Molybdenum-99 Production and Its Impact on the Medical Community

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Molybdenum-99 ($^{99}$Mo)

Parent of technetium-99m

Technetium-99m

Modern nuclear medicine imaging workhorse

Worldwide

80% of 30 million diagnostic nuclear medicine procedures performed annually\(^1\)

United States

50,000 procedures daily\(^2\)
Technetium-99m (\(^{99}\text{mTc}\))

30 Million Procedures Annually\(^3\)

<table>
<thead>
<tr>
<th>Region</th>
<th>Number of Procedures Performed Annually</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>12-15 million (40-50%)</td>
</tr>
<tr>
<td>Europe</td>
<td>6-7 million (20-23%)</td>
</tr>
<tr>
<td>Asia/Pacific</td>
<td>6-8 million (20-27%)</td>
</tr>
<tr>
<td>Other world regions</td>
<td>0.5 million (2%)</td>
</tr>
</tbody>
</table>

(Russian Federation, China, Central Asian countries not included because of a lack of data)

*Estimated worldwide growth through 2020: 1%-2% annually\(^3\)
# Global Molybdenum-99 Production & Consumption

<table>
<thead>
<tr>
<th>Country/Region</th>
<th>Production</th>
<th>Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Union</td>
<td>45%</td>
<td>22%</td>
</tr>
<tr>
<td>Canada</td>
<td>40%</td>
<td>4%</td>
</tr>
<tr>
<td>South Africa</td>
<td>10%</td>
<td>-----</td>
</tr>
<tr>
<td>Australia</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Other</td>
<td>-----</td>
<td>12%</td>
</tr>
<tr>
<td>Russia</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Japan</td>
<td>0%</td>
<td>14%</td>
</tr>
<tr>
<td><strong>USA</strong></td>
<td><strong>0%</strong></td>
<td><strong>46%</strong></td>
</tr>
</tbody>
</table>


$^{99}$Mo/$^{99m}$Tc Supply Chain

1. Nuclear Reactor
   Neutron bombardment of uranium target produces numerous daughter isotopes including $^{99}$Mo

2. Isotope production
   $^{99}$Mo extraction & purification

3. $^{99}$Mo/$^{99m}$Tc Generator manufacture

4. $^{99}$Mo/$^{99m}$Tc Generator distribution
   Hospitals
   Radiopharmacies
$^{99}$Mo/$^{99m}$Tc Supply Chain is Fragile

Entire worldwide production
< 10 sites (NONE in the United States)

Reactor Age

> 45 yrs. old: NRU in Canada, HFR, Osiris, & BR2 in Europe, & Safari in South Africa account for 95% of world $^{99}$Mo production

Decommissioning (2017-2020)
Extensive downtime (2008-2010)
NRU: 15 months
HFR: 13 months

Highly enriched uranium (HEU) availability
US to stop exporting HEU
\[^{99}\text{Mo/}^{99\text{m}}\text{Tc Supply Chain Interruption Consequences}\]

Potentially wreak havoc on patient care

Effects on diagnostic testing*
  Postponed/cancelled studies
  Alternative, less desirable radiopharmaceuticals
  Alternative, more expensive procedures

Effects on patient care
  Delays in diagnosis
  Delays in treatment

*United States 2008-2012: 16 million $\rightarrow$ 14.5 million (-9%)\(^5\)
Coping with $^{99}$Mo/$^{99m}$Tc Supply Chain Interruptions (2008-2010)

Short Term Solutions

More frequent generator elution
Maximizes $^{99m}$Tc activity extracted, improving yield

Revised examination schedules
Maximizes amount of $^{99m}$Tc available
Provides greater access to patients in most need
Results in cancelled studies
Coping with $^{99}$Mo/$^{99m}$Tc Supply Chain Interruptions (2008-2010)

Short Term Solutions

Decrease administered activity
  Longer imaging times $\rightarrow$ loss of image quality

Alternative radiopharmaceuticals

Nuclear cardiology (60% of $^{99m}$Tc studies)
  Thallium-201
    Inferior image quality
    Increased patient radiation exposure
    Increased downstream testing$^6$
    Increased cost$^6$
Coping with $^{99}$Mo/$^{99m}$Tc Supply Chain Interruptions (2008-2010)

Short Term Solutions

Alternative radiopharmaceuticals

**Nuclear cardiology** (60% of $^{99m}$Tc studies)
- Nitrogen-13, Rubidium-82
- Limited number of PET imaging systems vs. SPECT imaging systems

**Bone scintigraphy** (20% of $^{99m}$Tc studies)
- Fluorine-18
- Limited number of PET imaging systems vs. SPECT imaging systems
- Not yet reimbursable
What is Needed?

Readily available consistent supply of $^{99}$Mo ($^{99m}$Tc) to facilitate performance of nuclear medicine procedures necessary for patient care
Long Term Solutions

Decentralize $^{99}$Mo production

Entire worldwide production < 10 sites (NONE in the US)

Develop reliable domestic $^{99}$Mo source
Long Term Solutions

Develop reliable domestic $^{99}$Mo source

Two companies currently active

**NorthStar Medical Technologies (WI/ MO)**
- Neutron capture technology
- Phase I groundbreaking: 2014
- Applied for FDA approval
- Operational: ? 2015

**Shine Medical Technologies (WI)**
- LEU technology
- ? up to 1/3 world’s $^{99}$Mo needs
- Construction approval pending
- Operational: ? end of 2017
- Major obstacle: Financial
References

1 Van Noorden R. Nature. 2033;504:202-204.
Acronyms

- **BR2** – Belgian Reactor 2
- **FDA** – US Food and Drug Administration
- **HEU** – highly enriched uranium
- **HFR** – High Flux Reactor
- **LEU** – low enriched uranium
- **$^{99}\text{Mo}$** – Molybdenum-99
- **NRU** – National Research Universal Reactor
- **$^{99m}\text{Tc}$** – Technetium-99m