Direct Production of $^{99m}$Tc: Progress of the TRIUMF-led Consortium

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TRIUMF was founded in 1968 and has delivered nearly 50 years of science and innovation for Canada.

Owned & operated by a consortium of 19 universities.

- 12 MEMBERS
- 7 ASSOCIATE MEMBERS
• Funding from federal government to develop alternate supply methods for medical isotopes
• TRIUMF joined with four other institutions to implement direct production of $^{99m}\text{Tc}$
  – University of British Columbia
  – British Columbia Cancer Agency
  – Centre for Probe Development and Commercialization
  – Lawson Health Research Institute
2009 to Present: Project Mandate

**Goals:**

- Demonstrate routine, reliable, commercial-scale production of $^{99m}$Tc via $^{100}$Mo(p,2n) at multiple sites, multiple brands;
- Obtain regulatory approval for clinical use in humans;
- Establish a business plan;
- Disseminate, commercialize the technology

**Hypothesis:** Future production will be from variety of sources (neutron, proton, electron) and market driven

Our Philosophy

Cyclotron + ARTMS Technology

Radiopharmacy

Clinic
Cyclotrons by the Numbers

• Direct production of $^{99m}$Tc mimics PET production (eg. $^{18}$F-FDG)
  – Daily, just-in-time
• Retrofit Canada’s existing cyclotrons
  – Suits concentrated population regions
• Decentralized Production
  – $^{99m}$Tc locally produced, locally used, competitively priced
  – Redundant supply to avoid widespread shortages
  – Fits with existing radiopharmacy distribution model
  – Complementary to:
    • other medical isotopes produced by cyclotrons ($^{18}$F)
    • other sources of $^{99m}$Tc
100Mo Targets

300 µA, 18 MeV, 5.4 kW

450 µA, 24 MeV, 10.8 kW

130 µA, 16.5 MeV, 2.1 kW

Technology Developed

100Mo Target
Cyclotron Modification
Optimize Irradiation
Purify 99mTcO4
Regulatory QA/QC
100Mo Recovery
### Real and Projected Yields of $^{99mTc}$

<table>
<thead>
<tr>
<th>Cyclotron Modification</th>
<th>Optimize Irradiation</th>
<th>Purify $^{99mTcO_4}$</th>
<th>Regulatory QA/QC</th>
<th>$^{100}$Mo Recovery</th>
</tr>
</thead>
</table>

#### 100Mo Target

<table>
<thead>
<tr>
<th>GE PETtrace</th>
<th>TR19</th>
<th>TR30 (@24 MeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.5 MeV, 130 μA</td>
<td>18 MeV, 300 μA</td>
<td>24 MeV, 500 μA</td>
</tr>
<tr>
<td>Theoretical 4.9 Ci (6h)</td>
<td>Theoretical 15.4 Ci (6h)</td>
<td>Theoretical 39 Ci (6h)</td>
</tr>
<tr>
<td>Achieved 4.7 Ci</td>
<td>Achieved 15.0 Ci (@ 300 μA)</td>
<td>Achieved ~32 Ci (@ 450 μA)</td>
</tr>
<tr>
<td>Expected Satn: 75.6 mCi/μA</td>
<td>Expected Satn: 103 mCi/μA</td>
<td>Expected Satn: 156.8 mCi/μA</td>
</tr>
</tbody>
</table>

- **TR19**: 18 MeV, 300 μA
  - Theoretical: 15.4 Ci (6h)
  - Achieved: 15.0 Ci (@ 300 μA)
  - Expected Satn: 103 mCi/μA

- **TR30 (@24 MeV)**: 24 MeV, 500 μA
  - Theoretical: 39 Ci (6h)
  - Achieved: ~32 Ci (@ 450 μA)
  - Expected Satn: 156.8 mCi/μA

Graph showing yield (Ci) over irradiation time (hrs) for different energy levels and currents.
Recycling method determined, recycled targets not yet implemented.

*Recycling $^{100}$Mo for direct production of $^{99m}$Tc on medical cyclotrons.*

• Issue: Mo/Tc generator approved in Canada as a medical device
• $^{99m}$Tc Pertechnetate requires Market Authorization
  – Small clinical trial to demonstrate same performance as generator derived pertechnetate
  – Quality data for 3 different radiopharmaceutical kit formulations (cationic, anionic, neutral)
• Clinical Trial approved by Health Canada
• 60 subject trial completed over 3 locations in Canada
• Trial data being analyzed & report prepared
• Kit study underway
• Full NDS submission anticipated imminently
• Assumptions
  – 1 6hr run/day, 5 days/wk, 48 wks/yr
  – 555 MBq pertechnetate dose, require 4x dose (due to decay)
  – 3% of Canadian population require a scan each year

<table>
<thead>
<tr>
<th>Machine</th>
<th>Pertechnetate Released Per run (GBq)</th>
<th>Annual Production (GBq)</th>
<th># Available Today</th>
<th>Possible Annual Production (GBq)</th>
<th>Canadian Annual Demand (GBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR24</td>
<td>874</td>
<td>210,000</td>
<td>4</td>
<td>840,000</td>
<td>2,331,000</td>
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<tr>
<td>TR19</td>
<td>334</td>
<td>80,000</td>
<td>3</td>
<td>240,000</td>
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<td>PETtrace</td>
<td>112</td>
<td>27,000</td>
<td>7</td>
<td>188,000</td>
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<tr>
<td>Cyclone18</td>
<td>167</td>
<td>40,000</td>
<td>3</td>
<td>120,000</td>
<td></td>
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<tr>
<td>Our Consortium only</td>
<td>134,000</td>
<td>Total Potential</td>
<td></td>
<td>1,388,000</td>
<td></td>
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</tbody>
</table>
• New Facility
  – Multi-institutional research hub
  – Ensure isotope supply security for the province
• TR24 cyclotron
• Facility ready 2021
• Ramp up from local $^{99m}$Tc supply (est. 90,000 doses/year) to provincial (est. 140,000 doses/year)
• Provincial Ministry of Health interested but not yet committed
• Be an OEM supplier of equipment for $^{99m}$Tc production to major cyclotron manufacturers
• Supply $^{100}$Mo solid targets to $^{99m}$Tc producers
• Supply other solid target plates to research and clinical users.

ARTMS Products Inc. Partners with Alliance Medical to Modernize, Stabilize UK Medical Isotope Supply Chain
• The teams at TRIUMF, BCCA, UBC, LHRI, CPDC, and TRIUMF Innovations

• TRIUMF receives federal funding via a contribution agreement with the National Research Council of Canada
Canada's national laboratory for particle and nuclear physics

Laboratoire national canadien pour la recherche en physique nucléaire et en physique des particules

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