The Global Medical Isotope Crisis: Winnipeg to the Rescue!

Jeff Martin
University of Winnipeg
and
Prairie Isotope Production Enterprise

Inaugral Lecture Series 2009

Collaborating Institutes:
U. Winnipeg, Acsion Industries, Health Sciences Centre

Research Interests

- Parity-violating electron scattering as a probe of new physics
  - “Q-weak” experiment (~70 collaborators)
    - UWinnipeg: scanner detector and diamond detector
- Neutron experiments
  - ultracold neutron source to produce world's highest density, for determination of electric dipole moment.
    - UWinnipeg: project leadership
- Isotope production

TRIUMF

International Spallation Ultracold Neutron Source

Spokespeople: J.W. Martin (Winnipeg), Y. Masuda (KEK)

Collaborators: J. Birchall, J.D. Bowman, L. Buchmann, L. Clarke, C. Davis, B.W. Filippone, M. Gericke, R. Golub, K. Hatanaka, M. Hayden, T.M. Ito, S. Jeong, I. Kato, S. Komamiya, E. Korobkina, E. Korkmaz, L. Lee, K. Matsuta, A. Micherdzinska, W.D. Ramsay, S.A. Page, B. Plaster, I. Tanihata, W.T.H. van Oers, Y. Watanabe, S. Yamashita, T. Yoshioka

(KEK, Winnipeg, Manitoba, ORNL, TRIUMF, NCSU, Caltech, RCNP, SFU, LANL, Tokyo, UNBC, Osaka, Kentucky)

We propose to construct the world's highest density source of ultracold neutrons and use it to conduct fundamental and applied physics research using neutrons.

News: $10.9M proposal now funded in Canada and Japan.

Advertisement

- Please come see my talk in Chemistry on January 22, 2010 on “Ultra-cool Neutrons”.

Group Members as of Today

- Mr. Alex Coppens (PhD, 2010) (electron scatt.)
- Ms. Jie Pan (G) (electron scatt.)
- Mr. David Harrison (G) (neutron decay)
- Mr. Mark McCrea (G) (neutron capture)
- Mr. Troy Dawson (G) (ultracold neutrons)
- Mr. Mark Abotossaway (UG) (neutron decay)
- Dr. Vladas Tvaskis (PDF) (electron scatt.)

Major partnerships with UM, Acsion Industries, HSC, TRIUMF, UNBC, international

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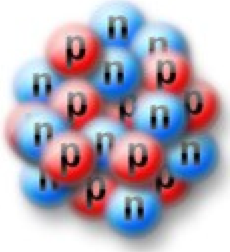
THE UNIVERSITY OF WINNIPEG acsion Health Sciences Centre Winnipeg

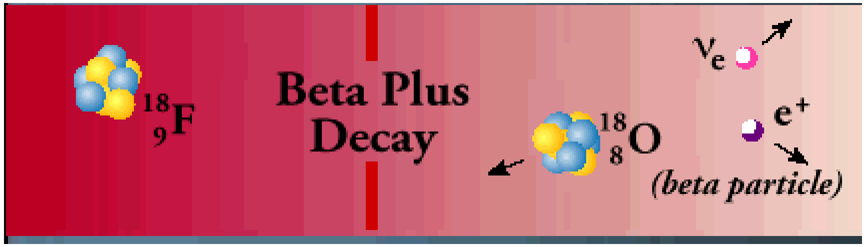
The Nucleus

- Atoms contain nuclei, orbited by electrons
- Nuclei can have different numbers of neutrons
  - e.g. Potassium (K) has 19 protons
    - K-39 has 20 neutrons, 93.26%
    - K-40 has 21 neutrons, 0.012%
    - K-41 has 22 neutrons, 6.73%
  - All three isotopes exist in nature



Radioisotopes

- If a nucleus decays by emitting radiation, it's called a radioisotope.
- e.g. Naturally occurring K-40 is a radioisotope.
  - Decays by beta-emission.



- Three types of decay:
  - alpha (α) - nucleus emits a helium nucleus
  - beta (β) - nucleus emits an electron or positron
  - gamma (γ) - nucleus emits a photon
- Gamma rays can pass through matter.

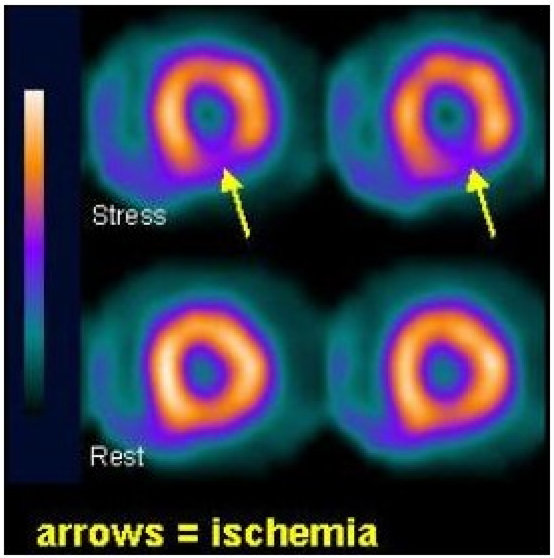
Tc-99m

- Technetium-99m is the most widely used radioisotope for nuclear medicine procedures in the world and accounts for 85% of all procedures.

$$^{99m}Tc \rightarrow ^{99}Tc + \gamma$$

- Procedure: inject patient with drug containing Tc-99m. Image the patient with a gamma ray camera and see where the uptake of the drug occurred.

Some Images Made with Tc-99m



The upper row shows two short-axis slices after pharmacological stress; the lower row shows the same slices when the body is at rest in conventional cardiac SPECT with Tc-99m tetrofosmin as a radiotracer. Arrows indicate a small perfusion defect on the back side of the heart -- visible only on the stress images -- showing ischemia in this region of the heart wall. Image courtesy of Drs. Oliver Gaemperli and Philipp Kaufmann, University Hospital Zurich, Switzerland.

Source: Soc. of Nuc. Med.

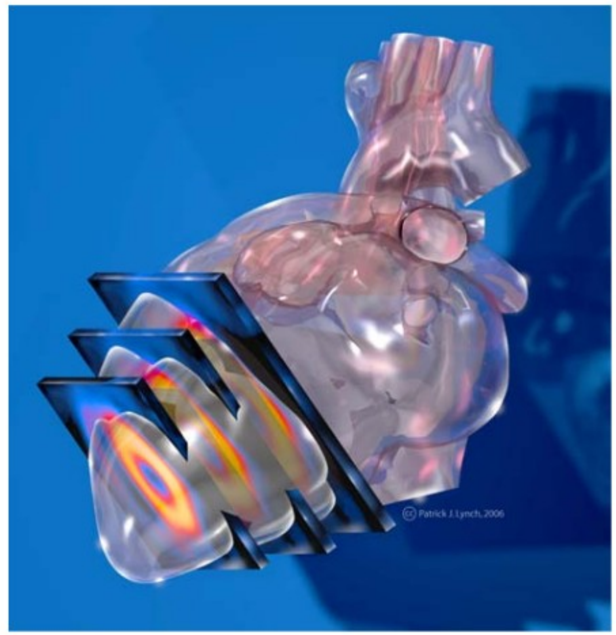
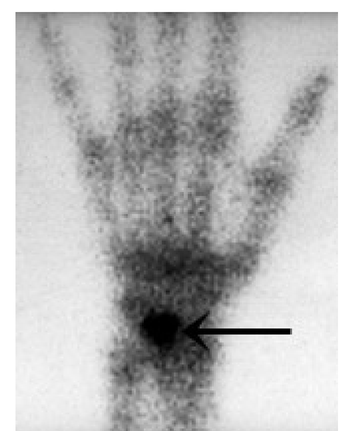


Figure 2.1: Short-axis views of the heart showing SPECT nuclear imaging. Credit: Patrick J. Lynch, medical illustrator; C. Carl Jaffe, MD, cardiologist.

Source: TRIUMF

Used for studies in:

- Cardiac Function
- Blood Flow
- Bone Metastases



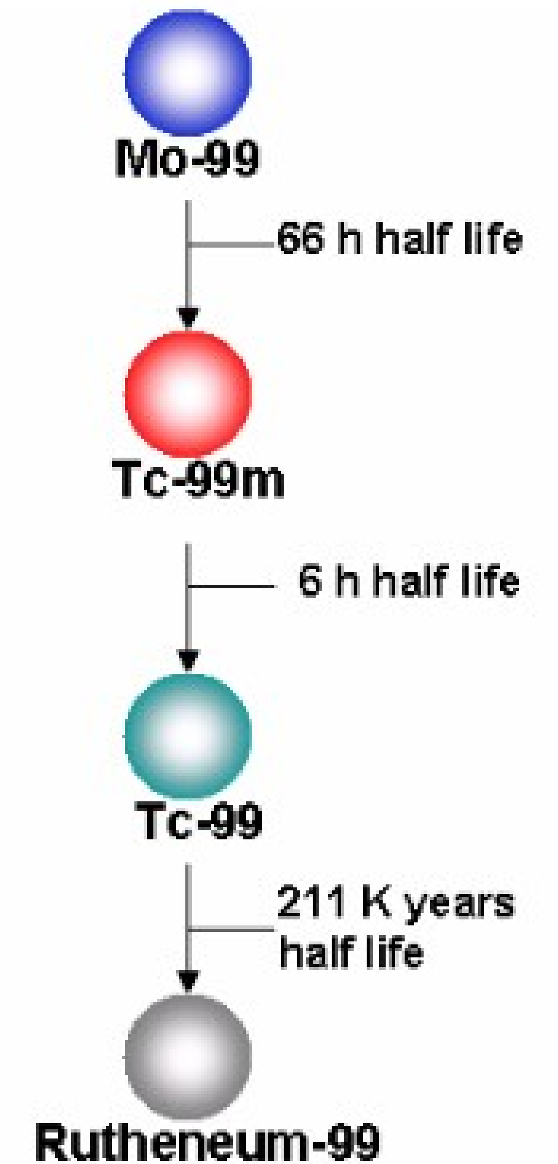
Tc-99m MDP image of wrist indicating bone lesion
source: Harvard Med School

Fun Facts about Technetium (Tc)

- How come I've never heard of “Technetium”?
- All Tc is radioactive and therefore it decays. So it is exceedingly rare in nature.
- Tc was the first element discovered in a laboratory (as opposed to being found in nature).
- It's interesting to search for Tc in nature because it's only found where nuclear reactions are taking place (e.g. in stars).

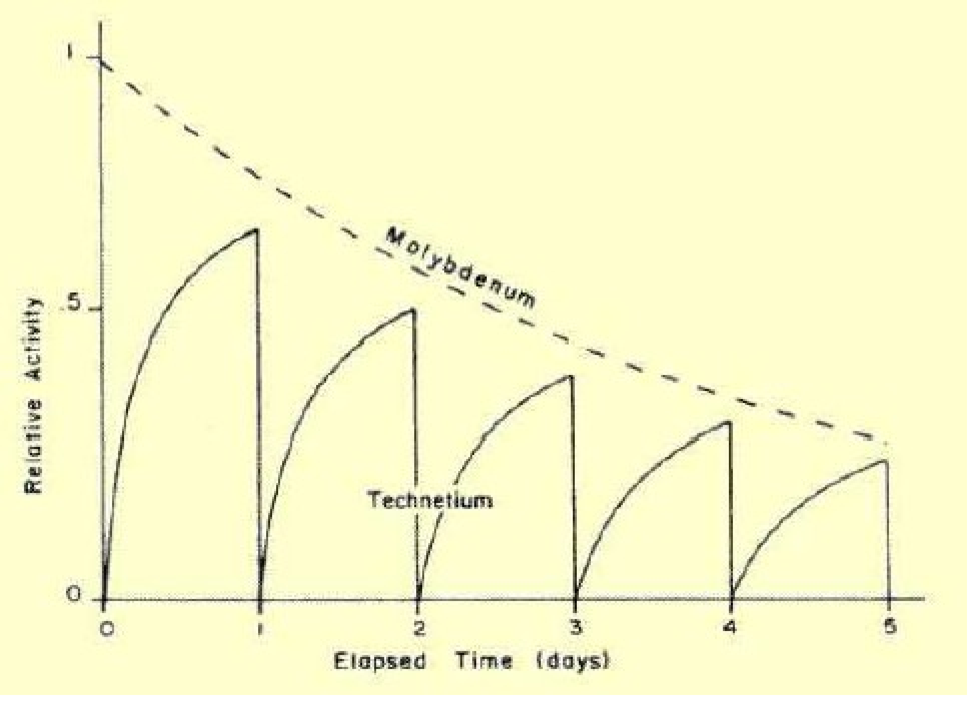
How to Make Tc-99m

- Tc-99m is produced from the decay of Molybdenum-99, another isotope.
- Mo-99 is currently produced at nuclear reactors, via fission of Uranium-235 (“highly enriched uranium”).
- Mo-99 lives for 66 hours.



The Tc-99m "generator"

- After about 24 hours, the Mo-99 has made about as much Tc-99m as it can (i.e. as much Tc-99m is decaying as is being produced).
- Then, it is time to milk the technetium cow.



Who makes Moly?

Worldwide Supplies of Moly

Most molybdenum-99, feedstock for the most-used radioisotope in medical imaging, comes from just five aging reactors. A little is made by newer reactors, such as OPAL. Outages at older reactors have created shortages, prompting calls to make moly in the United States.

Country	City, Province	Facility Name	Reactor Age (Years)	% World Supply of Moly	Power Output (Megawatts)
Canada	Rolphton, Ontario	NRU Chalk River	52	33%	135
The Netherlands	Petten	HFR	47	33%	45
Belgium	Mol	BR2	47	10%	100
France	Saclay	OSIRIS	42	8%	70
South Africa	Pelindaba	SAFARI	43	3%	20
Australia	Sydney	OPAL	2	N/A	20

Source: sciencenews.org

- News flash: Canada's reactor is currently shut down due to concern over water leaks (until next year). Status = learning to weld.

Consequences

Specialist 'very concerned' about cancelling isotope-needing scans

Last Updated: Wednesday, June 10, 2009 | 4:36 PM ET
CBC News

Doctors are looking for alternatives to maximize the supply of medical isotopes. (CBC)

As the supply of medical isotopes dwindles across Canada, specialists in nuclear medicine expressed concerns Wednesday that patients' appointments to undergo diagnostic scans may be cancelled.

"As we go further into this week, we're very concerned that we're going to have to turn patients away, look for alternate sites for them to be imaged," said Kevin Tracey, medical director of nuclear medicine at Hôtel-Dieu Grace Hospital in Windsor.

The concern is for some patients with life-threatening pulmonary embolisms — blockages in the arteries of the lung — who urgently need lung scans with isotopes because they are allergic to the contrast dye used in CT scans, the normal way of diagnosing the condition, Tracey said.

Without proper diagnosis, a patient without the disease may be improperly treated with a blood thinner, which could put them at long-term risk of bleeding complications. Occasionally, patients may have extensive clots in their lungs that were unexpected and could go untreated, with risk of sudden death.

- Problem not unique to Canada.
- Major initiatives in the US and elsewhere to solve the shortage as fast as possible.

U.S. Situation

- 60,000 diagnostic procedures per day based on Tc-99m; ex.: monitor blood perfusion into heart tissue following cardiac stress tests.

- White House launched a federal interagency panel to look at developing homemade moly — perhaps, on an emergency basis, as early as spring 2010.

H.R.3276 - American Medical Isotopes Production Act of 2009: To promote the production of molybdenum-99 in the United States for medical isotope production, and to condition and phase out the export of highly enriched uranium for the production of medical isotopes

Prairie Isotope Production Enterprise

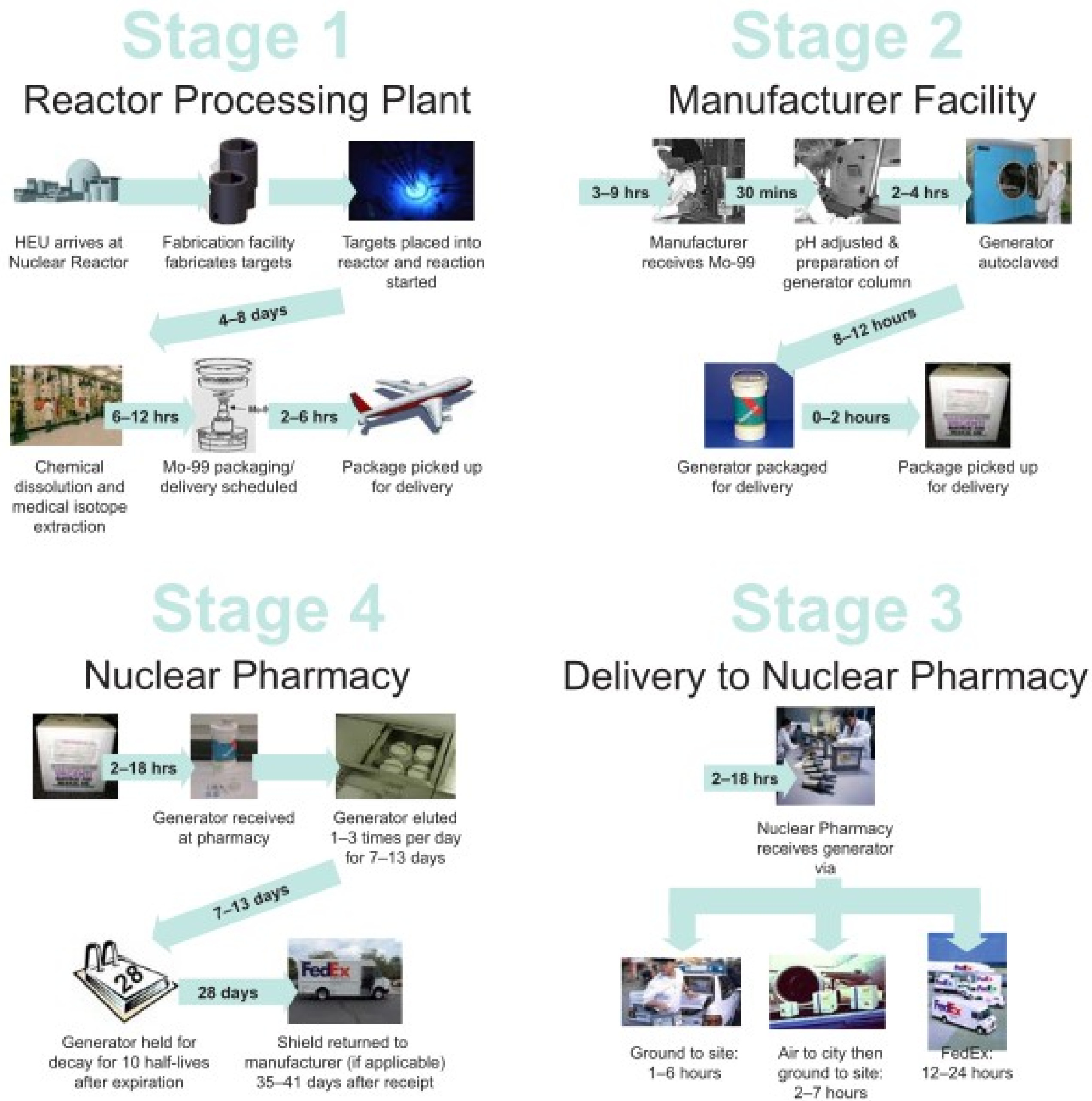
U.S. Situation

Short term Option: Irradiate targets in existing facilities in U.S. and send to Canada to have their moly extracted (a few reactors already exist)

Long-term Options:

- The top two homegrown candidates for supplying moly are the 43-year-old MURR, in Columbia, Mo., and a reactor still undergoing development by Babcock & Wilcox Co. of Lynchburg, Va. Both rely on designs that are conceptually old. Both are proposing to be ready by 2013.
- Rensselaer Polytechnic Institute: proposing Mo-99 from accelerators.
- Advanced Medical Isotope Corp: EB treatment of heavy water (deuterium oxide) and uranium; neutron production to induce fission, producing some Mo-99.
- Northstar – EB production of Mo-99 using Mo-100

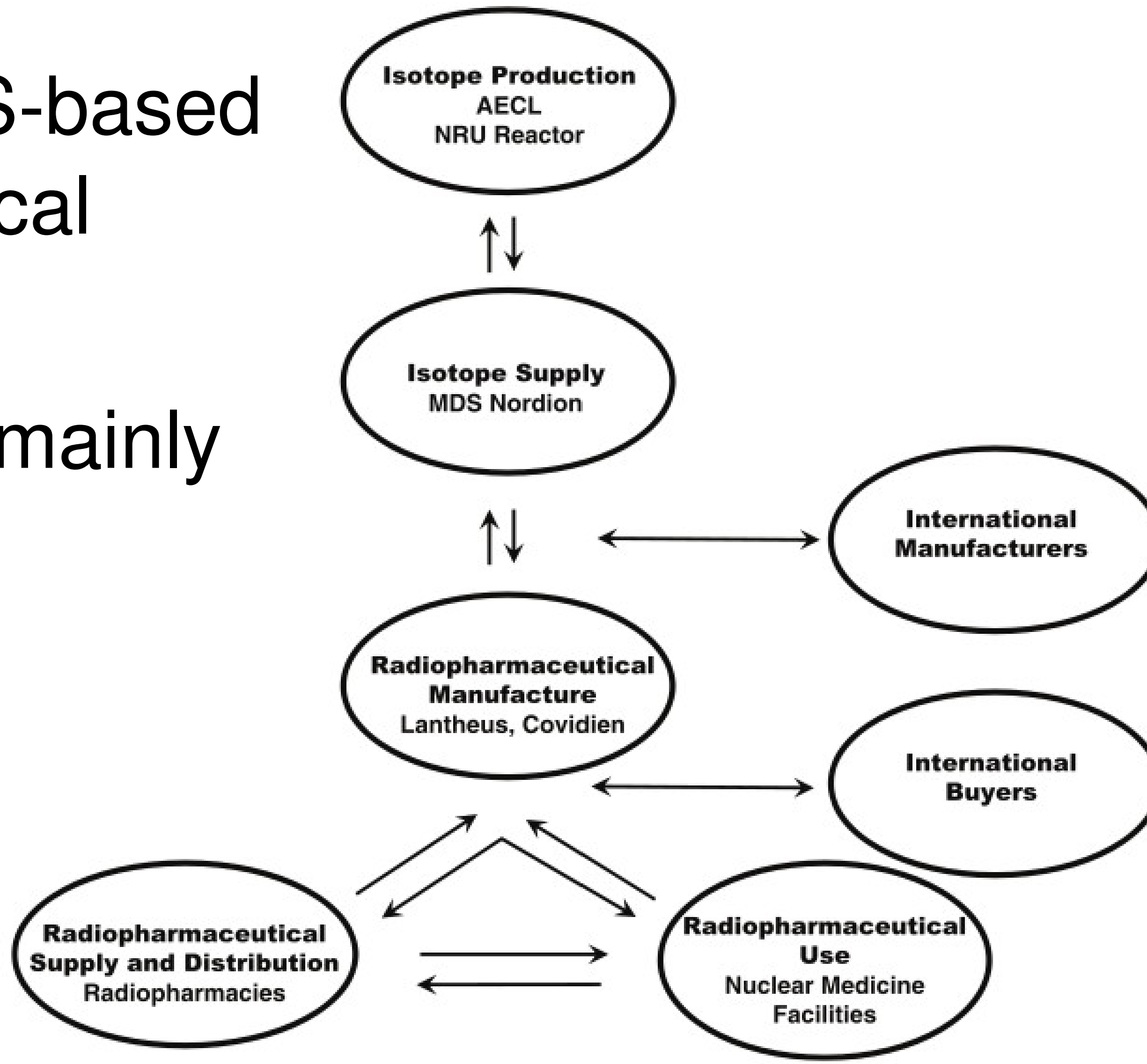
Tc-99m supply chain



Source: TRIUMF

How does Moly come to Manitoba?

- We buy it from US-based radiopharmaceutical manufacturers
- We currently buy mainly from Covidien

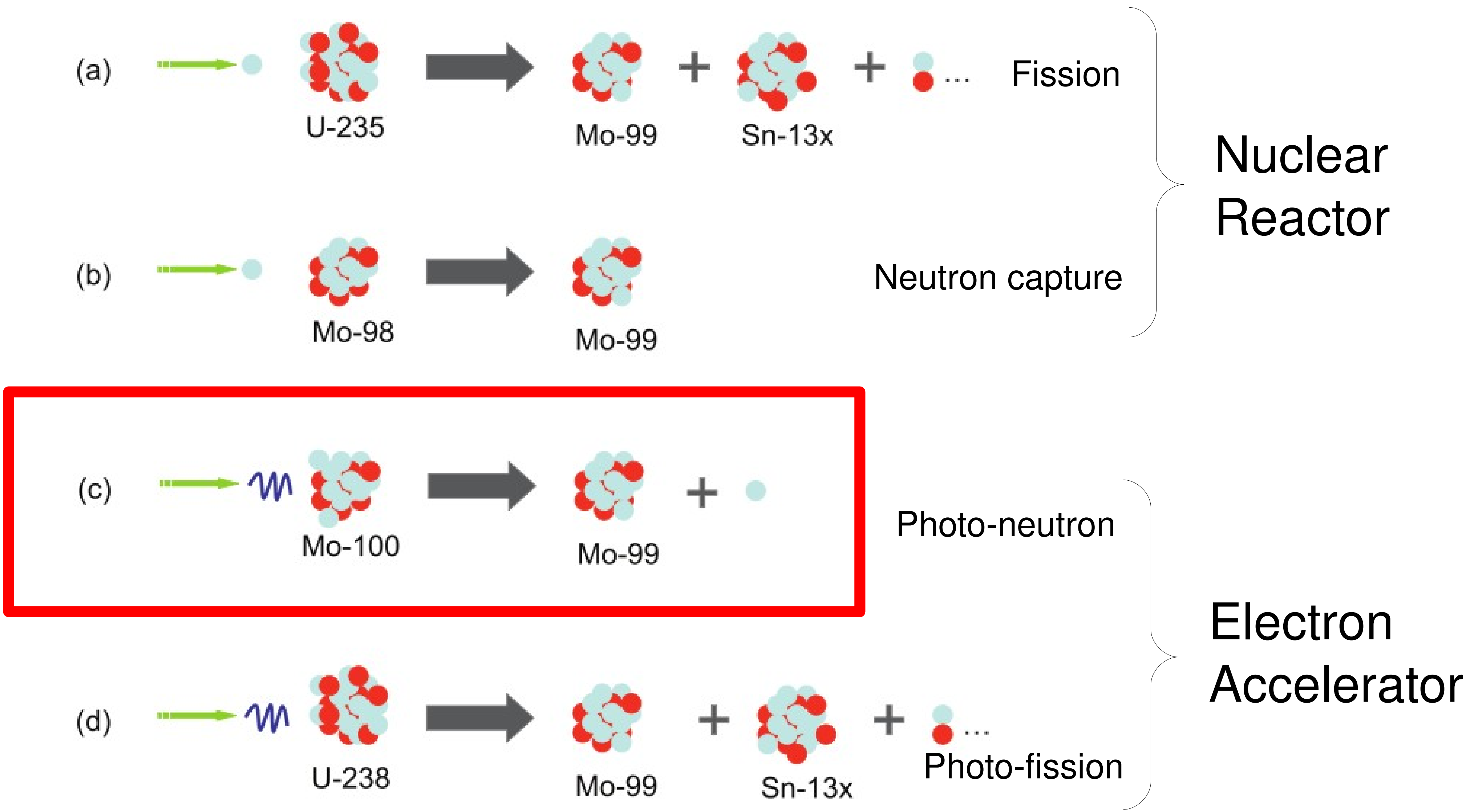


How can Winnipeg help?

- Two unique aspects to our proposal:
  - Alternate technology for Mo-99 production done using a small electron accelerator.
  - Conversion of the Mo-99 into a generator of Tc-99m also done within the province.

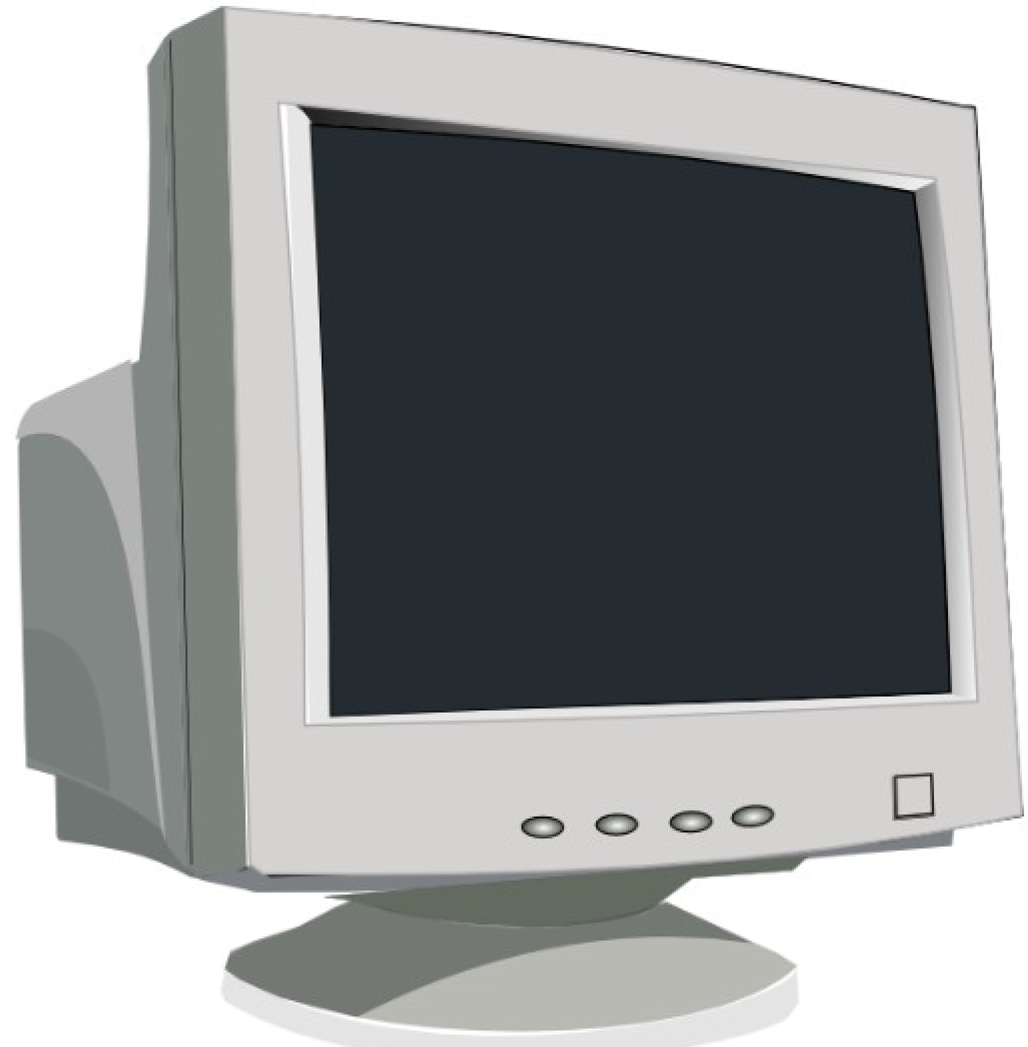
Prairie Isotope Production Enterprise

Ways to produce Mo-99



An example of a small electron accelerator

- Electron energy: 10,000 Volts.



An example of a bigger electron accelerator

- Electron energy: 10,000,000 Volts.

Acsion's Accelerator Facility in Manitoba

An example of a big electron accelerator

- Electron energy: 10,000,000,000 Volts.

Jefferson Lab, Newport News, VA

(I use all three of these electron accelerators.)

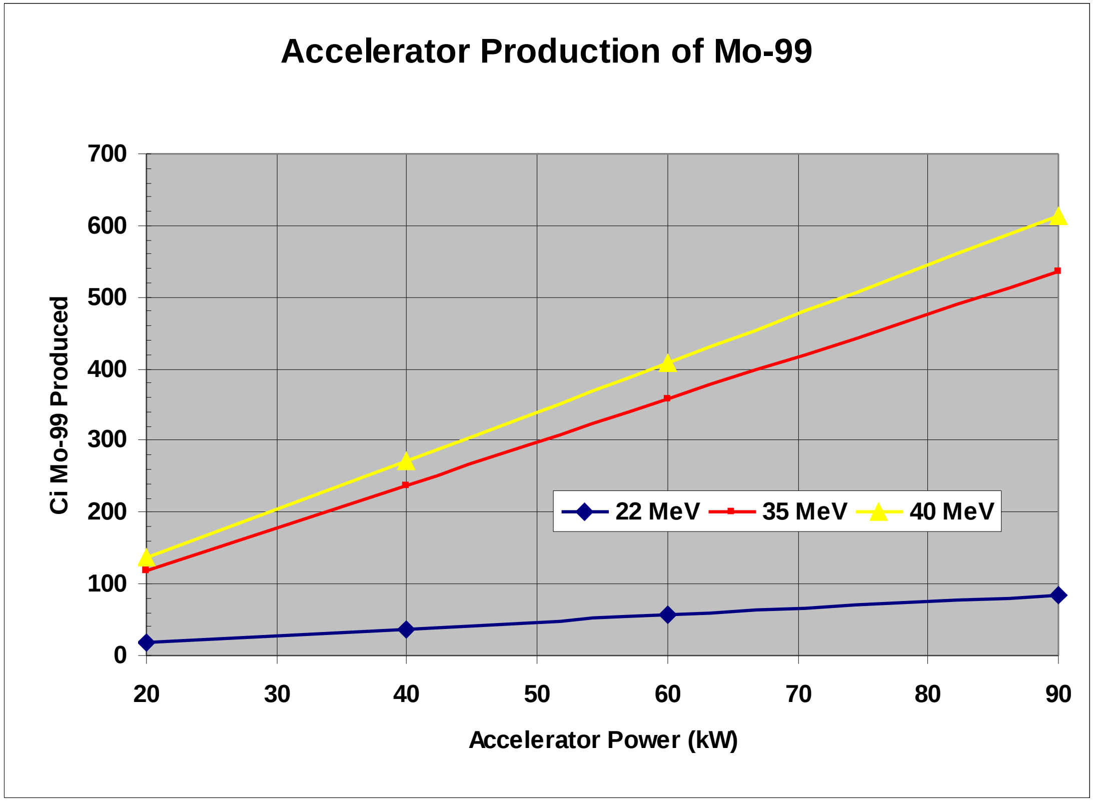
Desired Accelerator

- 35,000,000 Volt, 60 kW electron accelerator
- You can buy one. (From Mevex Corp, ON)

MEVEX
THE ACCELERATOR TECHNOLOGY COMPANY

Estimated daily production of Mo-99 on enriched Mo-100.

Canadian demand = 500 Ci/wk.



Electron accelerators

- Electron energy: 10,000,000 Volts.
- Note this is a very green technology: no long-lived radioactive waste.
- Very safe – accelerators already in use at hospitals today.

Acsion's Accelerator Facility in Manitoba

Processing the Moly Metal

- We must now take Moly Metal and liberate Mo-99 from it to make into a Tc-99m generator.
- This is different from taking U-235 and liberating Mo-99 (the usual process)

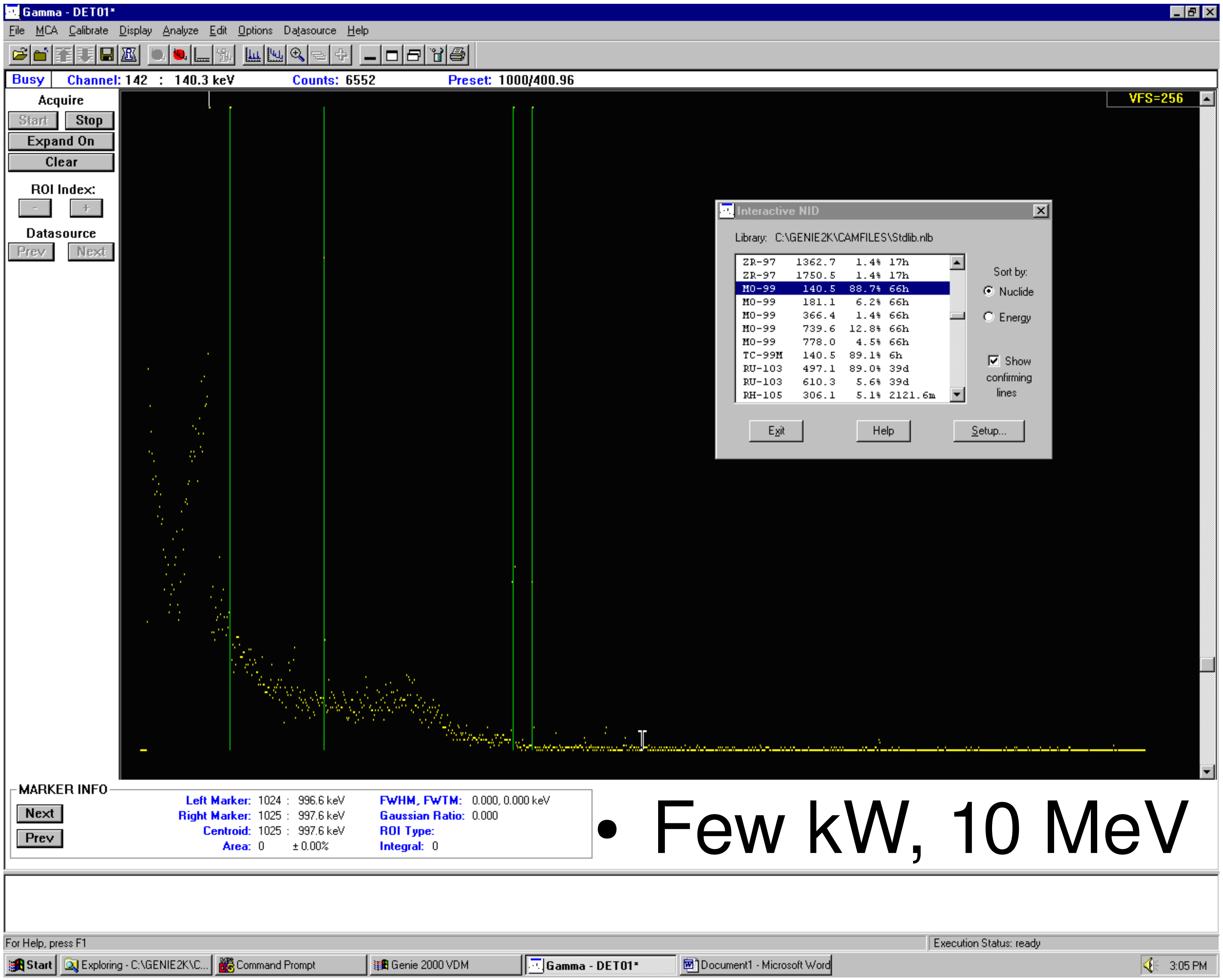
➢ Commercial processing technologies are available to convert Mo-100/Mo-99 targets with low activities into Tc-99m generators. Three extraction methods are used for Tc-99m; gel-moly method (zirconium molybdate) developed in several countries, a melt technology developed in the U.S and a powder technology (MoO_3 crystallization)

- You can buy one.
- UM Radiopharmacy is on board.

Schedule

- “Expression of Interest” submitted to Natural Resources Canada: July 2009 – answer in late Nov 2009.
- Produce Mo-99: October 2009. (We did it in Pinawa.)
- Generate Tc-99m: late 2009.
- Confirm Pharmaceutical qualities of Tc-99m: early 2010.
- Optimize process 2010 ~ 2011.
- Construct new accelerator and radiopharmaceutical facility 2012.
- Total project cost $35M over three years.
- Compare to nuclear reactor > $500M and 10 yrs.

Success in making Mo-99/Tc-99m at Acsion Industries, Pinawa



- Few kW, 10 MeV

Moving to the radiopharmacy

- Once sufficient Mo-99 in hand
  - fabricate generator of Tc-99m
  - radiopharmaceuticals, purity, clinical trials (WRHA)
  - Health Canada, CNSC licensing
  - Build facility

2. Clinical Utility – Selected radpharms to be labeled and tested.

   NB: 1Ci Mo >> 14GBq Tc (~80% yield, Day 2 cal.)

   i. MDP – upto 18.5GBq – Bone (metastases, fracture)
   ii. MIBI/Myoview – 5.5GBq/9GBq – Heart
   iii. Ceretec – 1.1GBq – Brain
   iv. Sulphur colloid – 2GBq – Liver/spleen/lymphatic system
   v. DTPA – 6GBq – Renal
   vi. MAG3 – 3GBq - Renal

K. Mang'era, UM/HSC

Possible Location for the New Facility

- Next to this:

New U. Winnipeg Science Complex and Richardson College for the Environment

Completion in 2011

Cutting-edge Science Complex for Winnipeg

Use them here

Make isotopes here

Going Beyond

- Should this technology work out, it could revolutionize the way radioisotopes are produced worldwide.
- Instead of being centralized at a few nuclear reactors, radioisotopes would be produced at local facilities close to hospitals.
- “Maybe we can franchise it.” -- Randy Kobes.

Our Team

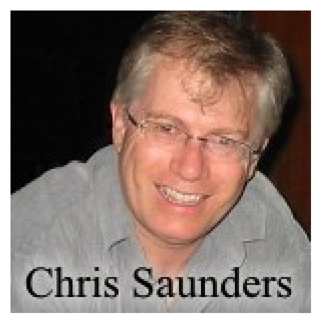
Rod

Randy

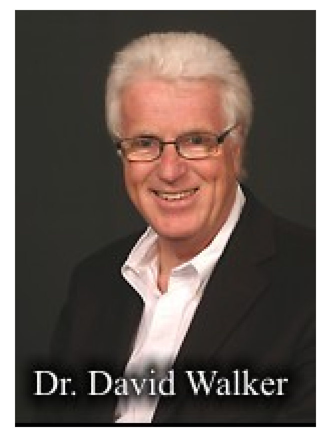
Jeff

John

Kennedy



Chris



David

Jennifer

Lloyd

Missing: Paul, Chris W., New Guy

Conclusions

- Current medical isotope shortage is preventing nuclear medicine imaging from occurring in hospitals worldwide.
- Science finds other ways of doing things in a crisis.
- Scientists from Winnipeg (and Pinawa) have a plan to produce Tc-99m based on commercially available technology that can be ready by 2012.

References

- Our website: http://pipe.uwinnipeg.ca
- Thank you for the slides I borrowed:
  - Chris Saunders, Acsion Industries
  - Kennedy Mang'era, UM/HSC Radiopharmacy
  - Tom Ruth, BCCA/TRIUMF
  - “Making Medical Isotopes: Report of the Task Force on Alternatives for Medical-Isotope Production”, TRIUMF, 2009.