Production of medical radioisotopes using the experimental fast reactor Joyo

*Yuto Sasaki, Masaki Okagaki, Shigetaka Maeda

Experimental Fast Reactor *Joyo*, Japan Atomic Energy Agency

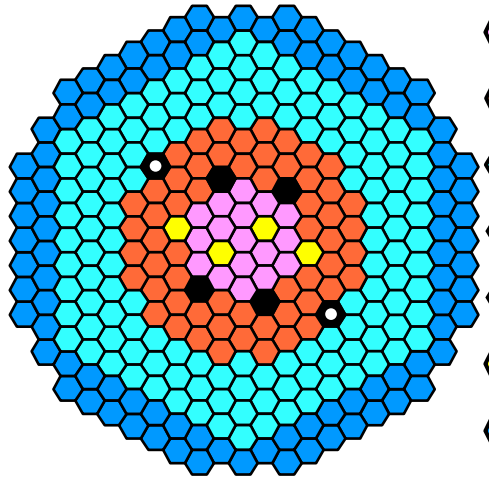
Index

- Introduction
- The Domestic Situation of Radioisotope
- Potential of Medical Radioisotope Production in Joyo
  - ^{225}Ac Production in the Fuel Region
  - ^{99}Mo Production in the Moderator Region
- Summary

Introduction
-Overview of Experimental Fast Reactor Joyo-

◆Experimental fast reactor for developing fuels and materials for future fast reactors.

- ✓ Thermal Power 100 MW
- ✓ Coolant Liquid sodium
- ✓ Core Diameter 78 cm
  Height 50 cm
- ✓ Fuel U-Pu mixed oxide pellet
  ^{235}U: 18wt% enriched
  Pu: < 32wt%

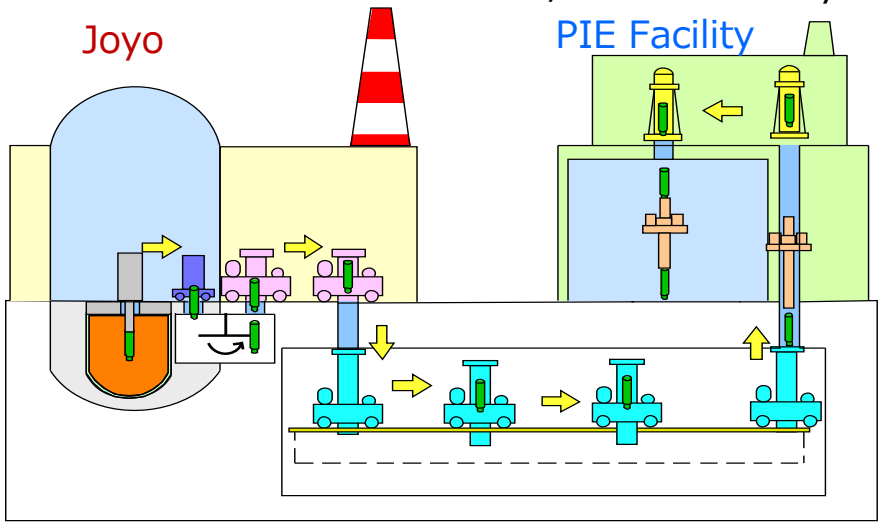


Core configuration

- Inner fuel S/A
- Outer fuel S/A
- Reflector (SS)
- Control Rod (B_4C)
- Backup C/R (B_4C)
- Irradiation test S/A
- Shielding S/A (B_4C)

S/A: Sub-Assembies

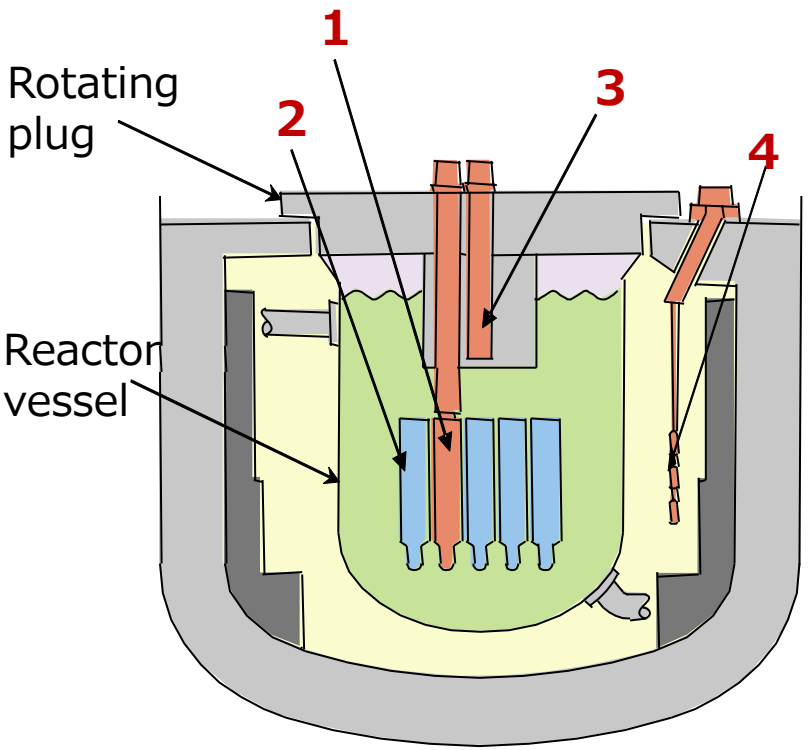
Takes 4 days to disassemble the S/A in PIE facility



Takes 2 days to transport S/A from Joyo to PIE facility

Introduction
-Irradiation Field in Joyo-

1. Fuel region (450～750℃)
2. Reflector region and moderate region (400～700℃)
3. Upper core region (550℃～)
4. Irradiation hole outside reactor vessel (200～600℃)

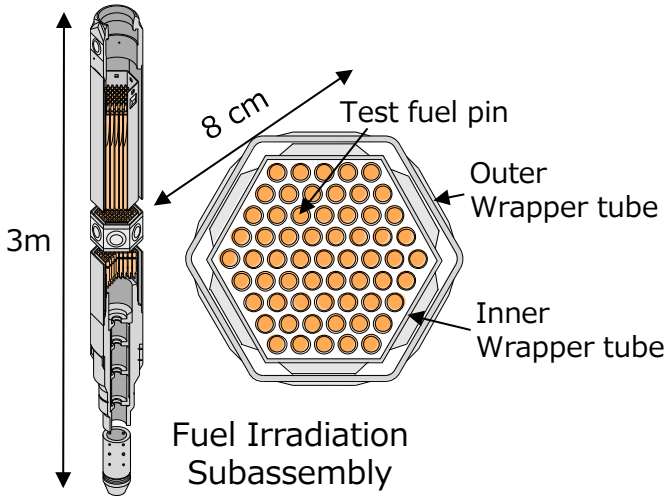


	Unit: n/(cm²·s)		Spectrum ratio
	Total neutron flux	Fast neutron flux (E≧0.1MeV)	
1	～4×10^{15}	～3×10^{15}	0.6～0.7
2	10^{14} ～ 2×10^{15}	10^{13}～ 2×10^{15}	0.2～0.5
3	10^{11} ～ 10^{13}	10^{10} ～ 10^{13}	10^{-1}
4	～ 10^{12}	～10^{10}	～10^{-2}

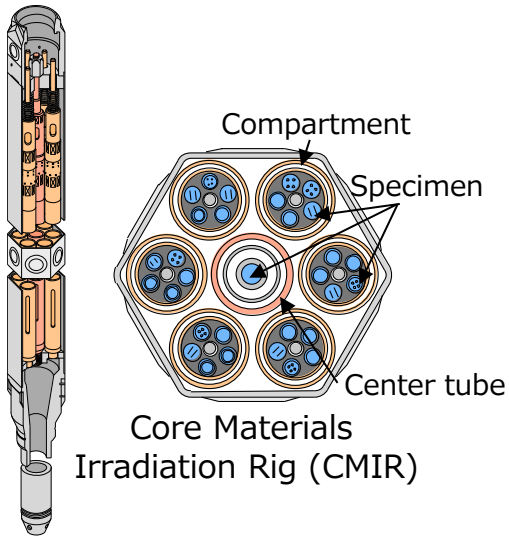
Introduction
-Representative Irradiation Rigs-

In fuel region

Irradiation field for fuels and core materials for fast reactor



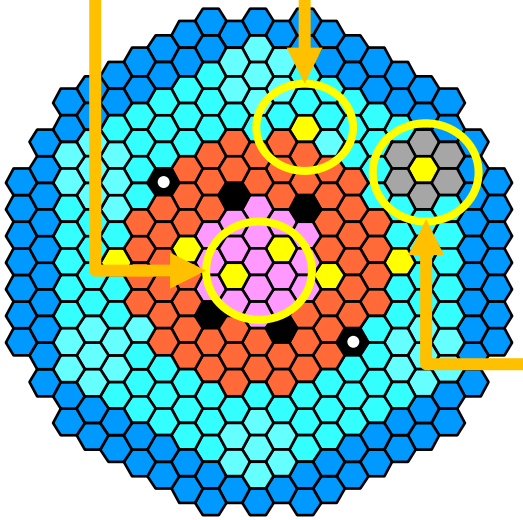
Fuel Irradiation Subassembly

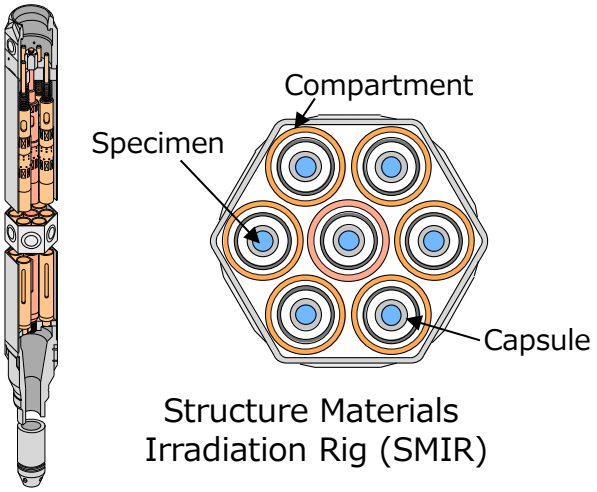


Core Materials Irradiation Rig (CMIR)

In reflector region

Irradiation field for testing materials for fast and fusion reactors



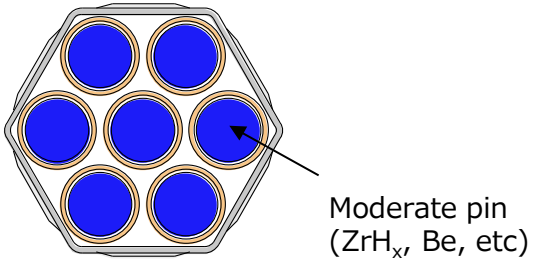


Structure Materials Irradiation Rig (SMIR)

- Inner fuel S/A
- Outer fuel S/A
- Reflector (SS)
- Control Rod (B_4C)
- Backup C/R (B_4C)
- Irradiation test S/A
- Shielding S/A (B_4C)
- Moderator S/A

In moderate region

Moderators are loaded in the reflector region to create irradiation fields with reduced neutron energy



Moderator Subassembly

The Domestic Situation of Radioisotope

The Action Plan for Promotion of Production and Utilization of Medical Radioisotopes (Outline)

31st May, 2022 Atomic Energy Commission, Japan

Background

Expectations for Radioisotope therapy

- Increased focus on *"theranostics"* (therapy+disgnosis)

Movements and Problems in Japan

- Restart of research reactors that can produce large amounts of radioisotopes (JRR-3)

On the other hand, insufficient number of

- Hospital beds for radioisotope therapy
- Human resources who promote production and utilization of radioisotopes

International Situation

- Vast investment for radioisotope production and R&D
- Forming network of research reactors and accelerators
- Accelerated competition for acquisition of radioisotopes and their raw materials

Goals to be Achieved during next decade

①Establishment of a stable Radioisotope Diagnostic System through *partial domestic production of Mo-99/Tc-99m*
②Implementation of *Radioisotope Treatment Using Domestic Radioisotopes*
③*Dissemination of Radioisotope Treatment* in Medical Setting
④Making Radioisotope-Related Fields, centered on Medicine, as a *"Strength" of Japan*

Contents of the Action Plan

(1)Promoting initiatives for Domestic Production and Stable Supply of "Important Radioisotopes "
- Strengthening R&D for mass production of ***Ac-225*** using "Joyo" and accelerators
(**Production demonstration by JFY2026 with *"Joyo"***)

(2)Establishment of systems and structure to promote utilization of radioisotopes in medical setting

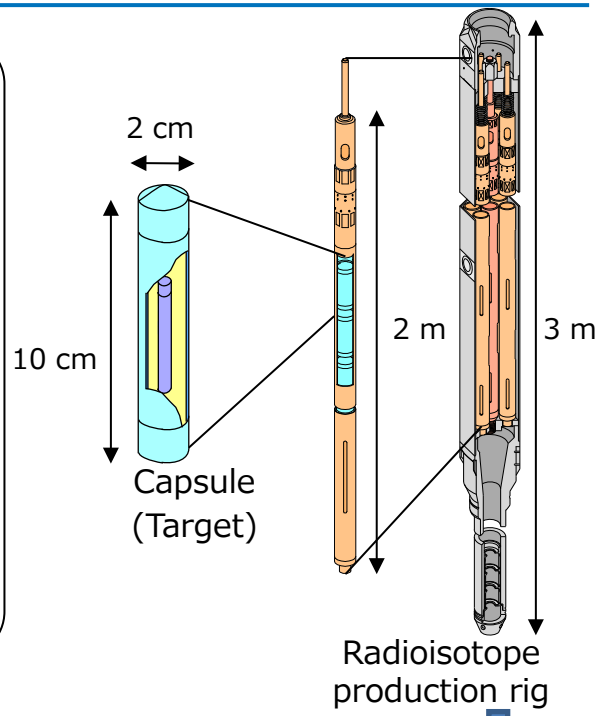
(3)Promoting R%D Contributing to Production of Radioisotopes

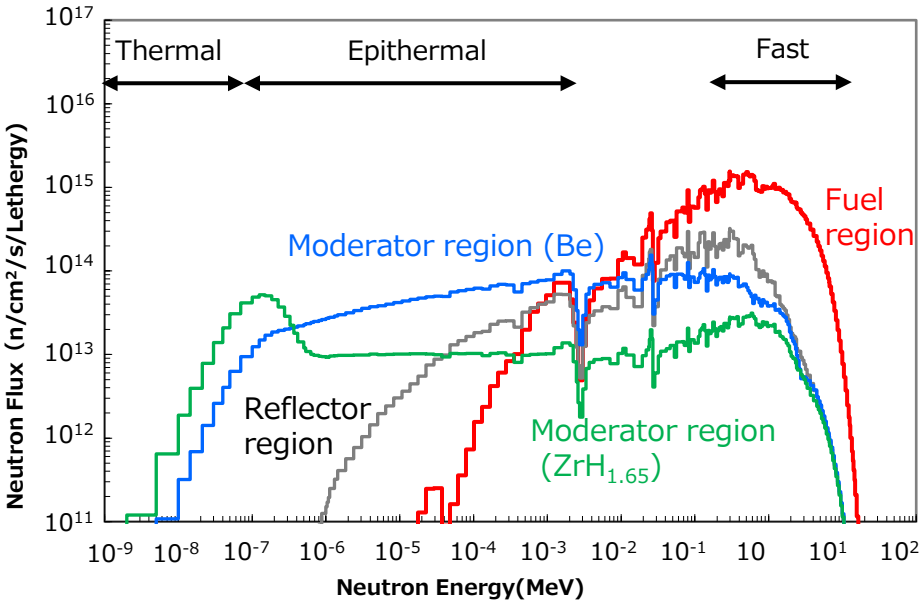
(4)Strengthening Research Infrastructures, and Networks for Production and Utilization of Radioisotopes

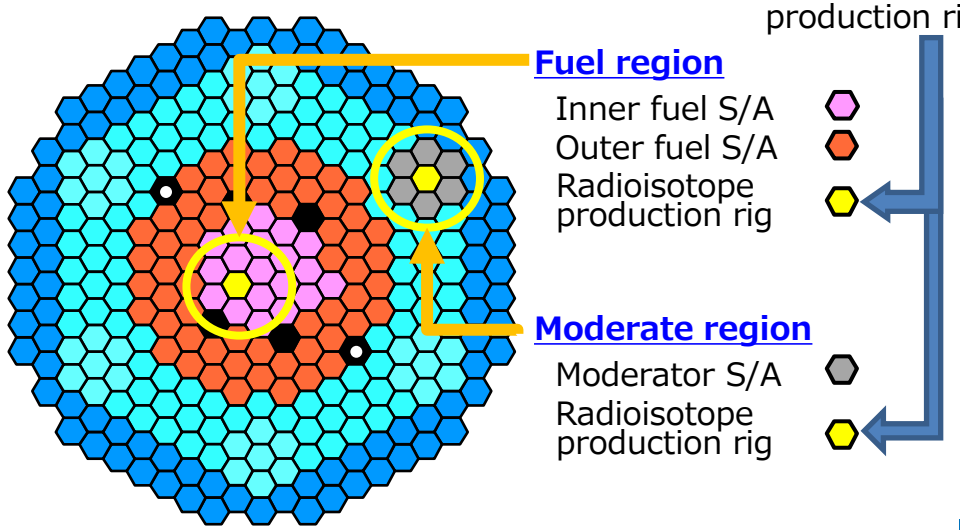
https://www.aec.go.jp/kaigi/other/siryo03/siryo3.pdf (In Japanese)

Potential of Medical Radioisotope Production in Joyo

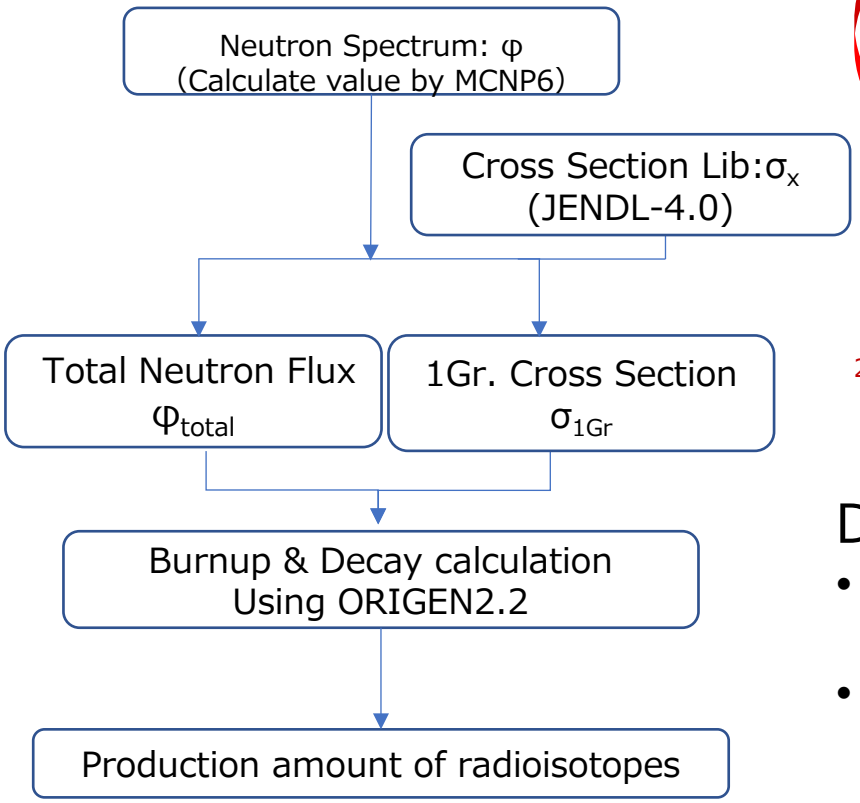
- **Providing a wide range of neutron energies to induce the aiming nuclear reactions**
  - ✓ Production of various radioisotope is possible
    - Fuel region : (n,2n) reaction
      ^{225}Ac
    - Moderator region : (n,γ) reaction
      ^{99}Mo、^{177}Lu、^{198}Au
- **Characterized by high neutron flux and large capacity for specimen loading**
  - ✓ Large-scale production is possible

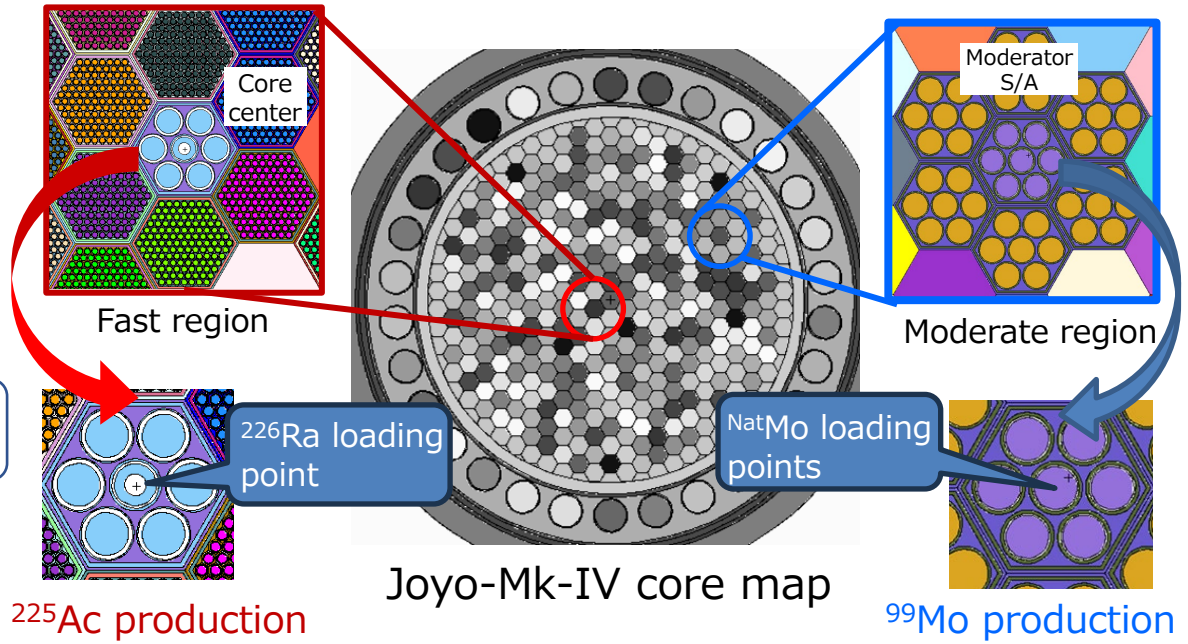






Evaluation Method of Medical Radioisotope Production in Joyo





Detailed evaluation using MCNP code

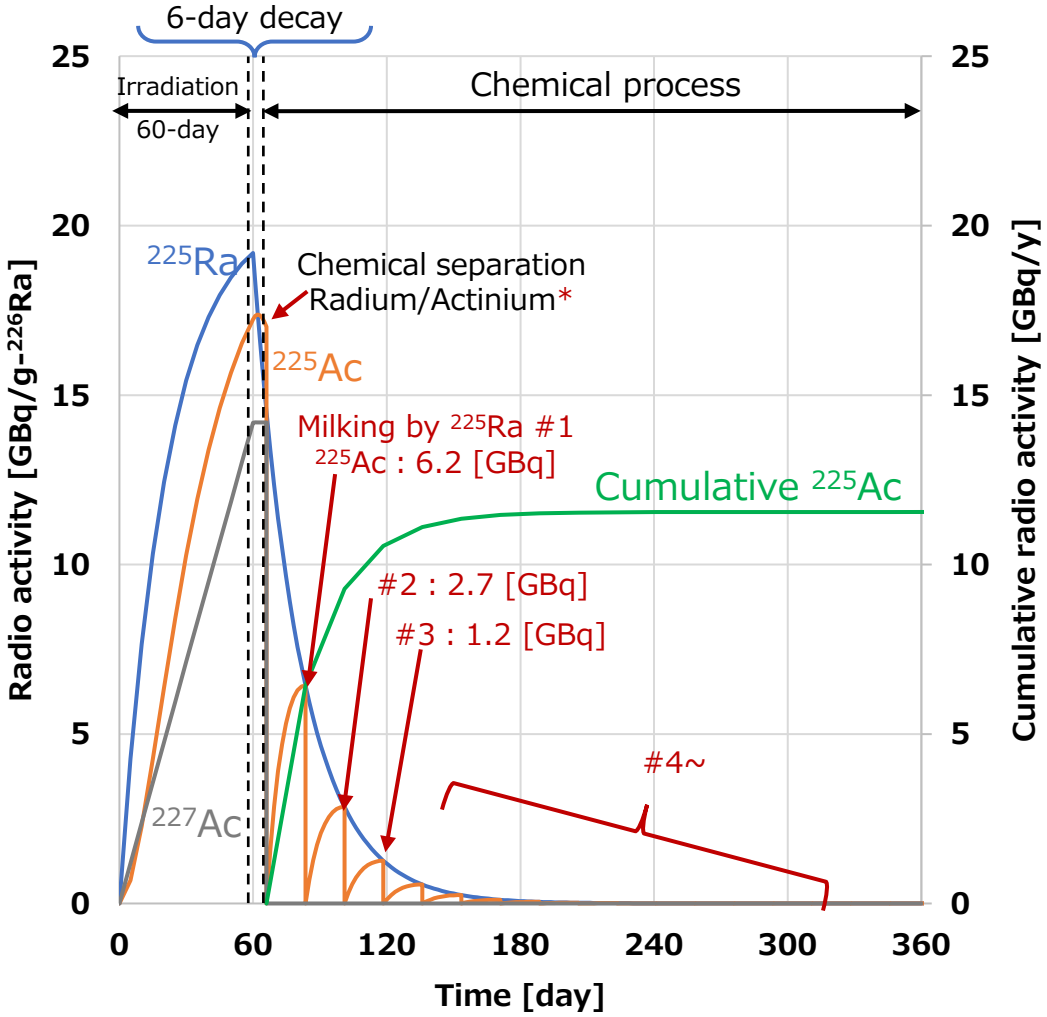
- Body data
  3D modeling for all subassemblies in the reactor vessel
- Material composition data
  Burnup compositions

Radioisotope Production in the Fuel Region

Ex. $^{226}Ra(n,2n)^{225}Ra \rightarrow ^{225}Ac$

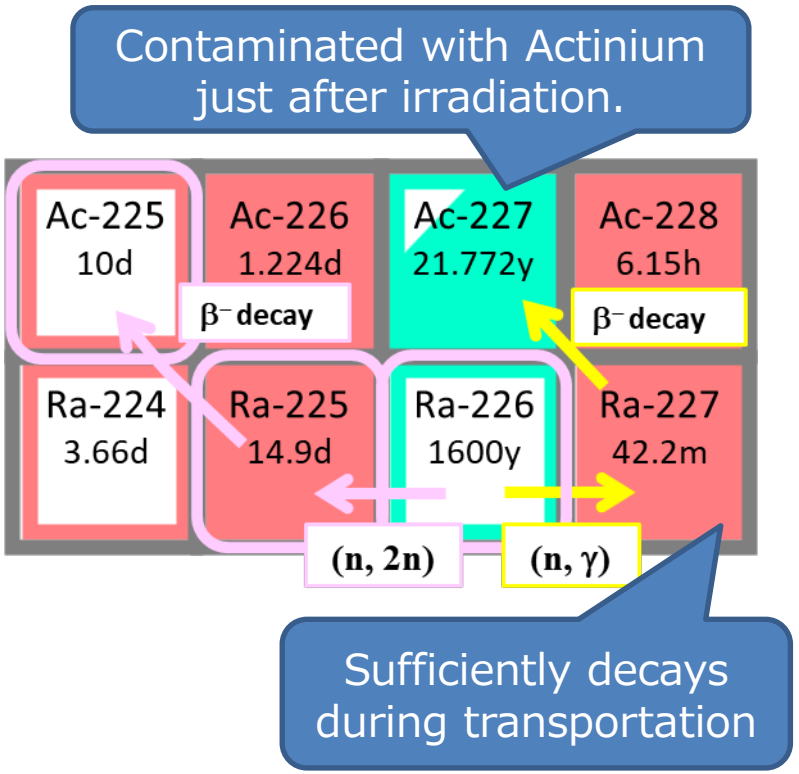
Evaluated Production Amount of ^{225}Ac in Joyo

60-day irradiation of 1g ^{226}Ra



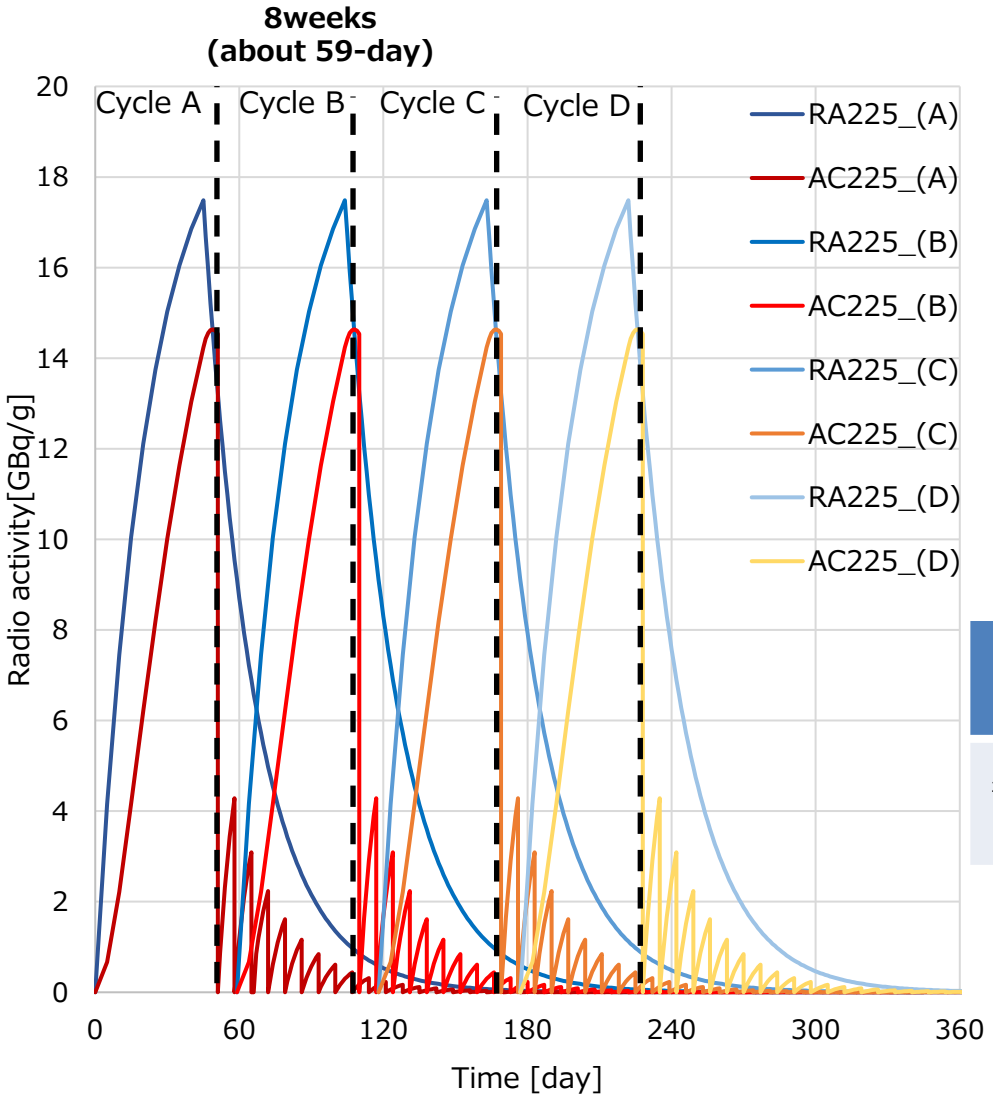
^{225}Ac is extracted through repeated milking operations every 17.5-day

The cumulative production amount of ^{225}Ac is 11.3 GBq



* The first separated ^{225}Ac cannot be used for medical purposes because it is contaminated with ^{227}Ac.

Operating Patterns Adopted to the Medical Needs



Medical needs
- 4 doses per patient at 8 weeks interval
- 100 kBq/kg-weight* → 6 MBq / patient (≒60kg)

Operation Pattern
- Irradiation : 45-day/cycle
- Fuel exchange and maintenance : 14-day/cycle
- Operation Cycle : 4 cycle/y

Other conditions
- Ra-226 target : 1 g/cycle
- Milking interval : 1 week

Milking	#1	#2	#3	#4	#5	#6~	Total	
							1cycle	Annual
^{225}Ac [GBq] (patient)	4.28 (710)	3.09 (520)	2.23 (370)	1.61 (270)	1.16 (190)	3.00 (500)	15.4 (2,560)	**61.5**

** Clemens Kratochwil, Frank Bruchertseifer, et at. Targeted aTherapy of Metastatic Castration-Resistant Prostate Cancer with 225Ac-PSMA-617: Swimmer-Plot Analysis Suggests Efficacy Regarding Duration of Tumor Control, J Nucl Med 2018; 59:795–802*

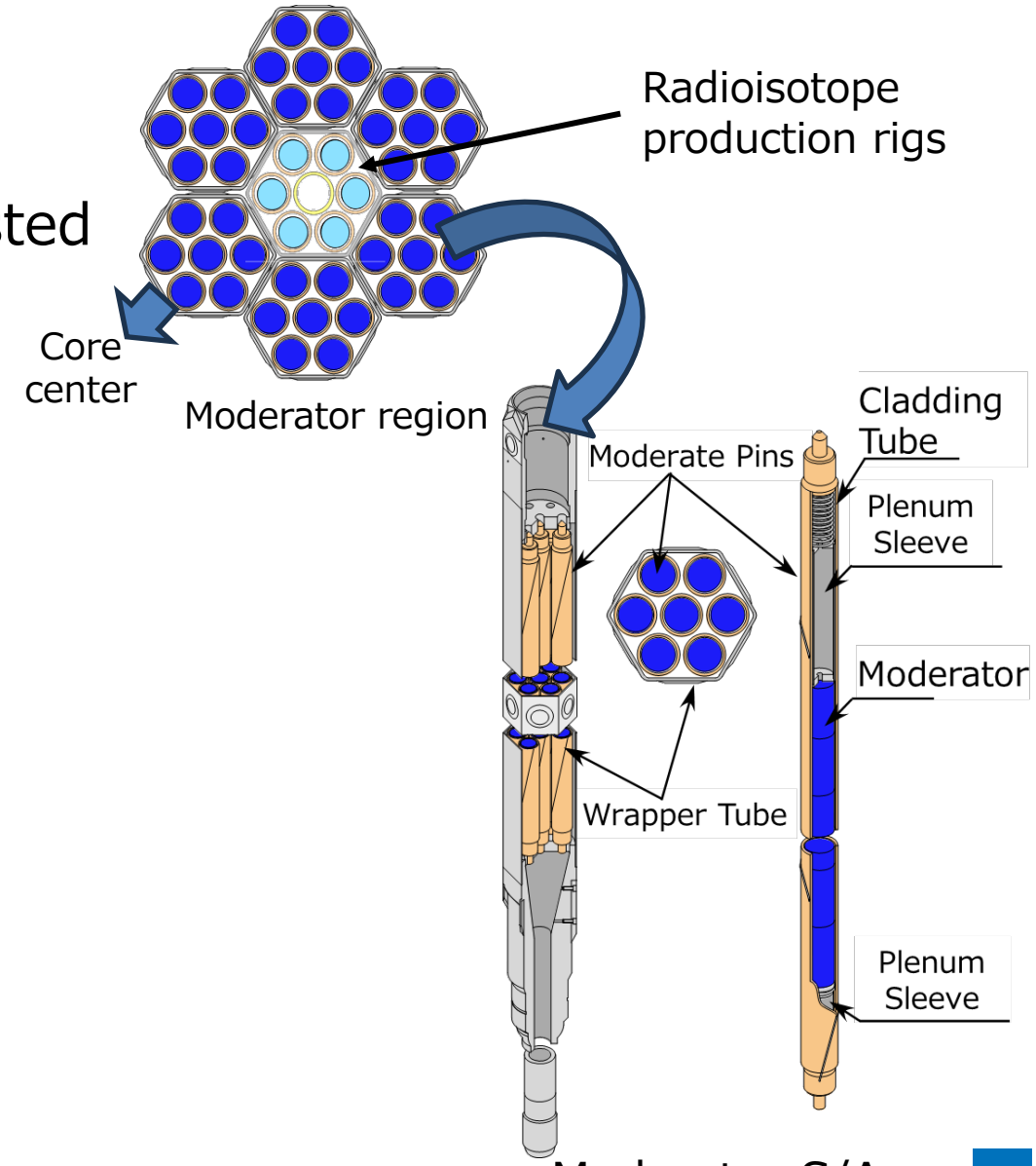
Radioisotope Production in the Moderator Region

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

Irradiation Conditions Suitable for ^{99}Mo Production

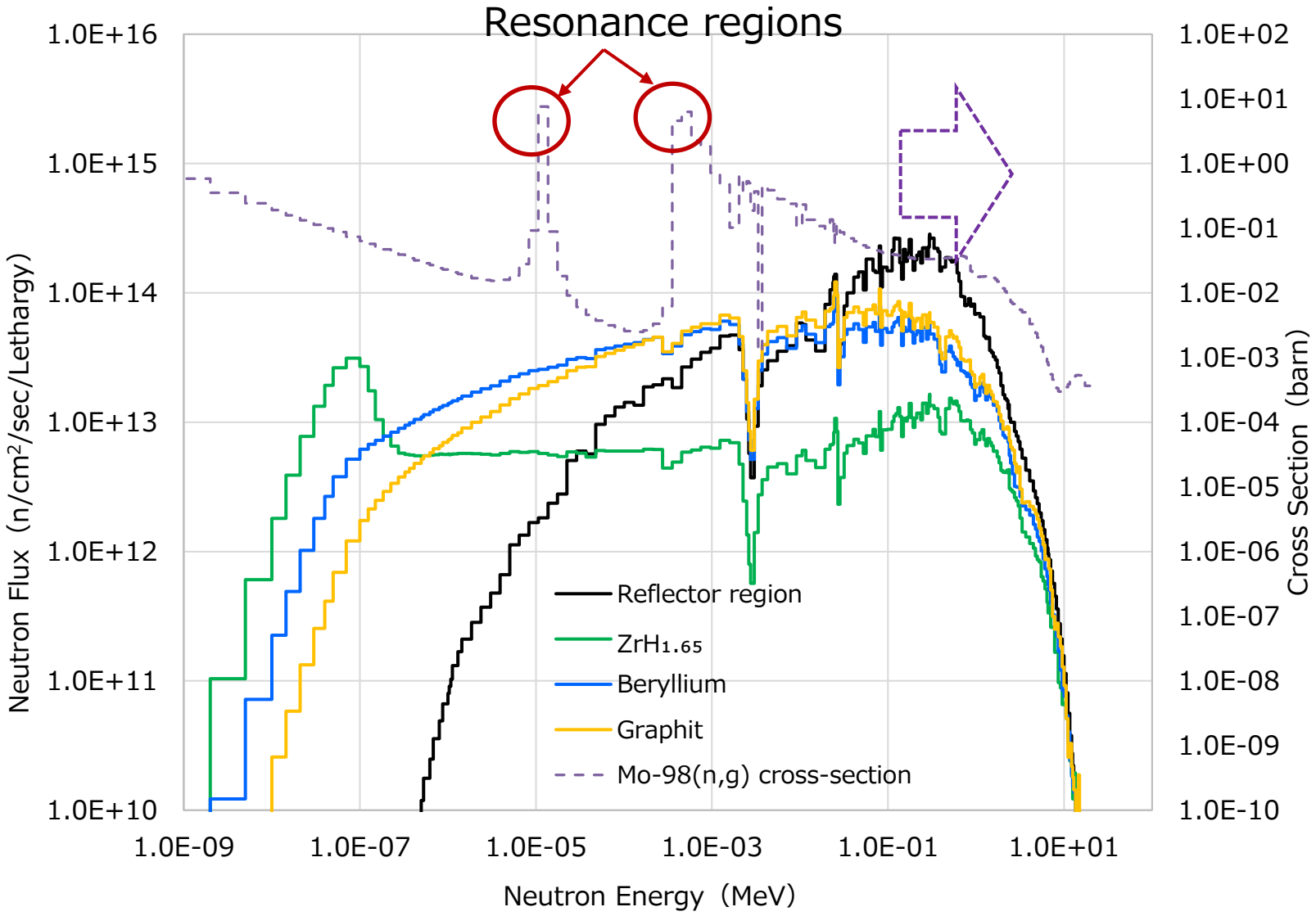
- Moderator material can be adjusted according to irradiation sample

- Evaluate irradiation conditions suitable for ^{99}Mo production
  -Moderator material
  (ZrH_x, Beryllium, Graphite, etc)

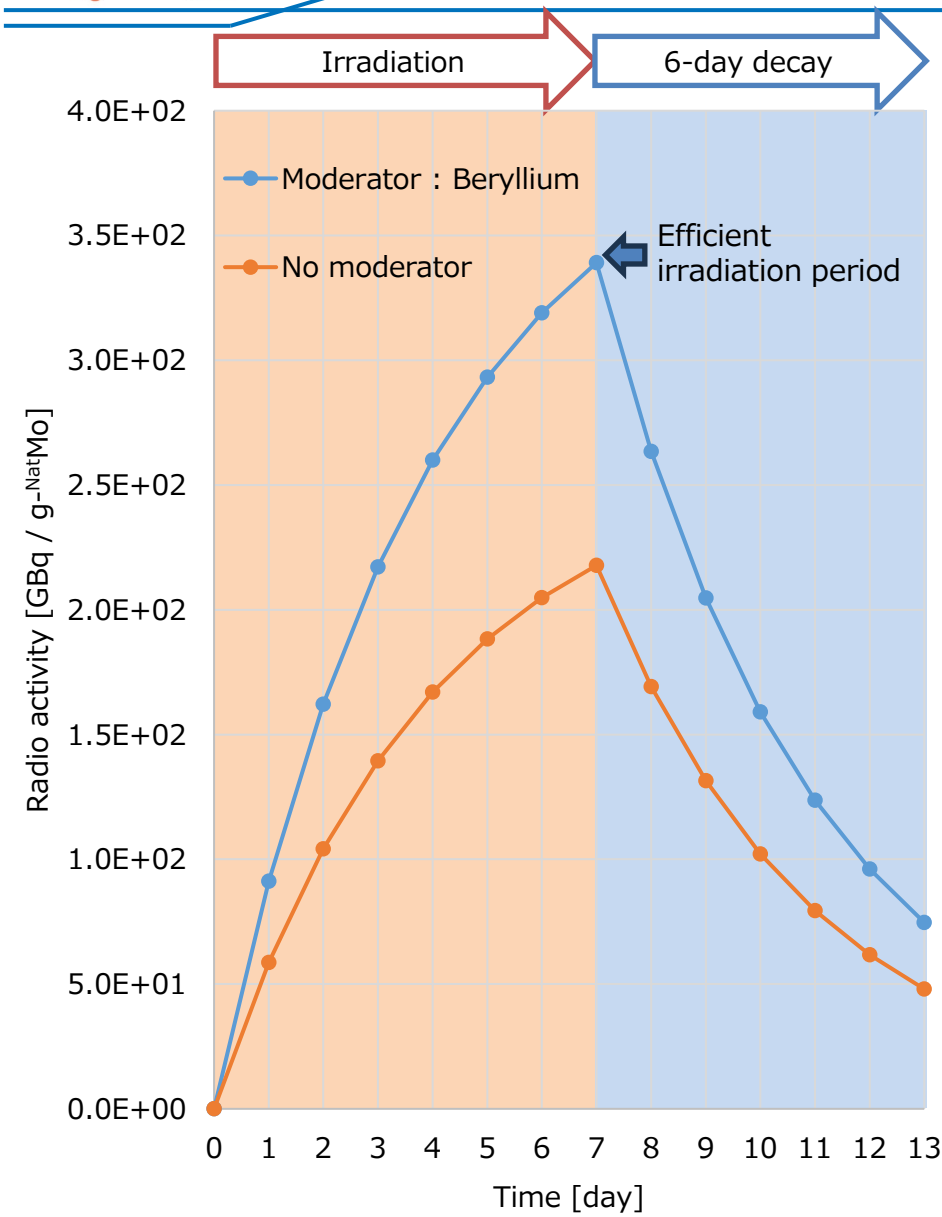


Difference of Earned Spectra with Moderator Materials

Using Beryllium as a moderator is effective for ^{99}Mo production, as it allows utilization of two resonance regions



Efficient Production of ^{99}Mo Using Moderator



Amount of ^{99}Mo available for supply

- No moderator
  47.9 GBq / g-^{Nat}Mo
- Moderator : Beryllium
  74.6 GBq / g-^{Nat}Mo

By installing a moderator, ^{99}Mo production increased by 1.5 times.

Tailoring the neutron spectrum through moderator materials also enables efficient production of radioisotopes.

Summary

Fuel region (Fast neutron)

- Utilizing the fast neutrons characteristic of Joyo, ^{225}Ac can be produced via the $^{226}Ra(n,2n)$ reaction.
  - By irradiating 1 g of ^{226}Ra for 60-day and repeated milking at 17.5-day intervals, would produce 11.3 GBq of ^{225}Ac.
  - By irradiating a few grams of ^{226}Ra, it is possible to produce the world's annual supply (63 GBq).

Production demonstration plan is ongoing for JFY2026

Reflector and moderator region (Epithermal neutron)

- A certain medical radioisotopes can be produced in the reflector region via (n,γ) reaction.
- Using a moderator is expected to enhance production efficiency.
  - Beryllium as a moderator increases the ^{99}Mo production yield by 1.5 times.

Currently in the feasibility study phase

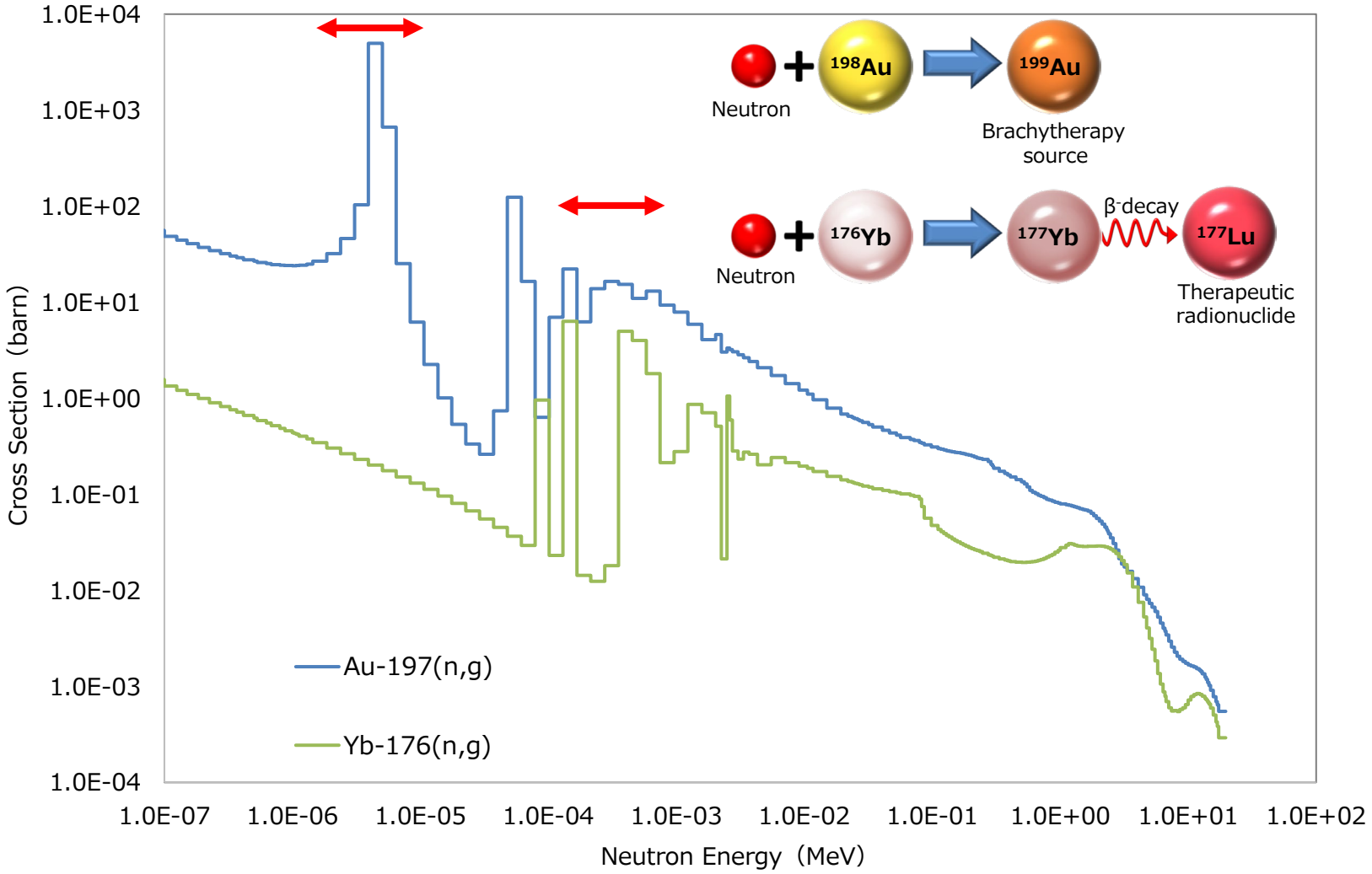
This work is supported by MEXT Innovative Nuclear Research and Development Program Grant Number JPMXD0220354346.

Thank you for your attention.

Appendix

Applicability of Moderators for Other Medical Radioisotopes

In the case of Au-198 production, a spectrum in the range of 1 eV to 10 eV is suitable.
On the other hand, for Lu-177, a spectrum in the range of 0.1 keV to 1 keV is suitable.



Schedule of ^{225}Ac Production in Joyo

2023/7/26
Obtained a license for operation
(Permission with new regulatory standards)

2023 - 2025
Works for safety improvement


Seismic reinforcement on the exhaust stacks


Ground improvement

2024/2/29
Cooperation agreement between
National Cancer Center and JAEA


Cooperation Agreement for Research and Development of Radiopharmaceuticals

2024/10/22
Obtained a license for multiple usages;
include production of radioactive isotopes

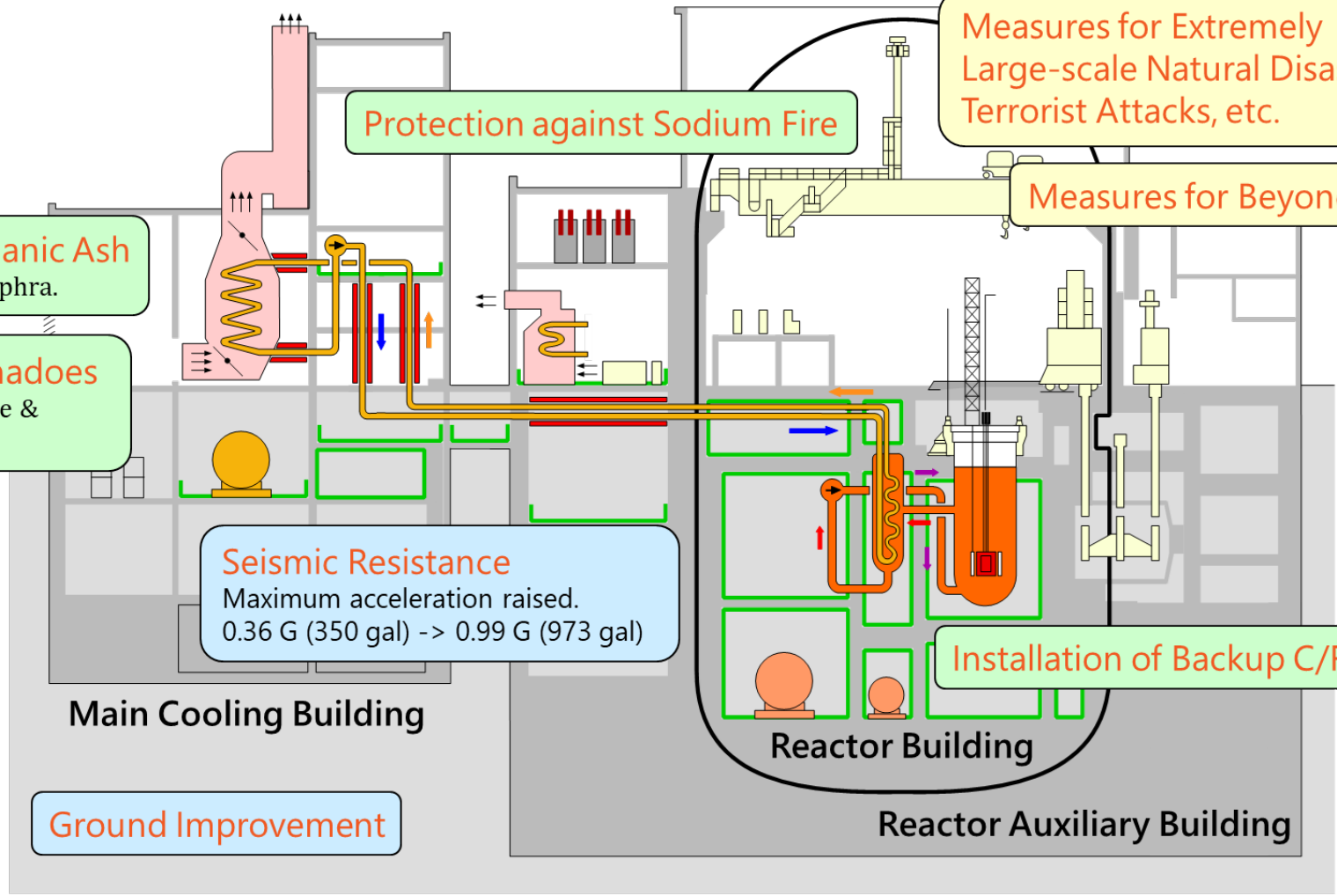
JFY2026
Restart operation of Joyo

Demonstrating ^{225}Ac production in Joyo

JFY2028 -
Scale-up of ^{225}Ac production

JFY: Japanese Financial Year (April to March)

Outline of Compliance with Regulation



More details were reported in Session 3 Safety & Security I