Domestic production of Ac-225 using the experimental fast reactor Joyo

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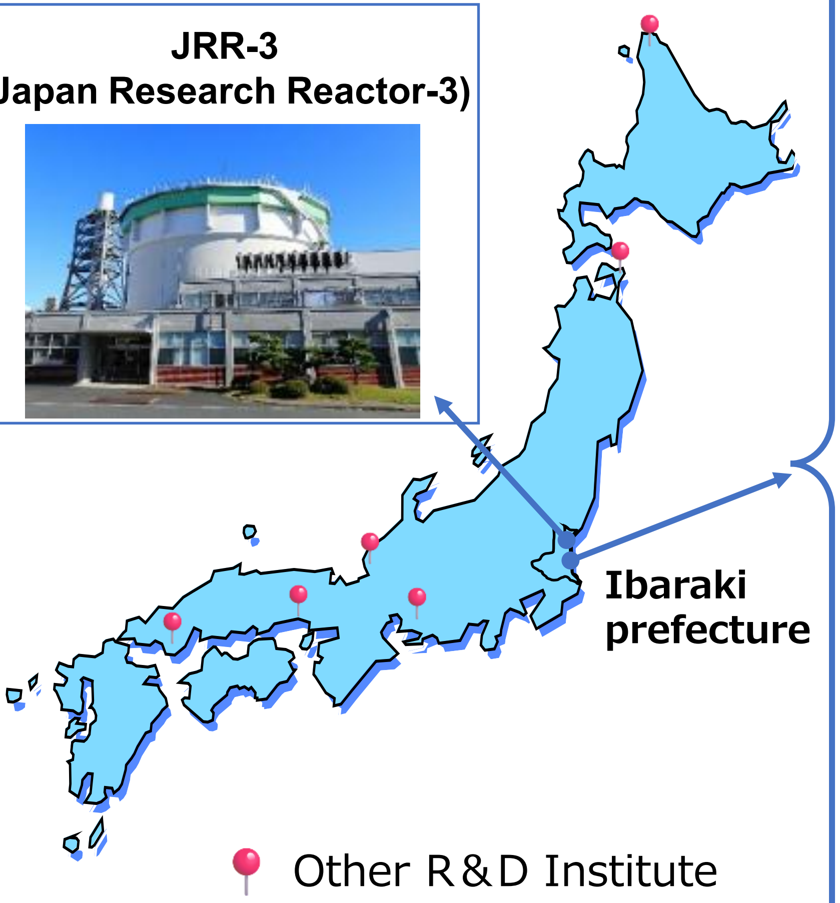
1. Introduction of JAEA

JAEA's role and major institutes

- R&D on advanced reactors by utilizing **Joyo, HTTR and related facilities**
- R&D on **Fukushima Daiichi NPP** decommissioning and radioactive waste management

JRR-3 (Japan Research Reactor-3)



Experimental Fast Reactor Joyo

R&D on Fast Reactor and its Fuel Cycle Technology

HTTR (High Temperature Engineering Test Reactor)

R&D on HTGR and Related Heat Application Technology

Sustainable

Stable energy supply
Enhancing resource efficiency and energy security

Reduction in environmental impact
Reduction of radioactive waste

Ubiquitous

Contributing to healthcare through cancer drug manufacturing
Production of Medical Radioactive Isotope（RI）

Space and nuclear fusion development, basic physics support
Provision of fast neutron irradiation field

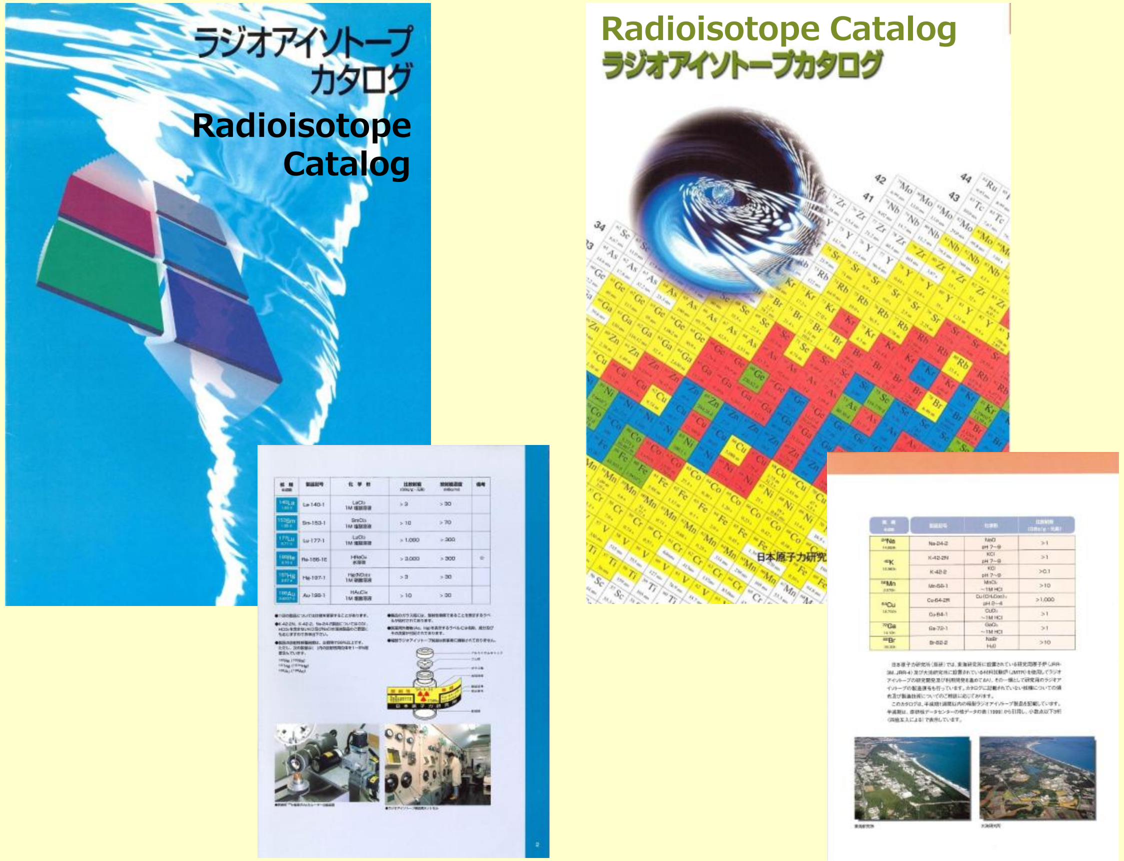
Synergy

Harmonization with renewable energy
Compensation for power fluctuations by adjustable power supply

Contributing to carbon neutrality
Hydrogen production, high-temperature heat utilization (industrial use)

Brief History of Radioisotope Production in JAEA

JAERI, the predecessor of JAEA, used to produce and distribute a variety of radioisotopes domestically



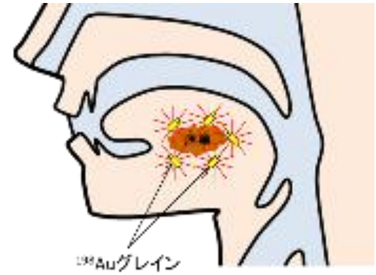
The catalog of Radioisotopes from the JAERI era

1995 Cabinet Decision

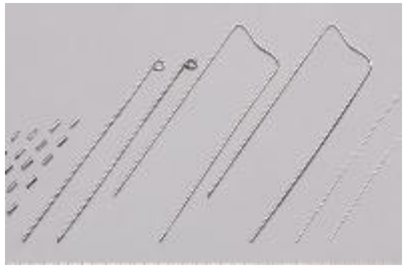
- The production of medium- to long-lived radioisotopes that can be imported from overseas was discontinued.
- The production of industrial-use radioisotopes with stable and high demand was transferred to the private sector.

The JAEA's production of radioisotopes was limited to

- ^{60}Co (for industrial use)
- ^{192}Ir (for industrial and medical use)
- ^{198}Au (for medical use)



^{198}Au for brachytherapy

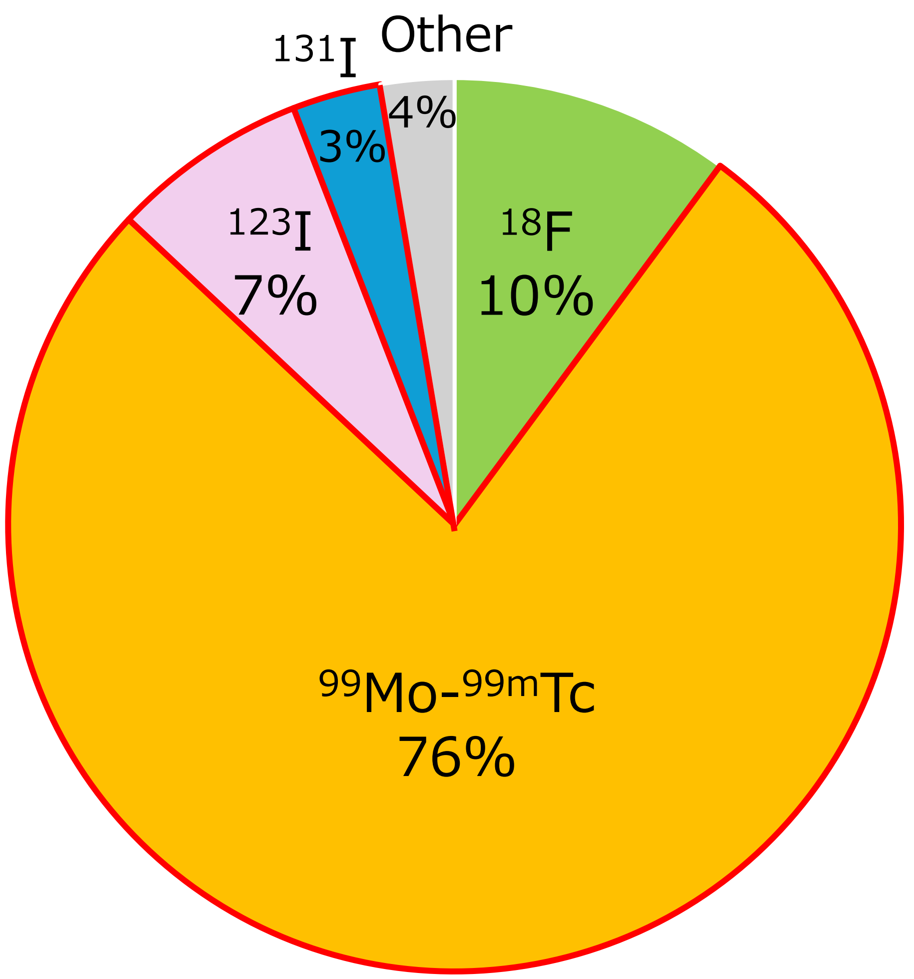


^{192}Ir for RALS
(Remote After Loading System)

2. Medical radioisotope landscape in Japan

Current supply situation and Recent Trends of RI

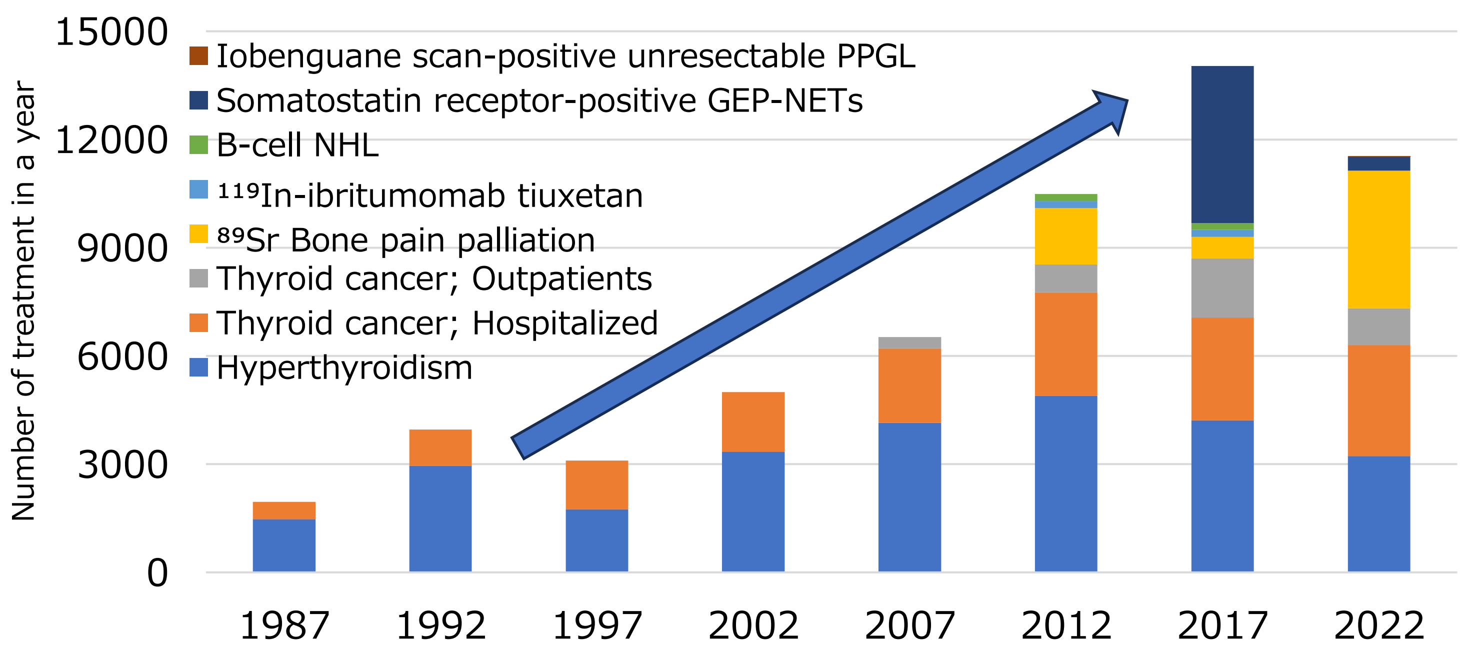
Domestic utilization ratio of unsealed radioisotopes (2019)



Red frame(86%): Import-dependent nuclides

https://www.jrias.or.jp/pdf/riyotokei2019_3.pdf

Number of unsealed radionuclide therapy



- Major Radioisotopes is becoming dependent on imports
- Expectations for Medical Radioisotopes is growing
- Western countries are ramping up medical radioisotopes production and research

https://www.jrias.or.jp/pdf/A4Pamphlet2024.pdf

National Action Plan for RI Production and Utilization (Outline)

31st May, 2022 Atomic Energy Commission, Japan

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)

3. Production methods of Ac-225 worldwide

Production method of Ac-225 worldwide

Existing method Th-229 generator

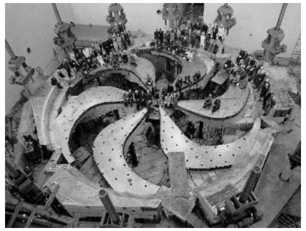
Extract Th-229 (Ac-225 generator) from U-233[*1]

Ac-225 extracted from the Th-229 generator

Stable supply is possible

Supply is limited

Alternative method Accelerator method



High Power Cyclotron[*2]
(Th-232(p,x)Ac-225)

Middle Power Cyclotron / Rhodotron [*3]
(Ra-226(p,2n)Ac-225)

QST

HITACHI Inspire the Next

Linac [*4]
(Ra-226(γ,n)Ra-225→Ac-225)

High specific radioactivity and good handling

Alternative method Reactor method

Experimental Fast Reactor *Joyo*
Fast Reactor
(Ra-226(n,2n)Ra-225→Ac-225)

High Flux Isotope Reactor@ORNL[*5]
Light Water Reactor
(Ra-226(3n,2β)Th-229
→Ra-225→Ac-225)

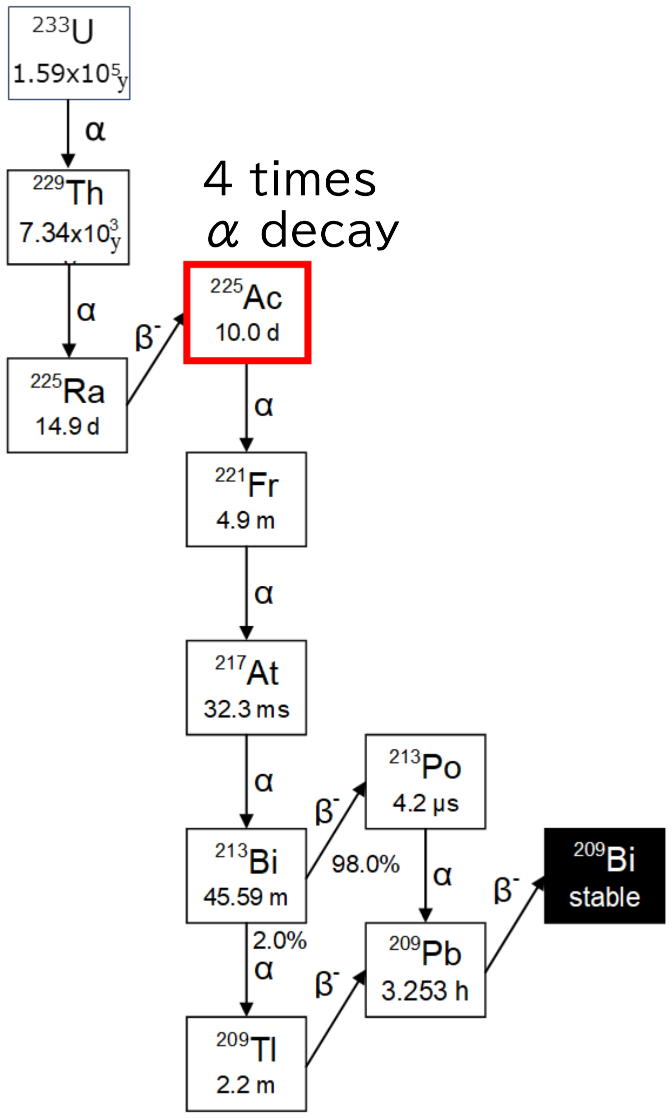
Mass production is possible

Scheduled annual-inspection shutdown

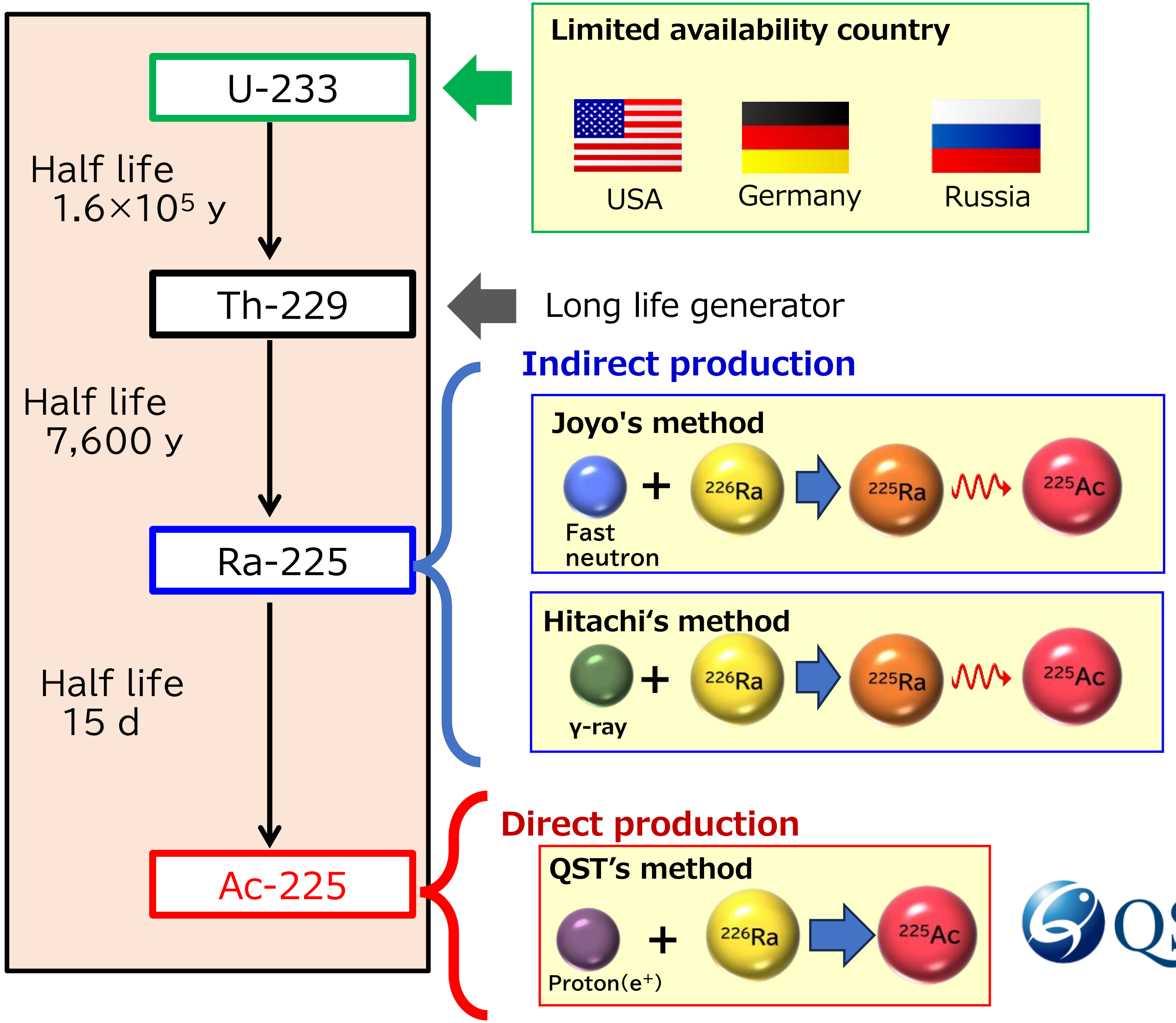
Advantages, Disadvantages

*1 https://isotopes.gov/BNL-AP-Hot-Cells
*2 https://cycops.triumf.ca/homepage/opsphotos.htm
*3 https://www.northstarnm.com/radiopharmaceutical-therapy/actinium-225/
*4 https://www.raris.tohoku.ac.jp/facility/mikamine/%e5%a4%a7%e5%bc%b7%e5%ba%a6%e9%9b%bb%e5%ad%90%e7%b7%9a%e5%bd%a2%e5%8a%a0%e9%80%9f%e5%99%a8/
*5 https://neutrons.ornl.gov/hfir

Reaction pathways



Neptunium series

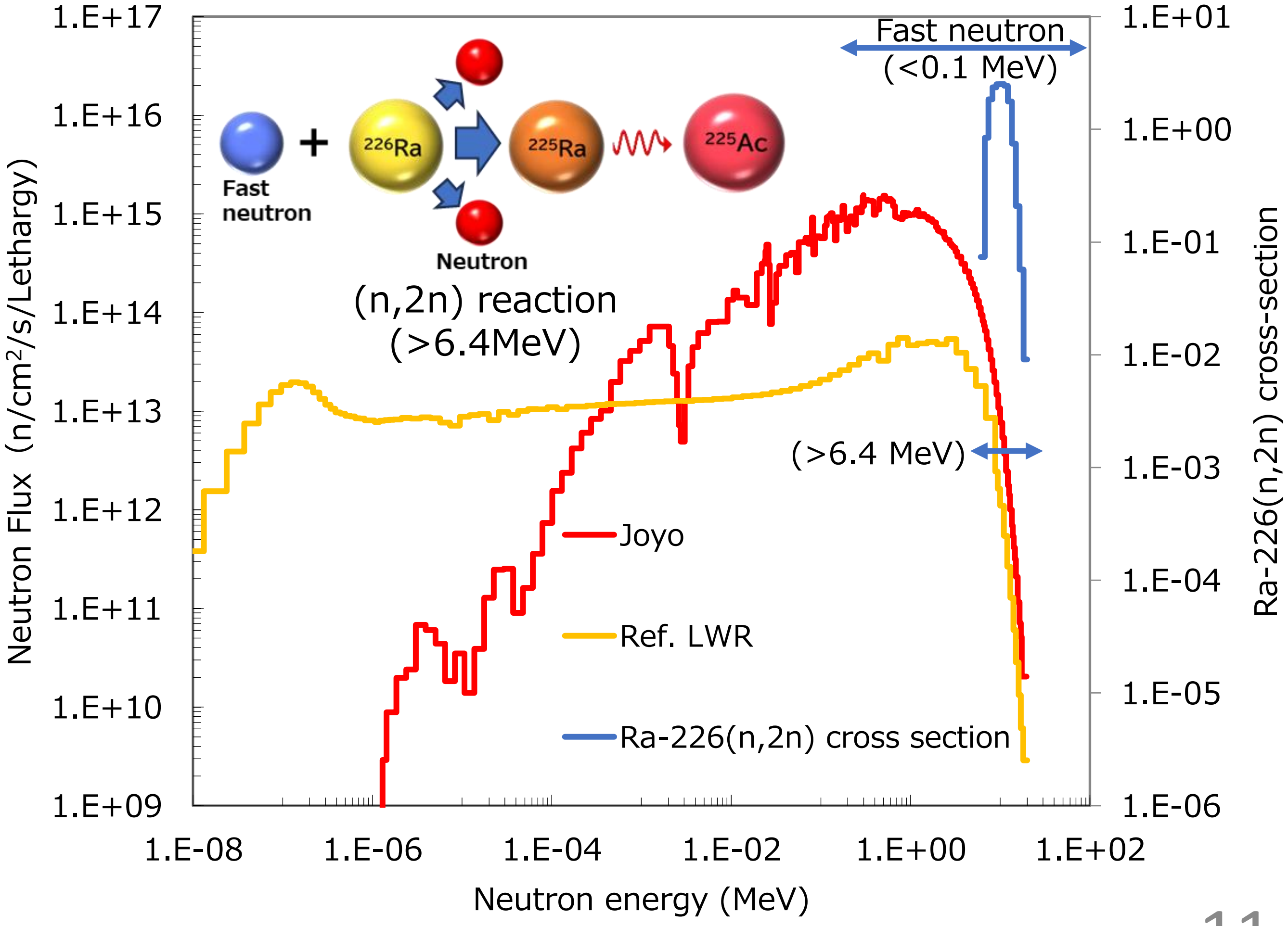


4. Ac-225 production at Joyo

Experimental Fast reactor *Joyo*

- Joyo was constructed as experimental reactor of the first step of Fast Breeder Reactor development in Japan.
- It is used for a versatile of purposes, from fast reactor development and fundamental research to industrial applications.

Main specifications of Joyo	
Purpose	Development of ・Fast reactors ・New fuel and material <u>Production of medical radioisotopes</u>
Reactor type	Sodium cooled fast reactor
Fuel	MOX(Mixed Oxide) fuel
Thermal power	100MW
Core model	Cylinder (Diameter : 78cm、Height : 50cm)
Operation period	60 day/cy ： 1～3cy/year



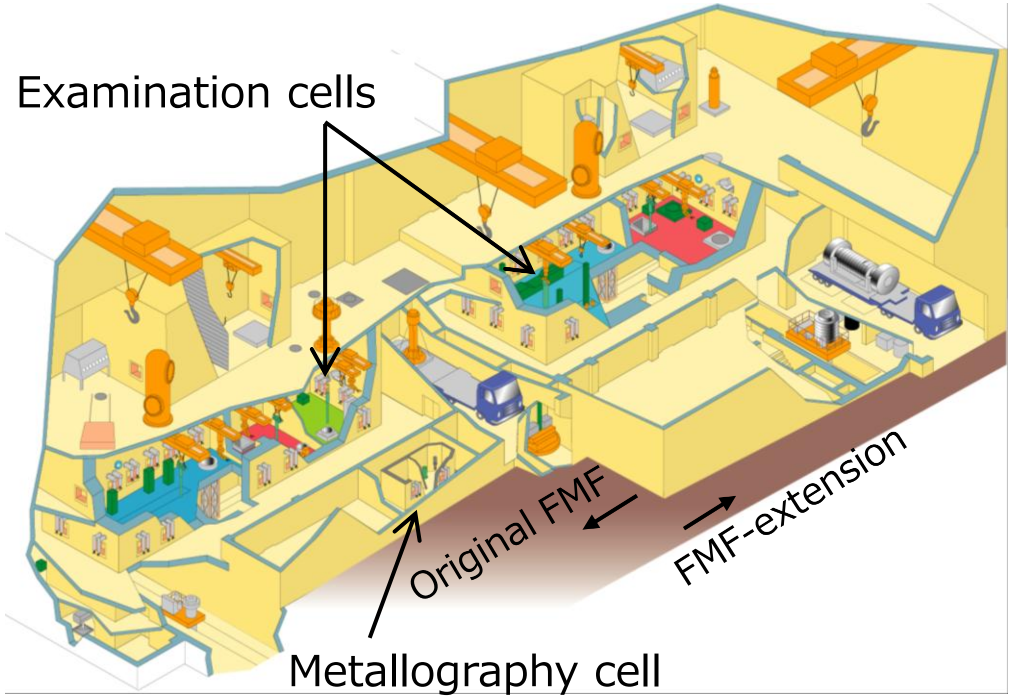
FMF (Fuel Monitoring Facility)

- FMF, which is connected to Joyo via sub-assembly (S/A) transportation route, is a large, heavily shielded, hot cell facility designed for remote examination of highly irradiated fast reactor (FR) fuel.
- It has various post irradiation examination (PIE) capabilities which have been applied for characterization of not only FR fuels irradiated in Joyo but also fuel debris retrieved from the TEPCO Fukushima Daiichi Nuclear Power Station.
- After Joyo restart, the fabrication of ^{226}Ra target for irradiation in Joyo, and the chemical separation of ^{225}Ac from irradiated ^{226}Ra target will be carried out in FMF.

Appearance of FMF

PIE capabilities of FMF

Non destructive characterization	X-ray CT, Visual inspection, Profilometry, Gamma scanning, etc.
Destructive characterization	SEM/EPMA,TEM, SIMS, TIMS, XPS, etc.

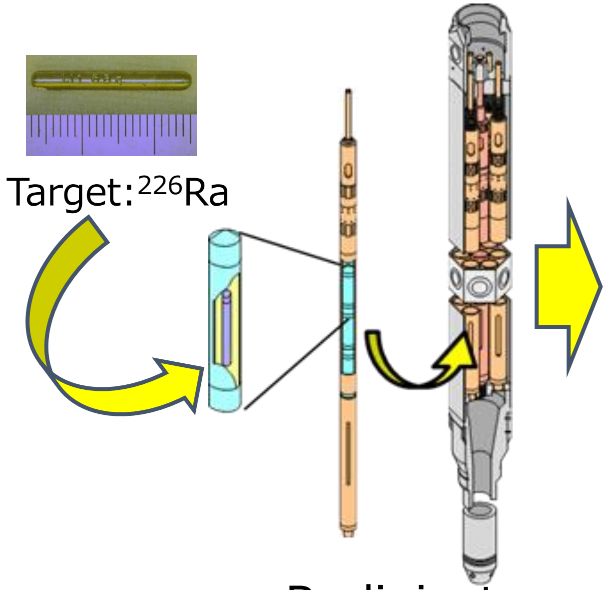


Ac-225 production process at Joyo

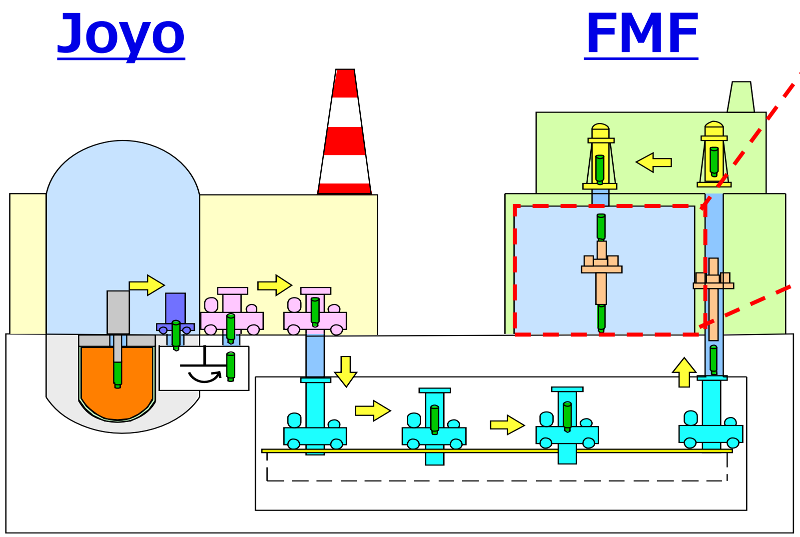
Process of ^{225}Ac production

1. Load ^{226}Ra into a radioisotope production S/A
2. Irradiate the S/A with Joyo
3. Transport from Joyo to FMF (Through the underground)
4. The S/A is disassembled at the FMF
5. Chemical separation of ^{225}Ac

} As short as 6 days

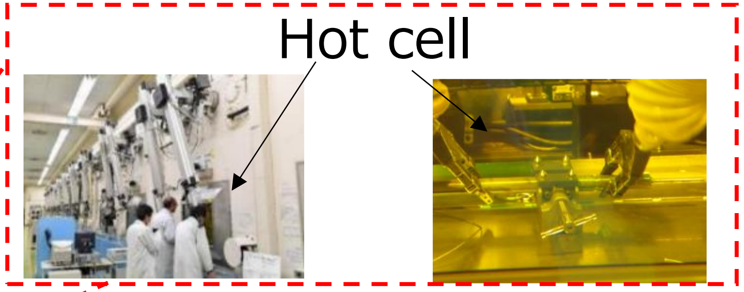


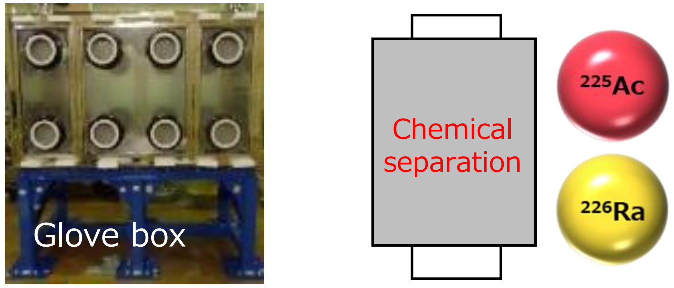
Radioisotope production S/A



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

Takes 3 days to disassemble the S/A



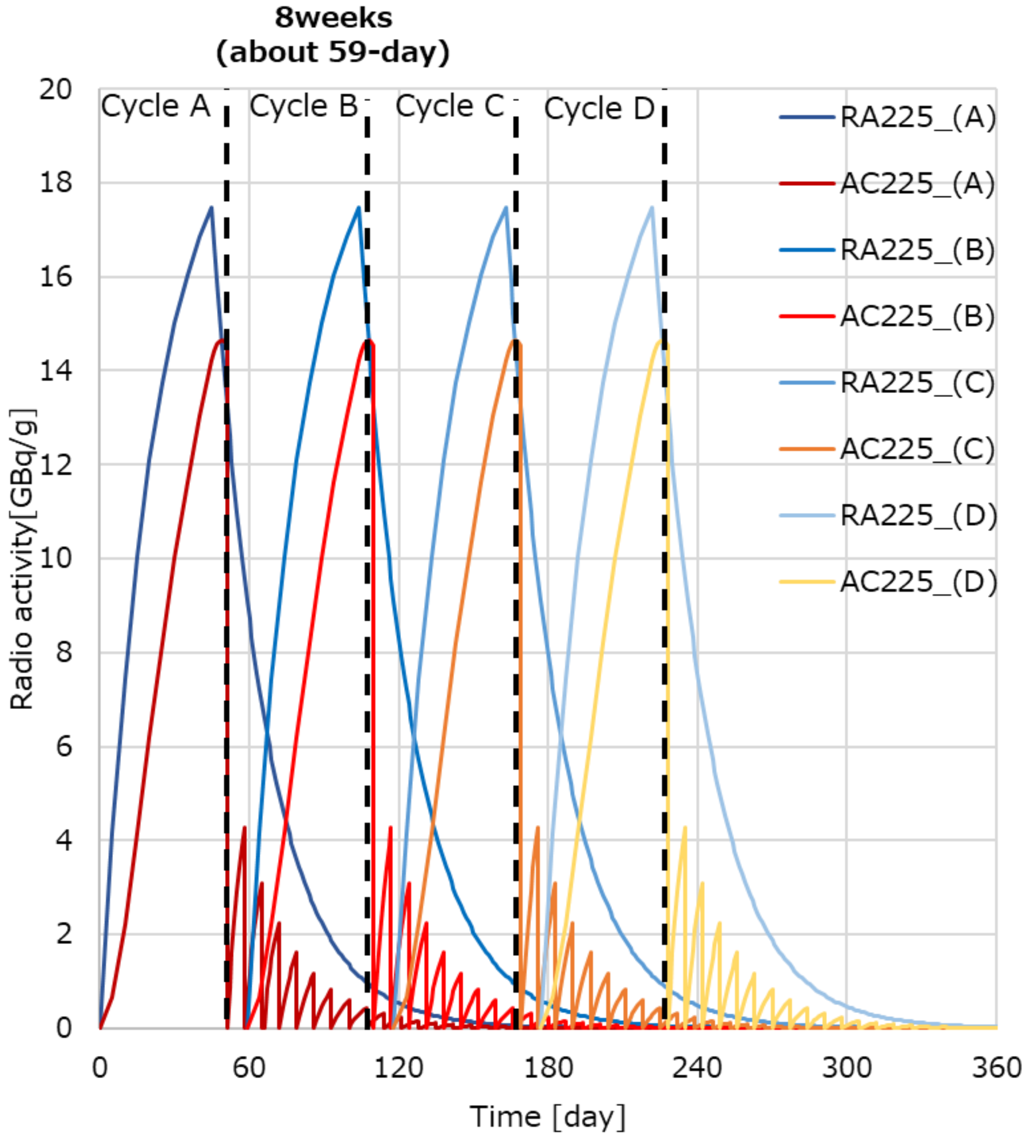


Takes 1 day to chemical separation

S/A : Subassembly

Estimated supply capacity of Joyo

Capable of meeting 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

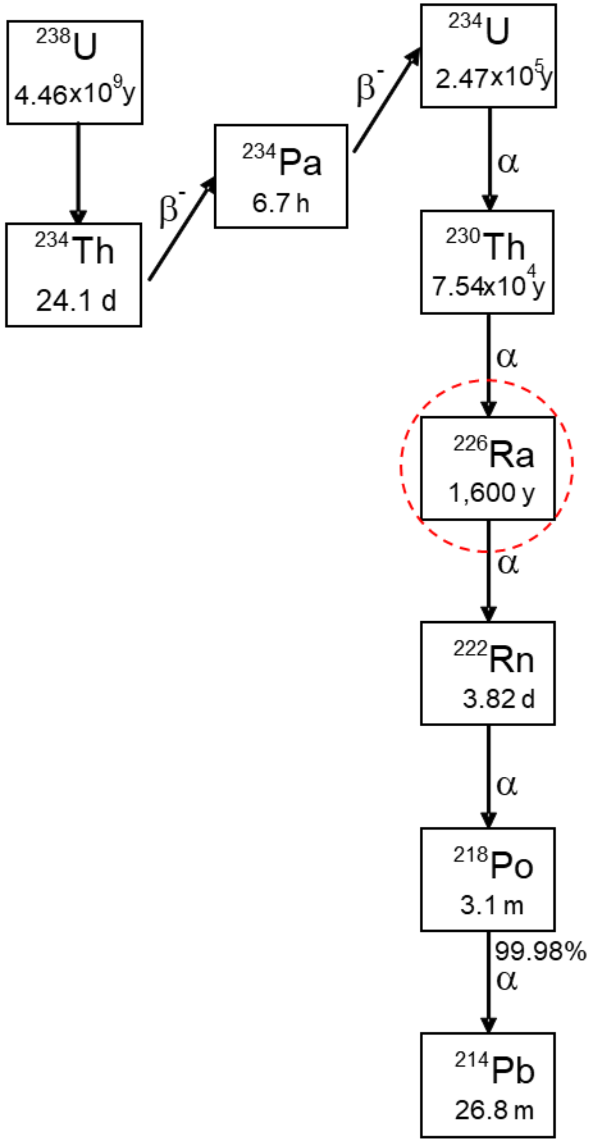
Milking	#1	#2	#3	#4	#5	#6~	Total	
							1cycle	Annual
^{225}Ac [GBq] (patient)	4.28 (710)	3.09 (520)	2.23 (370)	1.61 (270)	1.16 (190)	3.00 (500)	15.4 (2,560)	**61.5**

** 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*

5. Procurement of Ra-226

What is Ra-226

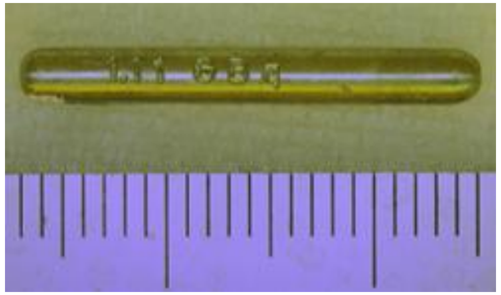
Nuclides in radioactive equilibrium with Nat-Uranium



Uranium series	
Nuclide	***weight (g)***
^{238}U	9.93×10^{5}
^{234}U	5.04×10^{1}
^{234}Pa	2.17×10^{-10}
^{234m}Pa	2.17×10^{-10}
^{234}Th	1.44×10^{-5}
^{230}Th	1.48×10^{1}
^{226}Ra	**3.09×10^{-1}**
^{222}Rn	1.98×10^{-6}
^{218}Po	1.10×10^{-9}
^{214}Po	9.51×10^{-16}
^{210}Po	6.79×10^{-5}
^{214}Bi	6.96×10^{-9}
^{210}Bi	2.46×10^{-6}
^{214}Pb	9.31×10^{-9}
^{210}Pb	3.98×10^{-3}
^{206}Pb	7.58×10^{1}

In the 1920s

Industrial use



Calibration source

Medical use

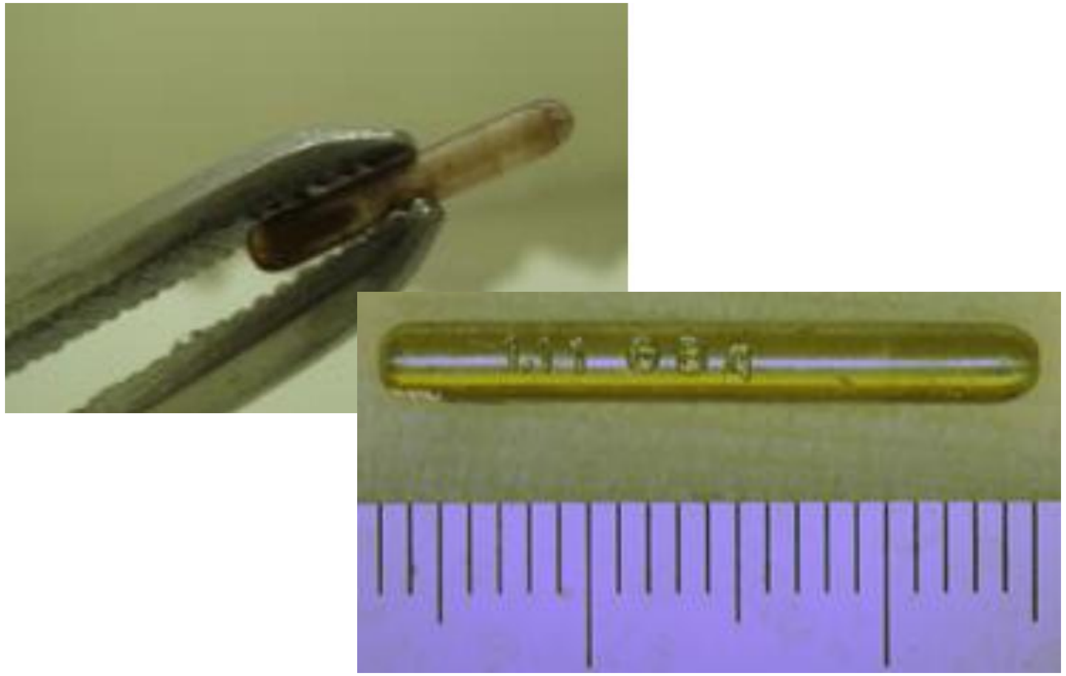
Therapeutic radiation source

https://www.aec.go.jp/kaigi/teirei/2023/siryo20/1-2_haifu.pdf

Procurement route of Ra-226

Procurement from

①Discarded radiation sources



②Natural uranium mines

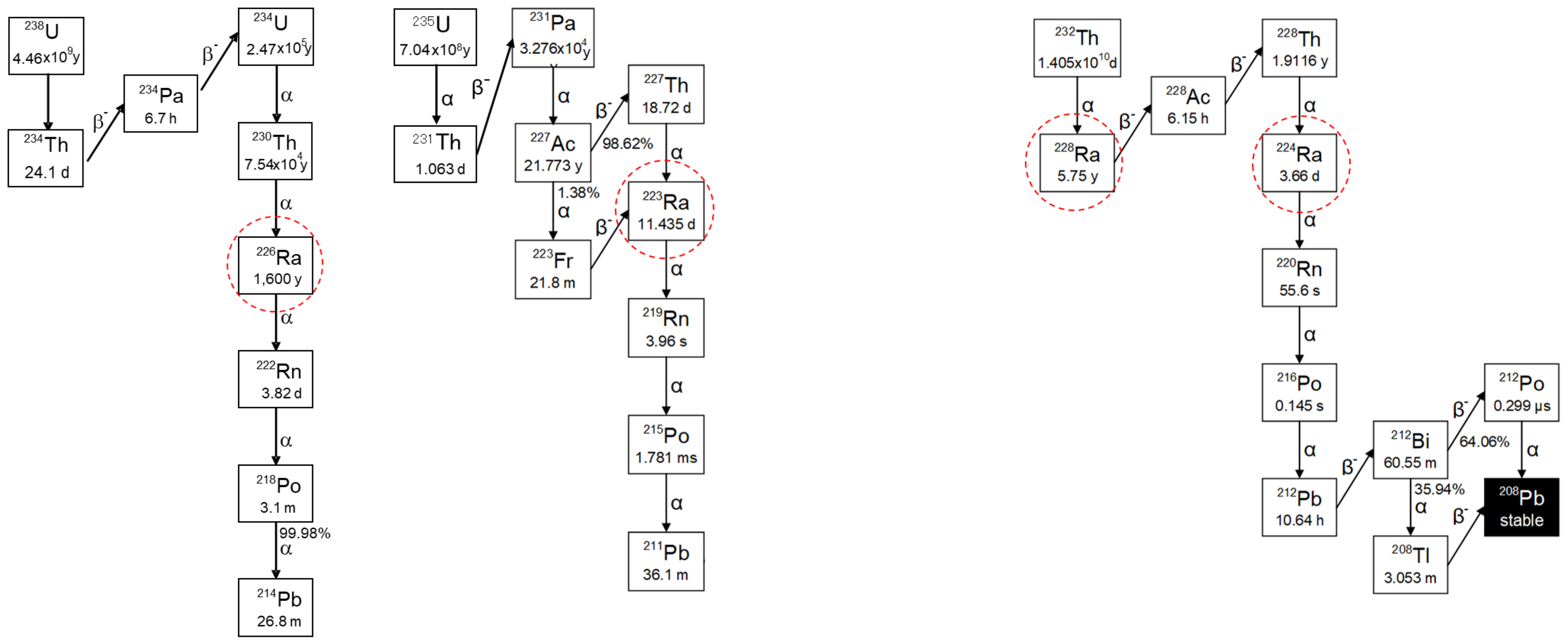
Production of new Ra-226 sources ceased in the 1960s, resulting in limited availability

→

It is necessary to recover Ra-226 from uranium mines

https://www.aec.go.jp/kaigi/teirei/2023/siryo20/1-2_haifu.pdf

②Procurement from natural uranium



Uranium series   Actinium series   Thorium series

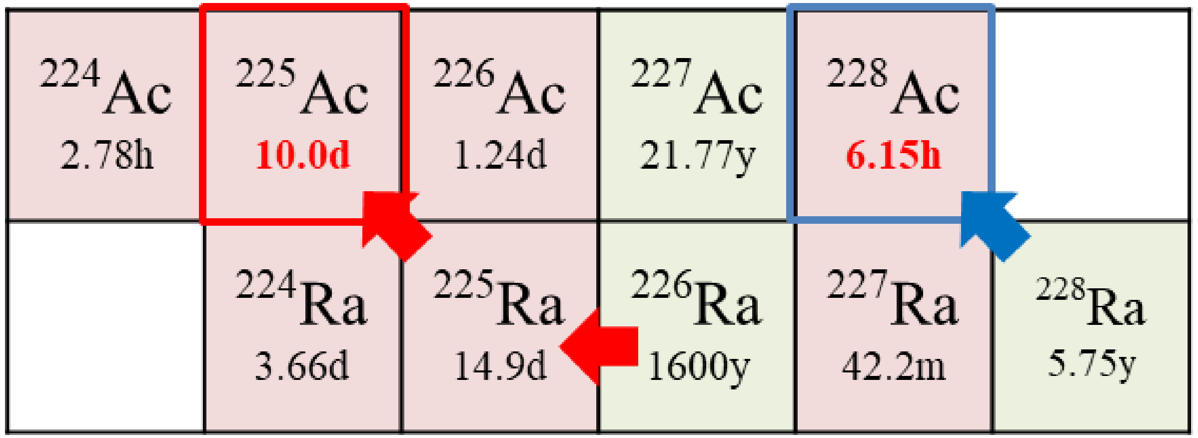
^{226}Ra	^{223}Ra	^{228}Ra	^{224}Ra
1600y	11.435d	5.75y	3.65d

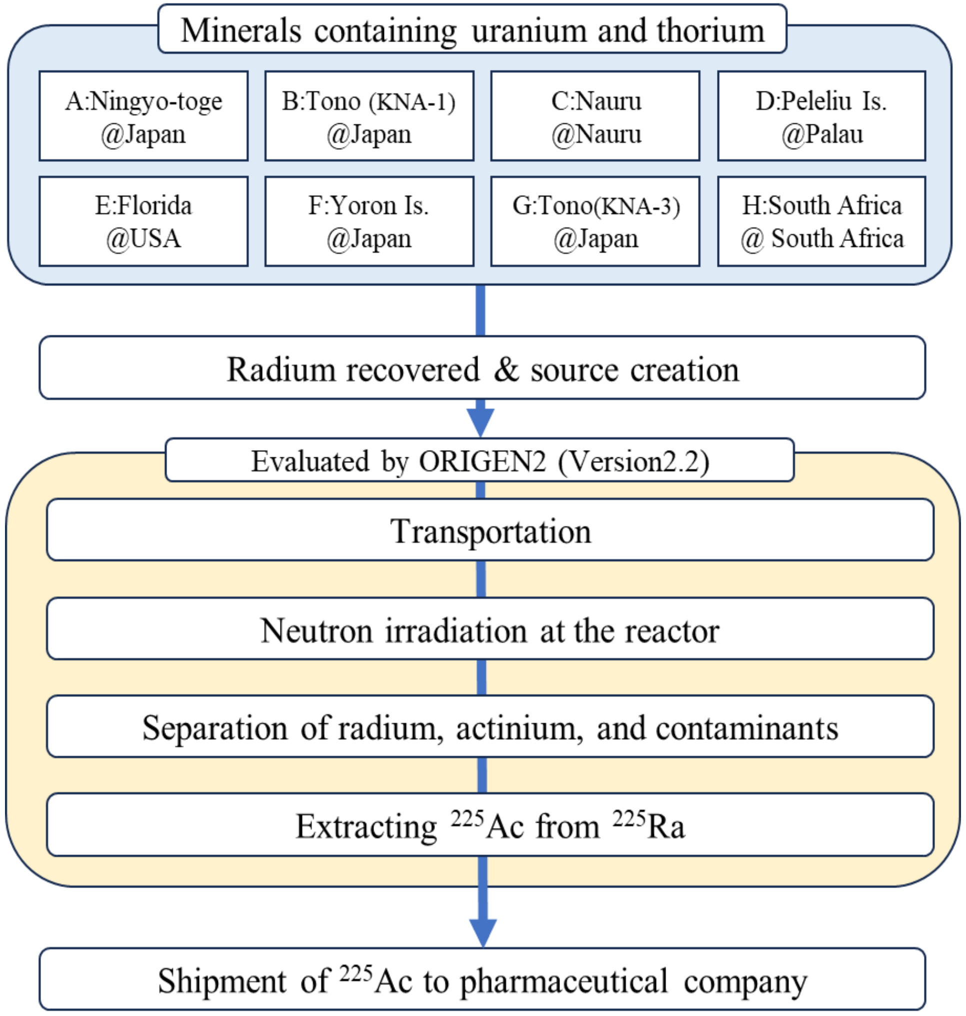
Uranium-Thorium ore

Impact of ^{228}Ra on ^{225}Ac Production

Purity of uranium or thorium ore

	Weight ratio(wt%)							
	A	B	C	D	E	F	G	H
^{Nat}U	99.7%	99.3%	98.8%	96.6%	90.1%	52.4%	40.3%	5.9%
^{Nat}Th	0.3%	0.7%	1.2%	3.4%	9.9%	47.6%	59.7%	94.1%
^{228}Ra	0.0004%	0.0009%	0.0016%	0.0046%	0.01%	0.12%	0.19%	2.0%
^{226}Ra	99.9%	99.9%	99.9%	99.9%	99.9%	99.8%	99.8%	97.9%

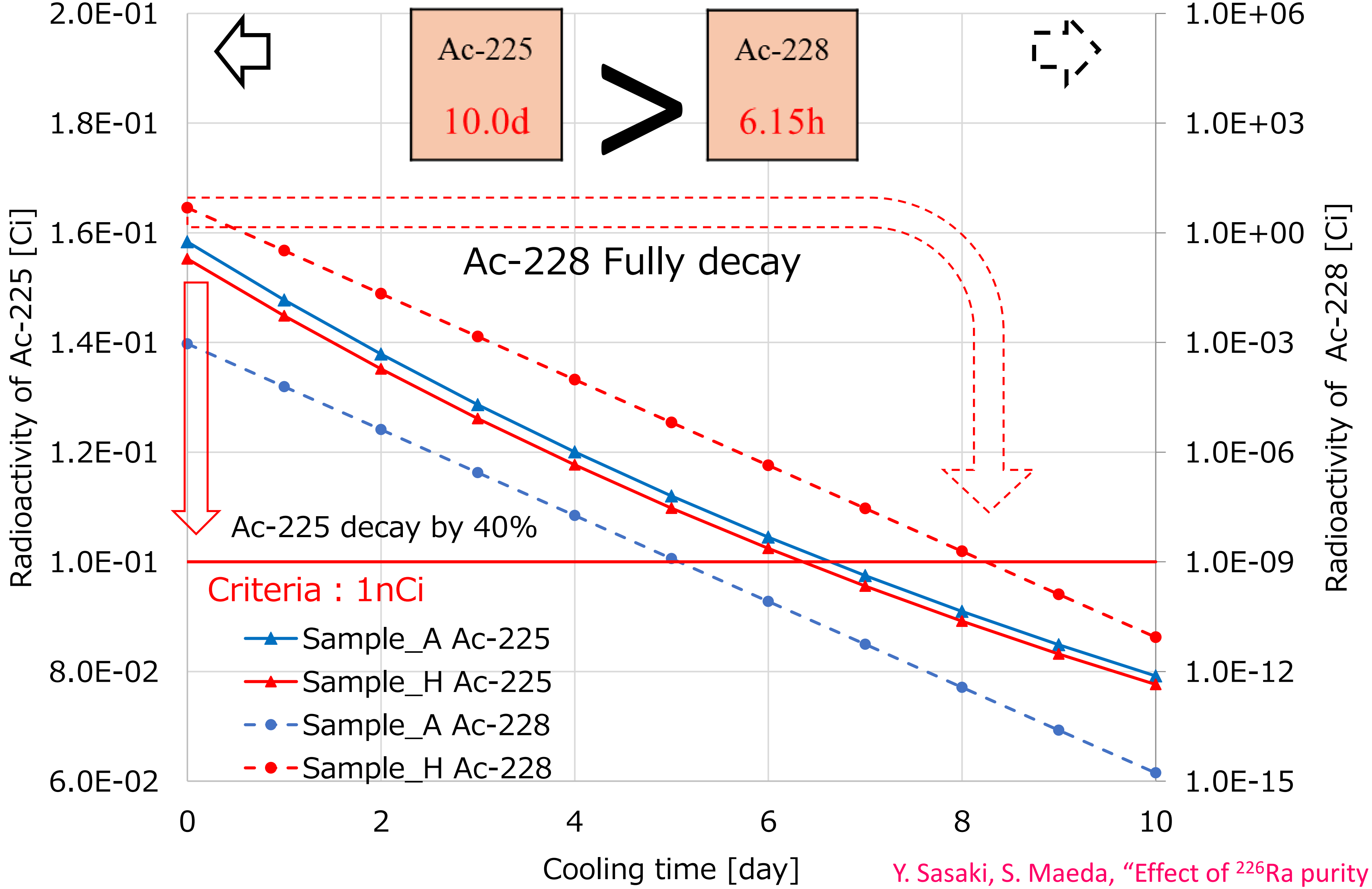




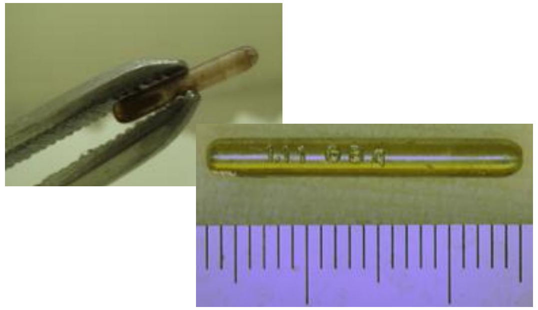
Evaluation flow

Y. Sasaki, S. Maeda, "Effect of ^{226}Ra purity as a target for ^{225}Ac production using a fast reactor" *Journal of Radioanalytical and Chemistry*, Published online, 2024 https://doi.org/10.1007/s10967-024-09397-7

Impact of ^{228}Ra on ^{225}Ac Production



①Discarded radiation sources



are preferable because Ra-228 decays within about 60 years (2025s → 1960s)

Y. Sasaki, S. Maeda, "Effect of ^{226}Ra purity as a target for ^{225}Ac production using a fast reactor" *Journal of Radioanalytical and Chemistry*, Published online, 2024 https://doi.org/10.1007/s10967-024-09397-7

Summary

- Global competition for Ac-225 production is accelerating.
- JAEA is leveraging the fast reactor *Joyo* for large-scale radioisotope production.
- Regulatory milestones achieved in JFY2024 include obtaining a license for changes in reactor installation for radioisotope production.
- Discarded radiation sources from the 1960s promise to be a viable source for producing Ac-225 from Ra-226

- *Joyo* is scheduled to restart in JFY2026 with Ac225 production demonstration planned using discarded Ra-226 sources within the same FY.

Thank you for your attention.