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Photonuclear production of Mo-99/Tc-99m using molybdenum trioxide and activated carbon

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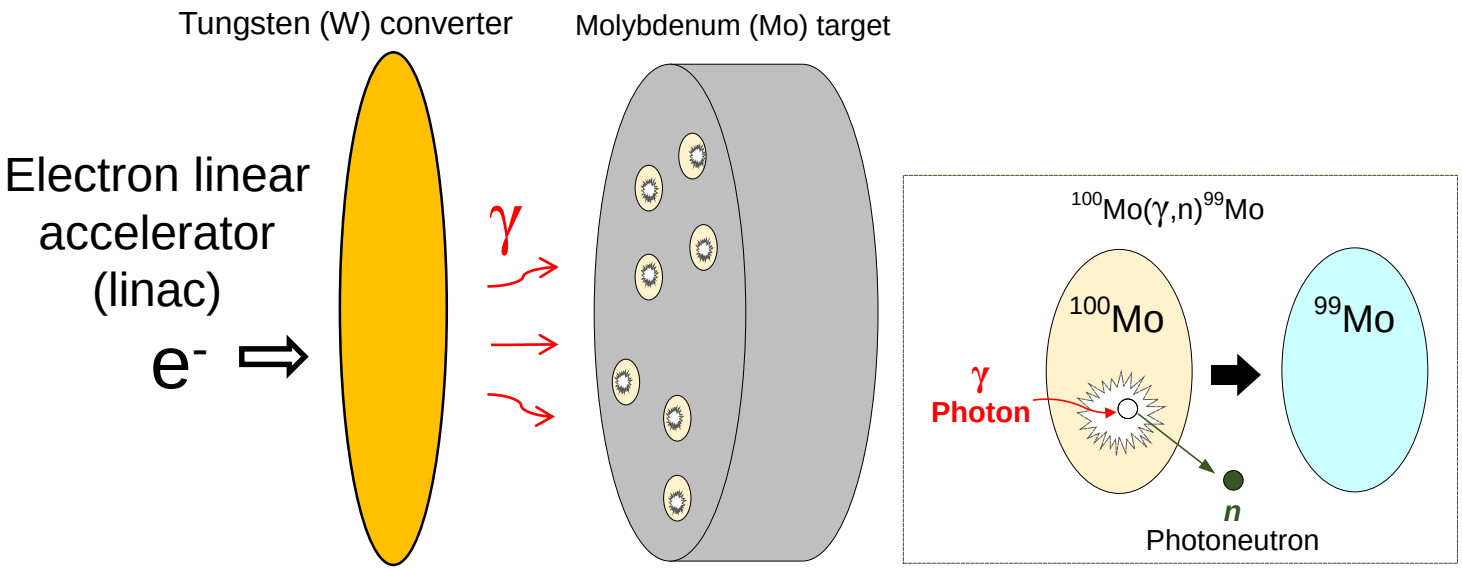
Contents

1. ^{99}Mo production via $MoO_3(\gamma,n)$
2. ^{99m}Tc separation and purification using TcMM
3. ^{100}Mo recovery from spent $Na_2MoO_4(aq)$
4. Electron linear accelerator design
5. Summary and current works

Photonuclear production of ^{99}Mo



^{100}Mo$(\gamma,n)^{99}$Mo

- Nuclear reaction between photons (γ) and a ^{100}Mo nucleus
- Threshold is ~8 MeV; electron linac can be used as the source of these high-energy photons (bremsstrahlung)
- We irradiate MoO_3 pellets rather than metallic Mo disks

  – Why?

Merits of using MoO_3 over metallic Mo

[1]	MoO_3  Spark plasma sintering	Metallic Mo  Spark plasma sintering
Molar mass ($g\ mol^{-1}$)	143.94	95.94
Melting point (K)	1068.15	2895.15
Boiling point (K)	1428.15	4912.15
Mass density ($g\ cm^{-3}$)	4.69	10.28
Pros	• Simple dissolution, and hence • Easy ^{100}Mo recovery from spent $Na_2MoO_4(aq)$ • Easy palletization	• High density in both powder and pellet forms • Efficient target cooling

[1] K. Ishikawa et al. (2011), AESJ 2011 Annual Meeting, Fukui University, Fukui, Japan.

Pelletization: MoO_3 vs. Metallic Mo

[1]	MoO_3  Spark plasma sintering	Metallic Mo  Spark plasma sintering
Powder mass density ρ_{pow} (g cm^{-3})	4.69	10.28
Pellet theoretical density ρ_{pel} (g cm^{-3})	4.45 ($= 0.95\ \rho_{\mathrm{pow}}$) at $T_s = 873.15$ K sintering temperature	7.29 ($= 0.71\ \rho_{\mathrm{pow}}$) at $T_s = 1373.15$ K

⇧

MoO_3 is pelletized
at lower T_s and hence shorter sintering time!

[1] K. Ishikawa et al. (2011), AESJ 2011 Annual Meeting, Fukui University, Fukui, Japan.

MoO_3 irradiation using L-band e^- linac


[1]

L-band (1.3 GHz) electron linac at KURRI[2], Japan

- Beam energy: 30–46 MeV
- Average beam power: ~10 kW
- We have been irradiating [^{nat}Mo]MoO_3 and [^{enr}Mo]MoO_3 pellets using this linac (enriched in ^{100}Mo)

We will address experimental results conducted on Dec. 12–22, 2016; the irradiation conditions were

Beam energy	35 MeV
Average beam power	1.19 kW
Beam-on time	10 min
[^{nat}Mo]MoO_3 pellets  Before & after irradiation	• ϕ 10 mm, 3 mm-thick, 1.06 g • Three such pellets were irradiated

[1] http://www.rri.kyoto-u.ac.jp/en/facilities/ela
[2] KURRI stands for Kyoto University Research Reactor Institute.

Low specific activity (LSA) of (γ,n)^{99}Mo

$$\frac{2\ \text{mg Mo}}{\text{g Al}_2\text{O}_3} \times x\ \text{g Al}_2\text{O}_3 = 4\ \text{mg Mo}$$

$x = 2$[1]

- $\frac{2\ \text{mg Mo}}{\text{g Al}_2\text{O}_3}$: Mo adsorption cap. of alumina[2]
- $x\ \text{g Al}_2\text{O}_3$: Amount of alumina per column
- $4\ \text{mg Mo}$: Amount of Mo per column

$$A_{sp,F-Mo} \cong 1.85 \times 10^5\ \text{GBq/g}$$[1]

fission

$$\left(4\ \text{mg Mo} \times \frac{1.85 \times 10^5\ \text{GBq}}{\text{g Mo}}\right) = 7.4 \times 10^2\ \text{GBq} = 20\ \text{Ci}$$

(Before calibrated to six-day Ci)

$$A_{sp,\gamma-Mo} \cong 67.35\ \text{GBq/g}$$ (2,747 times lower)

photonuclear — Monte Carlo simulation result

$x = 5,494$

To obtain the same ^{99}Mo activity per ^{99m}Tc generator using photonuclear-produced ^{99}Mo, ~5.5 kg of alumina is required
→ New ^{99m}Tc generator compatible with LSA ^{99}Mo is needed

[1] IAEA (2013), Non-HEU Production Technologies for Molybdenum-99 and Technetium-99m.
[2] A. Dash, F. F. R. Knapp, Jr., and M. R. A. Pillai (2013), ^{99}Mo/^{99m}Tc separation: An assessment of technology options. *Nucl. Med. Biol.* 40(2): 167–176.

Technetium Master Milker (TcMM)

TcMM

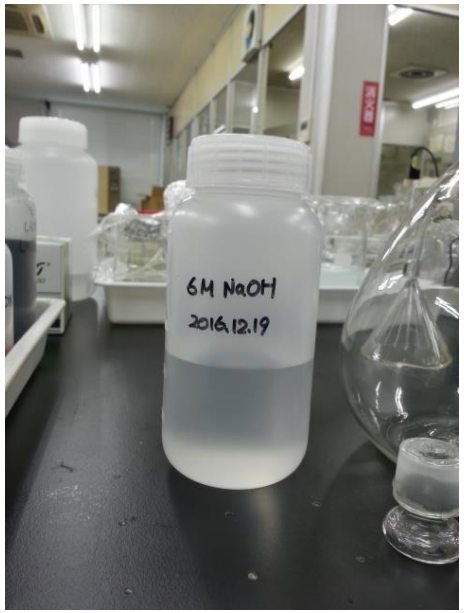
- Developed by **Kaken Inc., Mito, Japan**
- Can be used with both LSA- and HSA-^{99}Mo
- Uses two columns of:
  - Activated carbon (AC), which adsorbs Tc(VII) oxoanions but not Mo(VI) ones (opposite of alumina)
  - Activated alumina (AA), which adsorbs Mo(VI) oxoanions in the eluate of Tc(VII) oxoanions
- Exhibits ^{99m}Tc elution efficiencies of $\geq$ 90%[2]
- Consists of six steps; these will be explained step by step

Related articles

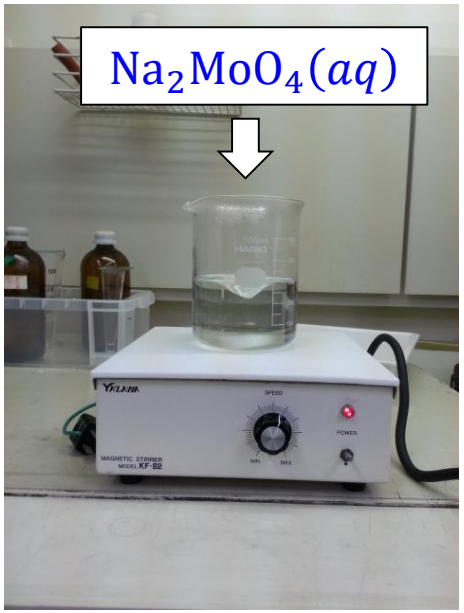
[1] S. Sekimoto et al. (2017), Separation and purification of ^{99m}Tc from ^{99}Mo produced by electron linear accelerator, *J. Radioanal. Nucl. Chem.* 311(2): 1361–1366.
[2] K. Tatenuma et al. (2016), Generator of Highly Concentrated Pure ^{99m}Tc from Low Specific Activity ^{99}Mo Produced by Reactor and/or Electron Linear Accelerator, 2016 Mo-99 Topical Meeting, St. Louis, Missouri.
[3] K. Tatenuma et al. (2016), Method of recovering enriched radioactive technetium and system therefor, US Patent 9,236,153.
[4] K. Tatenuma et al. (2014), A mass-production process of a highly pure medical use 99mTc from natural isotopic Mo(n,γ)99Mo without using uranium, *RADIOISOTOPES* 63(11): 501–513.

① Dissolution of irradiated MoO_3 pellets

Irradiated MoO_3 pellets



6-M $NaOH(aq)$



Magnetic stirrer

- MoO_3 pellets were dissolved in a 6-M $NaOH(aq)$ solution, simply by

$$MoO_3(s) + 2NaOH(aq) \rightarrow H_2O(l) + \underbrace{Na_2MoO_4(aq)}_{2Na^+(aq) + [MoO_4]^{2-}(aq)}$$

- Diluted to 200 mL, the $Na_2MoO_4(aq)$ solution had an average pH of 8.12 out of three such solutions

② ^{99m}Tc adsorption to activated carbon

2.0-g AC column

Activated carbon (AC)

- Has a high surface-to-volume ratio
- Used in purifying air and water, etc.
- Adsorbs $[TcO_4]^-(aq)$ ions but not $[MoO_4]^{2-}(aq)$ ones

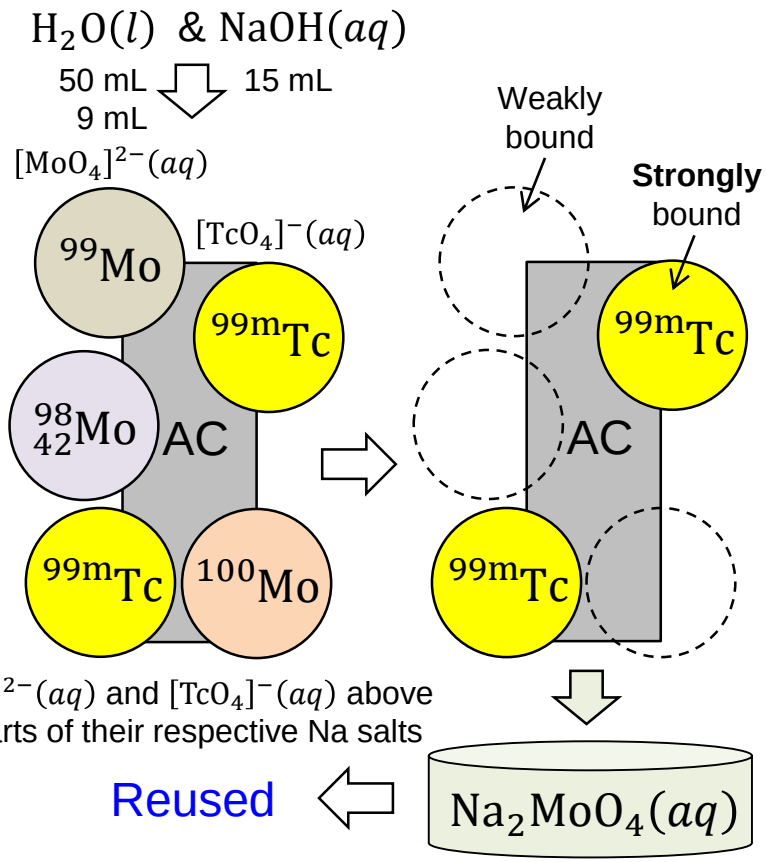
Why?

The principle of selective adsorption of $[TcO_4]^-(aq)$ to AC remains unclear; we are investing and planning experiments.

- The 200-mL $Na_2MoO_4(aq)$ solution, containing $[MoO_4]^{2-}(aq)$ constantly decaying to $[TcO_4]^-(aq)$, was poured into the AC column.
- $[TcO_4]^-(aq)$ ions, where Tc consists of ^{99m}Tc and a small amount of ^{99g}Tc, were then tightly bound to the AC, while only marginal amounts of the $[MoO_4]^{2-}(aq)$ ions, where Mo consists of various Mo isotopes, were captured by the AC.

③ ^{99}Mo removal from activated carbon

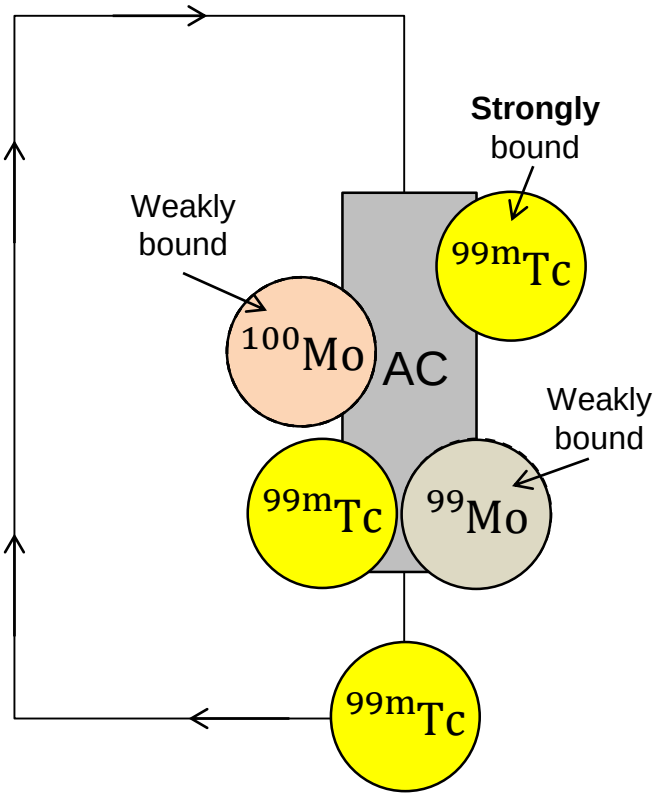
2.0-g AC column



- The minute amounts of $[MoO_4]^{2-}(aq)$ ions were flushed into the poured $Na_2MoO_4(aq)$ solution with $H_2O(l)$ and $NaOH(aq)$.
- The $Na_2[^{99}Mo]MoO_4(aq)$ solution was then allowed to decay to $Na[^{99m}Tc]TcO_4(aq)$ and poured again into the AC column.

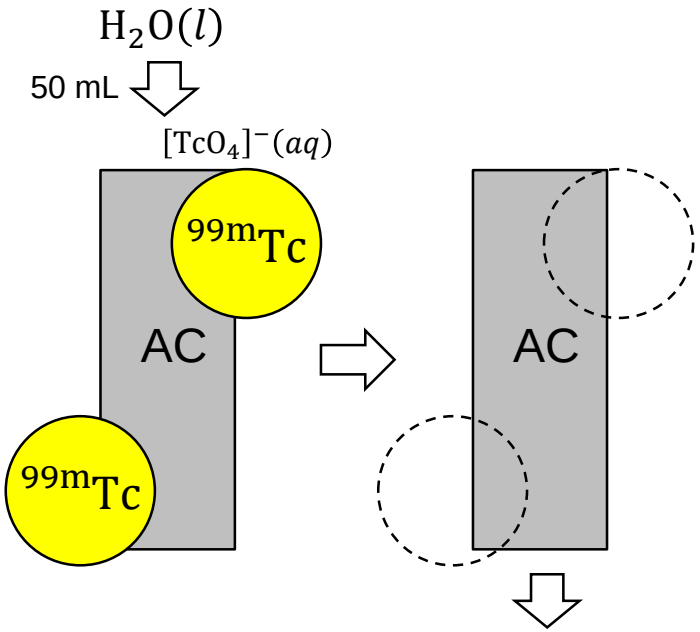
③ ^{99}Mo removal from activated carbon

- This "AC-filtered" $Na_2MoO_4(aq)$ solution in which ^{99}Mo decays to ^{99m}Tc is reused until the ^{99}Mo loses most of its activity



④ ^{99m}Tc elution from activated carbon

2.0-g AC column

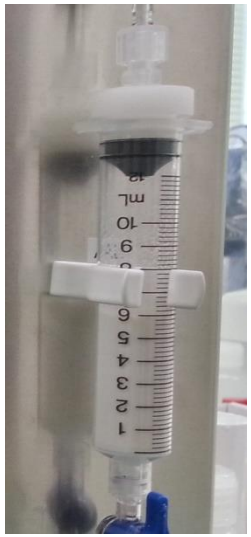


- The AC-captured $[TcO_4]^-(aq)$ ions were then eluted with water.
- Still, the excessive $Na^+(aq)$ ions, a part of $NaTcO_4(aq)$, and trace amounts of ionic compounds of Mo and Nb needed to be removed.

⑤ ^{99m}Tc purification by activated alumina

5-cc IER column

+



6-g AA column

Ion exchange resin (IER)

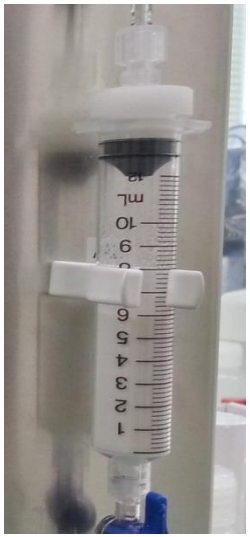
- Removes $\mathrm{Na}^+(aq)$ ions

Activated alumina (AA)

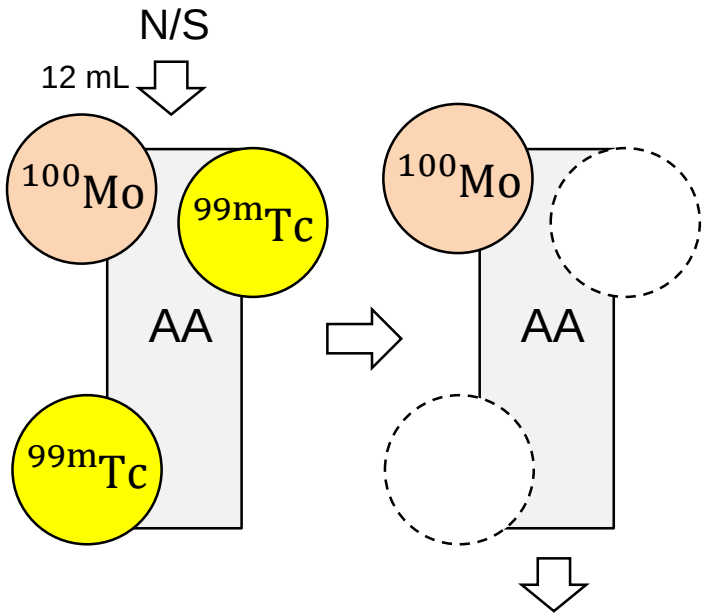
- Adsorbs $\mathrm{Na}^+(aq)$ ions and ionic compounds of Mo and Nb

- The $\mathrm{Na}^+(aq)$ ions and ionic compounds of Mo and Nb in the $\mathrm{NaTcO_4}(aq)$ eluate were removed by columns of 5-cc IER and 6-g AA, respectively.
- A column of 12-g AA can do the same task without IER.

⑥ ^{99m}Tc elution from activated alumina



6-g AA column



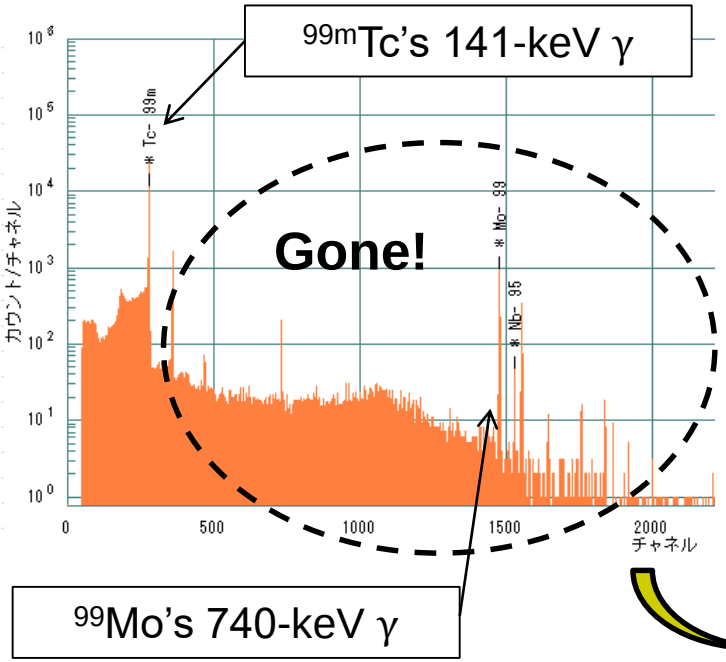
$$Na[^{99m}Tc]TcO_4(aq)$$

$Na^+(aq)$ ***not*** in excess

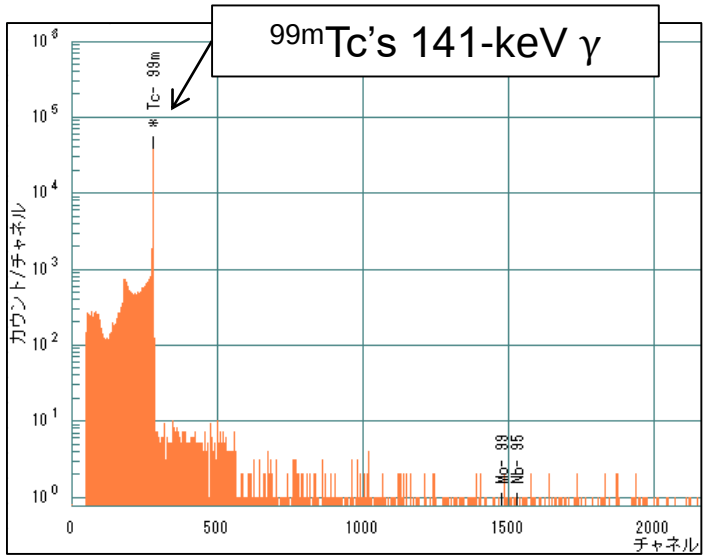
- Finally, highly pure ^{99m}Tc was eluted with N/S in the form of $NaTcO_4(aq)$, or to be exact, $[TcO_4]^-(aq)$.

^{99m}Tc elution efficiency

$Na_2MoO_4(aq)$ solution before TcMM



$NaTcO_4(aq)$ solution (eluate) after TcMM



- Virtually all Mo and Nb species were eliminated.
- ^{99m}Tc elution efficiency: 81.17% on average out of the three irradiated [^{nat}Mo]MoO_3 pellets, about 10% lower than it could be.
  → Short elution time could be the reason: 40-min TcMM experiments showed elution efficiencies of 90–95%, but in this TcMM experiment the elution time was only 20 mins

[1] K. Tatenuma et al. (2016), 2016 Mo-99 Topical Meeting, St. Louis, Missouri.

TcMM actual use history using $^{98}Mo(n,\gamma)^{99}Mo$

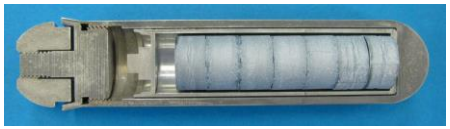
$^{98}Mo(n,\gamma)^{99}Mo$

JRR-3, JAEA, Tokai, Japan

NUCEF-BECKY, JAEA, Tokai, Japan

Oct. 5–12, 2010

- Irradiated [^{nat}Mo]MoO_3 capsule:



  Three such capsules, weighed 293.4 g (Mo: 195.6 g) in total, were irradiated for a week
- ^{99}Mo yield: 2.99 TBq (80.81 Ci)
- ^{99}Mo specific activity: 14.8 GBq/g

Oct. 13–27, 2010

- Separation and purification of ^{99m}Tc using TcMM
- ^{99m}Tc elution efficiency: 90–98%
- ^{99m}Tc radionuclidic purity as a gamma emitter: 6N (99.9999%)

Having proved its high accuracy and precision many times, TcMM is ready to be commercialized

[1] http://jrr3.jaea.go.jp/jrr3e/1/11.htm
[2] https://www.jaea.go.jp/english/04/ntokai/hot/hot_04.html

TcMM summary

ϕ 20 mm; 10 mmt

MoO_3 powder
[^{nat}Mo] or [^{enr}Mo]

Pelletization

e$^-$ linac

γ-irradiation of MoO_3 pellets

[^{LSA}Mo]MoO_3 dissolution by NaOH(*aq*)

$Na_2[^{LSA}Mo]MoO_4(aq)$

LSA: low specific activity
^{nat}Mo: naturally occurring Mo
^{enr}Mo: enriched to >95% in ^{100}Mo
^{LSA}Mo: ^{99}Mo having LSA

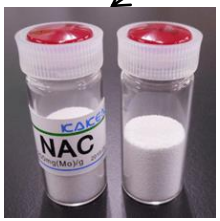
^{100}Mo recycle by precipitation

^{enr}Mo

^{nat}Mo

Liquid waste

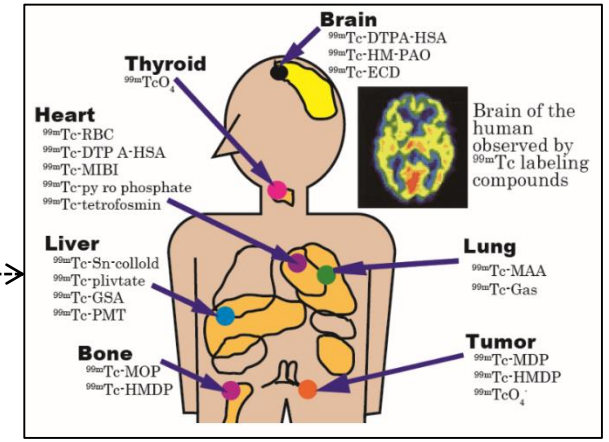
Spent $Na_2MoO_4(aq)$



Nano-sized alumina

$Na[^{99m}Tc]TcO_4(aq)$

^{99m}Tc-radiopharma.



^{100}Mo recovery from spent $Na_2MoO_4(aq)$

$[^{enr}Mo]MoO_3$ pellets —(γ, n)→ $[^{99}Mo]MoO_3$ pellets

Dissolution by

$$[^{99}Mo]MoO_3(s) + 2NaOH(aq) \rightarrow H_2O(l) + \mathbf{Na_2[^{99}Mo]MoO_4}(aq)$$

$\mathbf{Na_2[^{99}Mo]MoO_4}(aq)$

TcMM → $\mathbf{Na[^{99m}Tc]TcO_4}(aq)$

Spent $Na_2MoO_4(aq)$ containing "expensive" non-activated ^{100}Mo

Purification of $Na_2MoO_4(aq)$ by AC, etc.

Precipitation → Liquid waste

$MoO_3(s)$

Purification and drying

MoO_3 powder

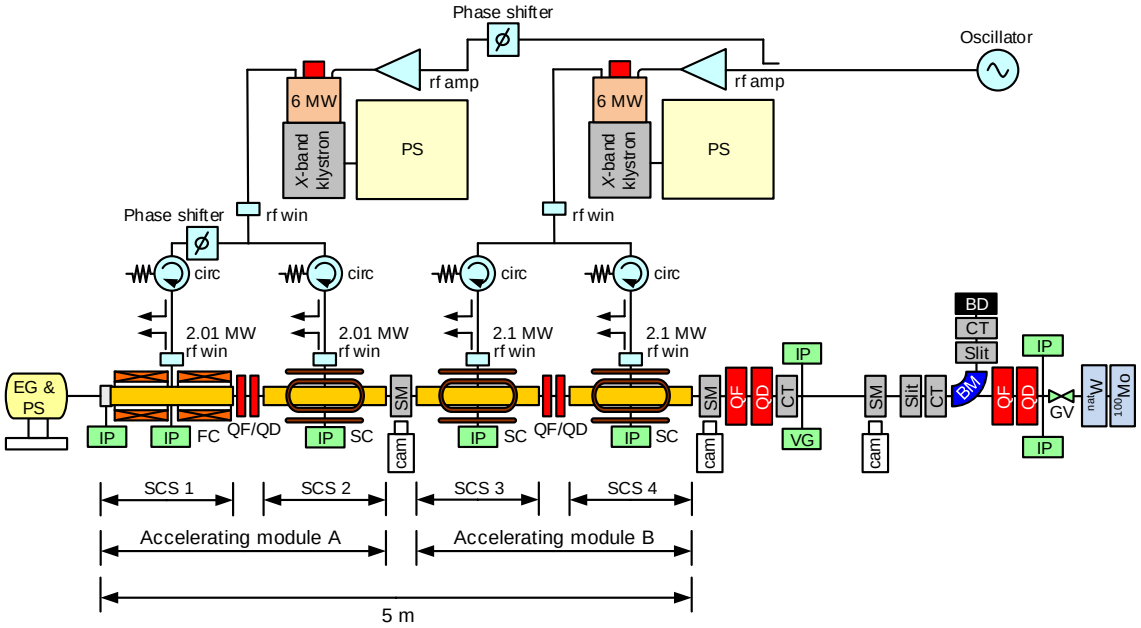
Powder → Pellet by spark plasma sintering

^{100}Mo recovery schematic

Goal recovery rate: ≥99%

X-band e^- linac dedicated to ^{99}Mo production

[1,2]



- Commissioned in 1965, the KURRI L-band electron linac is used for experiments and education; an electron linac dedicated to ^{99}Mo production is necessary.
- We have designed such a ^{99}Mo-producing electron linac, downsized by adopting X-band radio frequency.
- Design beam energy and power (average) are 35 MeV and 9.1 kW, respectively[1-2].
- 11 of the designed electron linac can meet the Japanese ^{99}Mo/^{99m}Tc demand[1].

[1] J. Jang, M. Yamamoto, and M. Uesaka (2017), Design of an X-band electron linear accelerator dedicated to decentralized ^{99}Mo/^{99m}Tc supply: From beam energy selection to yield estimation, *Phys. Rev. Accel. Beams* 20(10) 104701.

[2] J. Jang, M. Yamamoto, and M. Uesaka (2016), Development of a compact X-band electron linac for production of Mo-99/Tc-99m, IPAC'16, Busan, Rep. of Korea.

Summary and future work

Summary

- We use MoO_3 because of its simpler dissolution and easier pelletization compared with those of metallic Mo.
- TcMM can extract ^{99m}Tc from photonuclear-produced LSA-^{99}Mo as well as fission-produced HSA-^{99}Mo with an average elution efficiency of $\geq 90\%$, and is ready for commercialization.
- We designed a compact X-band electron linac dedicated to decentralized ^{99}Mo production; 11 such linacs can make Japan self-sufficient in ^{99}Mo/^{99m}Tc.

Current work

- The principle of $[\mathrm{TcO_4}]^-(aq)$ adsorption to AC remains elusive; we are investigating and planning experiments.
- Recovering non-activated ^{100}Mo from a spent $\mathrm{Na_2MoO_4}(aq)$ solution is also under investigation.

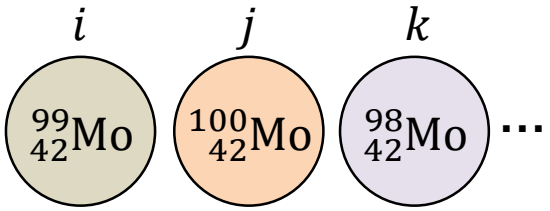
Thank you for attention

Low specific activity of $^{100}Mo(\gamma, n)^{99}Mo$

$$A_{Mo}(t_{irr} = 72h) = 687\ GBq$$

Monte Carlo simulation results at 35 MeV, 260 μA, and $\mathcal{V} = 1\ cm^3$

$$A_{sp,i} = \frac{A_i}{m_i + \sum_{j \neq i} m_j}$$



$A_{sp,i}$: specific activity of a radionuclide i
A_i: activity of a radionuclide i

m_i: mass of a radionuclide i
m_j: mass of all nuclides (stable or radioactive) isotopic with i

Mo mass density $\rho = 10.2\ g\ cm^{-3}$
Mo target volume $\mathcal{V} = 1\ cm^3$

$$A_{sp,Mo}\ (72\ h) = \frac{687\ GBq}{10.2\ g} = 67.35\ GBq/g$$

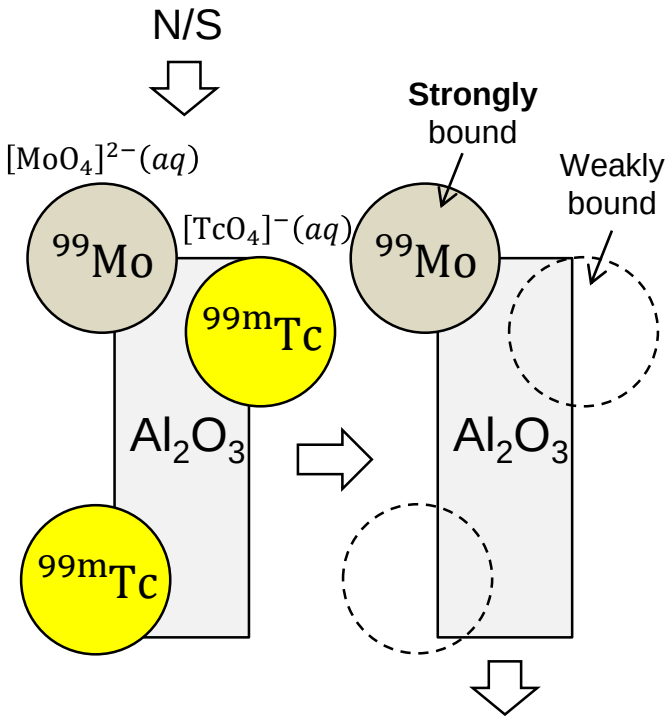
$GBq\ ^{99}Mo/g\ ^{all}Mo$

Alumina vs. Activated carbon

Alumina chromatography

- Can be used for F-^{99}Mo
- Stationary phase: $Al_2O_3(s)$
- Mobile phase: normal saline

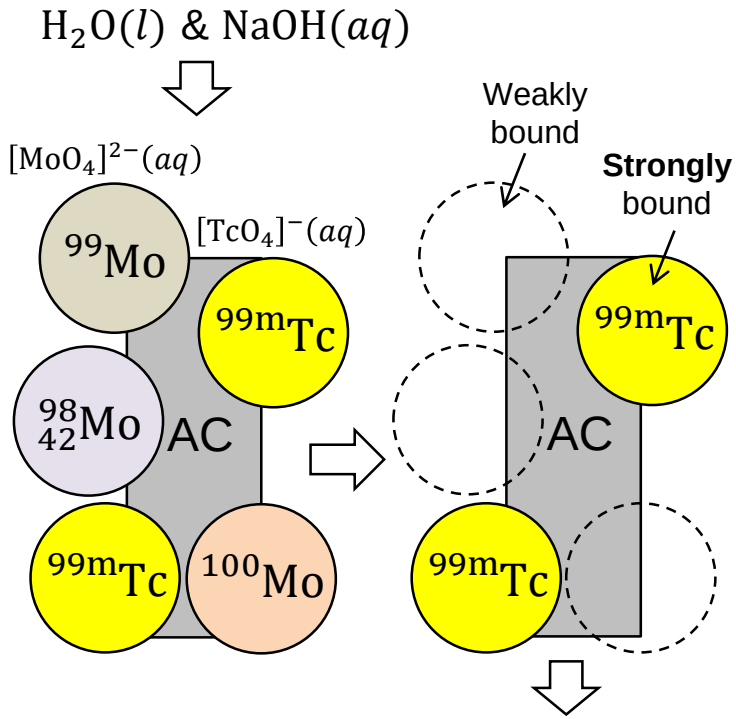
N/S; 0.9% NaCl(*aq*)



$NaTcO_4(aq)$
Sodium pertechnetate

AC chromatography (TcMM)

- Can be used for F-^{99}Mo and γ-^{99}Mo
- Stationary phase: activated $^{nat}C(s)$
- Mobile phase: $H_2O(l)$ and $NaOH(aq)$



$Na_2MoO_4(aq)$
Sodium molybdate

$[MoO_4]^{2-}(aq)$ and $[TcO_4]^{-}(aq)$ above are parts of their respective Na salts