TRIUMF

Canada's national laboratory for particle and nuclear physics
Laboratoire national canadien pour la recherche en physique nucléaire
et en physique des particules

Direct production of Tc-99m including a Mo-100 supply.

TJ Ruth

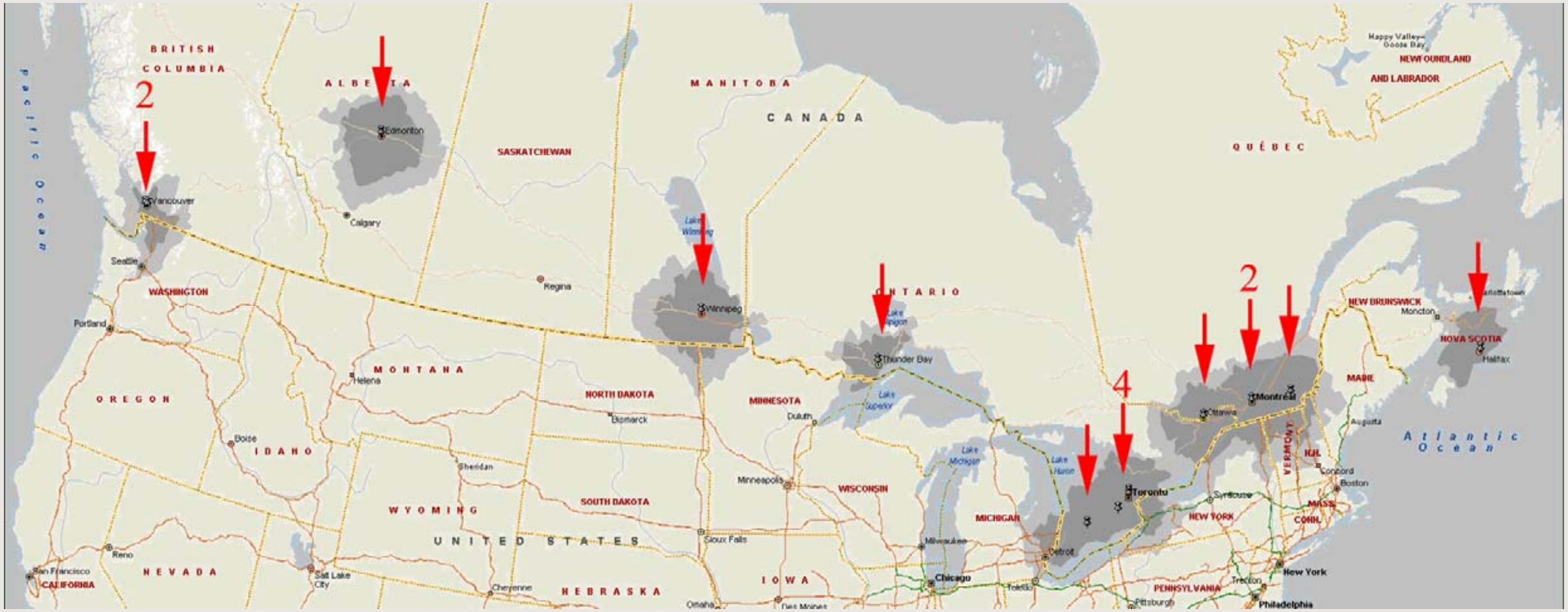
TRIUMF/BCCA

NSERC CRSNG

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Natural Resources Canada
Ressources naturelles Canada
Canada

Networking Canada’s Cyclotrons



Red arrows indicate operational or nearly operational medical cyclotron facilities. Some arrows indicate more that one facility. Dark and light gray shading represent 120 and 180 minute land transportation regions.

BC Cancer Agency CARE + RESEARCH
TRIUMF
LAWSON HEALTH RESEARCH INSTITUTE
NSERC CRSNG
CIHR IRSC

NISP Collaboration

TRIUMF

BC Cancer Agency
CARE & RESEARCH
An agency of the Provincial Health Services Authority

LAWSON
HEALTH RESEARCH INSTITUTE

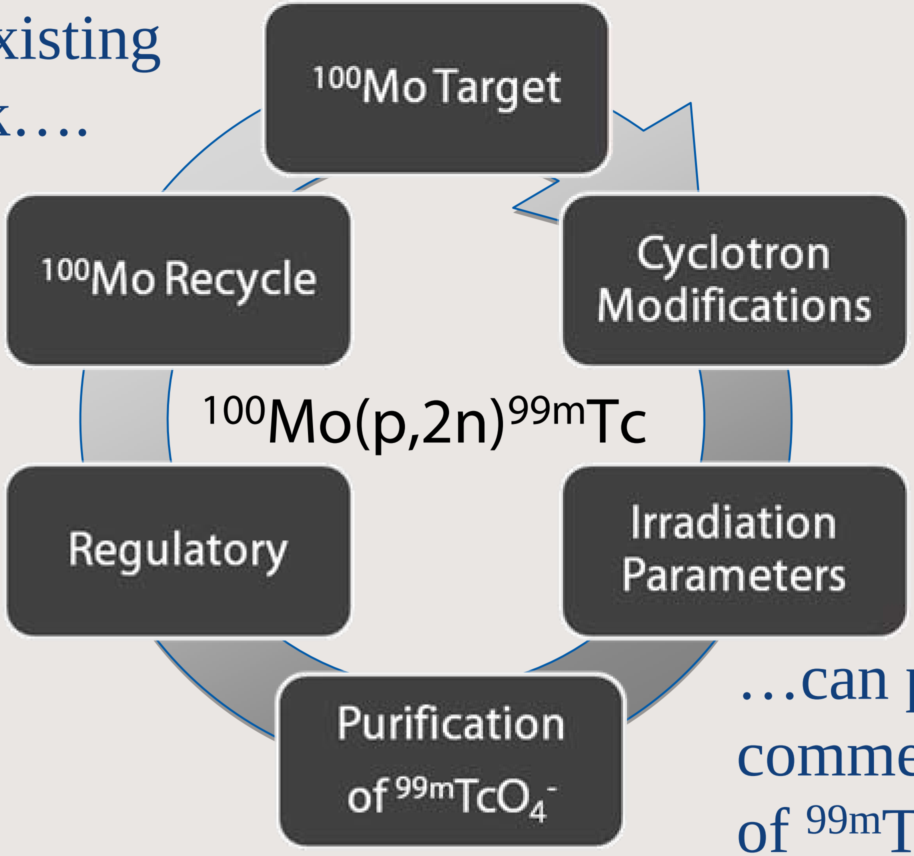
cpdc

With support from: GE, Nordion, AAPS

TRIUMF

The Process: Direct Production of ^{99m}Tc

To demonstrate existing cyclotron network….



…can produce commercial quantities of ^{99m}Tc

Goal: Help formulate policy on $^{99}Mo/^{99m}Tc$ medical isotope production

Technical Goals: Cyclotron-based Production

- Establish optimal irradiation conditions
  - Beam (energy, current)
  - Target characteristics (purity, plate, housing, transfer, recycle)
  - Time (irradiation, cooling)
- Goals
  - Establish production quantity
  - Identify impurities
    - Specific activity (99m/99g ratios, other long-lived Tc)
      - Implications in radiopharmaceutical chemistry, patient dose
    - Radionuclidic purity / other non-Tc isotopes present
      - Implications in production waste, recycling, patient dose
  - Identify/Understand regulatory space
    - Production specifications, transport, shelf-life, etc.
    - To meet healthcare system demands, maximize safety
  - Economics

5

Team Equipment/Capabilities

- TR19 (vaulted), PETtrace (self-shielded, vaulted)

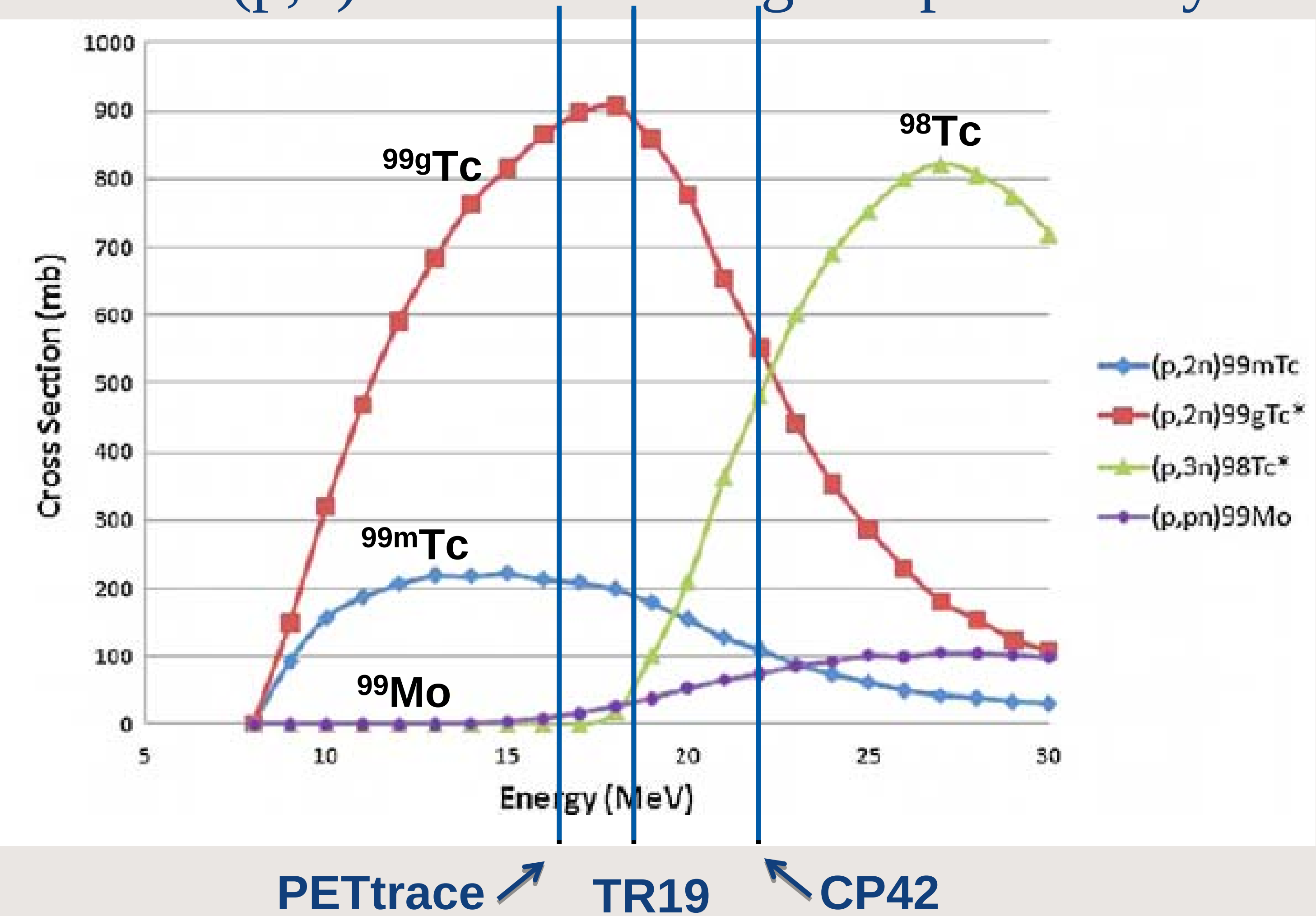
TR19
13-19 MeV, ≤200μA
Upgrade to:
300 μA (approved)

GE PETtrace
16 MeV, ≤100 μA
Upgrade to: ≤150 μA

Not shown: CP42, 20-42 MeV, ≤200μA

Theor. Calculations: Beam Energy

^{100}Mo(p,x) reactions of highest probability



A. Celler, X. Hou, F. Bénard, T. Ruth, Phys. Med. Biol. 2011, 56, 5469

Infrastructure Requirements

1) Upgrade to **beam current** of GE PETtrace & ACSI TR19

2a) Solid target system for GE PETtrace

– suitable for self-shielded cyclotron installation

2b) Solid target system for ACSI TR19

– including local shield

3) Target plate

4) Target transfer system for both cyclotrons

5) Receive & Dissolve system for both targets

6) Purification system for separation of Tc-99m

7) Hot cells for process apparatus

8

Infrastructure Requirements

1) Upgrade to **beam current** of GE PETtrace & ACSI TR19

2a) Solid target system for GE PETtrace

– suitable for self-shielded cyclotron installation

2b) Solid target system for ACSI TR19

– including local shield

3) Target plate

4) Target transfer system for both cyclotrons

5) Receive & Dissolve system for both targets

6) Purification system for separation of Tc-99m

7) Hot cells for process apparatus

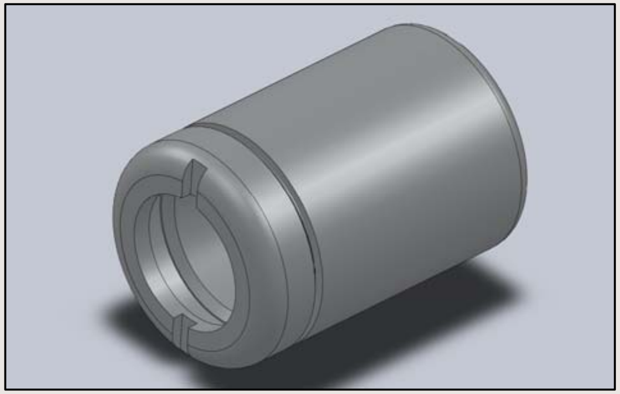
TRIUMF

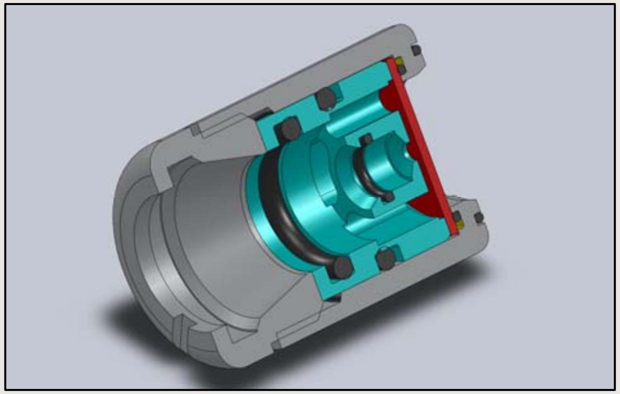
Beam Current Upgrades

- Purchased from respective cyclotron vendors
  - PETtrace to 150 μA
  - GE has obtained CNSC certification of upgraded PETtrace
  - TR19 to 300 μA
  - ACSI has applied for CNSC certification of upgraded TR19
- Installation to be completed in December
- TR19 upgrade includes beamline
- All three facilities need license amendments for operation at full current

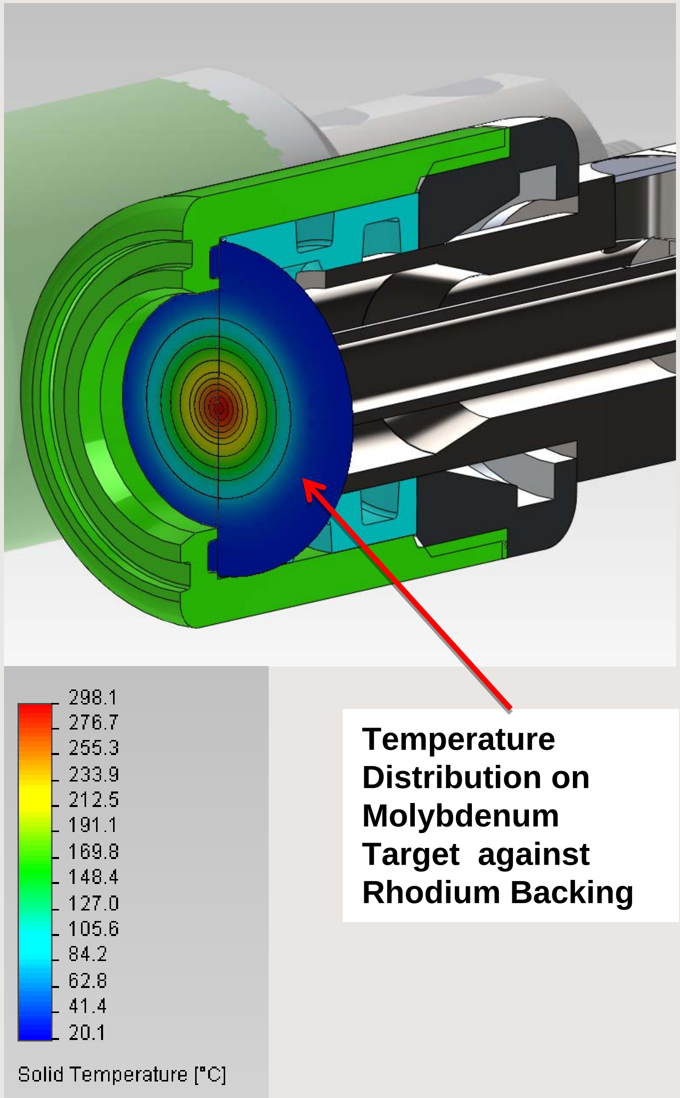
Solid Target System

- PETtrace

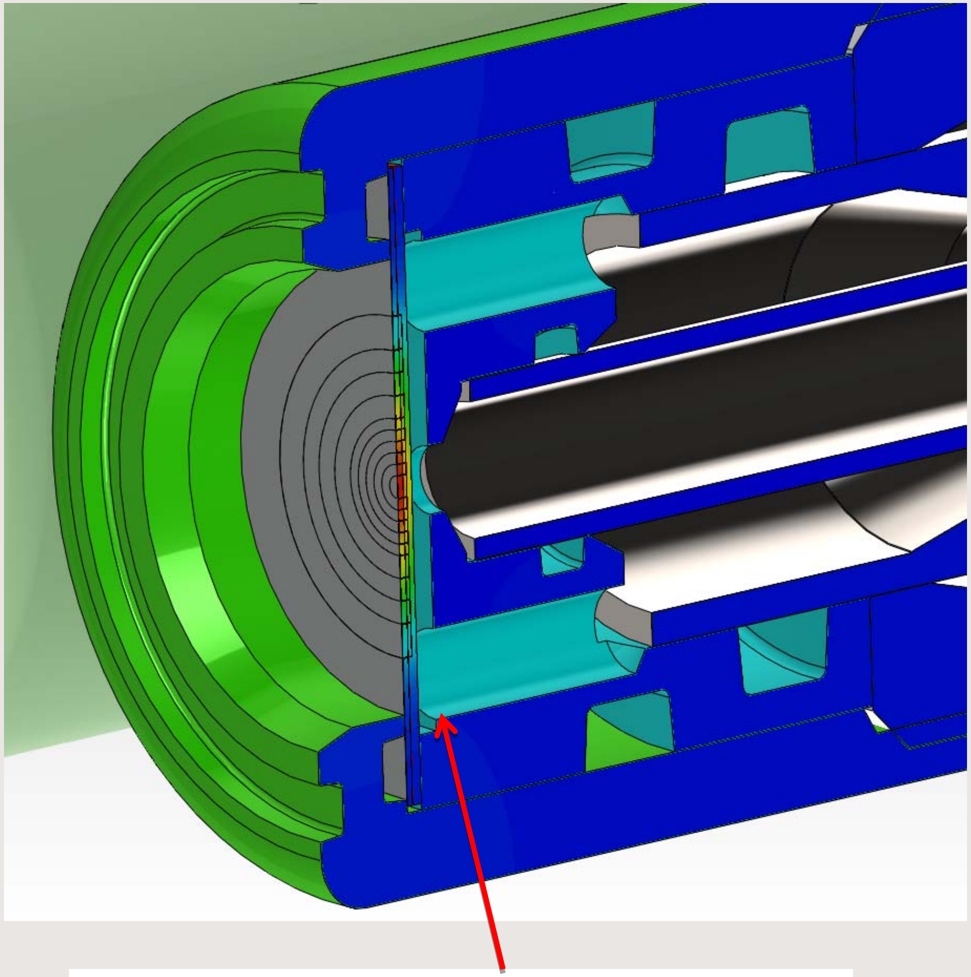




Target Plate: Simulation Results



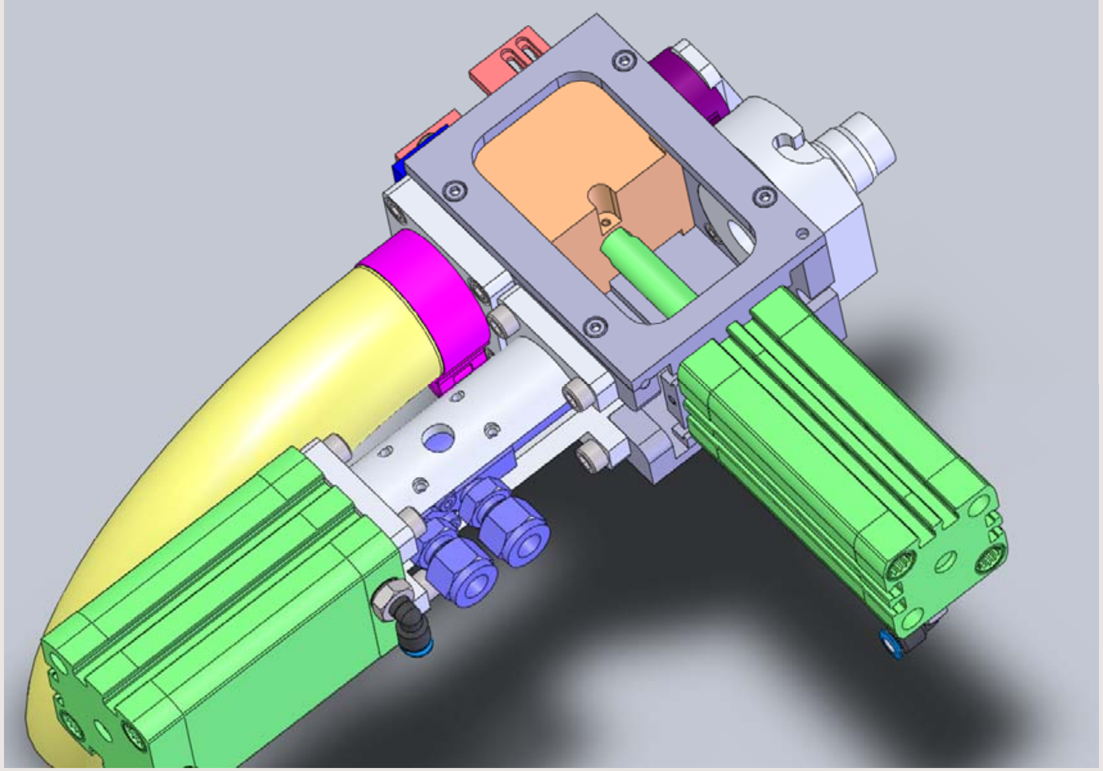
Temperature Distribution on Molybdenum Target against Rhodium Backing



Section View – Temperature distribution thru axial plane of ^{100}Mo GE Target Assembly

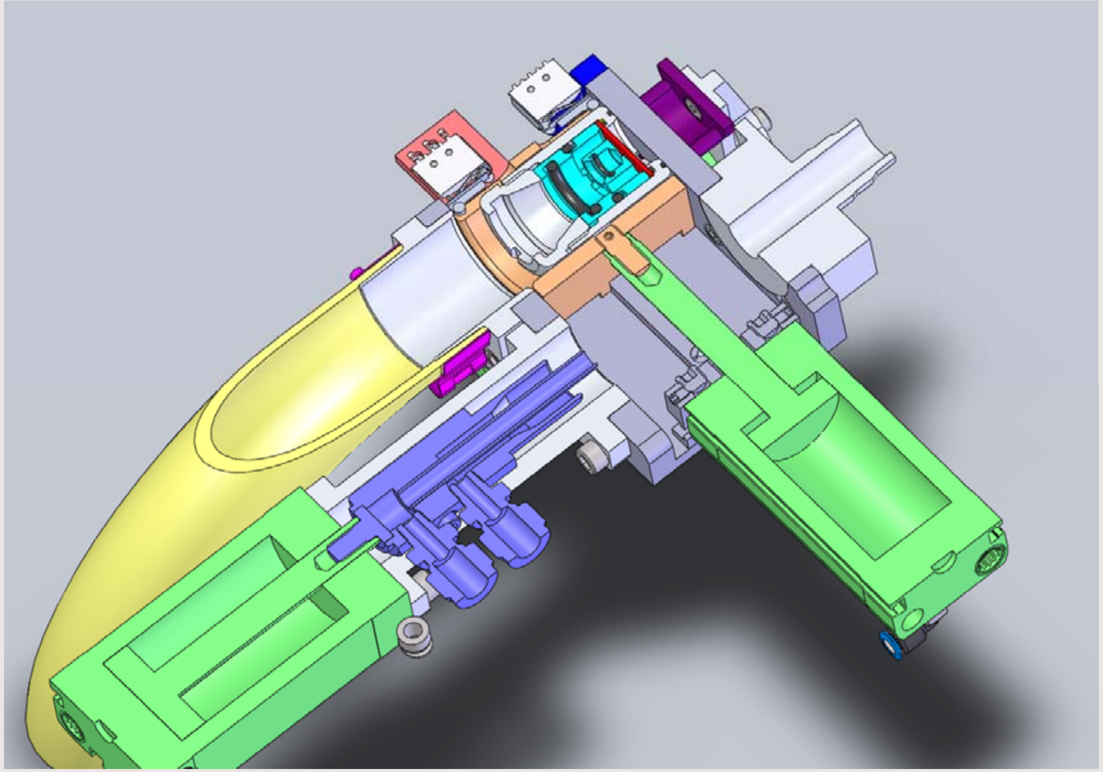
Solid Target System

- PETtrace target assembly
  - 20 x 20 x 10 cm



Solid Target System

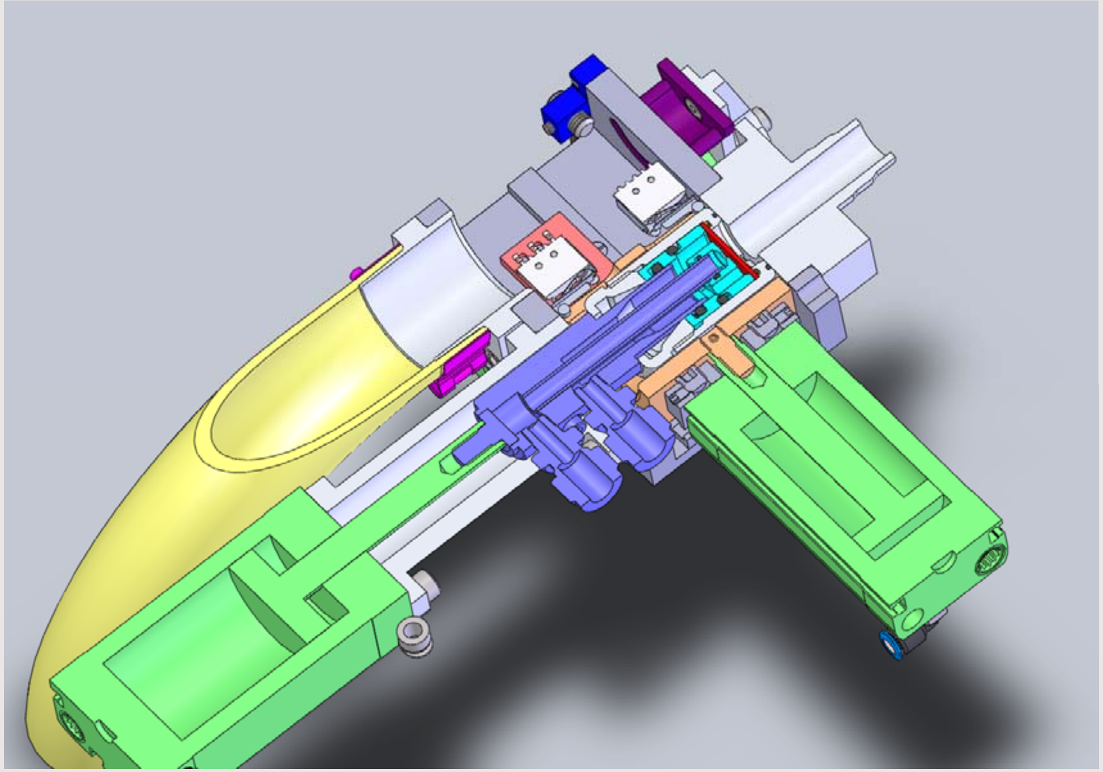
- PETtrace target assembly



14

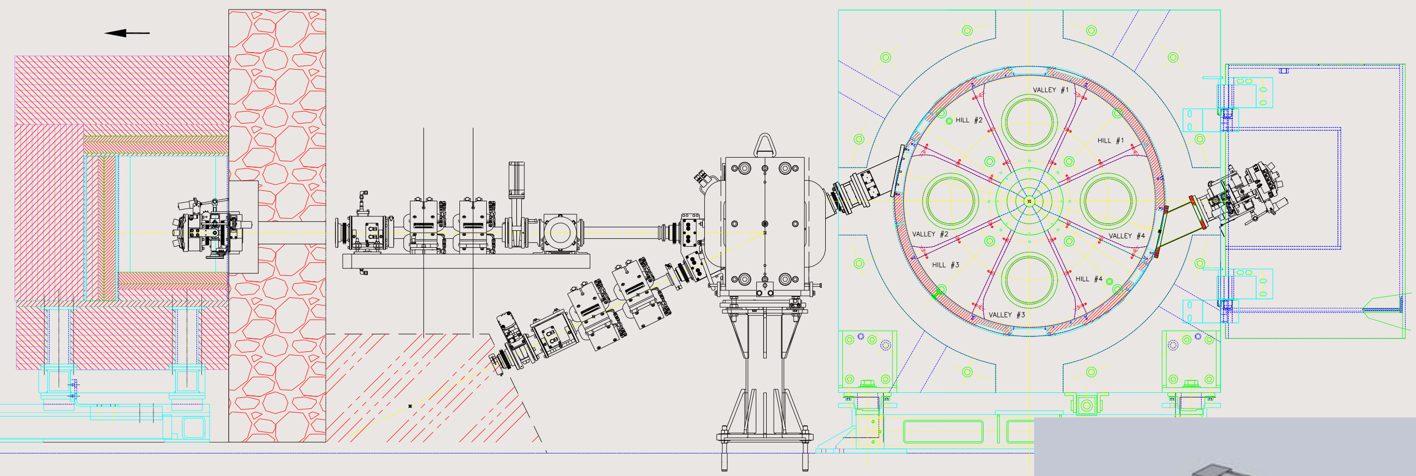
Solid Target System

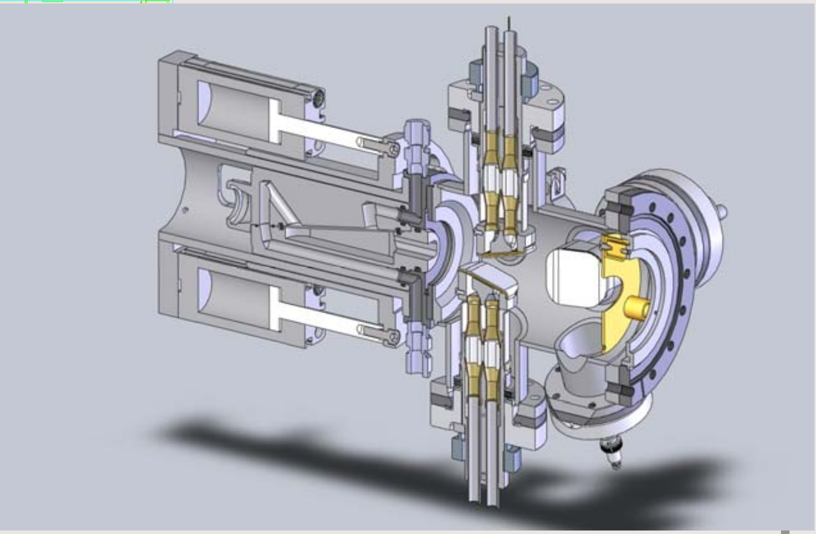
- PETtrace target assembly



Solid Target System

- TR19 beamline installation





Target Plate: Mo-100 coatings

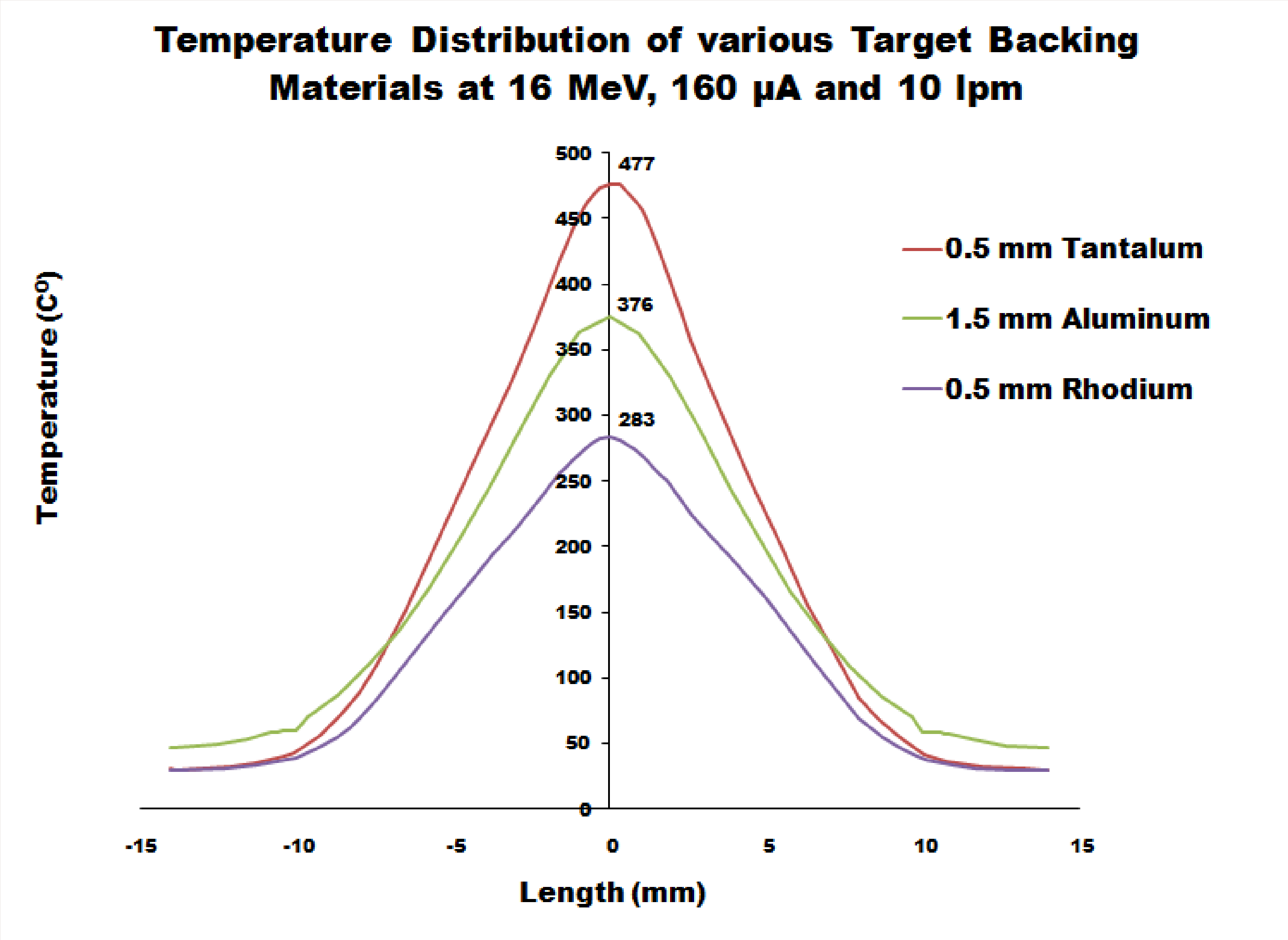
- Targets to utilize full beam power
  - GE PETtrace
    - 16.5 MeV, 150 μA
    - Dissipate 2.5 kW (1 kW in moly)
  - ACSI TR19
    - 18 MeV, 300 μA
    - Dissipate 5.4 kW (2.4 kW in moly)

TRIUMF

Target Plate: Design

- Targets to degrade beam energy to ~10 MeV
- Match or exceed beam area
- Utilize enriched Mo-100 (>97%)
  - $0.85/mg to $2.65/mg
- GE PETtrace
    - Range 0.3mm
    - 0.6g for 15 mm diameter beam
- ACSI TR19
    - Range 0.4mm
    - 0.8g for 10 x 20 mm beam

Target Plate: Temperature Distribution on Target Face



Methods to make ^{100}Mo coatings

- Two issues
  - Uniformity of coating
  - Adherence to backing
- Methods
  - Powder pressing & sintering
  - Electrophoretic deposition & sintering

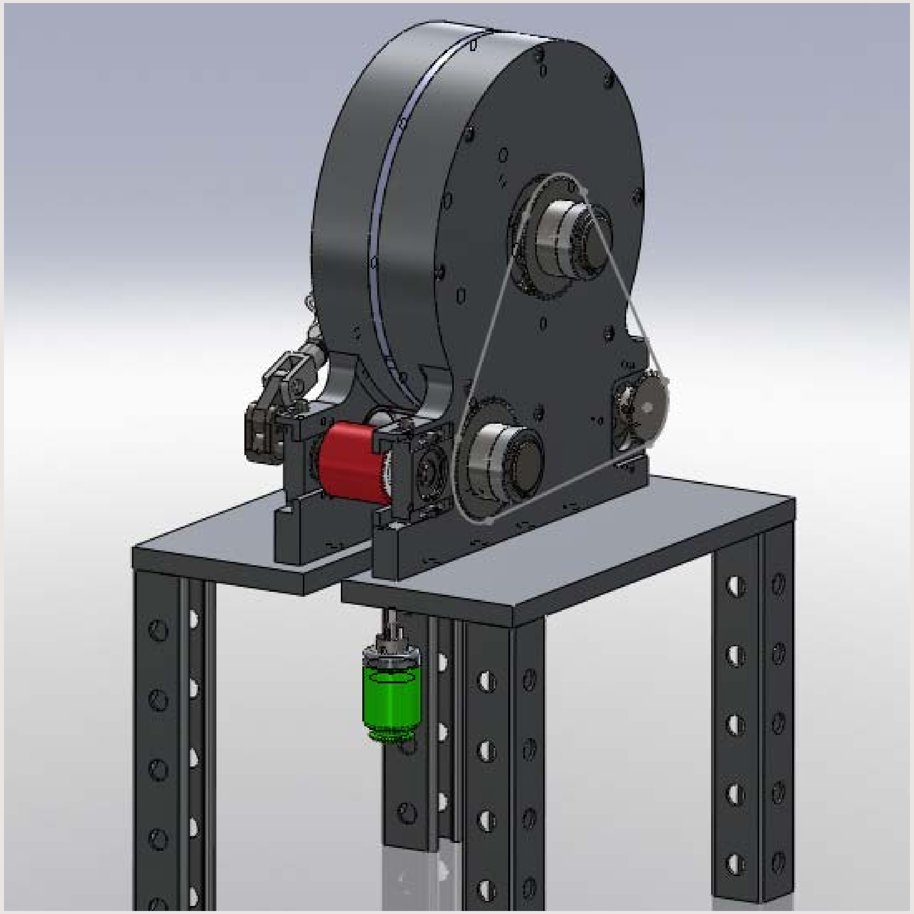
Electrophoretic Deposition

- Many commercial applications of the concept
- Deposit material from suspension
  - Not a chemical process
- Allows thin or thick coatings
- Suitable for orthogonal or oblique targets

Electrophoretic Deposition

- Achieved deposits up to 800 mg to date
- Irradiated at up to 80 μA to date
- Target production is ongoing

4) Target Transfer System

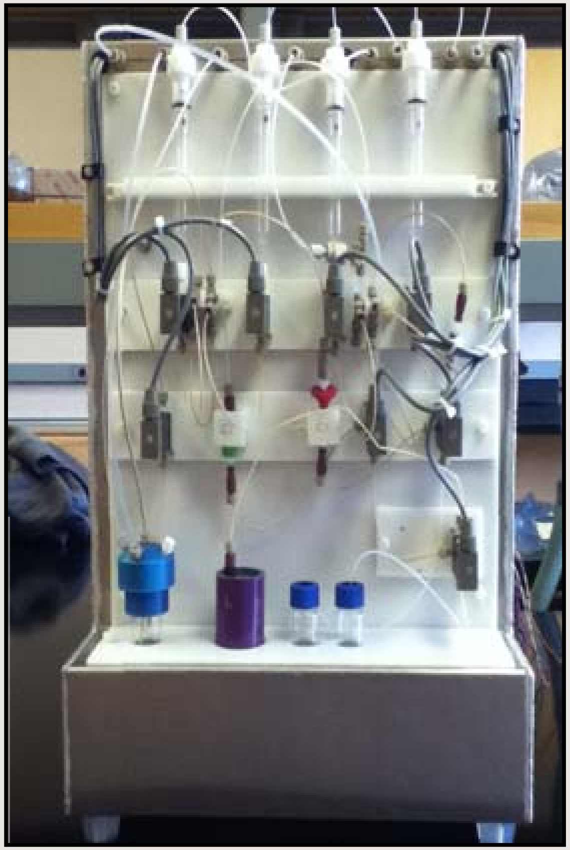


7) Capital upgrades

- TRIUMF MHESA lab

6) Automated Isotope Purification

Remote separation system



- **Dissolution:** rapid in H_2O_2
- **Ion exchange:** Dowex™ vs ABEC
- Dowex is flow dependent
- Capture @ <2mL/min, release @ <1 mL/min
- **Time:** complete in <30 min.
- **Efficiency:**
  - Dowex: 72% (35 min)
  - ABEC >90% (30 min)
- **Radiochemical Purity:** >99.99% TcO_4
- **Trace analysis:** <10 Bq Mo-99, <5 ppm Al^{3+}

- Other Tc isotopes detected: ^{97}Tc, ^{96}Tc, ^{95}Tc
- 97.39% enriched ^{100}Mo used
  - May require higher enrichement (99.1%)

T.J. Morley et al. Nuc. Med. Biol. 2011, in press

6) Product Losses, Impurity

Mo-100 irradiation				
EOB =	1137	Dose =	18.9	uAh
Target plate pre-dissolution =			86.9	mCi @ 1206
	Product vial =		70.8	mCi @ 1256
	Waste 1 vial =		6.87	mCi @ 1321
	ABEC column =		0.46	mCi @ 1544
	BioRad column =		0.78	mCi @ 1549
	Alumina column =		1.88	mCi @ 1553
Target plate post-dissolution =			1.41	mCi @ 1334
		Total =	82.2	mCi
	Module efficiency =		81.5%	

Waste vial - 2 hours EOB		
Isotope	t1/2	MBq
Nb-95m	86.6h	0.02
Nb-97	72m	337.23
Mo-99	66h	82.54
Tc-99m	6h	52.50

		Hours since EOB			
		0	3	25	80
Identity	t1/2	Activity (MBq)			
Tc-93g	2.75h	4.36	1.91	0.01	0.00
Tc-94g	293m	3.52	2.04	0.09	0.00
Tc-94m	52m	17.11	1.05	0.00	0.00
Tc-95g	20h	2.46	2.11	1.12	0.15
Tc-95m	61d	0.00	0.00	0.00	0.01
Tc-96g	4.3d	0.60	0.45	0.47	0.26
Tc-99m	6h	3056.20	2024.70	164.48	0.28

Sample values from a single experiment – work continues

TRIUMF-built Purification Rigs

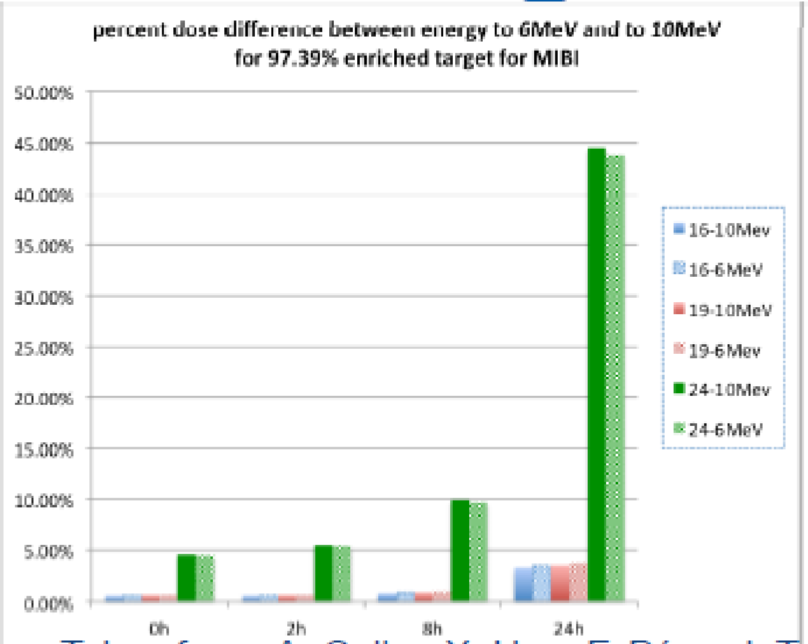
TRIUMF

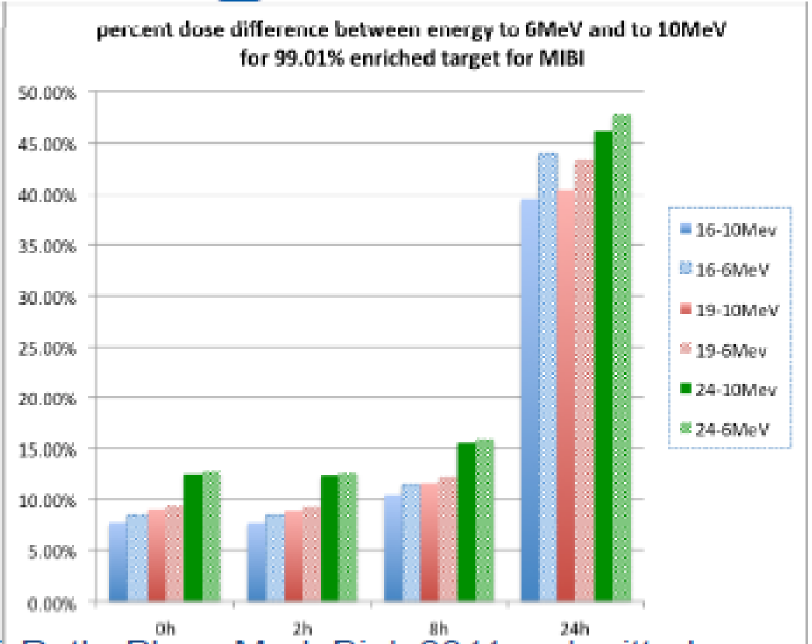
Summary and Conclusions

- ^{100}Mo: purchased from suppliers
  - Recycling chemistry demonstrated, 90.7(0.6)% efficiency
- Cyclotron capabilities
  - Range from 16-22 (or higher) MeV (16-19 optimal?)
  - Current range 150 - 300µA
  - Irradiation Time: to be determined (shorter may be better)
- Solid Target Station and Transfer System:
  - Assembly and installation underway
- Target Plates – established, optimization underway
  - Press & Sinter or Electrophoretic Deposition
- Dissolution and Purification
  - Automated systems built: ABEC, 90% efficient, 30 min, high purity
- Regulatory – Labeled 3 separate kits 3X; all passed USP specs

Theor. Calculations: Target Purity

Isotopes	Enriched			Natural
	A	B	C	
^{92}Mo	0.005	0.0060	0.09	14.85
^{94}Mo	0.005	0.0051	0.06	9.25
^{95}Mo	0.005	0.0076	0.10	15.92
^{96}Mo	0.005	0.0012	0.11	16.68
^{97}Mo	0.01	0.0016	0.08	9.55
^{98}Mo	2.58	0.41	0.55	24.13
^{100}Mo	97.39	99.54	99.01	9.63

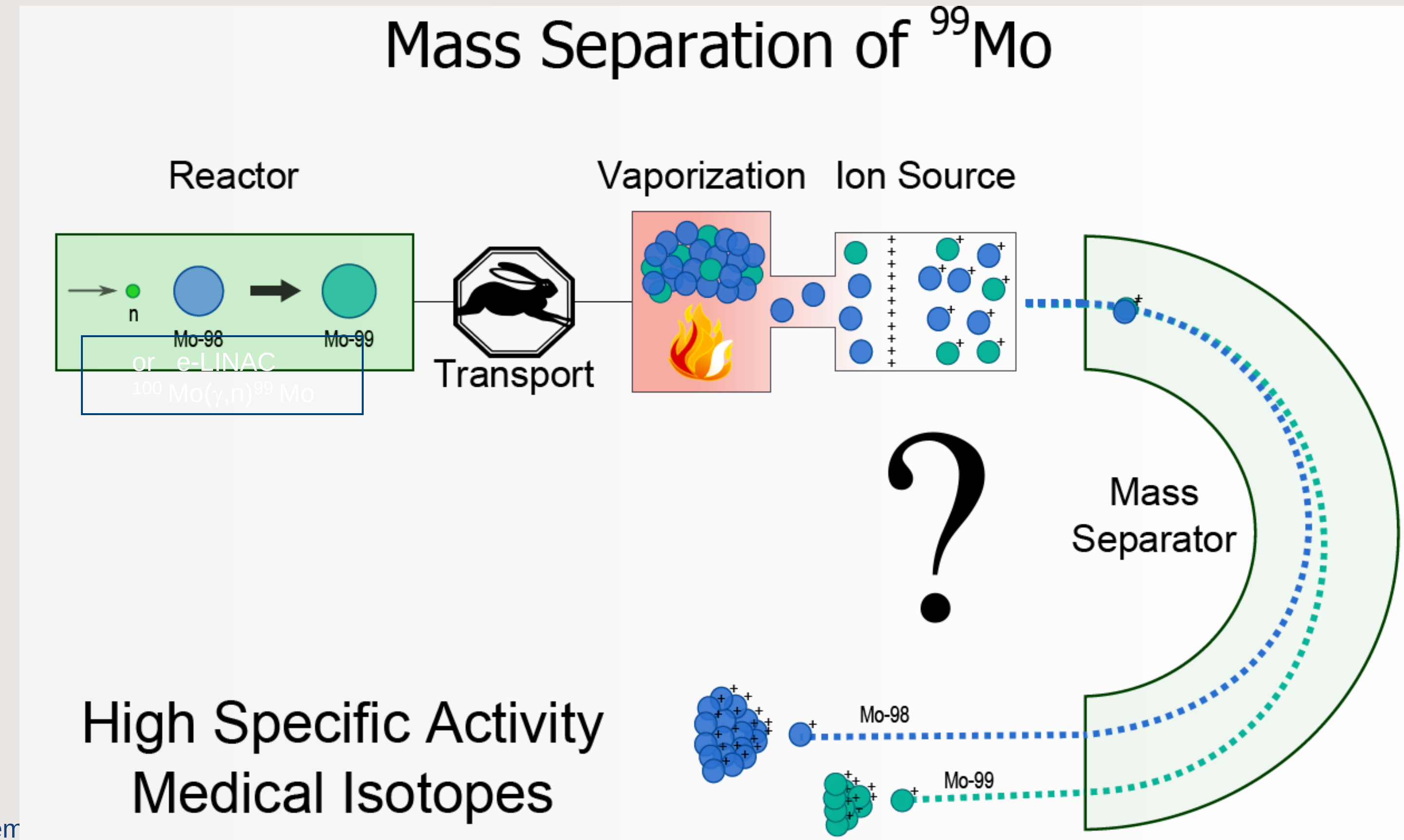




Taken from: A. Celler, X. Hou, F. Bénard, T. Ruth, Phys. Med. Biol. 2011, submitted

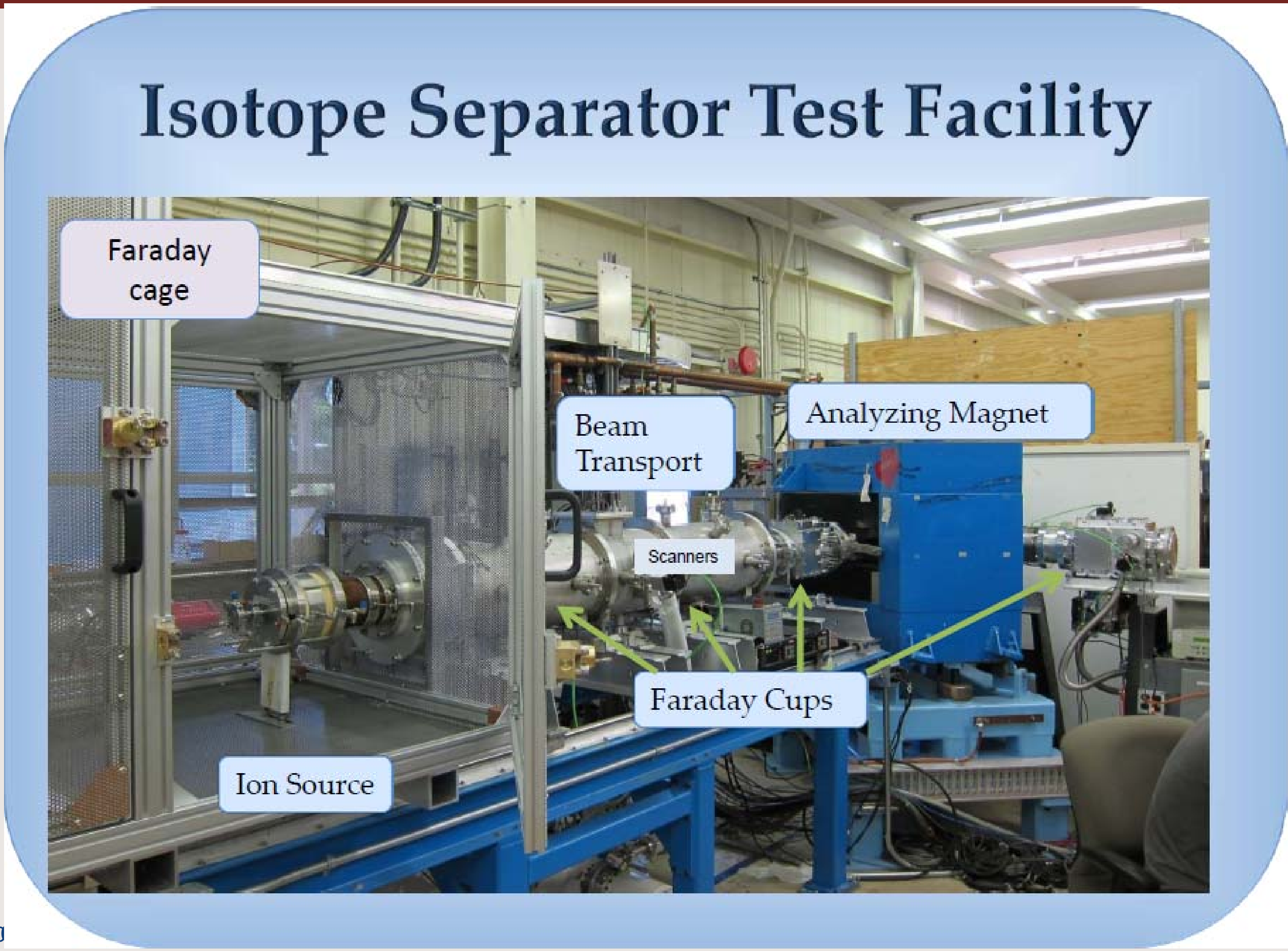
All NISP Proposals require Mo-100

MoRe developing an enhanced ion source and an electromagnetic mass separator pilot unit capable of enriching Mo-99/100 (and ^{186}Re) from a source derived from (n, γ) (1/100,000) or similar process with sufficient yields (high specific activities) to be commercially viable.

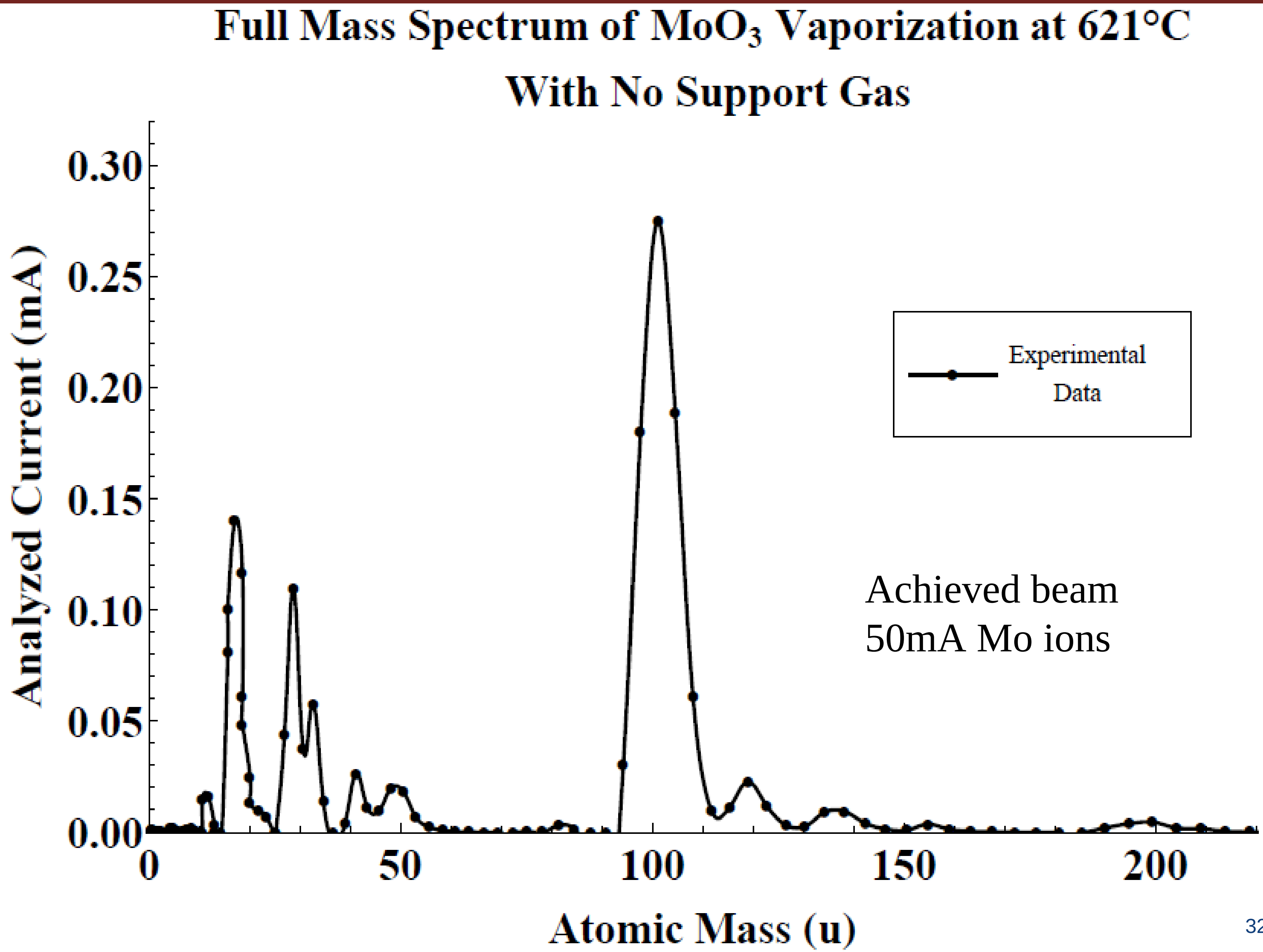


Specific activity = radioactivity per gram of material

Ion source test stand @ TRIUMF



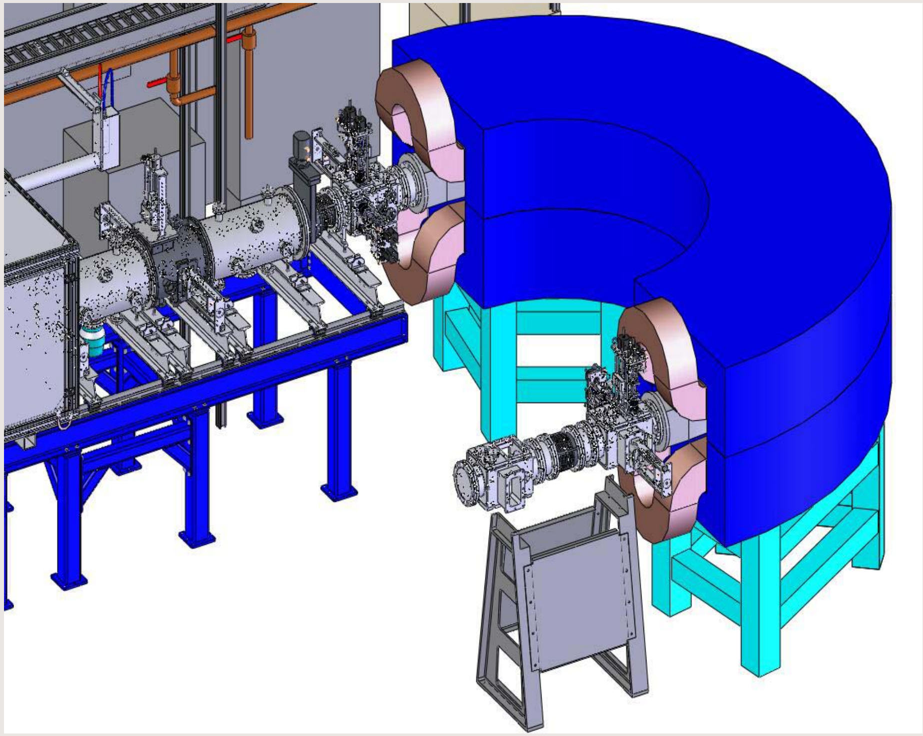
TRIUMF



Achieved beam
50mA Mo ions

$^{98/100}$Mo

- With beam currents in excess of 50 mA the ion source is suitable for enriching target materials .



TRIUMF

The Goal: Produce a 100 mA ion beam at ISTF

The MoRe Team

Name	Affiliation	Role/Title
Thomas Ruth	TRIUMF/BCCA	Principal Investigator
John D'Auria	AAPS contractor	Co-Investigator/ProjectManager (Tech.)
Paul Schmor	AAPS CSO	Ion Source Designer
Suzanne Lapi	WUSL	Co-Investigator
Keith Ladouceur	AAPS	Research Associate
Guy Stanford	AAPS contractor	Project Engineer
Peter Machule	TRIUMF/SFU	Mechanical Technician (shared)
Mark Preddy	AAPS contractor	Mechanical Technican (June-Aug., 2011)
Rod Keller	AAPS contractor	CHORDIS source Inventor/ Consultant
Chris Campbell	AAPS COO	Commercial/Business Leader

Acknowledgements

The Team

Tom Ruth, Paul Schaffer
Ken Buckley (Project Manager)
François Bénard
Mike Kovacs
Frank Prato
John Valliant
Chris Leon
Anne Goodbody
Eduoard Asselin
Tom Morley
Stefan Zeisler
Julius Klug
Vicky Hanemaayer
Philip Tsao
Milan Vuckovic
Jean Pierre Appiah
Maurice Dodd
Support from:
Machine shop,
Cyclotron staff
Radiation Safety Groups

Finances

Shirley Reeve, Rosemary Watters, Jenny Song
Steven Foster

Other Groups

Edmonton (S McQuarrie, K Gagnon, J Wilson)
CNSC

In-Kind

The GE Healthcare Team (Martin Orbe)

Funding

Natural Resources Canada / Ressources naturelles Canada
Canada

Selected Acknowledgments & References

- OECD NEA Mo-99 Production Technologies Report
  - http://www.oecd-nea.org/med-radio/reports/Med-Radio-99Mo-Prod-Tech.pdf
- Government of Canada response to Expert Review Panel Report
  - http://nrcan.gc.ca/eneene/sources/uranuc/pdf/isotopes-gc-re-eng.pdf
- *Nature* essay on accelerator-based production techniques
  - http://www.nature.com/nature/journal/v457/n7229/full/457536a.html
- NRCan medical isotope programs
  - http://nrcan.gc.ca/eneene/sources/uranuc/mediso-eng.php
- Accelerator-based Mo-99 technologies
  - http://www.triumf.ca/sites/default/files/Making-Medical-Isotopes-PREPUB.pdf
- CLS linac technology
  - http://www.cap.ca/sites/cap.ca/files/article/1278/Jan10-Offprint-Ross.pdf
- TRIUMF cyclotron technology
  - http://www.triumf.ca/nrcan-nisp

36

Thank you!

Merci!

TRIUMF: Alberta | British Columbia | Calgary | Carleton | Guelph | Manitoba | McMaster | Montréal | Northern British Columbia | Queen's | Regina | Saint Mary's | Simon Fraser | Toronto | Victoria | Winnipeg | York