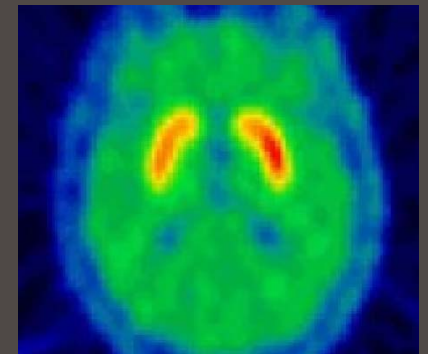
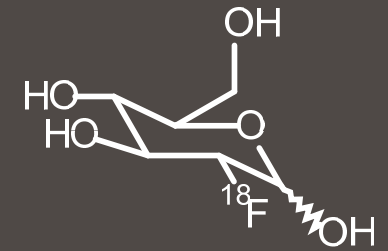


Hot and Fast:

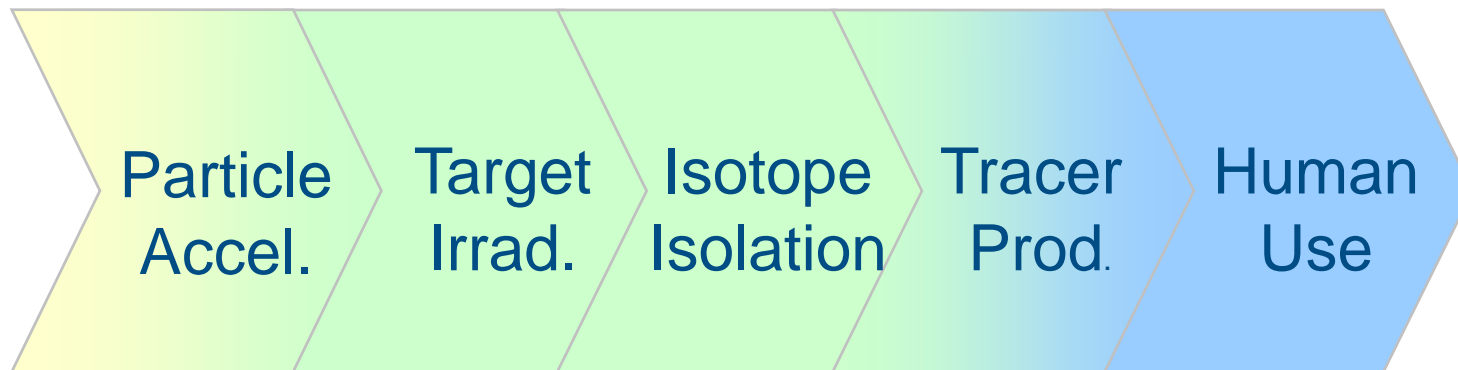
Radiochemistry with Isotopes for Medicine

Paul Schaffer | Head, Nuclear Medicine | TRIUMF



Overview

- Objectives of this talk:
 - Define molecular imaging, why use isotopes in medicine?
 - Illustrate the radiopharmaceutical process (a chemist's perspective)



- Isotope Crisis: Innovative solutions with existing infrastructure

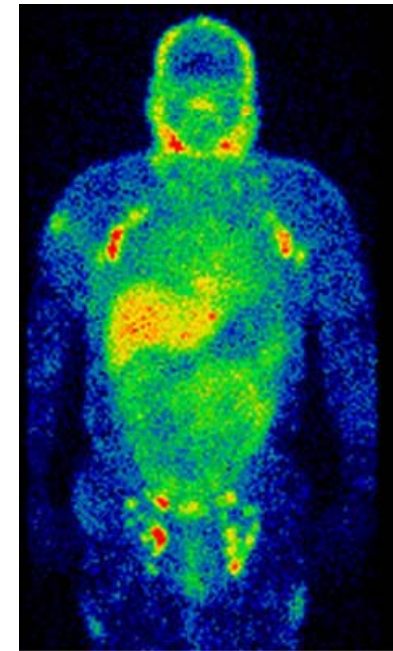
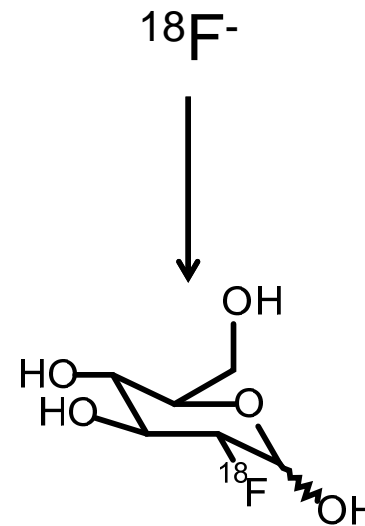
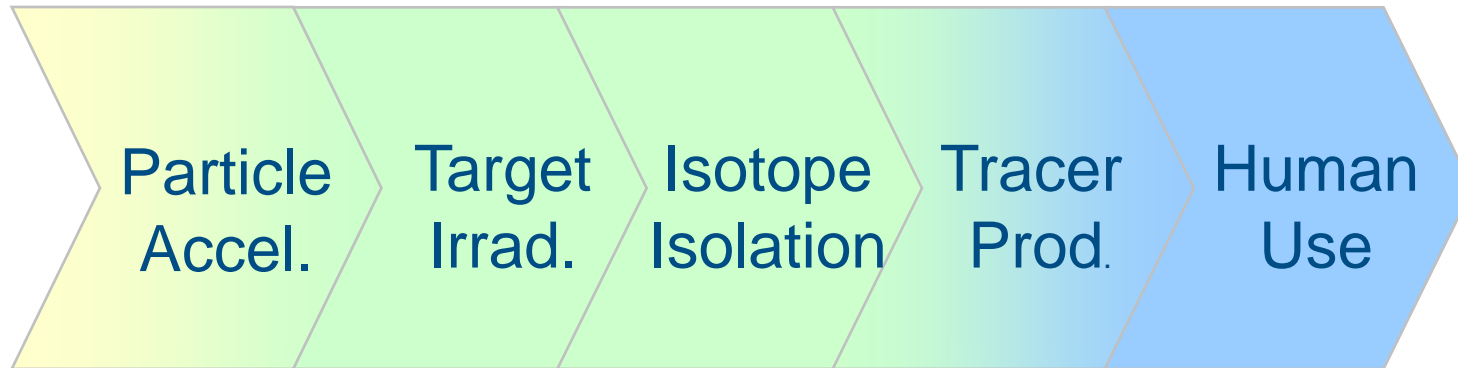
Molecular Imaging Defined

- Goals of MI
 - Non-invasive evaluation of:
 - Physiological function – initiation of disease
 - Aberrant cell/tissue behavior - disease progression
 - Treatment efficacy
 - Results in:
 - Personalized, more efficient healthcare
 - Increased patient safety - avoid unnecessary treatment

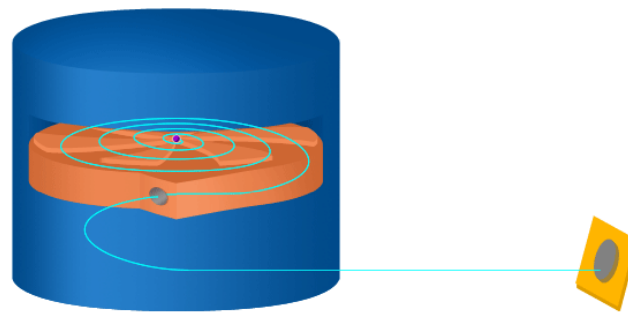
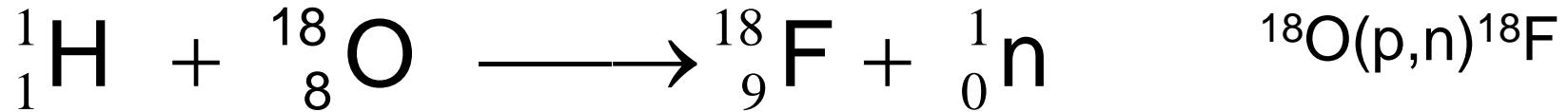
Requires:

- Adequate/Economical isotope production
 - Robust radiopharmaceutical process

The Radiopharmaceutical Process

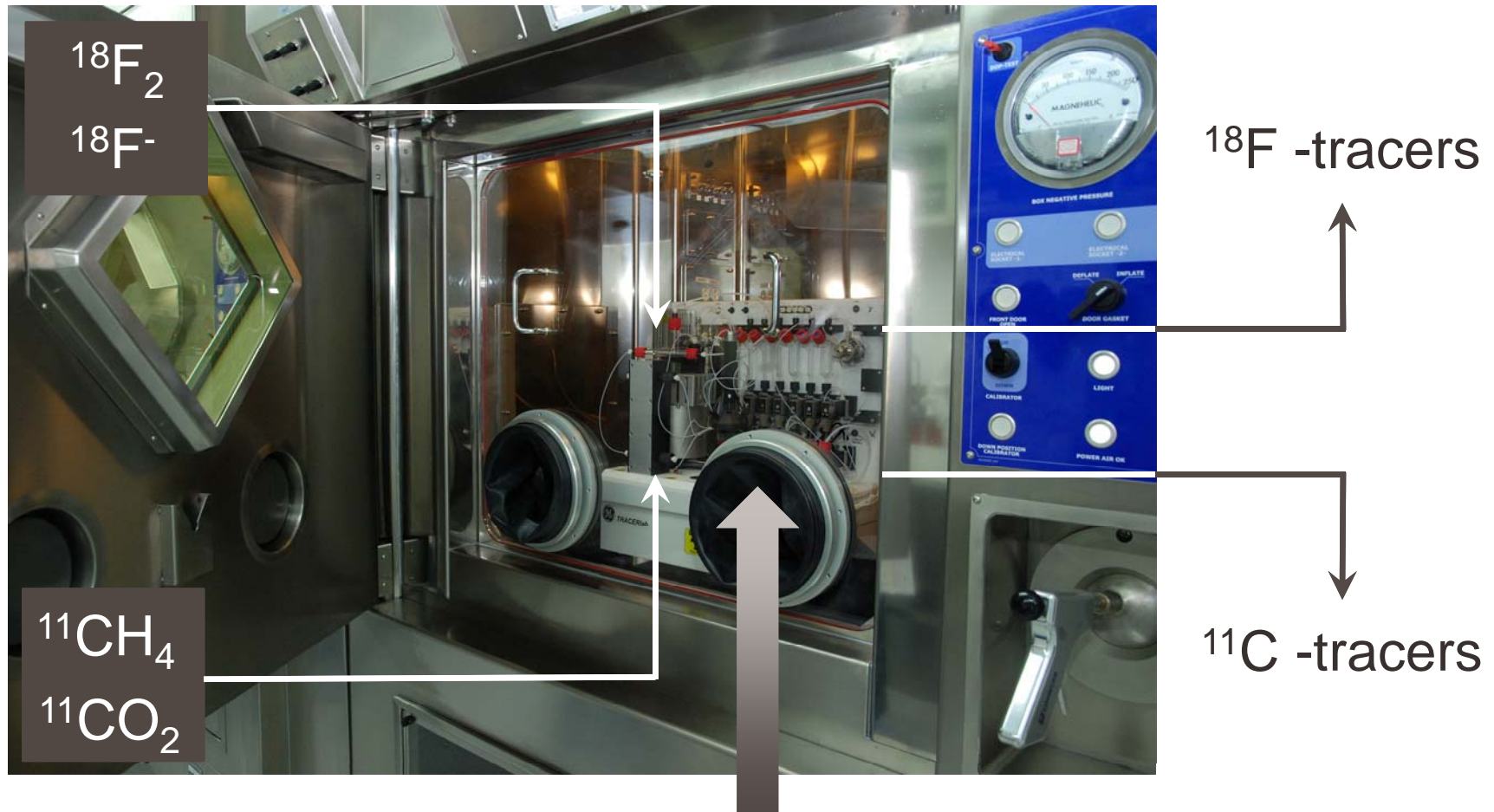


Isotope Production via Cyclotron



- Cyclotrons in Canada's major hospitals produce PET isotopes

Radiochemistry: Hot and Fast



Complex chemistry, purification, formulation

Radiochemistry: Hot and Fast

Fluorine-18

$t_{1/2}$: 110 min

Amenable to nucleophilic (F^-), electrophilic (F_2) addition

Carbon-11

$t_{1/2}$: 20 min

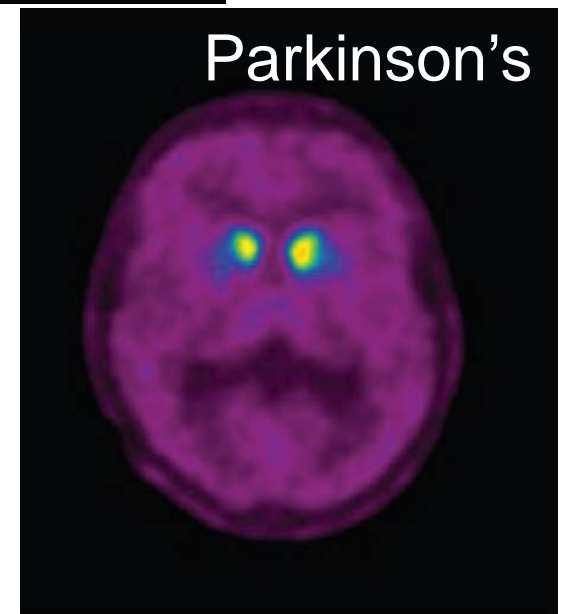
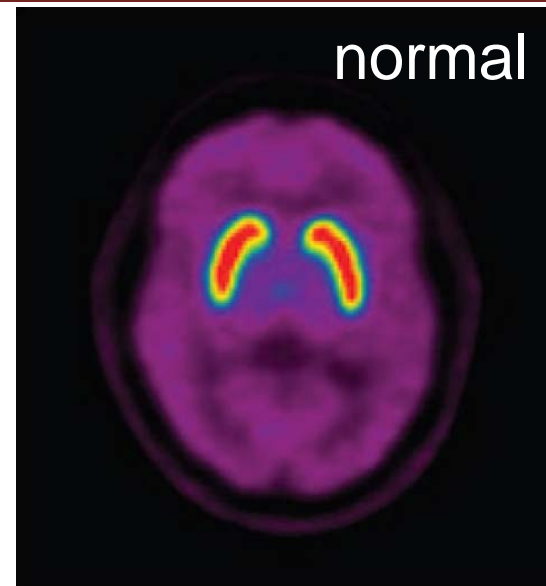
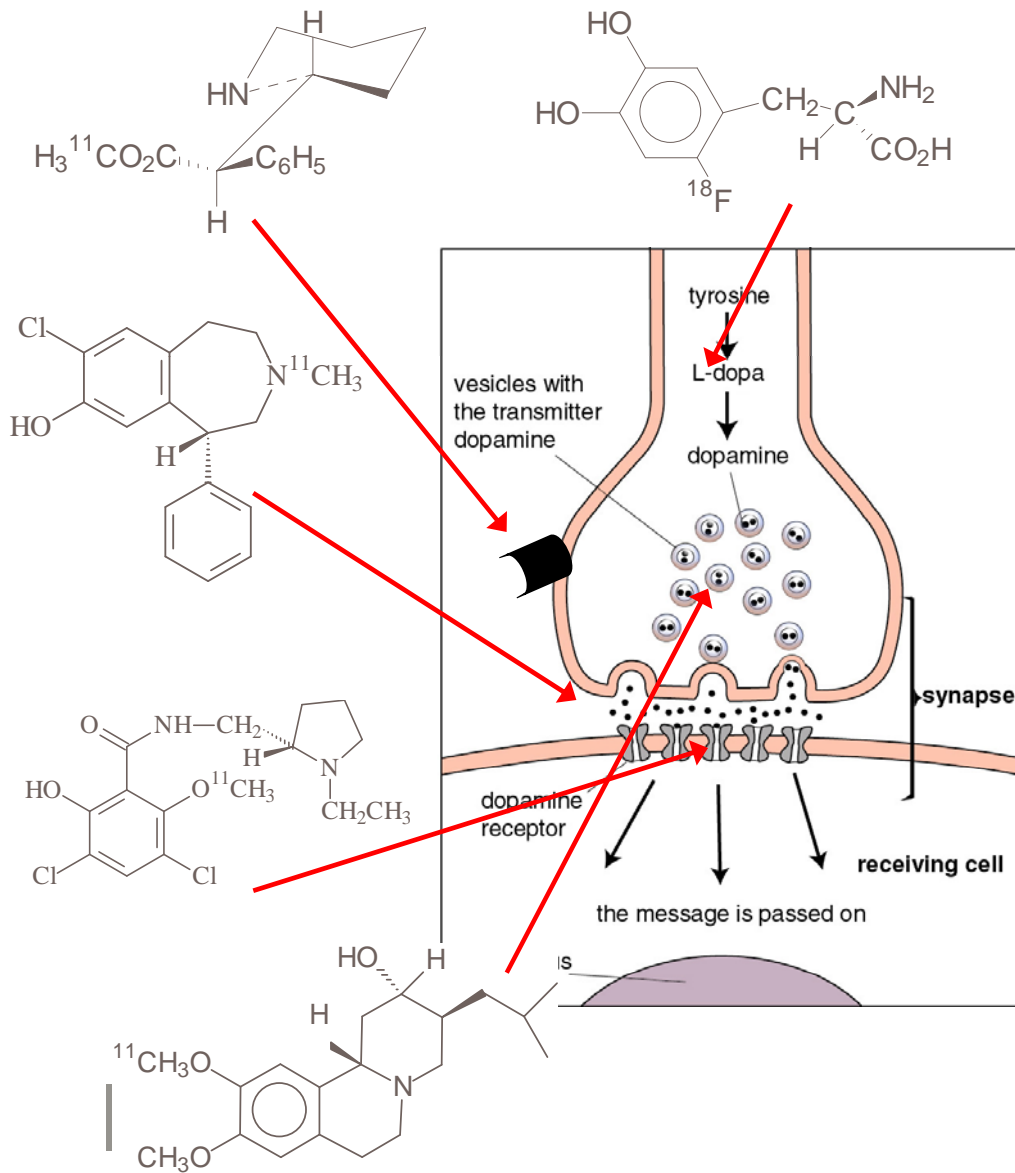
Amenable to heteroatomic modification (CO_2 , CH_3I)

Other isotopes: wide range of half-lives, chemistry

Process demands:

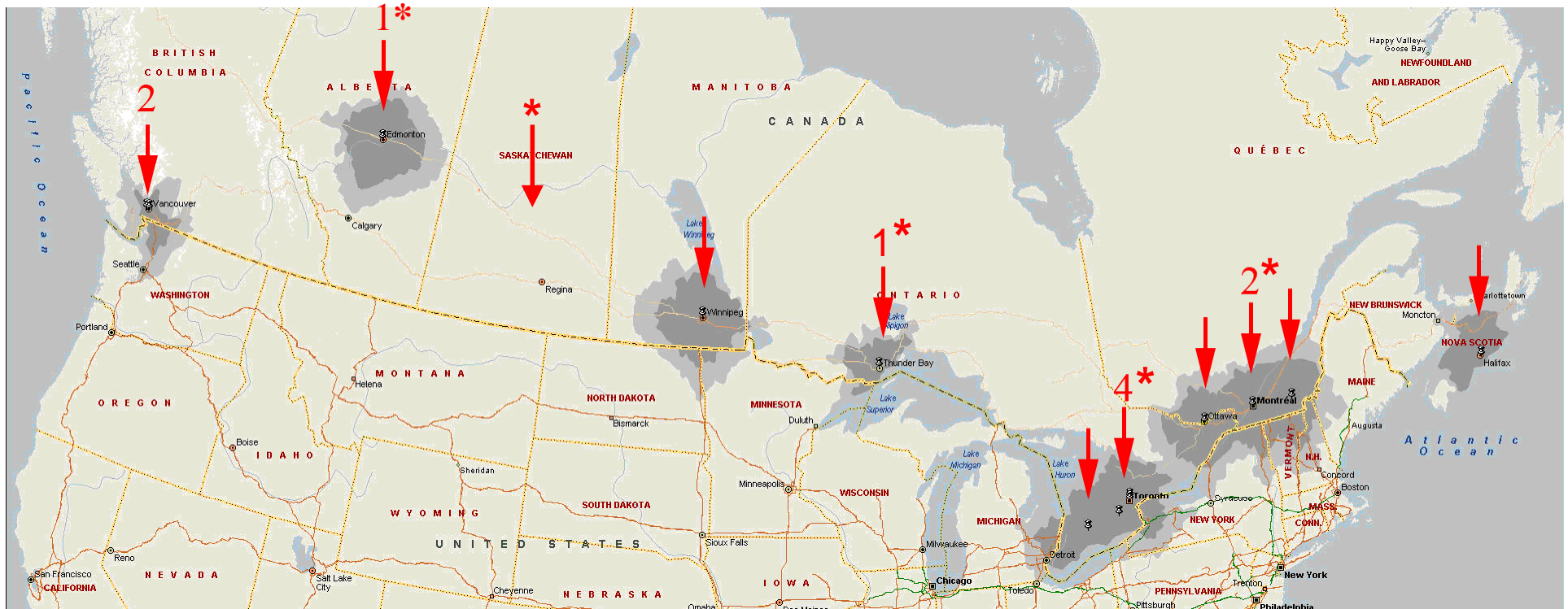
- Rapid isolation, chemical synthesis (40 min, start to finish)
- Automated/semi-automated chemistry, purification
- GMP (sterile, pyrogen free)
- Low mass (final prep contains ~100 ng of active drug)

Radiotracers for Molecular Imaging



Future of Nuclear Medicine in Canada

Canada has a growing cyclotron infrastructure



* New machines scheduled for installation

Disease focus: Oncology, Neurology and Cardiology

Up and coming tracers in Canada

Neurology*

^{11}C - raclopride
 ^{11}C - methylphenidate
 ^{11}C - DTBZ
 ^{11}C - Sch233900
 ^{11}C - PK11195
 ^{11}C - PiB
 ^{11}C - PMP
 ^{11}C - DASB
 ^{11}C - FLB
 ^{11}C - MRB
 ^{11}C - rolipram
 ^{11}C - raclopride
 ^{18}F -DOPA

Oncology*

^{11}C - methionine
 ^{11}C - choline
 ^{18}F -NaF
 ^{18}F - FDG
 ^{18}F - FES
 ^{18}F - FLT
 ^{18}F - FAZA
 ^{18}F - FET
 ^{18}F - EF5
 ^{68}Ga -DOTATOC
 ^{64}Cu -Annexin
 ^{64}Cu -Tz

Cardiology*

^{13}N - NH_3
 ^{82}Rb
 ^{11}C - CO
 ^{11}C - Carfentanil
 ^{11}C - acetate
 ^{11}C - HED
 ^{11}C - Losartan
 ^{18}F - RGD
 ^{18}F - flurpiridaz
 ^{18}F - FTHA
 ^{18}F - GLP1 (^{68}Ga)
 ^{18}F - FHBG
 ^{18}F - HFB
 $^{123/124}\text{I}$ -FIAU

*Partial audit across Canadian sites

MICAD** Database lists: 355 SPECT agents (64 in humans)
490 PET agents (110 in humans)

Accelerators to Address the Isotope Shortage

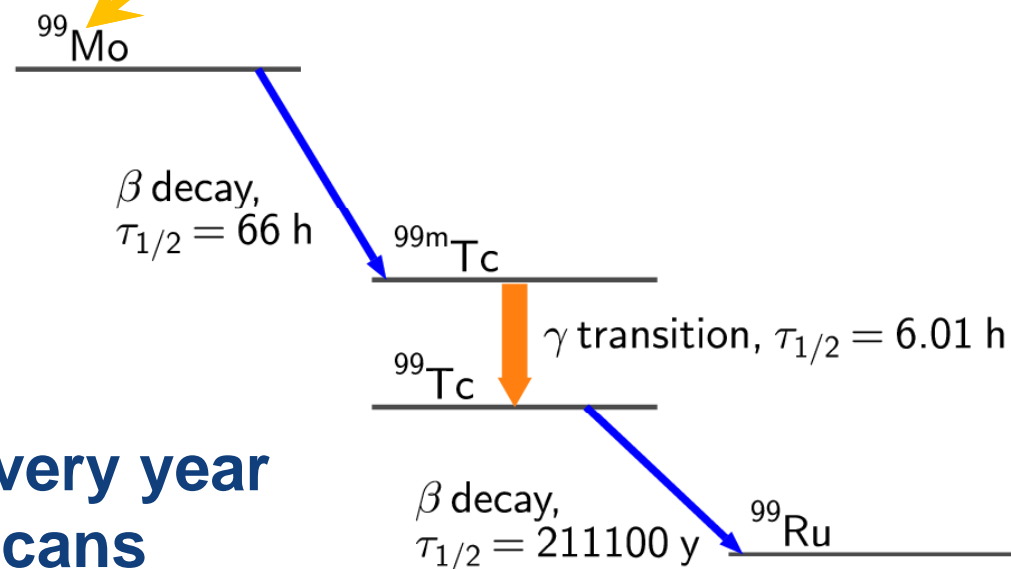
Moly 'Cow'



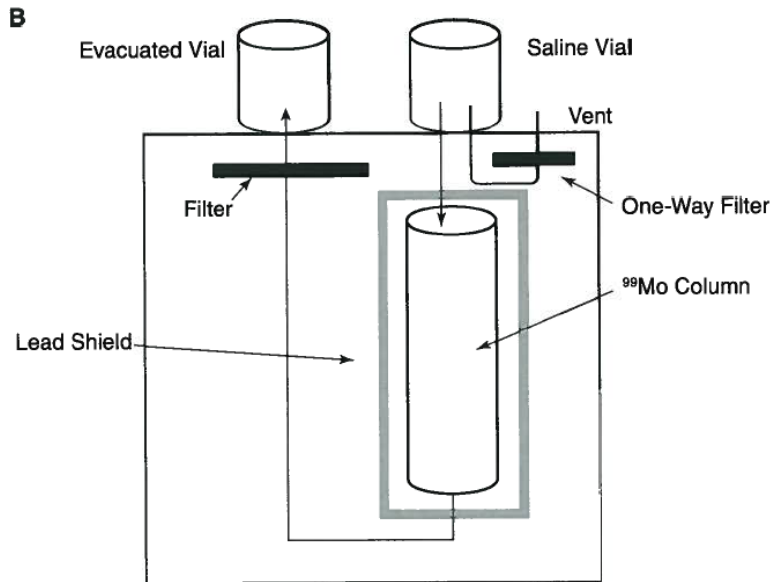
- Transportable
- Easy to use
- Enables 20-40 million procedures globally every year
- 85% of all Nuc. Med. scans



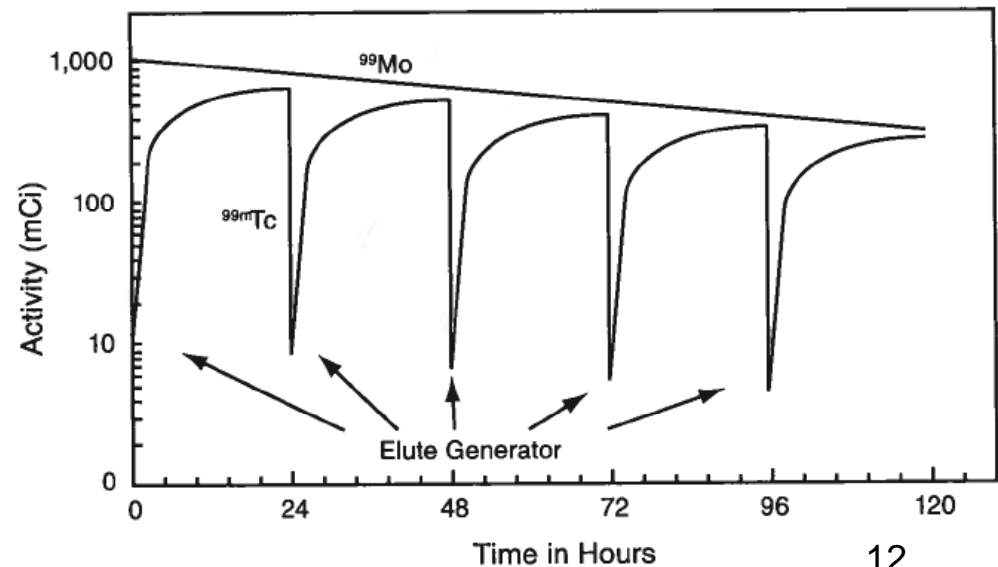
NRU – Chalk River
Enriched ^{235}U target



Moly Cow: Tc-99m Generators



- Tc-99m is “milked” from the generator
- Tc-99m is tagged to tracers and then injected into the patient



Production Alternatives

- Alternatives are well known
- at various stages of commercial-scale production:

Neutron ‘solution(s)’:



Photon ‘solution(s)’:

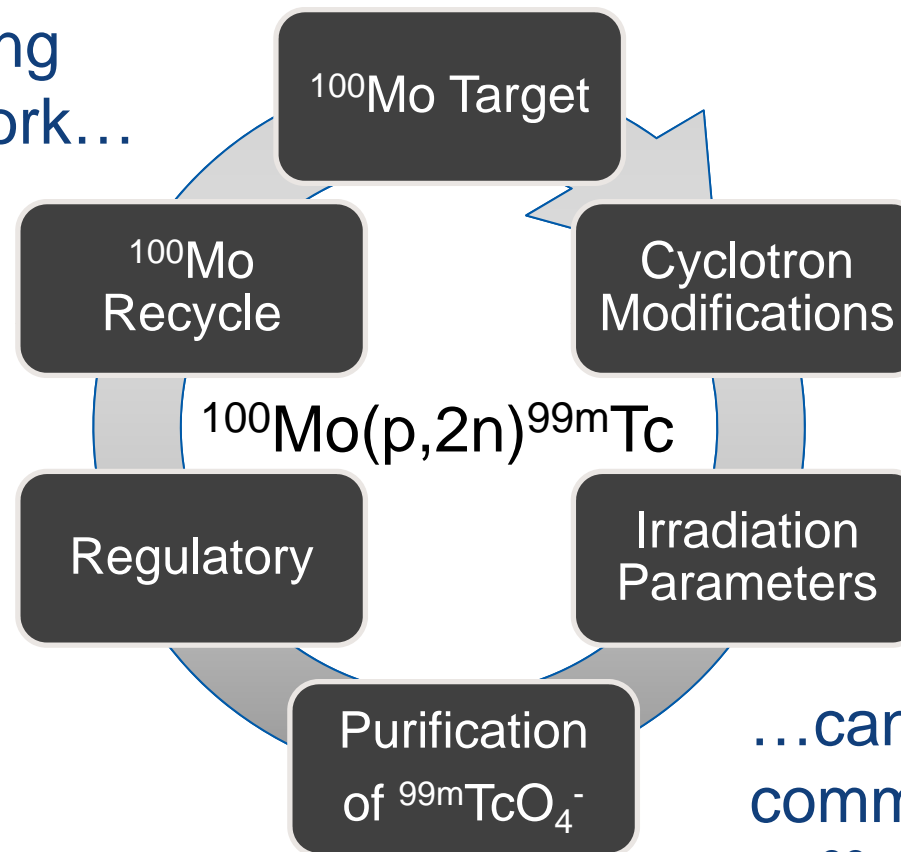


Proton ‘solution’:



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

Canada's existing
cyclotron network...



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

Goal: Formulate policy
on $^{99}\text{Mo}/^{99m}\text{Tc}$ medical isotope production

Team Equipment/Capabilities

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



BC Cancer Agency

TR19

13-19 MeV, $\leq 200 \mu\text{A}$

Upgrade to:
300 μA (approved)



Lawson

GE PETtrace

16 MeV, $\leq 100 \mu\text{A}$

Upgrade to: $\leq 150 \mu\text{A}$

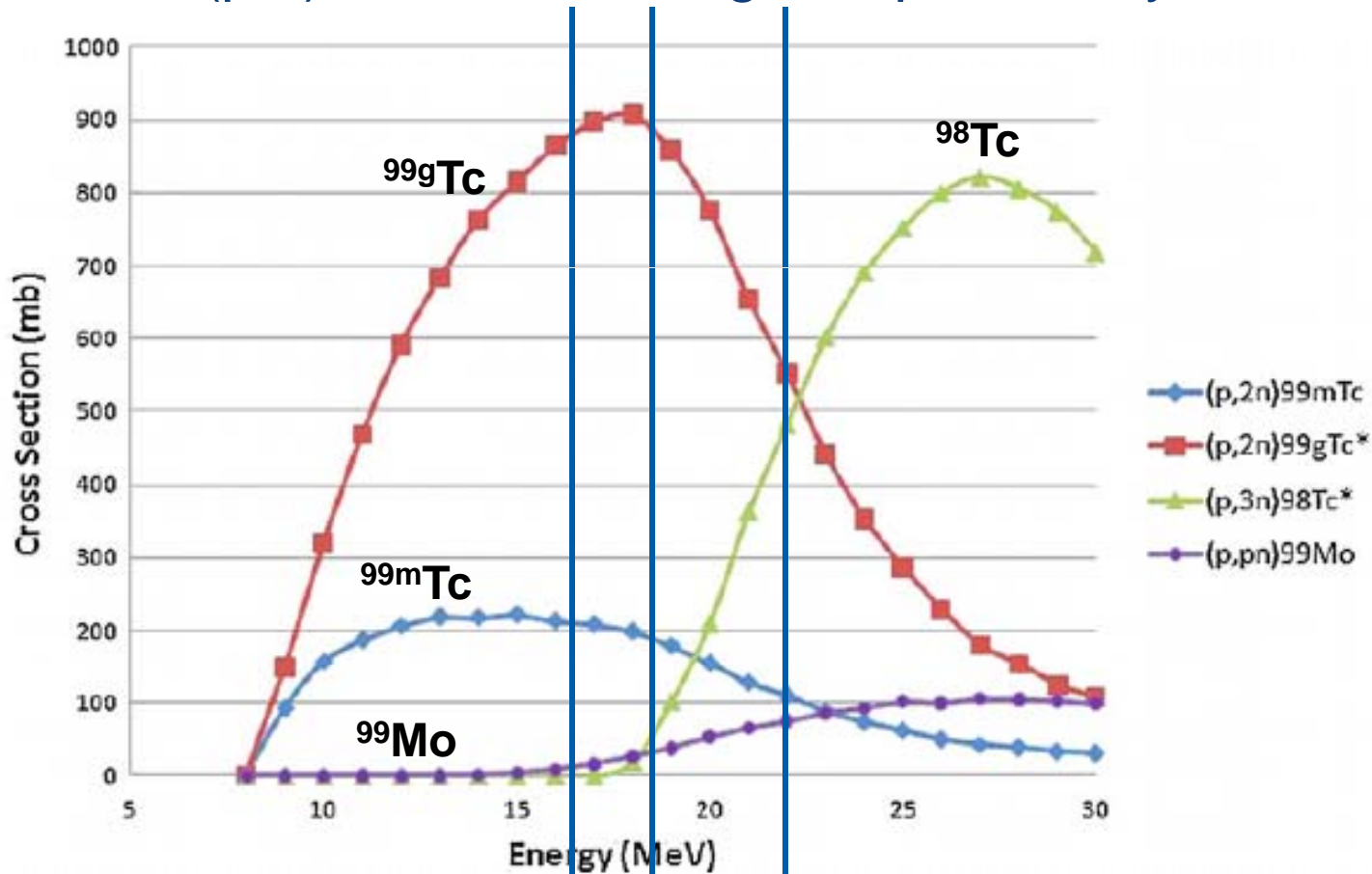


CPDC

Not shown: CP42, 20-42 MeV, $\leq 200 \mu\text{A}$

Theor. Calculations: Beam Energy

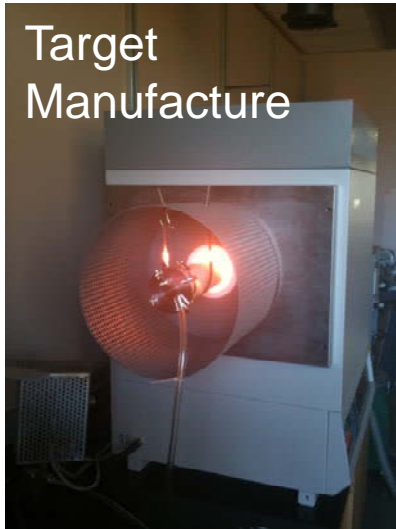
$^{100}\text{Mo}(p,x)$ reactions of highest probability



PETtrace ↗ TR19 ↖ CP42

Demonstrating Proof of Concept

Target
Manufacture



Target



Target Transfer



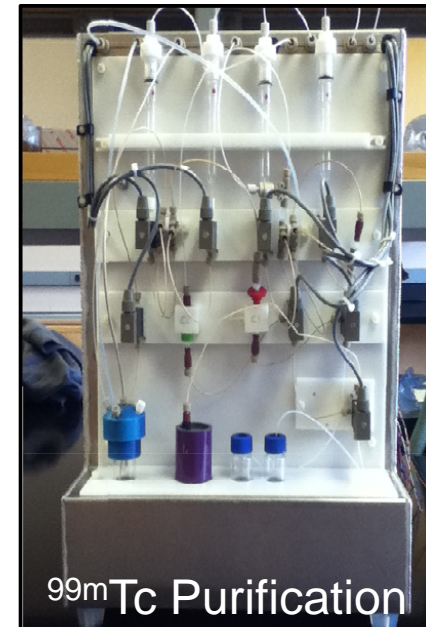
Target Holder



Cyclotron Target Station



^{99m}Tc Purification



Direct Production of ^{99m}Tc

- Production at multi-Ci quantities possible
 - TRIUMF and partners have produced up to or more than 1 Ci of ^{99m}Tc in two parts of the country
 - Production accomplished on two different types of medical cyclotron, three before end of March 2012.
- Use of existing cyclotron infrastructure feasible
 - Individual site capabilities (energy, current, time) will factor in output capacity/feasibility
 - Anticipated optimal metrics: 16-19 MeV, 100-300 μA , 3-6 hour irradiation(s) on a daily basis

Team is on track to deliver proof of concept and a production model based on a tested approach



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



Natural Resources Canada / Ressources naturelles Canada



NSERC
CRSNG



Thank you! Merci



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