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Extraction Properties of ^{99m}Tc from irradiated High-density MoO_3 Pellets Solution

Akira SHIBATA[1], Takuya ISHIDA[1], Takayuki SHIINA[2], Masaaki KOBAYASHI[3], Masakazu TANASE[2], Yoshiaki KATO[1], Akihiro KIMURA[1], Akio OHTA[2], Asaki YAMAMOTO[3], Yasumasa MORIKAWA[3], Kaori NISHIKATA[1], Nobuhiro TAKEUCHI[2] and Kunihiko TSUCHIYA[1]

1 : Japan Atomic Energy Agency, 4002 Narita, Oarai,Higashiibaraki, Ibaraki 311-1393, Japan
2 : Chiyoda Technol Corporation, 3681 Narita, Oarai, Higashiibaraki, Ibaraki 311-1313, Japan
3 : FUJIFILM RI Pharma Co. Ltd., 453-1 Shimo-okura, Matsuo, Sammu, Chiba 289-1592, Japan

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Introduction

^{99m}Tc, a daughter nuclide of ^{99}Mo, is commonly used as a radiopharmaceutical. In case of Japan, all of ^{99}Mo are imported from foreign countries. R&D on ^{99}Mo domestic production has been performed under the cooperation programs. ^{99}Mo production by (n, γ) method was adopted from viewpoints of nuclear proliferation resistance and waste management.

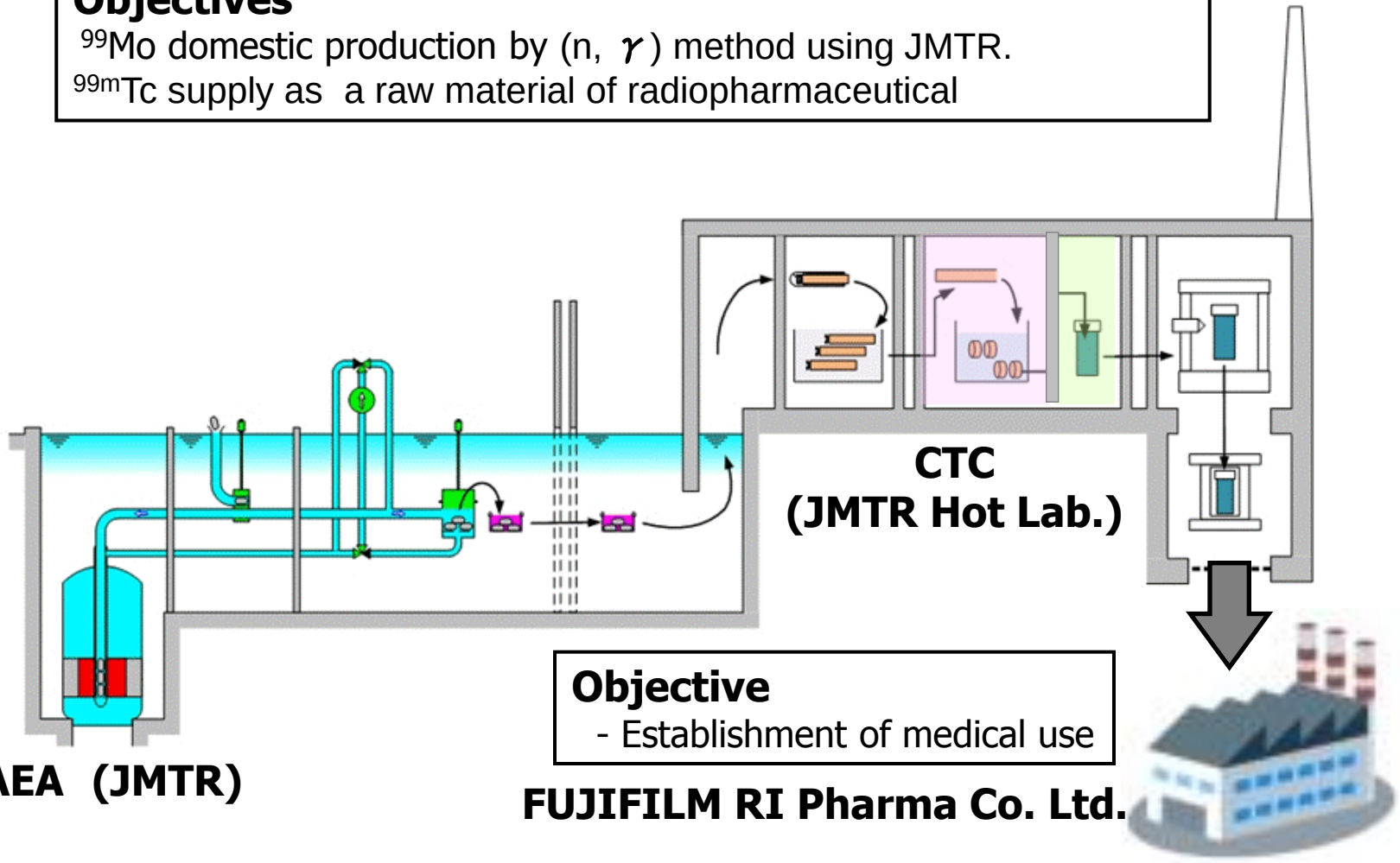
In this study, experiments of ^{99}Mo /^{99m}Tc production were performed to enhance recovery yields of ^{99m}Tc. Cold tests with Re were performed to optimize experimental condition. Then hot tests were performed. High-density MoO_3 pellets were irradiated in the Kyoto University Reactor (KUR). Solvent extraction method with MEK was used to extract ^{99m}Tc from ^{99}Mo /^{99m}Tc solution. And quality tests for the solutions were performed.

Background

Objectives

^{99}Mo domestic production by (n, γ) method using JMTR.

^{99m}Tc supply as a raw material of radiopharmaceutical



Goals of this experiment

In order to make adaptable production, recovery yields and impurities of product should be…..

(i) Recovery yields are more than 80%.

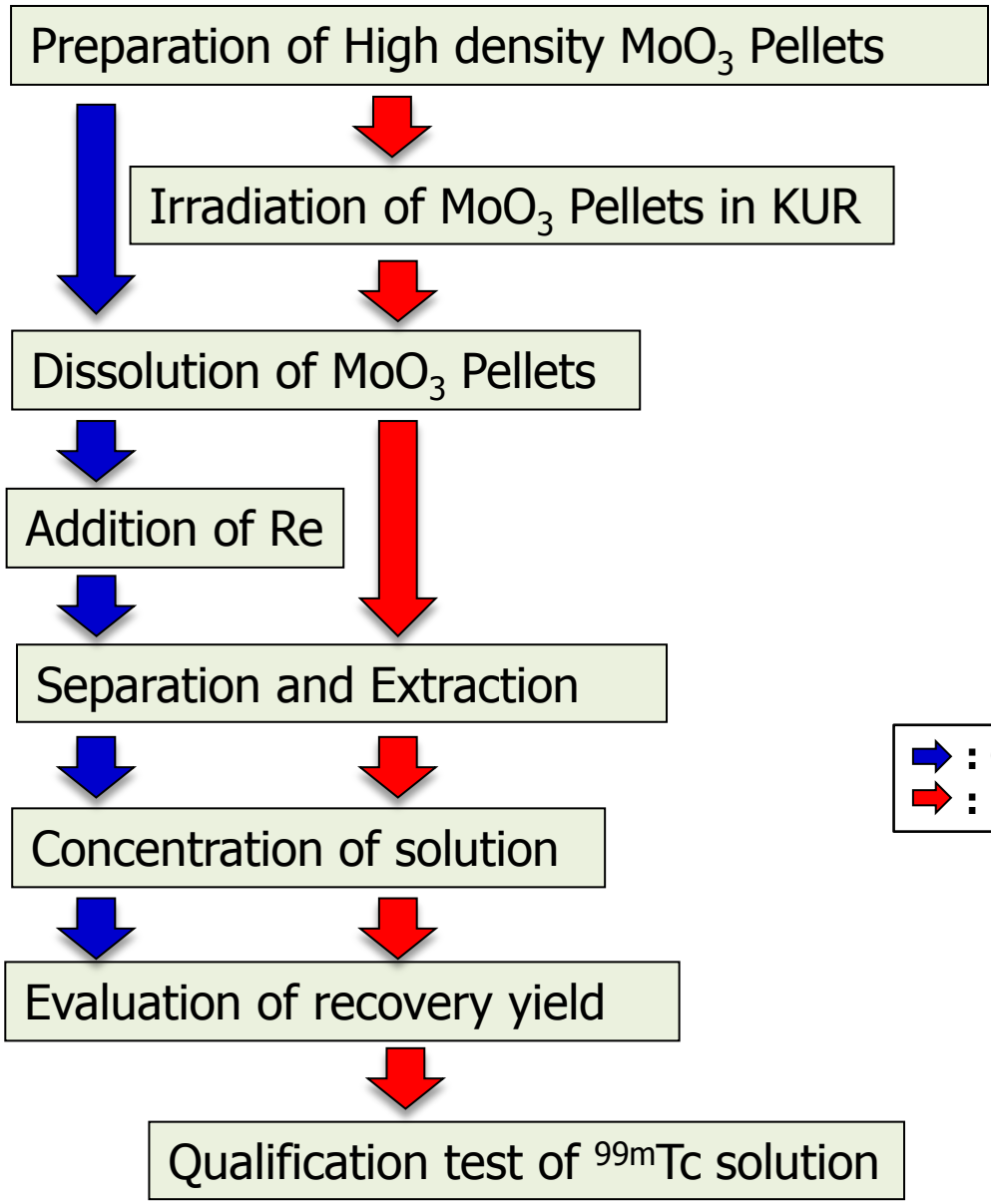
(ii) The impurities of ^{99}Mo and MEK in product are below the limits of standard which we made based on other standards of pharmaceutical production.

※ Such as “Guidance on the manufacture of sterile pharmaceutical product by aseptic processing” and “Radiopharmaceutical Standard” of Japan.

Flow of this experiments

Experimental Flow

Re and Tc are homologous elements



Properties of High-density MoO_3 Pellet

The high density MoO_3 pellets were fabricated by the plasma sintering method.

Production configuration

- Low temperature
- High pressure

Sintering properties of MoO_3 pellet

Items	Values
(1) Sintering conditions	
Temperature	530℃
Pressure	66.8MPa
Atomoshper	Air
Oxidation treatment	Ozone gas (80℃×2h)
(2) Properties	
Dimension	ϕ18×10 mm
Weight	11g
Density	91～93% T.D.
Impurities (ppm)	Na:<5, K:<5, MgO<1, CaO<1, W:20, Fe:<1, etc.

^{99}Mo/^{99m}Tc separation-concentration device

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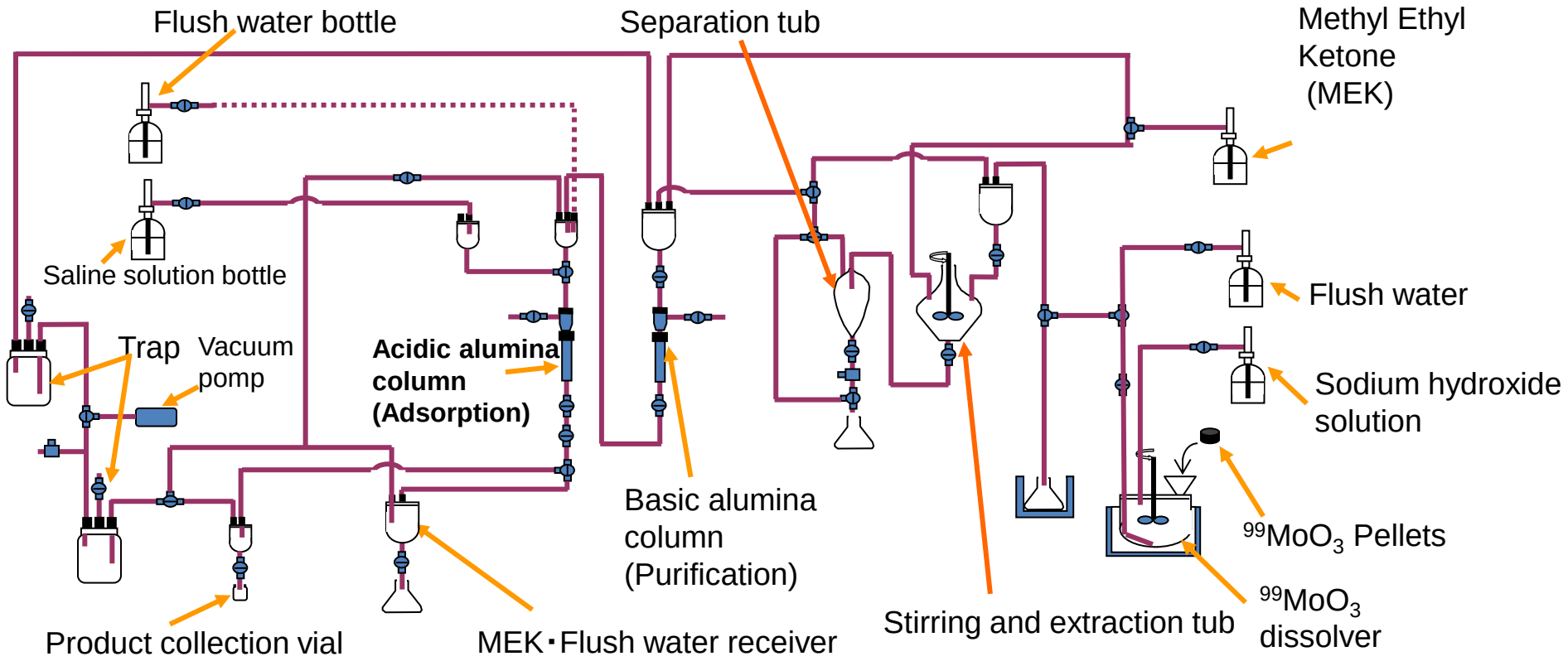


- **^{99}Mo Dissolver** : MoO_3 Pellets are dissolved by NaOH solution.
- **Stirring and extraction tub**: Methyl ethyl ketone (MEK) is added to the Mo Solution. Those are mixed and stirred. ^{99m}Tc is extracted to MEK and MoO_3 remain in Mo solution by this solvent extraction.
- **Separation tub**: Settled separation of Mo layer and MEK layer.
- **MEK・Flush water receiver** :Receiver of waste water and waste MEK.
- **Product collection vial**: ^{99m}Tc-Saline is collected in this vial

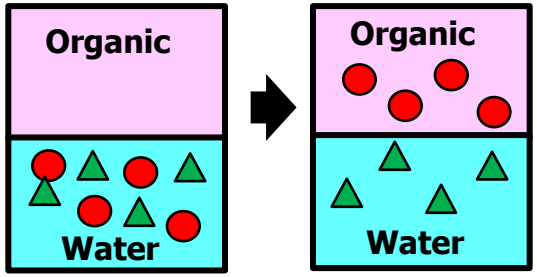
Extraction Tests with Rhenium (Cold test)

Re was used as a substitute of ^{99m}Tc. The amount of Re used in the extraction test was equivalent to 12.5 TBq (340 Ci) of ^{99m}Tc.

Experimental Flow

Separation and Extraction

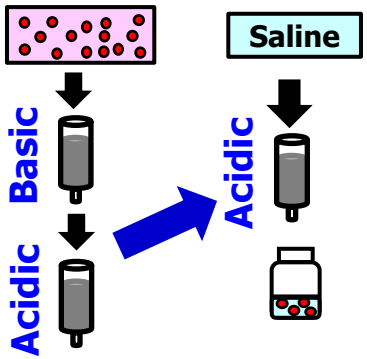
Water layer : Mo solution or Saline
Organic layer : Ketone type (MEK)



● : Target material (^{99m}Tc)

Concentration

Adsorption /elution



Extraction test : Re, the homologous element, was used as a substitute of ^{99m}Tc

Flow of Hot Test

Experimental Flow

Irradiation (in KUR)

Type A Package

(~20h)

^{99}Mo/^{99m}Tc Extraction/concentration (in JMTR Hot Lab.)

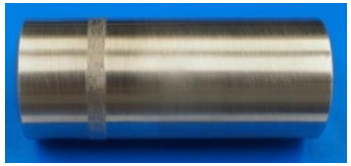
Type A Package

(~4h)

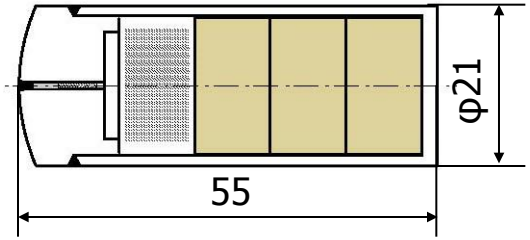
Inspection of ^{99m}Tc Solution (in FUJIFILM RI Pharma)

Preparation for test

MoO_3 pellets

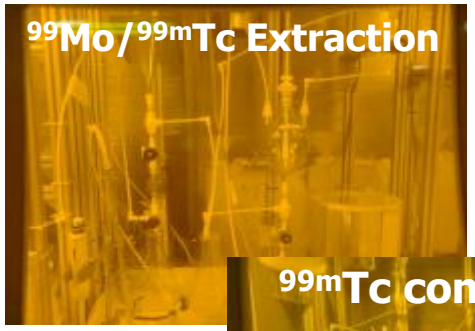


Al Container

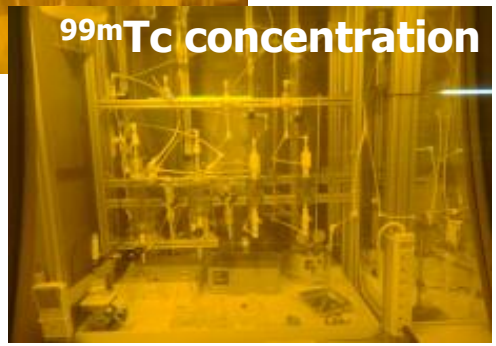


Irradiation target

Installation of device in hot cell (Lead cell No.2)



^{99m}Tc Solution

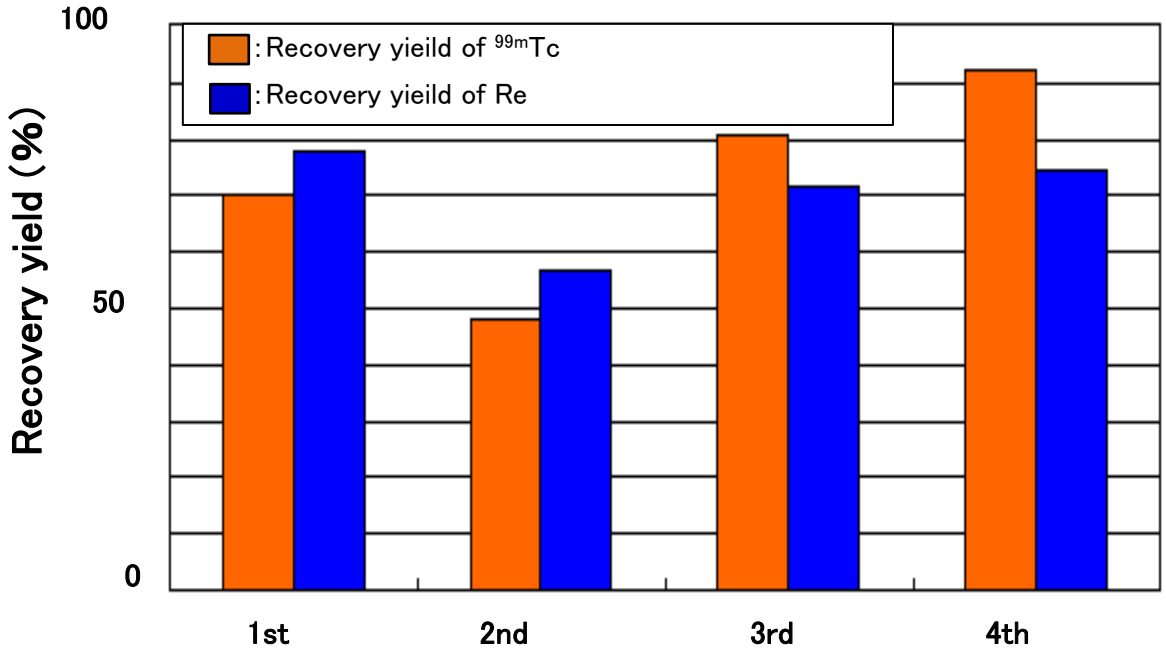


Irradiation conditions in KUR

Irradiation conditions in KUR

Items	Values
Thermal power	1MW
Thermal	$1.8\times10^{17}/m^2/s$
Fast flux	$8.8\times10^{16}/m^2/s$
Irradiation Temp.	about 50℃
Irradiation Time	3h12min

Results of cold tests and hot tests in 2013



Average recovery yield: ^{99m}Tc=73%※, Re=70%

→ Not achieved

(Experiments in FY2013)

Recovery rates of experiments in 2013.

Liquid flow condition

Difference between former alumina column and current alumina column.

Filing height **40mm**

Inside diameter **16mm**

Filing height **48mm**

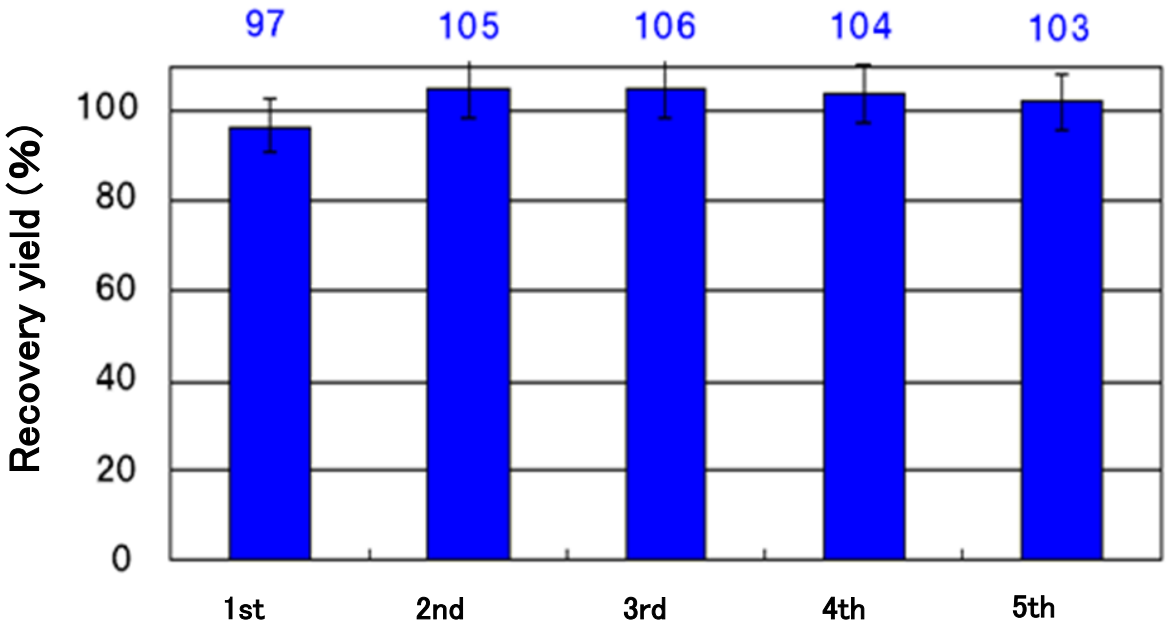
Inside diameter **14mm**

Flow rates and suction pressure

	Basic alumina Column (MEK)	Acidic alumina Column (MEK [adsorption])	Acidic alumina Column (Water [Rinsing])	Acidic alumina Column (Saline [Elution])
Flow rate of liquid	11.2±2.5 ml/min	9.4±2.3 ml/min	18.5±4.6 ml/min	4.0±0.2 ml/min
Suction pressure	(0.01MPa)	(0.005MPa)	(0.03MPa)	(0.005MPa)

Optimization of Liquid flow conditions

Recovery yield of cold tests



Average recovery yield (Re) = 103 %

Optimization of Liquid flow conditions

Recovery rate of this experiments enhanced to about 100% from 73% (in 2013).

Recovery yield of hot tests

- Amounts of 99mTc was evaluated by radio activity.
- The theoretical radioactivity of ^{99m}Tc was calculated by following equation

$$A_2 = 0.877 \times \{\lambda_2 /(\lambda_2 - \lambda_1)\} A_{10} \times \{\exp(-\lambda_1 t) - \exp(-\lambda_2 t)\}$$

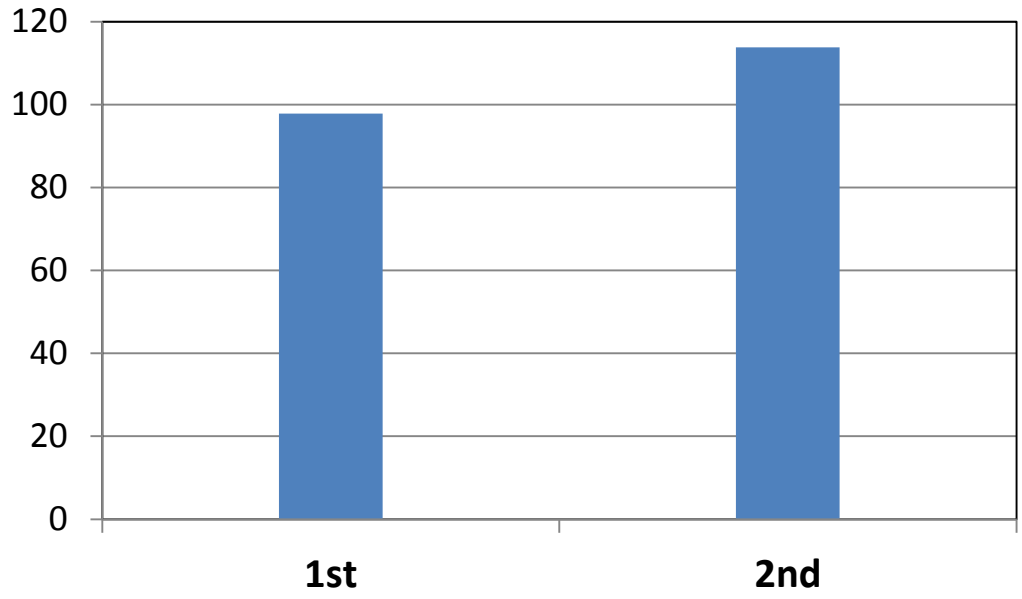
A_{10} : Activity of ^{99}Mo (Activity of ^{99m}Tc = 0)

λ_1 : Decay constant of ^{99}Mo

λ_2 : Decay constant of ^{99m}Tc

A_2 : Activity of ^{99m}Tc (Bq)

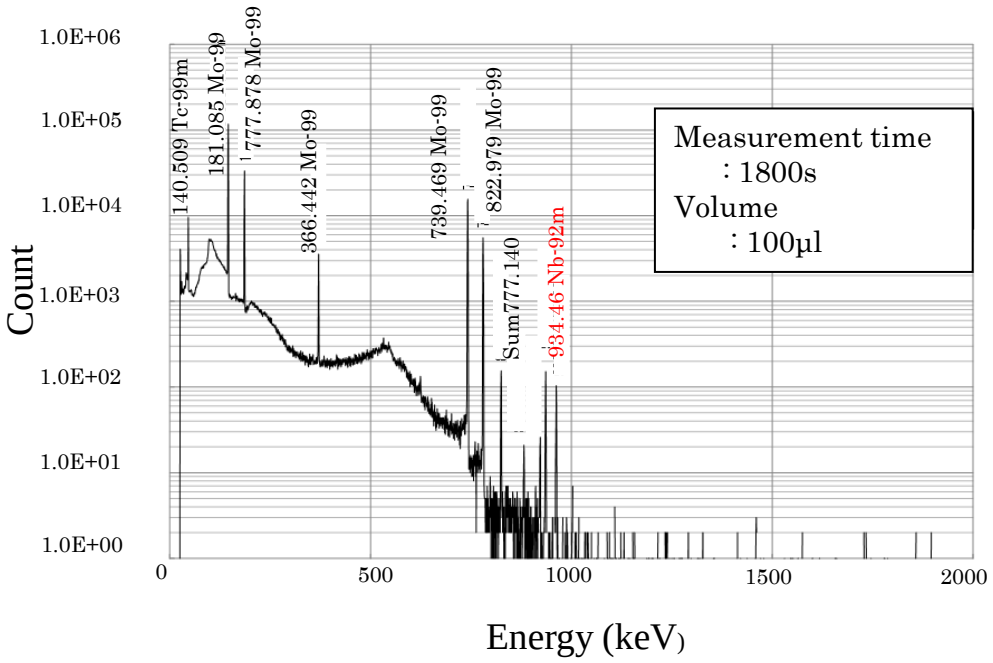
No.	Activities of ^{99}Mo (Bq)	Activities of ^{99m}Tc (bq)	Recovery yield (%)
1	1.09×10^9	9.71×10^8	97.8
2	8.53×10^8	7.53×10^8	113.8



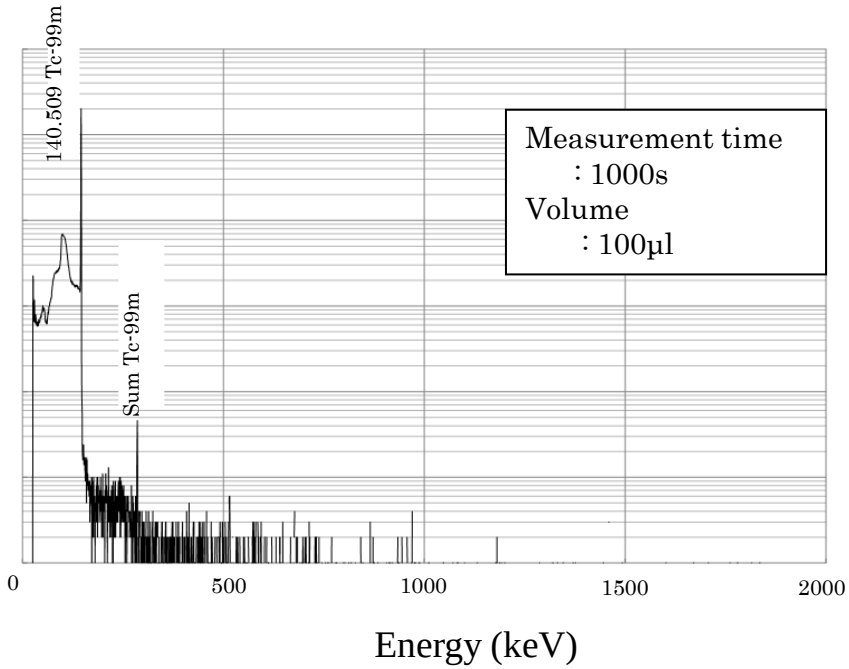
Average recovery yield of ^{99m}Tc = 106 %

High recovery yield also confirmed by the optimum liquid flow conditions in the hot tests.

Impurities in Solution



Gamma spectrum of ^{99}Mo solution



Gamma spectrum of ^{99m}Tc solution

Natural Mo contain ^{92}Mo of 14.8%
^{92}Mo(n,p)^{92m}Nb in Reactor

^{92m}Nb did not move from aqueous layer to organic layer

Results of Quality tests

	pH	Al (ppm)	Radionuclide Purity	MEK (ppm)	Radiochemical impurity	Osmotic pressure (mosm)	Endtoxine
This experiment	5.51	–	Peak of ^{99m}Tc only	404	2.00%	286 293	Negative
standard	4.5-7.0	≦10	≦0.015%	≦5000	≦5	270-300	Negative

Standard were set based on some of other guideline such as "Guidance on the manufacture of sterile pharmaceutical product by aseptic processing" from the Ministry of Health, Labour and Welfare of Japan and "Radiopharmaceutical Standard" of Japan

Average impurity of MEK : lower than that of standard by an order of magnitude.

Conclusions

(1) Inside diameter of alumina column was changed from 16mm to 14mm and flow rates of liquid in alumina columns were optimized. The recovery yields enhanced from 73% to about 100%. This shows that recovered yields of ^{99m}Tc as high as 80% at the shipping time was achieved.

(2)The impurities in ^{99m}Tc solution were evaluated and were efficiently low. And it is concluded that this method would be suitable for the radiopharmaceutical production.

In future, the solvent extraction demonstration tests will be carried out with high density MoO_3 pellets irradiated in JMTR.

This study was carried out for the "Research and Development of domestic ^{99}Mo production by (n, γ) method in JMTR" under the framework of Strategic Promotion Program for Basic Nuclear Research launched by the Ministry of Education, Culture, Sport, Science and Technology of Japan (MEXT).

Thank you for your attention!