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Development of Fundamental Technologies for Domestic Production of Medical Radioisotope (Technetium-99m)

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1. Introduction

- Technetium-99m (^{99m}Tc; $T_{1/2}$=6 h) is used in over 30 million medical imaging procedures worldwide every year. (about 80% of all nuclear medicine procedures)

- Japan is the world's third-largest consumer of ^{99}Mo (^{99}Mo; $T_{1/2}$=66 h, ^{99m}Tc is daughter nuclide of ^{99}Mo), and relies entirely on imports for its demand.

- Recently, it has been difficult to carry out a stable supply of ^{99}Mo/^{99m}Tc for some problems such as aging of reactors which producing ^{99}Mo and obstructions in transportation.

- The irradiation target for ^{99}Mo production has been changed to the low enriched uranium (LEU) from viewpoints of nuclear security and so on. However, ^{99}Mo production with LEU has some problems.

Thus, ^{99}Mo production by (n, γ) method has been developed as a resolution of the above problems under the project of the Tsukuba International Strategic Zone.
In this presentation, the R&D items and the experimental results for the ^{99}Mo/^{99m}Tc production development in this project is introduced.

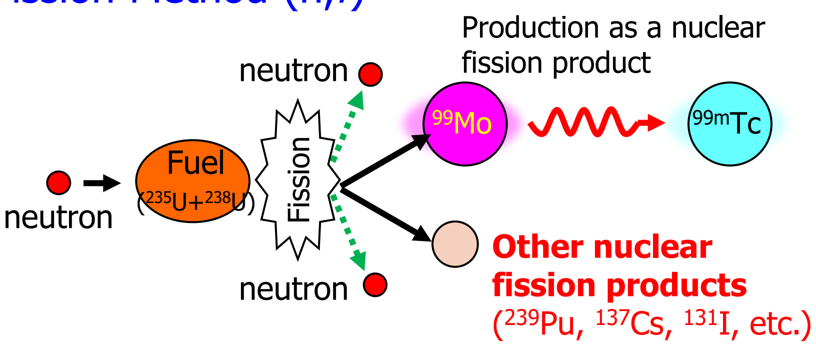
2. Selection for ^{99}Mo Production

^{99}Mo is produced almost all with enriched uranium.

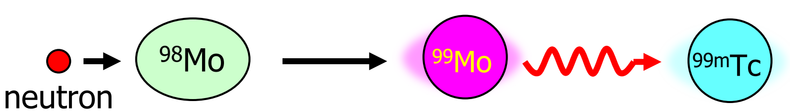
- Limited availability of highly-enriched Uranium,
- Necessity of a technology similar to nuclear fuel recycling
- Necessity of management in term of non-proliferation and nuclear security

Production Methods of ^{99}Mo

Fission Method (n,*f*)



Neutron Activation Method (n,γ)



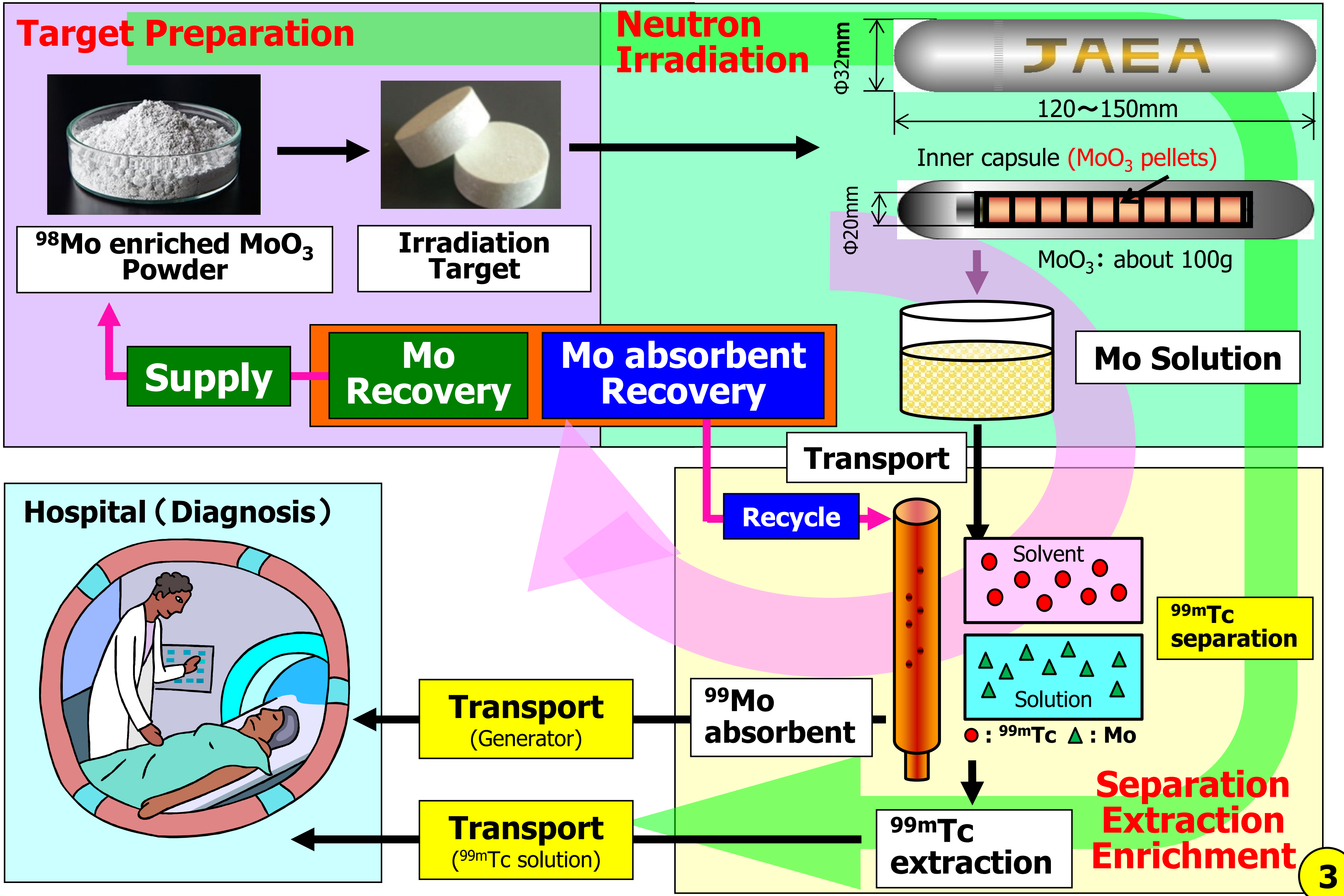
Comparison between Production Methods

	(n,*f*)	(n, γ)
Use of Uranium	**Yes**	**No**
Generation of Pu	**Yes**	**No**
Nuclear Proliferation Resistance	**Low**	**High**
Specific Activity	**High**	**(Low)**
^{99}Mo Production Cost	**High**	**(Low)**

Mar. 2012 : Seoul Nuclear Security Summit (Key actions)

1) Commitments from the governments of the four countries to support conversion of European production industries to non-HEU-based processes around 2017.
2) Support for U.S. exports of HEU to the European isotope producers to enable continued Mo-99 production until the facilities can convert to LEU targets.

3. Concept of Production Flow by (n, γ) ^{99}Mo



4. Extraction Methods of Tc-99m

The (n, γ)^{99}Mo is of **lower specific activity** than the fission ^{99}Mo. It is necessary for utilization of (n, γ)^{99}Mo to develop the **extraction and concentration methods** of ^{99m}Tc solution through the extraction devices or ^{99}Mo/^{99m}Tc generators.

Irradiated MoO_3 Pellets

↓

Dissolution
(Mo Solution)

Master-Milker

(Solvent extraction)

^{99m}Tc

Separation/Extraction*
(with MEK)

↓

Concentration/Purification*
(Al_2O_3 column)

↓

Conditioning
(**^{99m}Tc solution**)

Column Method

(^{99}Mo/^{99m}Tc generator)

^{99}Mo

Separation/Extraction*
(Mo Adsorbent)

↓

Washing/Assembly
(Generator)

↓

Conditioning
(**^{99m}Tc solution**)

*** : R&D items**

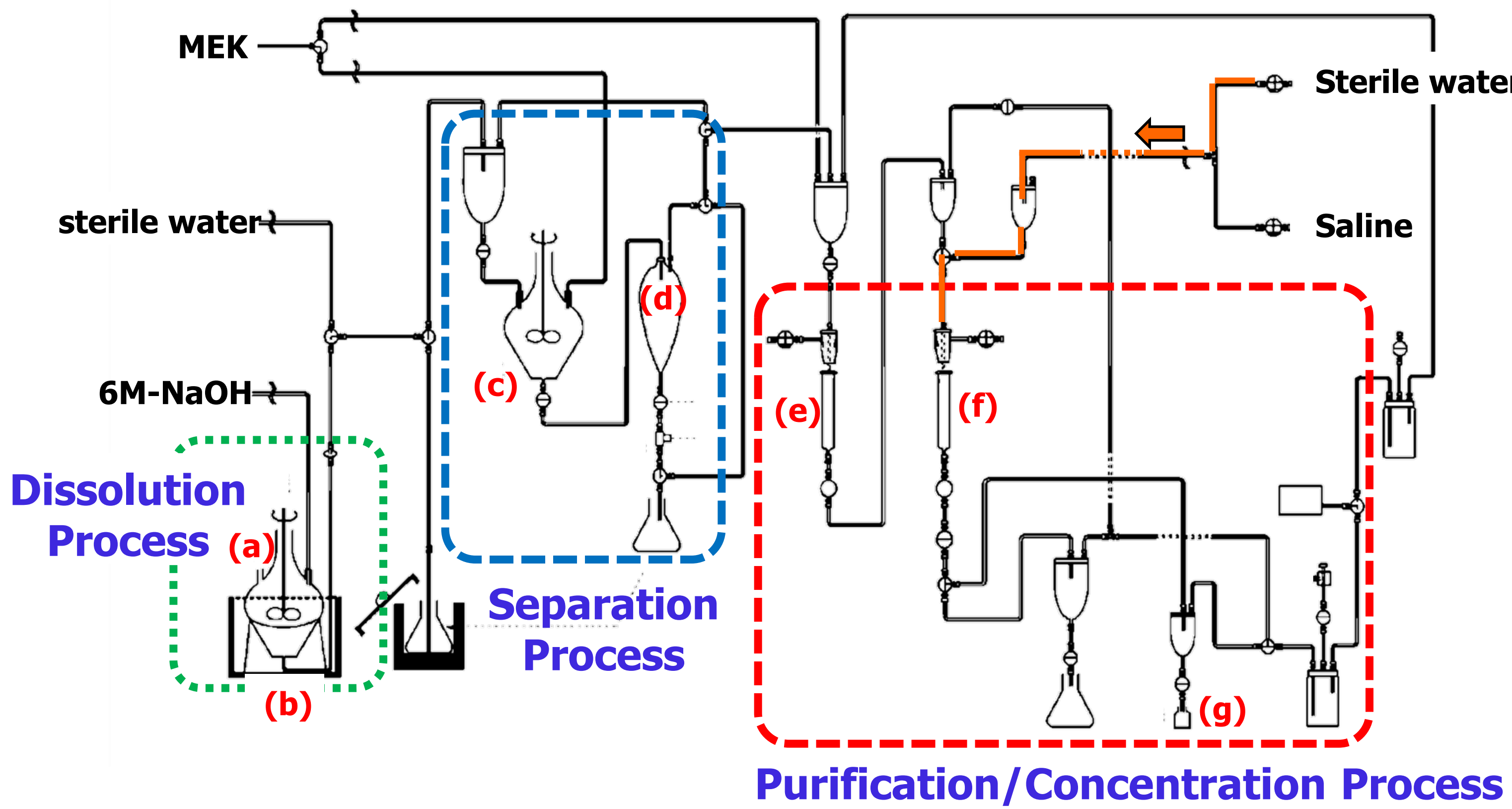
5. Solvent Extraction – Concept –

The preliminary extraction tests were performed with the MoO_3 pellets irradiated at JRR-3M in the JMTR hot laboratory.

[Process for Tc-99m Extraction]

Dissolution ➡ Separation ➡ Purification/Concentration

[Apparatus for Tc-99m Extraction]



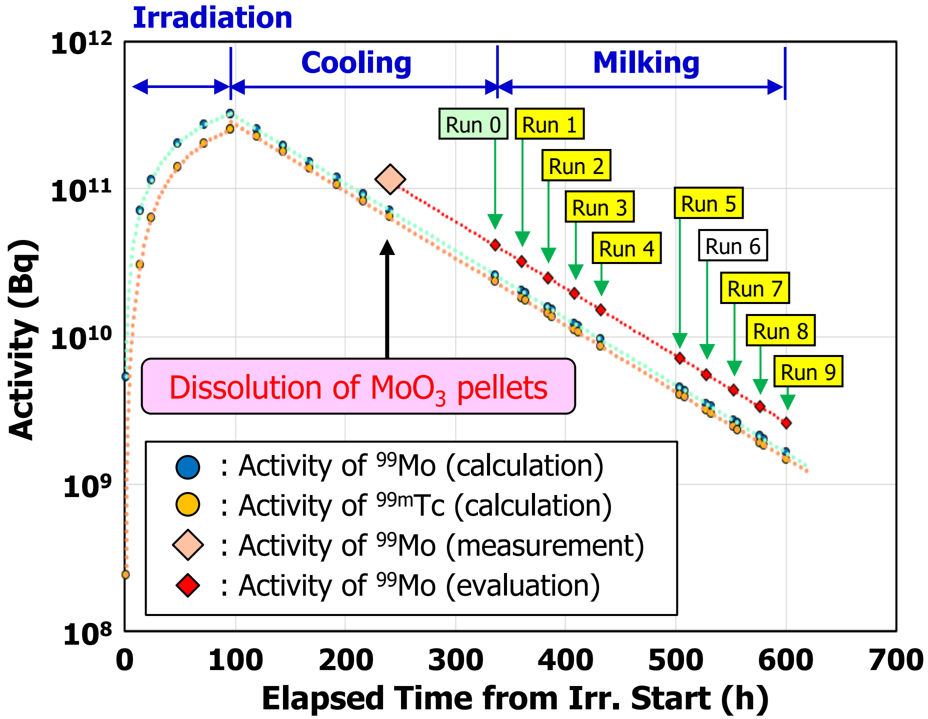
(a) Inlet of MoO_3 pellets, (b) Dissolution container, (c) Mixture container, (d) Separation and extraction container, (e) Basic-Alumina column, (f) Acidic-alumina column, (g) Recovery bottle

5. Solvent Extraction – Experimental Results (1) –

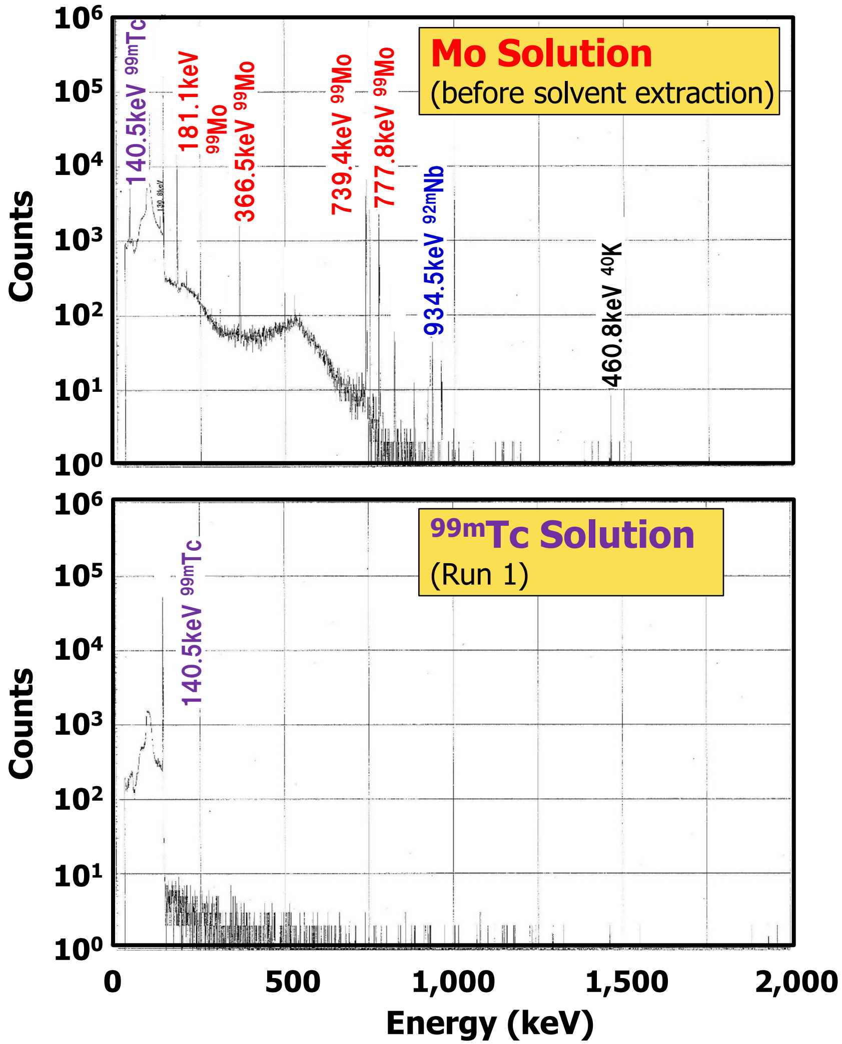
[Evaluation of Activity]

Irradiation Conditions

Irr. Reactor	: JRR-3
Irr. Device	: Hydric Rabit
ϕ_{th}	: 0.9 – 1.0x10^{14} n/cm^2/s
Irr. Time	: 4 days (96 h)



[γ-ray spectrum (Run 1)]



- In addition to ^{99}Mo and ^{99m}Tc, ^{92m}Nb was detected in the Mo solution.
- The ^{99m}Tc solution had only ^{99m}Tc peak, confirming its high purity.

5. Solvent Extraction – Experimental Results (2) –

Items	Standard values	Experimental Number				
		Run 1	Run 2	Run 3	Run 7	Run 8
Appearance	Colorless and transparent	Good	Good	Good	Good	Good
Radiochemical Purity	$\geq$ 95 %	98	98	97	99	99
Radionuclidic Impurity	$\leq$ 0.015 %	N.D.	N.D.	N.D.	N.D.	N.D.
pH	4.5 – 7.0	5.8	5.6	5.4	6.2	6.0
Osmotic Pressure	About 286 mOsm	292	294	291	289	286
Chemical Impurity						
Al (ppm)	< 10 ppm	< 10	< 10	< 10	< 10	< 10
Mo (ppm)	–	1.03	2.29	1.85	3.28	2.25
MEK (ppm)	< 5,000 ppm	117	99	59	166	102
Endotoxin	< 0.03 EU/mL	Bad	Good	Good	Bad	Good
Labeling Test	<10 %	3.5	3.0	3.2	4.2	5.3

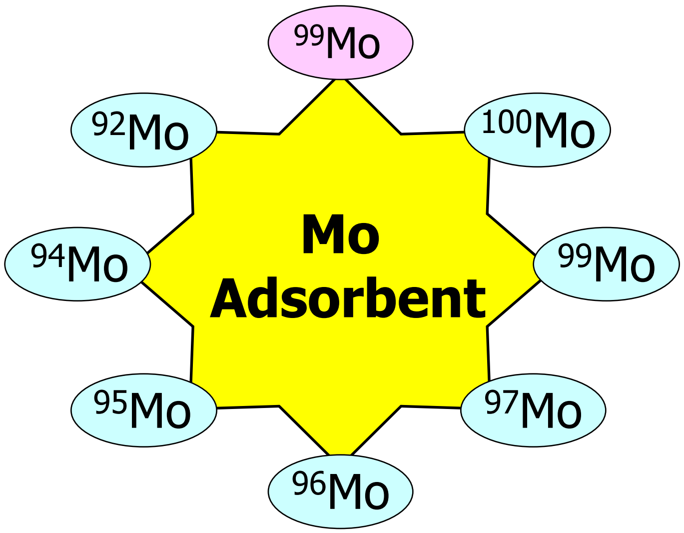
3 of 5 samples passed the quality test criteria. The remaining 2 samples failed the endotoxin test. The reason for the failures was inadequate cleaning of alumina and sterilization of the collected bottles.

6. Column Method – Mo Adsorbent Development –

It is necessary for $^{99}Mo/^{99m}Tc$ generators loaded with (n, γ)^{99}Mo to develop the Mo adsorbents with high Mo absorption amounts. Some Mo adsorbents have been fabricated and the characterization of these adsorbents was carried out.

[(n, γ)^{99}Mo]

1) Lower specific activity
2) Stable isotopes in Mo after irradiation



High Mo adsorption performance is required

[Candidate Mo adsorbent]

Inorganic polymer-based adsorbents

- Polyzilconium compound (PZC) (synthesized from Zirconium tetrachloride)
- New Polyzilconium compound (New PZC) (synthesized from zilconium alkoxide)
- Polytitanium compound (PTC)

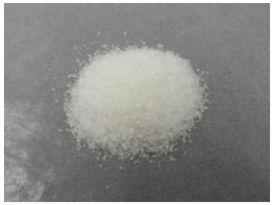
PZC, New PZC, and PTC have high Mo adsorption performance, but their use in pharmaceutical applications is challenging.

Alumina-based adsorbents

- Hierarchically macro-/mesoporous γ-alumina (HMMA)

6. Column Method – New typed Mo Adsorbent –

Mo absorption amounts

Mo Adsorbent	Mo Absorption Amounts	Appearance Image
PZC	250 mg/g	
New PZC	165 mg/g	
PTC	250 mg/g	
HMMA	90mg/g	

- HMMA was synthesized to develop a recyclable Mo adsorbent manufacturing technology as an alternative to Inorganic polymer-based adsorbents.
- The Mo adsorption capacity of conventional alumina is 20 mg/g, whereas HMMA achieved 90 mg/g.

Future challenges

- During Mo adsorption, the particle strength weakened, and particle fragmentation occurred.
- Improvement of particle strength is necessary.

7. Mo Recycling Development – Concept –

MoO_3 is used as the irradiation target for the production by (n, γ)^{99}Mo. Recycling technology development is proposed to recover molybdenum (Mo) for the effective use of resources and reduction of radioactive wastes.

[Subjects for Mo Recycling]

(a) Recovery of Mo resource

Mo recovery from the Mo solution and used ^{99}Mo/^{99m}Tc generators (PZC, etc.) and utilization of recovered Mo.

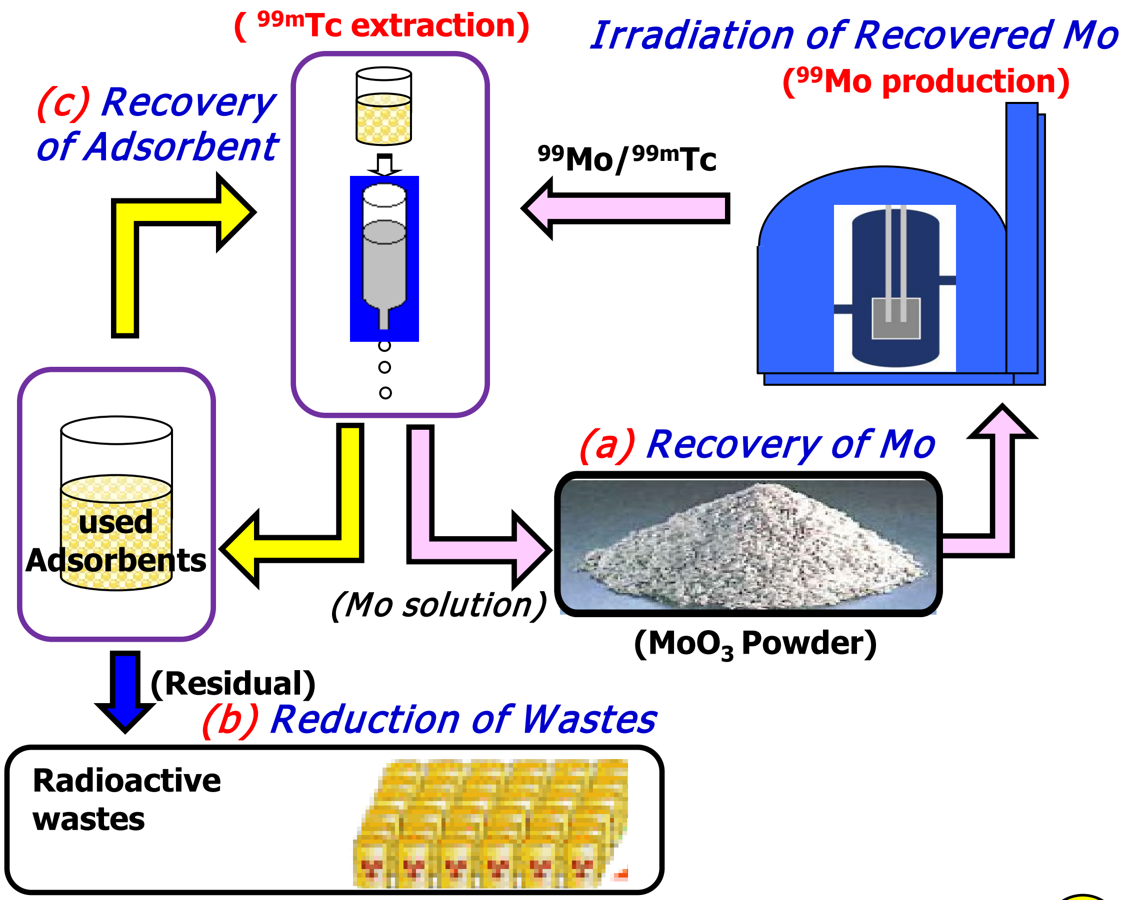
(b) Reduction of Wastes

Treatment and waste reduction of used MEK and adsorbents (PZC, etc.) and Mo solution

(c) Recovery of Mo adsorbent

Development of reusable ^{99}Mo/^{99m}Tc generators

[Mo Recycling System]

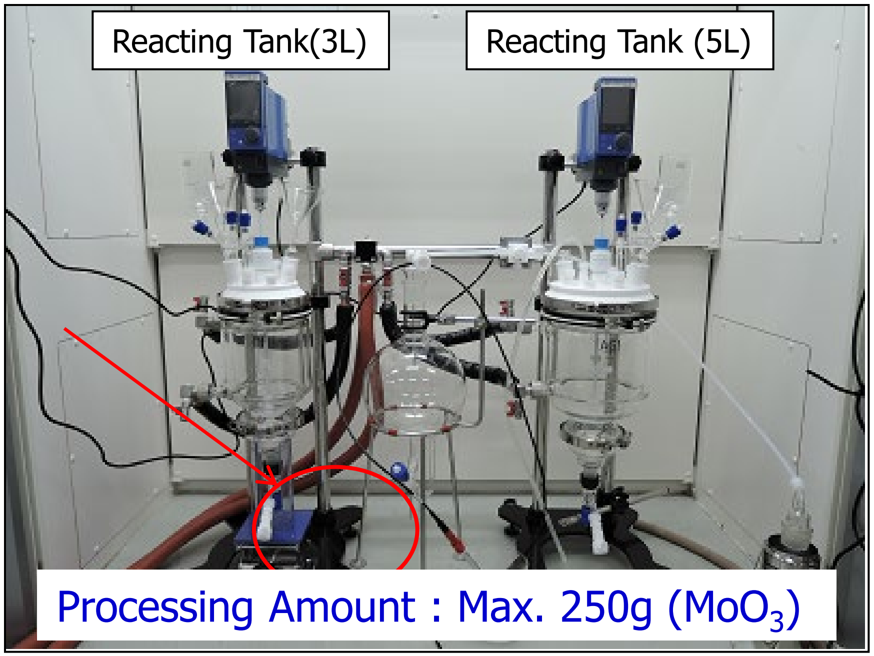


7. Mo Recycling Development – Experimental Results –

[Process for Mo Recycling]

Mo Solution → **Acid precipitation** → **Purification** → **Calcination** → **MoO_3 Powder**

[Apparatus for Mo Recycling]



- It is possible to recover Mo from Mo eluent from the column method.
- It is possible to recover Mo from Mo waste solution from the solvent extraction method.

[Experimental Results]

Process \ Methods		Column method	Solvent Extraction Method
Mo Solution	Mo Concentration (g/L)	54	33
	Na Concentration (g/L)	28	45
Acid Precipitation	Solution Volume (L)	2.72	2.56
	Mo Concentration (g/L)	0.218	0.238
Purification	Solution Volume (L)	5.49	5.32
	Mo Concentration (g/L)	0.307	0.389
	Mo Recovery Rate (%)	96.58	97.51
Calcination	MoO_3 Recovery Rate	90%	94%

The recovered MoO_3 powder was of high purity with an average particle size of 3 μm.

8. Conclusion

(1) In the solvent extraction with MEK, it is possible to remove impurities such as ^{92m}Nb from the Mo solution in which irradiated MoO_3 has been dissolved. Additionally, the quality of the obtained ^{99m}Tc solution largely achieved the research and development target values.

(2) Various Mo adsorbents with higher Mo adsorption performance were developed compared with existing Al_2O_3 adsorbents. New developed Al_2O_3 need to be improved Mo adsorption performance.

(3) Mo recovery rate from the used-Mo solution and the used-adsorbents was more than 90% and contribution to an efficient supply and low cost production can be realized by $(n, \gamma)^{99}Mo$.

Thank you for your attention