United States Nuclear Regulatory Commission

Protecting People and the Environment

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 (^{99m}Tc)

30 Million Procedures Annually[3]

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

(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[4]

Country/Region	Production	Consumption
European Union	45%	22%
Canada	40%	4%
South Africa	10%	------
Australia	2%	1%
Other	-----	12%
Russia	1%	1%
Japan	0%	14%
USA	0%	46%

^{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}Mo/^{99m}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 →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 ⟶ 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.

2 Cutler CS et al. J Nucl Med. 2014;55:1208–1213.

3 Report on Molybdenum-99 Production for Nuclear medicine 2010-2020 (APIES 2008)

4 Khlopkov A, et al. Ending HEU Use in Medical Isotope Production:Options for US – Russian Cooperation. NTI Report February 14, 2014.

5 IMV Market Report Dec. 26, 2013

6 Small GR, et al. Lessons from the Tc-99m shortage: implications of substituting Tl-201 for Tc-99m single photon emission computed tomography. Circ Cardiovasc Imaging. 2013;6:683-691.

Acronyms

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