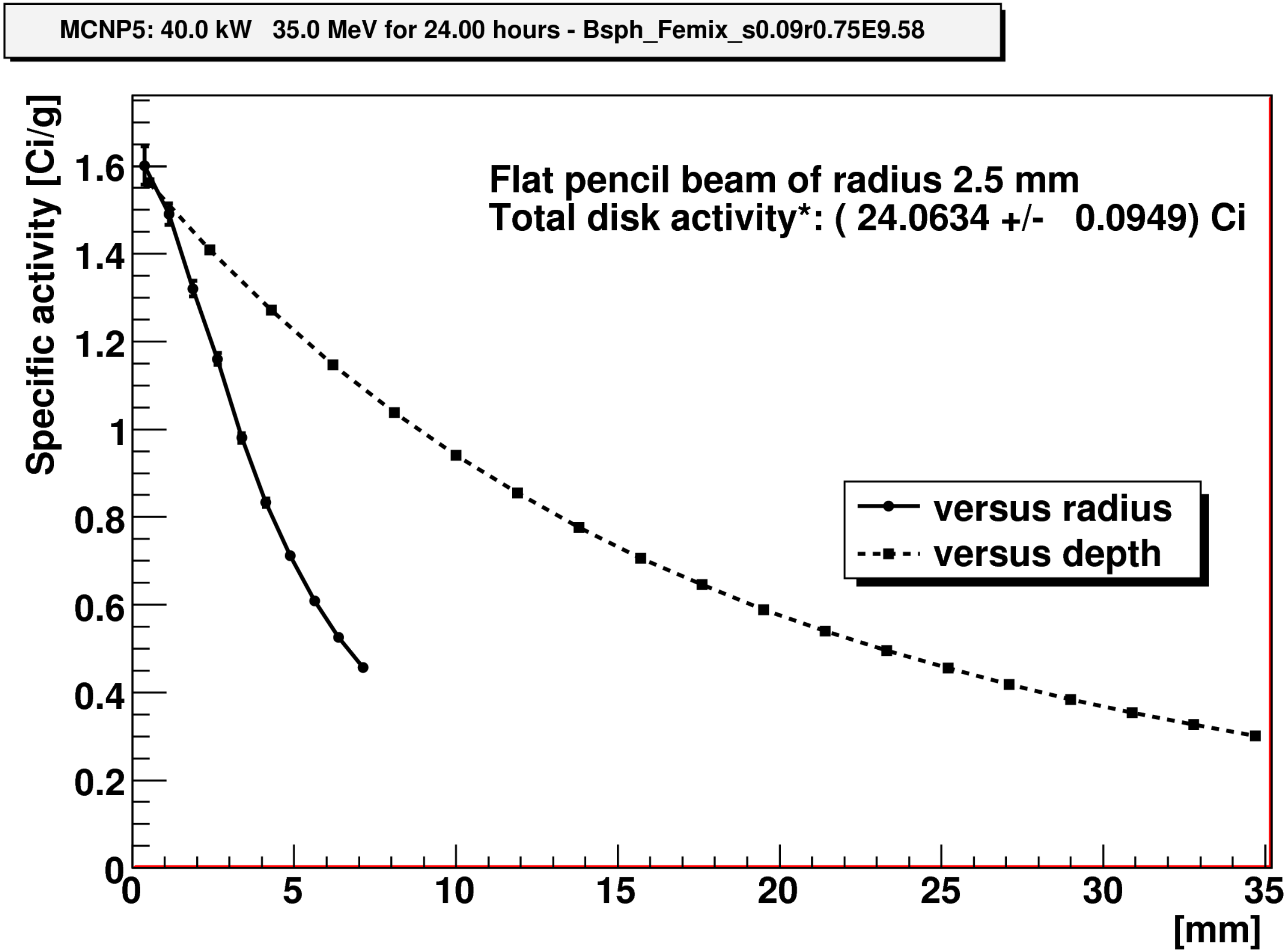


Photon Shower (EGS++)



Electrons and photons above 14 MeV shown

Mo-99 Specific Activity after 24 hours



Future for CLS Isotope Project

- Start commissioning linac this June, with first irradiations in August

- Work to end of current project (2013 March 31)
  - Demonstrate initial ~2.5 – 5 Ci (~100 – 200 GBq) per day production rate
  - Perform full suite of analysis tests on ^{99}Mo and extracted ^{99m}Tc at Winnipeg HSC
  - Continue with refining the processes and improving production rate for more than 20 Ci (800 GBq) per day at full power

- Explore commercialization options to manage the future development
  - Construct additional facilities elsewhere in Canada
  - Investigate possible production of other medical isotopes

- Obtain Health Canada approvals for this ^{99}Mo/^{99m}Tc production method
- Relocate present linac as a production facility
  - Possibly locate with the new PET cyclotron facility at U of Saskatchewan
  - Design with infrastructure suitable for routine production

Project Team

- Canadian Light Source Inc. (lead)
- National Research Council (INMS and IMI)
- Winnipeg Health Sciences Centre (U of Manitoba)
- Mevex Corp.
- Consultants:
  - retirees from AECL, Dupont, CNSC
  - DoyleTech Inc. – business case

With support from:

- University of Ottawa Heart Institute
- NorthStar Medical Radioisotopes LLC
- University Health Network (U of Toronto)
- Acsion Ltd. (member of PIPE)

Project Funding:

- Natural Resources Canada ($10M)
- Province of Saskatchewan ($2M)