

8th August, 2022
NAPAC 2022 at Albuquerque

Applications of Particle Accelerators

Mitsuru UESAKA,
Chairman, Japan Atomic Energy Commission
Professor of Emeritus, the University of Tokyo

- ***Downsizing of Accelerators***
- ***Medical RI Production by Best Mix of Research Reactors and Accelerators***
- ***Sustainable Social Infrastructure***
- ***Decommission of TEPCO Fukushima Daiichi Nuclear Power Station (FDNPS)***
- ***Summary***

Particle, Energy and Choice of Accelerators

100 keV

1 MeV

100 MeV

1 GeV

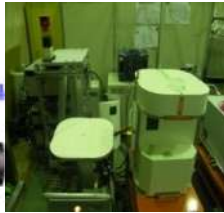
1 TeV



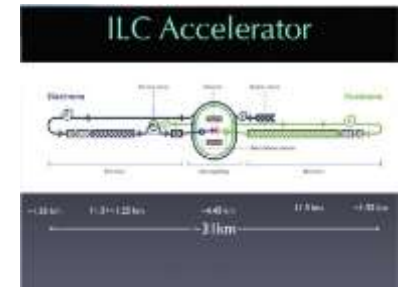
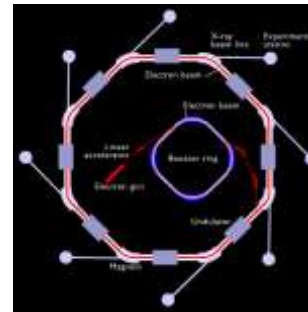
Electron



X-ray Tube



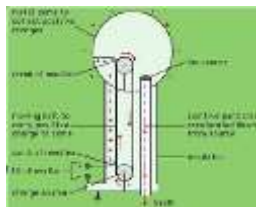
Linac



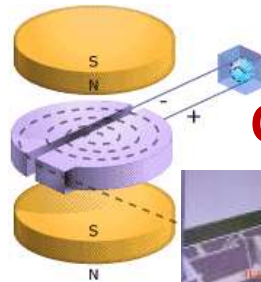
Linear Collider



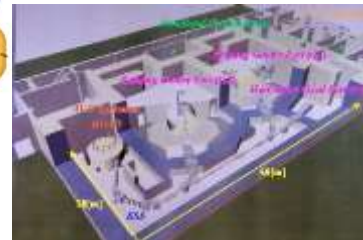
Ion



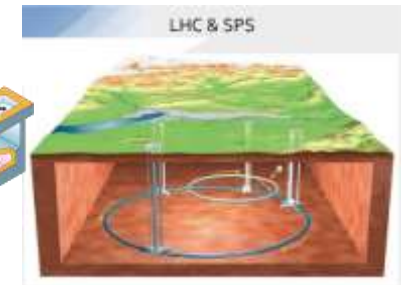
Electrostatic



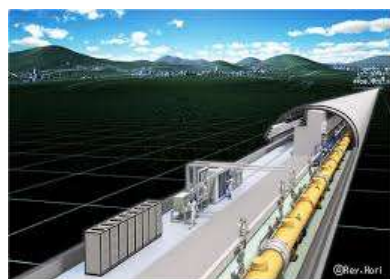
Cyclotron



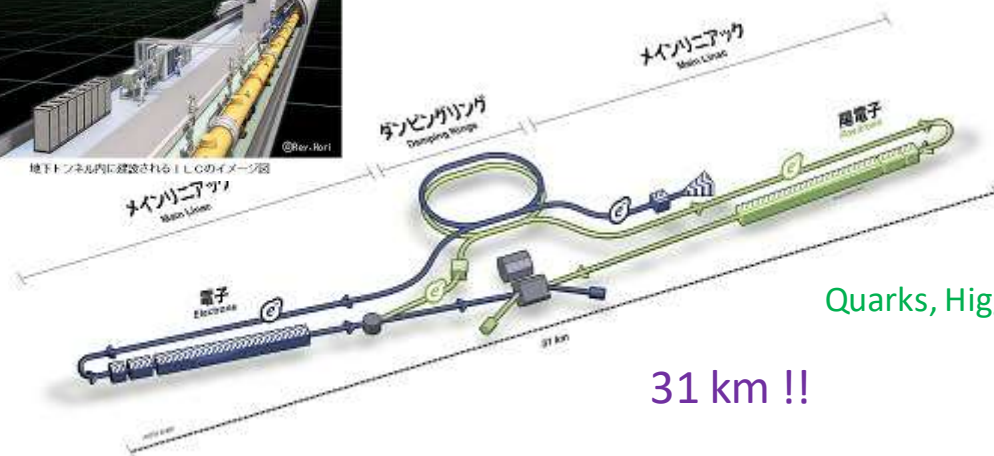
Synchrotron



Trials for Downsizing of International Linear Collider



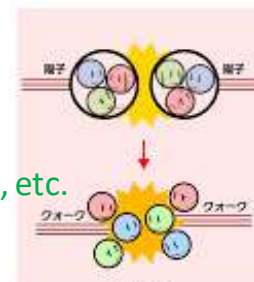
地下トンネル内に建設されるILCのイメージ図



31 km !!

Quarks, Higgs, etc.

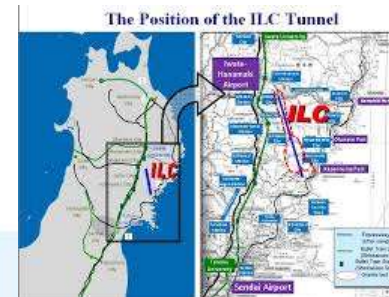
Proton



LHC

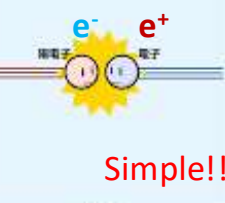
大型ハドロン衝突型加速器

基本粒子 (クォーク) が衝突して陽子と中性子の衝突



e^- e^+

Simple!!



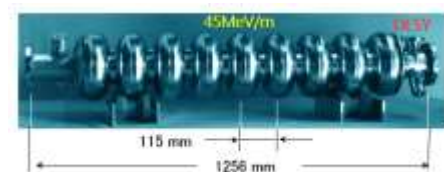
ILC

国際リニアコライダー

基本粒子 (レプトン) と同じの衝突

ILC Scheme | www.ilc.or.jp

Superconducting Linac



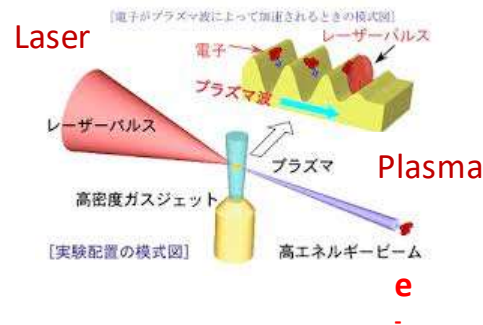
X-band
(11.424 GHz)
Linac



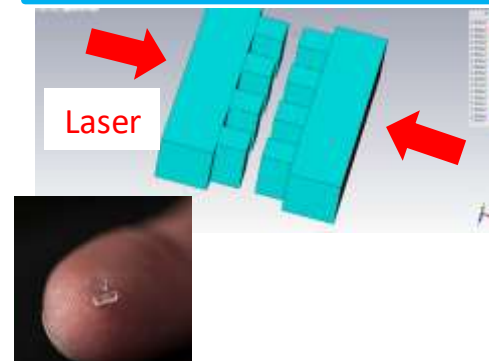
X-Band

11.424 GHz

Laser Plasma Accelerator



Optical Laser Dielectric Accelerator



Downsizing of Medical Accelerators by Advanced Technologies

Electron Linac with S/C/X-bands

<http://www.accuray.com/>

<http://www.accuthera.com/>

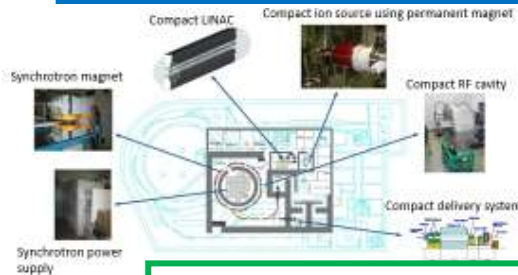


<http://www.varian.com/>

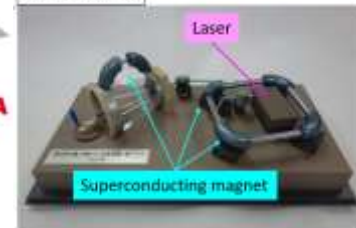
<http://www.accuray.com/>

<http://www.mhi-global.com/index.html>

Synchrotron with Layout / SC

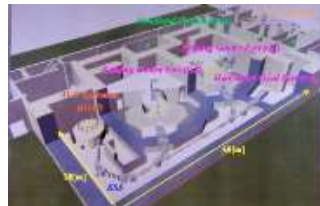


Hokkaido University and Hitachi
Quantum knife



Cyclotron with SC / Layout

<http://www.nirs.go.jp/ENG/core/ace/index.html>



https://www.toshiba.co.jp/about/t/press/2015_11/pr1001.htm

TOSHIBA



Review of
Accelerators for
Science and
Technology,
Vol.2(2009).p.154

Quantum Knife of QST

J-PARC

LANSE



Neutron Source and BNCT



RANS of RIKEN



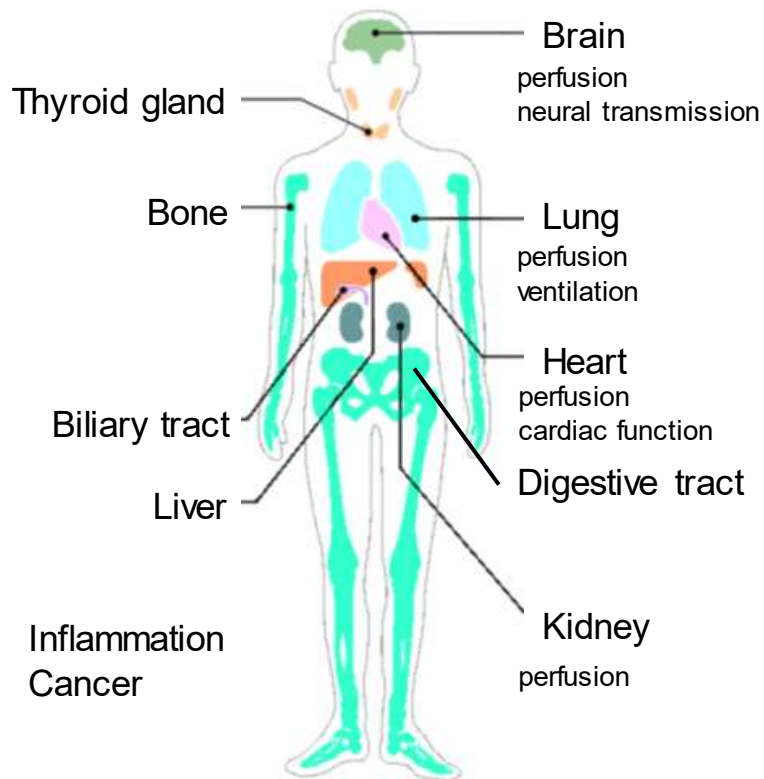
Cyclotron based BNCT
at Fukushima



- **Downsizing of Accelerators**
- **Medical RI Production by Best Mix of Research Reactors and Accelerators**
- **Sustainable Social Infrastructure**
- **Decommission of TEPCO Fukushima Daiichi Nuclear Power Station (FDNPS)**
- **Summary**

Clinical Nuclear Medicine

Uses of atomic energy for imaging of diseases and care for patients



	radioisotope	purpose
gamma-emitting RI	$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$, ^{123}I , ^{201}Tl , ^{67}Ga , ^{111}In , $^{89\text{m}}\text{Kr}$, etc.	SPECT ¹⁾ imaging
positron emitting RI	^{18}F , ^{11}C , ^{15}O , ^{13}N , ^{68}Ga , ^{89}Zr , etc.	PET ²⁾ imaging
beta-emitting RI	^{131}I , ^{90}Y , ^{177}Lu , ^{64}Cu , etc.	thyroid diseases malignant lymphoma neuroendocrine tumor
alpha-emitting RI	^{223}Ra , ^{225}Ac , ^{213}Bi , etc.	prostate cancer with metastasis, etc.

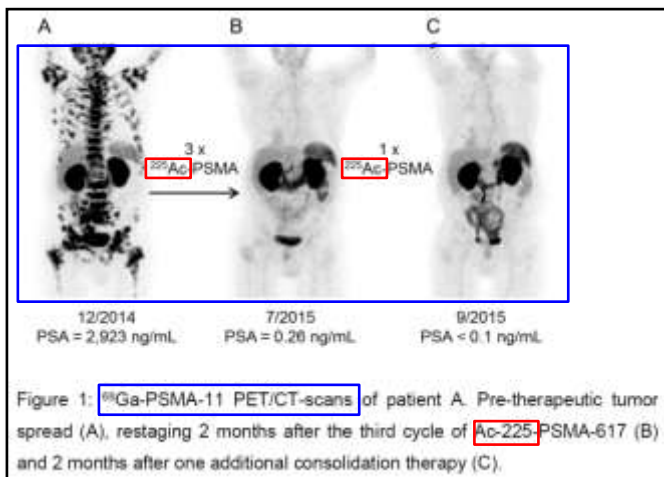
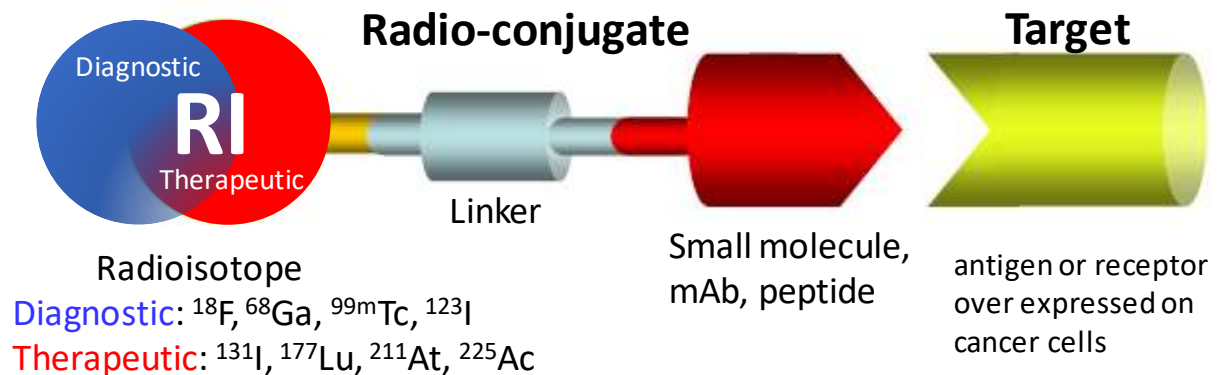
1) SPECT: Single Photon Emission Computed Tomography

2) PET: Positron Emission Tomography

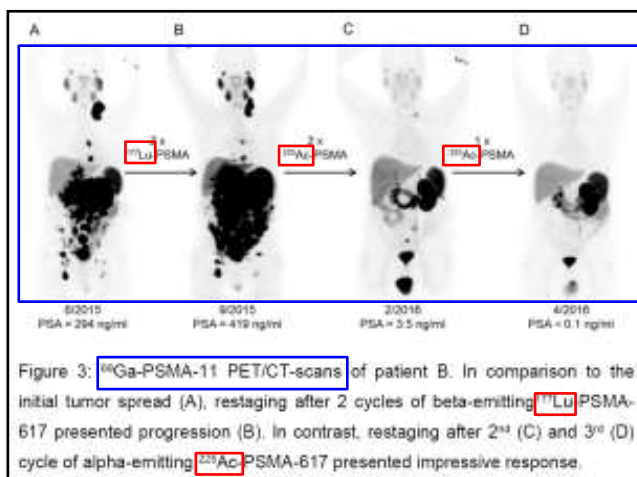
Theranostics is a concept of personalized medicine that combines **diagnostics** and **therapeutics** for **each patient**, using the **same** or **similar** diagnostic agent as the therapeutic agent, in order to 1) avoid harm to the patient and 2) ensure that the treatment is effective.

How it works?

Diagnostic or **therapeutic** isotopes bind to antibodies, peptides, or small molecules via chelation etc. Radio-conjugates bind specifically to antigens or receptors overexpressed on cancer cell membranes and emit radiation from those sites.



In the case of bone metastasis, β -particles are expected to cause side effects in bone marrow due to their long range \rightarrow Switch to treatment using α -emitters. (Pre-operative diagnostics)

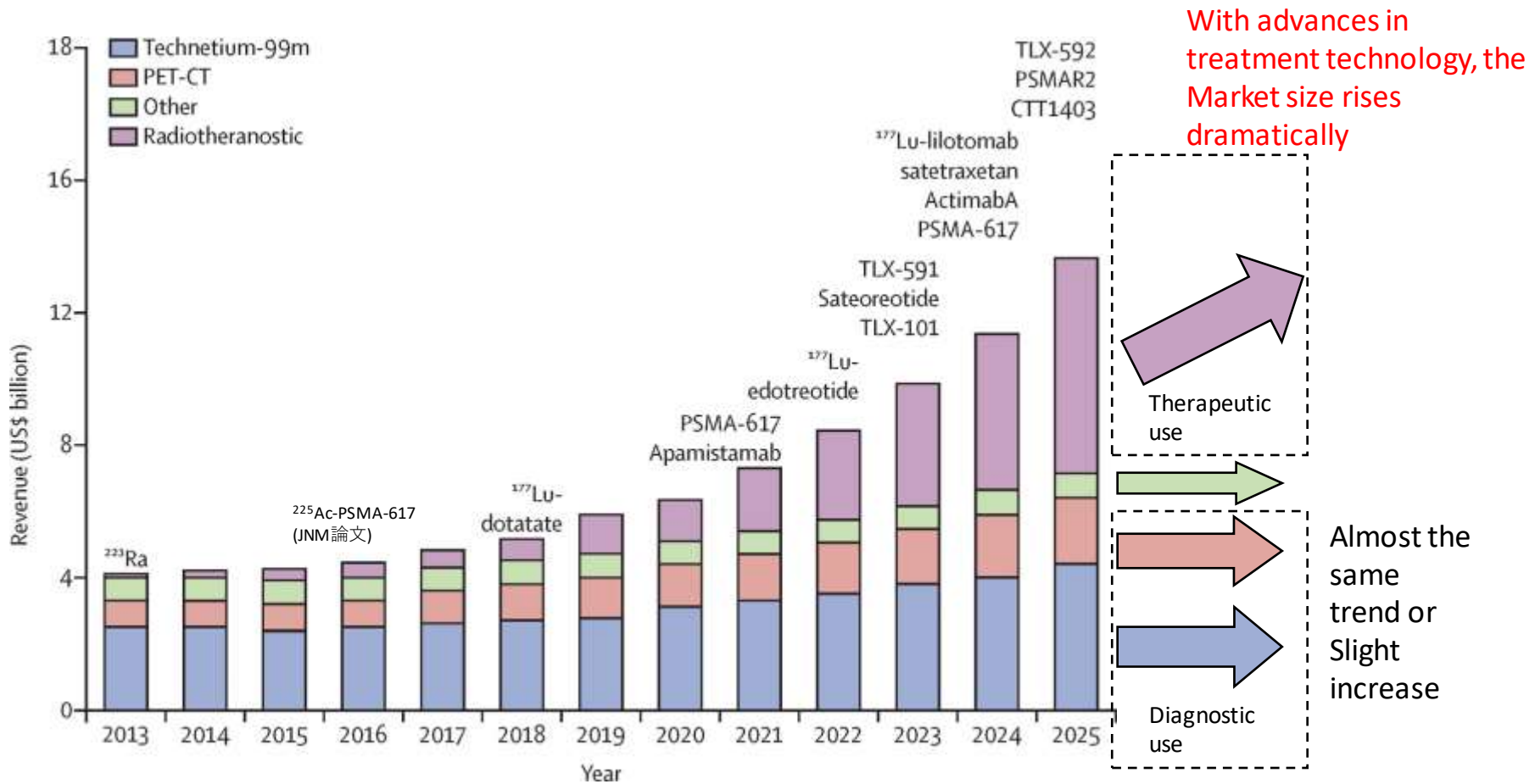


Preoperative and postoperative diagnosis that decided to use alpha emitter because beta emitter did not work.

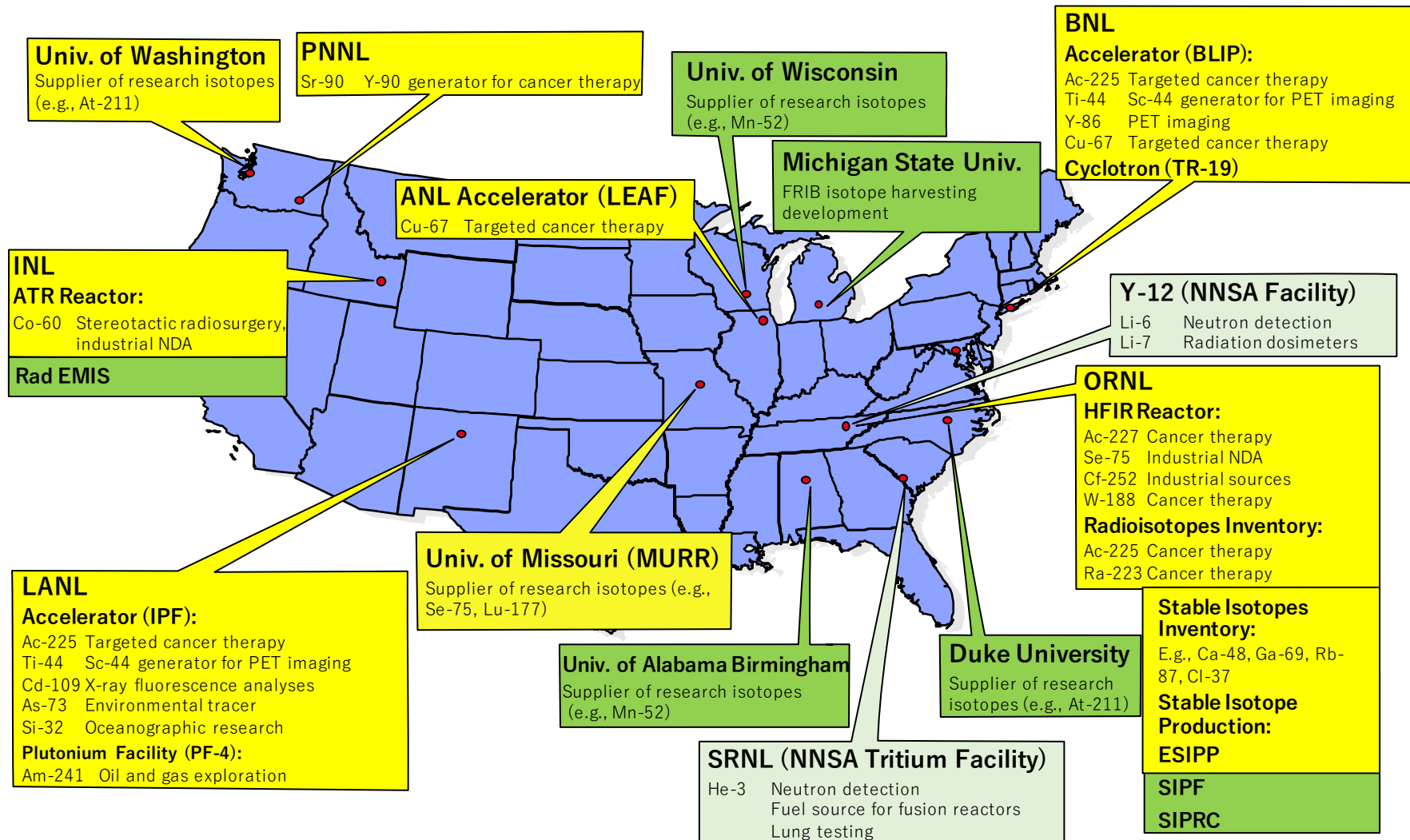
Kratochwil et al. J Nucl Med 2016;57:1941-1944

The left figures are notable for the fact that the ^{225}Ac -labelled agent has resulted in the complete remission of systemic metastases from prostate cancer. HOWEVER, the image is also symbolizing what theragnostics is all about. **We can optimize the treatment plan precisely for each patient using thragnostic technique.**

Revenue growth of the radiotheranostics field by market analysis



DOE Isotope Program Production Sites



TRIUMF & CNL

TRIUMF: トライアンフ研究所 (国立素粒子原子核物理研究所)
CNL (Canadian Nuclear Laboratories): カナダ国立原子力研究所



Institute for Advanced Medical Isotopes (IAMI)



^{225}Ac Production Milestones



Year	2020	2021	2022	2023	2024	2025
$^{225}\text{Ac}^*$ produced (Ci)	0.05	<0.15	0.5	Up to 3-6 Ci, depending on demand and revenue milestones		
$^{227,225}\text{Ac}^*$ produced (Ci)	0.2	<0.6	2.0	Up to 12-24 Ci, depending on demand and revenue milestones		

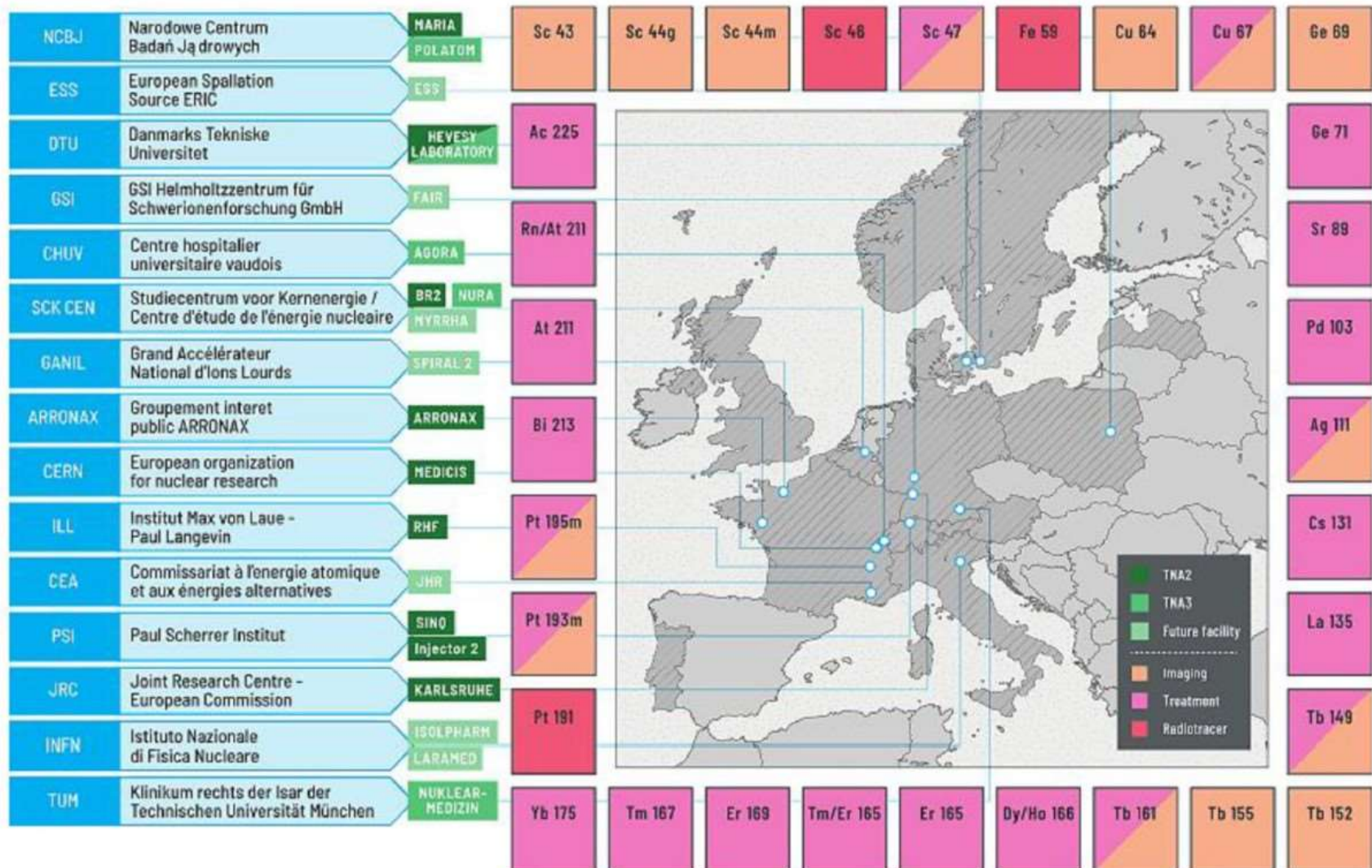


$^{229}\text{Th}/^{225}\text{Ac}$ ジェネレータ
148-185MBq(4-5mCi)/month



TRIUMFのツイッターコメントより
カナダ首相ジャスティン・トルドー氏が TRIUMF に 訪問 (2018/11/2) し、 Institute for Advanced Medical Isotopes (IAMI) の設立を国家的に支援すると宣言。IAMIではTc-99mやAc-225を製造。

PRoduction of high purity Isotopes by mass Separation for Medical Applicaion 2020

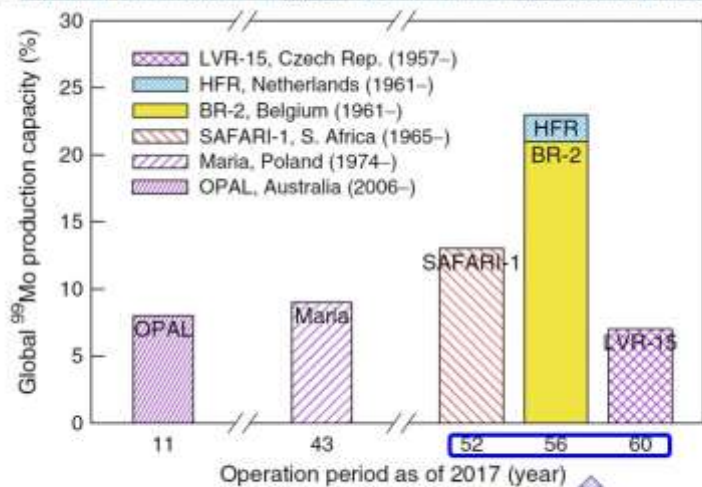


$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ Production Shift

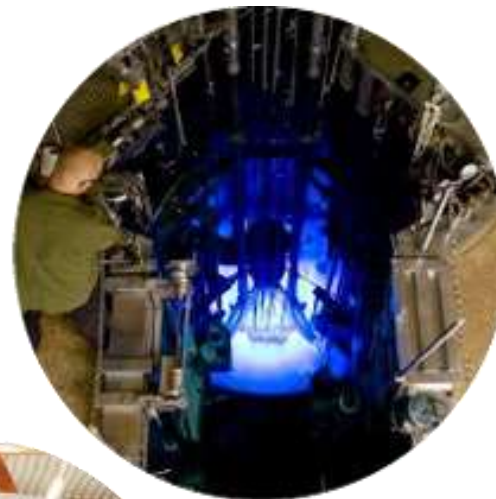
Highly Enriched U Research Reactors
and Air Transportation

Low Enriched U Research Reactors /
Medium Sized Accelerators
and Just-in Supply

From: J. Jang, M. Yamamoto, and M. Uesaka (2017), Phys. Rev. Accel. Beams 20, p. 104701



Three, out of six, are reaching the end of service lives
Alternative source of ^{99}Mo is necessary!



MURR



Electron Rhodotron



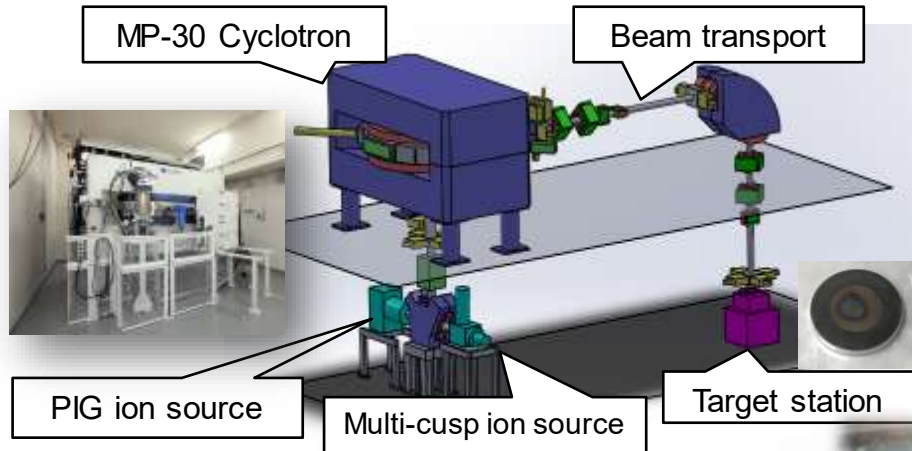
Electron Linac γ -ray Source

Production facilities of α -emitter ^{211}At in Japan

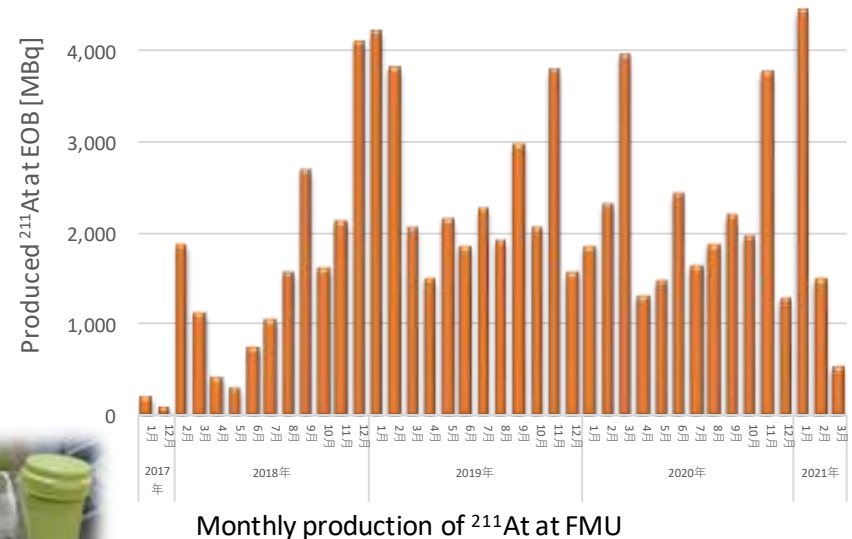
- ^{211}At production facilities (5 sites)
- ^{211}Rn production facilities (2 site)
- End-user facilities including production site (more than 18 users)



Advanced Clinical Research Center(ACRC): An ^{211}At Manufacturing and R&D site at Fukushima Medical University(FMU)



The MP-30 cyclotron and its irradiation system



Purpose of ACRC Establishment

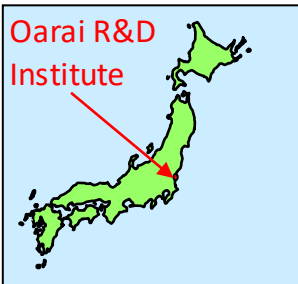
- Established as a center for early diagnosis of various diseases using PET/MRI and PET/CT.
- Aims to improve the level of medical care and research by establishing an environment that enables the translational research and clinical application
- Contribute to the healthcare of the Fukushima citizen by investigating and analyzing radioactive materials in the environment in collaboration with the Quantum Science and Technology Agency (QST).

Our ^{211}At R&D pipeline

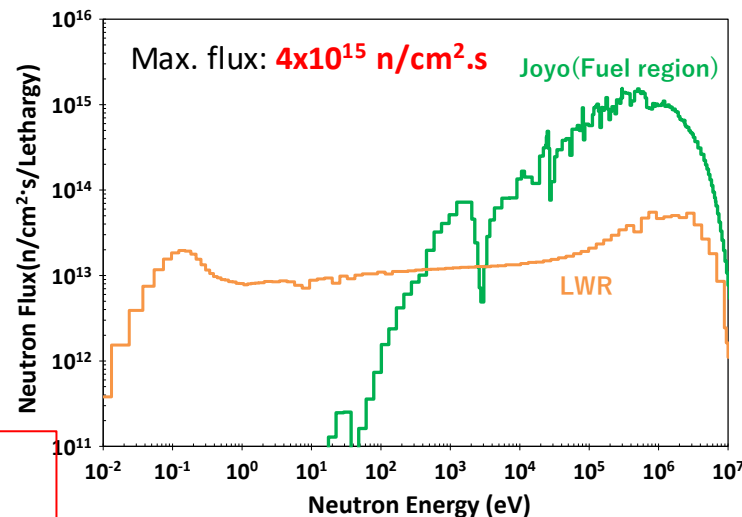
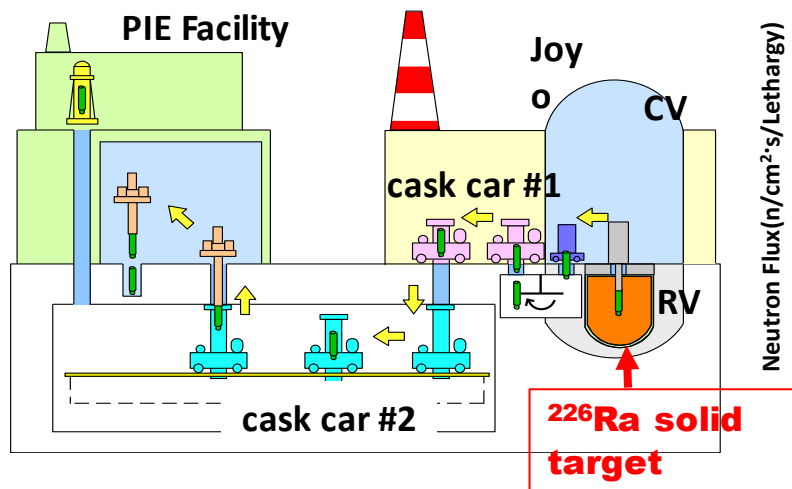
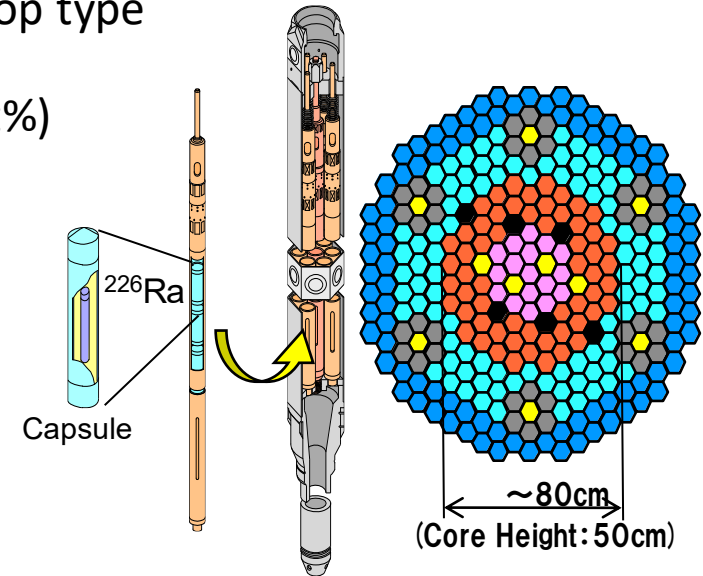
- Clinical trial using MABG (collaboration work with QST)
Ukon et al. Ann Nucl Med **36**, 695 (2022); EJNMMI Physics **7**, 58 (2020).
- Development of pretargeting strategy using low immunogenic streptavidin scFv conjugate and improved iminobiotin derivatives (collaboration work with UTokyo)
Washiyama et al., J Nulc Med **61** (suppl1) 1212 (2020).
- Development of ^{211}At labeled Bombesin derivatives
Aoki et al., Chem. Pharm. Bull. **68**, 538–545 (2020).
- ^{211}At labeled CXCR4 antibody for cancer stem cell targeted radionuclide therapy
Oriuchi et al., Sci Rep **10**, 6810 (2020).



^{225}Ac Production by Research Fast Reactor, Joyo



Type: Sodium-cooled fast reactor, loop type
 Output: **100 MWt**
 Fuel: MOX (^{235}U : 18 wt%, Pu: <30 wt%)
 Operation period: **60 days/cycle**



- ◆ Inner Fuel S/A
- ◆ Outer Fuel S/A
- ◆ Control Rod
- ◆ Irradiation Test S/A
- ◆ Reflector (Stainless Steel)
- ◆ Shielding S/A
- ◆ Moderator S/A

^{225}Ac Yield by solid ^{226}Ra and Proton Cyclotron

QST and Nihon Medi+physics

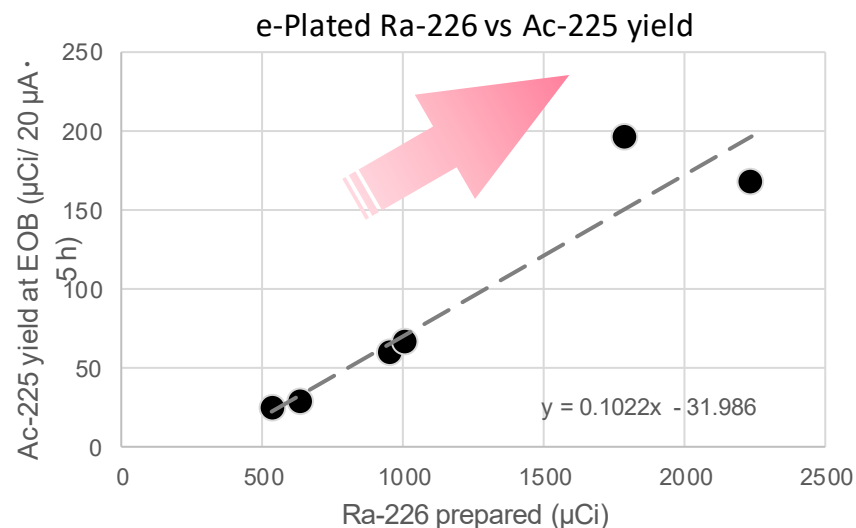
H_2^+ 34 MeV 15.6 MeV proton on target	#1	#2	#3	#4	#5	#6	#7
Ra-226 Target prepared	13.5 MBq (366 μCi)	35.4 MBq (956 μCi)	37.5 MBq (1.01 mCi)	19.8 MBq (536 μCi)	23.6 MBq (639 μCi)	66.2 MBq (1.79 mCi)	83.0 MBq (2.24 mCi)
e-Plating efficiency	94%	97%	97%	98%	97%	69%	88%
Activation ($\mu\text{A}\cdot\text{h}$)	20 $\mu\text{A}\cdot 3\text{ h}$	← — — — 20 $\mu\text{A}\cdot 5\text{ h}$ — — — →					
Ac-225 Yield (@EOS/ 4 d from EOB)	522 kBq (14 μCi)	2.23 MBq (60 μCi)	2.43 MBq (66 μCi)	904 kBq (24 μCi)	1.03 MBq (28 μCi)	7.25 MBq (196 μCi)	6.16 MBq (167 μCi)



Ra-dedicated Vertical
Target station *



Electroplated Ra (1 mCi)
on conical Au surface **



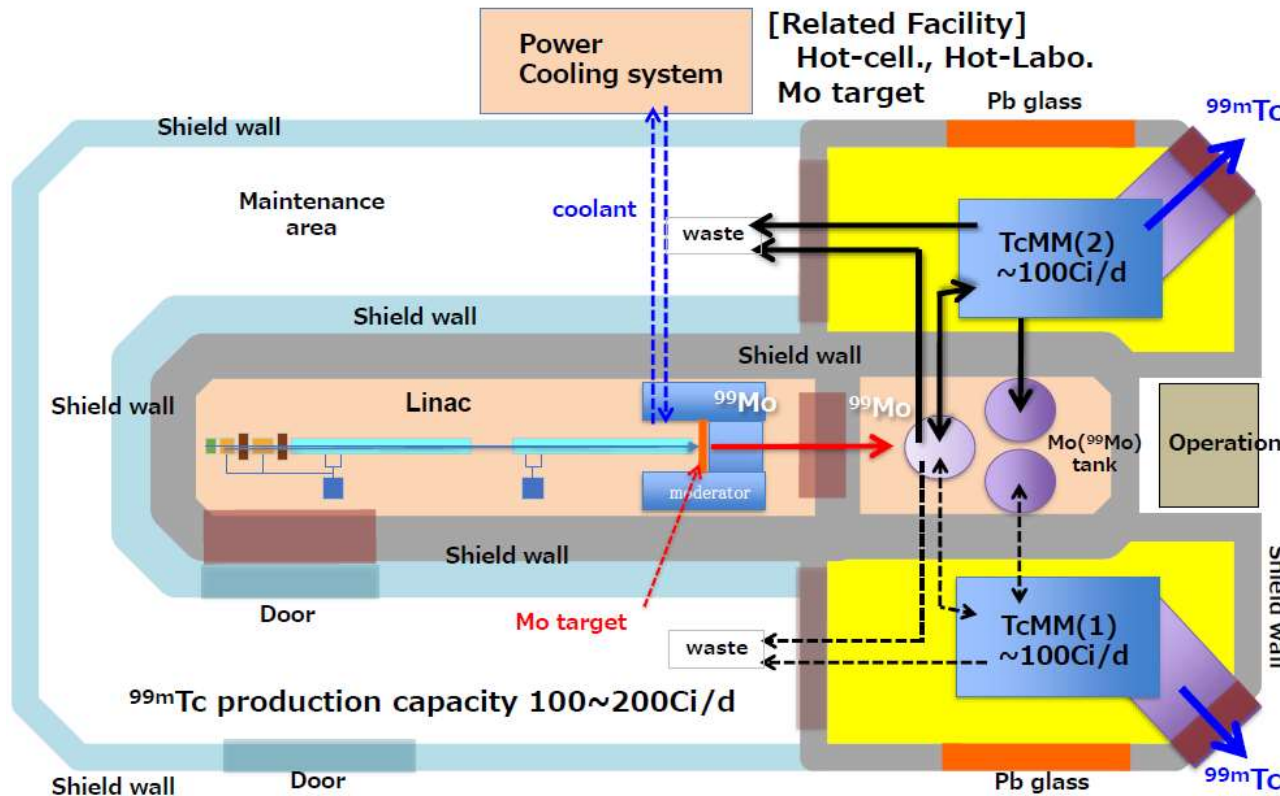
* Japanese Patented #6450211 (filed on Dec 14, 2018); ** Japanese Patent Application #2018-060672 (filed on Mar 27, 2018);
Nagatsu K, *Eur J Nucl Med Mol Imaging* (2021) 10.1007/s00259-021-05460-7

35 MeV 35 kW S-band Electron Linac γ -ray / Neutron Sources for Production of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ and ^{225}Ac

1. γ -ray / Neutron sources for $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ from ^{100}Mo / ^{98}Mo

$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ and Medicine Production Facility
Production Capacity is 100-200 Ci/week

~5 facilities in Japan
~100 in the world
(expected)



University of Tokyo
(Nuclear Professional
School/Dept Nucl
&Eng/Bioeng Dept/
Isotope Sci Center)
Kyoto University
Hitachi Co.
Accuthera Inc.
KAKEN

2. γ -ray sources for ^{225}Ac production from ^{226}Ra target

Similar scale
(expected)

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 + diagnosis)

Movements and Problems in Japan

- Restart of research reactors* that can produce large amounts of radioisotopes (JRR-3, “Joyo”) 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

Developing the Action Plan that aims to provide domestic radioisotopes to patients

The Action Plan contributes to

- Improvement of people’s welfare by enhancing the medical system through cutting-edge nuclear science and technology
- Ensuring economic security in terms of medical services

Goals to be Achieved during next decade

- Establishment of a Stable Radioisotope Diagnostic System through *partial domestic production of Mo-99/Tc-99m*
- Implementation of *Radioisotope Treatment Using Domestic Radioisotopes*
- Dissemination of Radioisotope Treatment* in Medical Setting
- Making 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”

- Stable supply of *Mo-99/Tc-99m* using JRR-3 and accelerators (Manufacturing approximately *30% of domestic demand* by the end of FY2027 as far as possible, and supply to domestic)
- Strengthening R&D for mass production of *Ac-225* using “Joyo” and accelerators (Production demonstration by FY2026 with “Joyo”)
- Strengthening efforts to commercialize *At-211* (Indicating usefulness as a pharmaceutical product by FY2028)

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

- Establishment of hospital rooms for radioisotope treatment (Average number of months to wait for radioisotope treatment: *3.8m (2018) -> 2m (2030)*)
- Preparation for commercialization of new radiopharmaceuticals (Th-227, Ga-68)

(3) Promoting R&D Contributing to Domestic Production of Radioisotopes

- Technical development support for production by research reactors and accelerators
- Promotion of initiatives by the Fukushima International Research and Education Organization
- Establishment of systems of non-clinical studies of radiopharmaceuticals

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

- Strengthening Human Resources in the Field of R&D and Medical Setting
- Strengthening the Supply Chain in line with Domestic Production
- Study of Mechanisms for Waste Treatment and Disposal

Japan's Stance toward Radioisotope Production (Tentative Translation)

Basic Policy on Economic and Fiscal Management and Reform 2022 「骨太の方針」(Approved by the Cabinet on June 7, 2022)

Chapter 4 Medium-to long-term economic and financial management

5. Promoting education and research activities that support socioeconomic vitality

(omitting the beginning)

We will implement the "Sixth Science, Technology and Innovation Basic Plan" ¹⁶² and **sector-specific strategies**¹⁶³ to bring about a sustainable economy and society through public-private partnerships.
(omitting the beginning)

<注釈>

【162】Approved by the Cabinet on March 26, 2021

【163】AI, biotechnology, quantum technologies, materials, environmental energy, safety/security, health/medical care, space, oceans, food/agriculture, forestry and fisheries are positioned as strategically important fields in the "6th Science, Technology and Innovation Basic Plan". **We will also pursue efforts in accordance with "The Action Plan for Promotion of Production and Utilization of Medical Radioisotopes "**.

The following government documents also mention the promotion of "The Action Plan for Promotion of Production and Utilization of Medical Radioisotopes " :

Grand Design and Action Plan for a New Form of Capitalism Follow-Up「新しい資本主義」 (Approved by the Cabinet on June 7, 2022)

Integrated Innovation Strategy 2022「統合イノベーション戦略」 (Approved by the Cabinet on June 3, 2022)



Rays of Hope

Cancer care for all

Rays of Hope will integrate the breadth of the IAEA's expertise to support Member States in the diagnosis and treatment of cancer using radiation medicine.

The Global Cancer Burden



Over 70% of cancer deaths occur in LMICs.

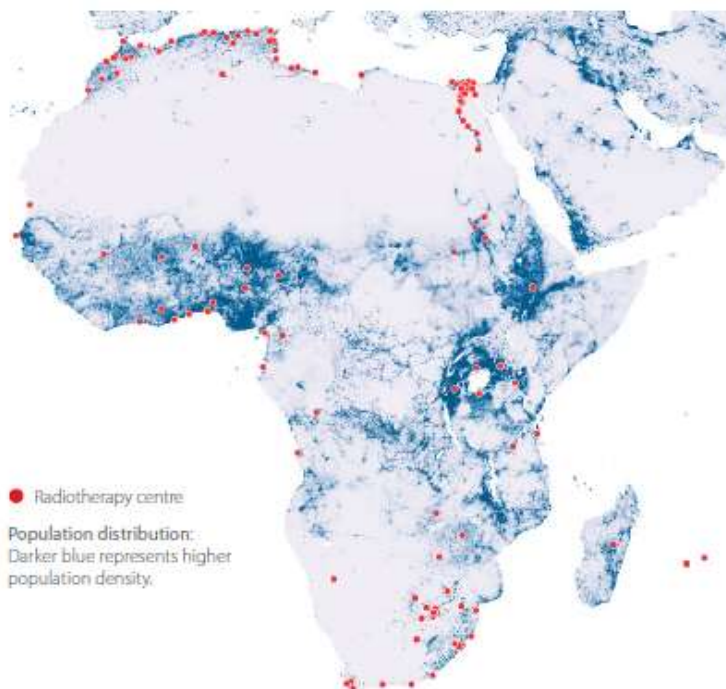
70%

Only 5% of global spending on cancer goes to LMICs.



About half of cancer patients require radiotherapy.

OVER 70% OF THE POPULATION OF AFRICA DOES NOT HAVE ACCESS TO RADIOTHERAPY.



In Africa, over 700,000 people died of cancer in 2020.
More than 20 African countries have no radiotherapy treatment unit.

Nuclear Medicine from Nuclear Waste by University of Tokyo's Group

**α emitter ^{225}Ac for cancer
therapy from waste (^{226}Ra)
at U-fuel production**

Chemical extraction
of ^{226}Ra from U mining
waste

($\sim 15\text{g } ^{226}\text{Ra}$ from 30km^3)



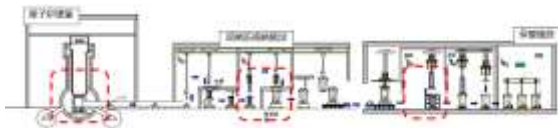
Fuel Cycle Plant



Decommissioning Plant



Debris without Fuel Materials



Solid or
Liquid
 ^{226}Ra
Targets



Supply for
Fundamental
Research

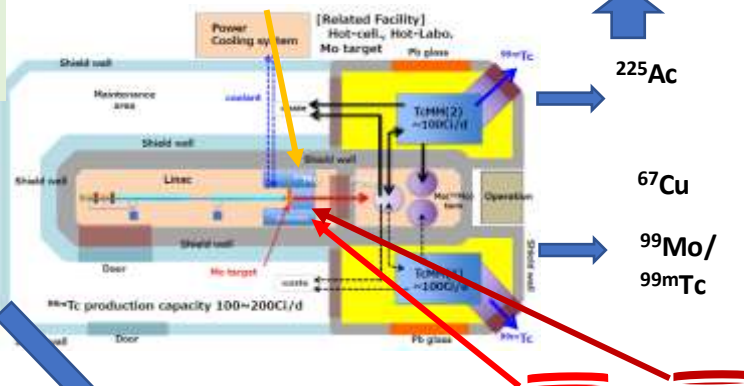


Supply for
Clinical Uses



$^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ (SPECT),
100 B¥/year @ JAPAN

^{67}Cu (PET)
 ^{225}Ac (α)
(Theranotics=
Therapeutic+Diagnosis)



Mixer-Settler

^{68}Zn

$^{98,100}\text{Mo}$



γ Emitter RIs ($^{99}\text{Mo}/^{99\text{m}}\text{Tc}$) for
cancer diagnosis from spent
fuel waste (Mo)

Best Mix of Supply

Energy



Medical RIs



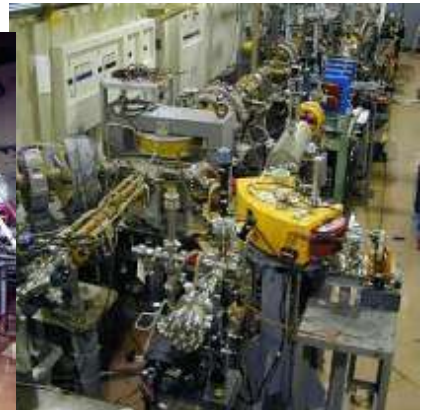
**LEU
Research Reactor**



Fast Reactor



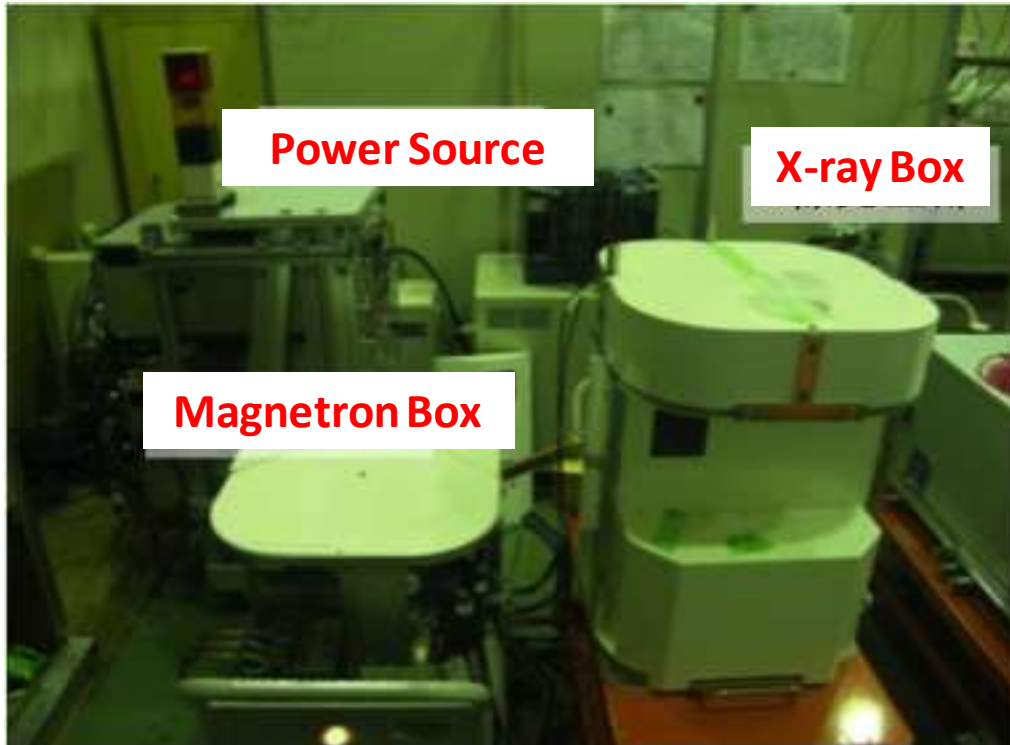
Proton Cyclotron



**Electron
Linear Accelerator**

- **Downsizing of Accelerators**
- **Medical RI Production by Best Mix of Research Reactors and Accelerators**
- **Sustainable Social Infrastructure**
- **Decommission of TEPCO Fukushima Daiichi Nuclear Power Station (FDNPS)**
- **Summary**

Portable X-band (9.3 GHz) 950 keV System by University of Tokyo



According to the Japanese Law on radiation safety, an electron beam source below 1 MeV is not defined as an accelerator. Thus, we comply with the Regulations on radiation safety, which is rather reasonable.

Thus, we use it any place by setting our self-designed radiation controlled area.

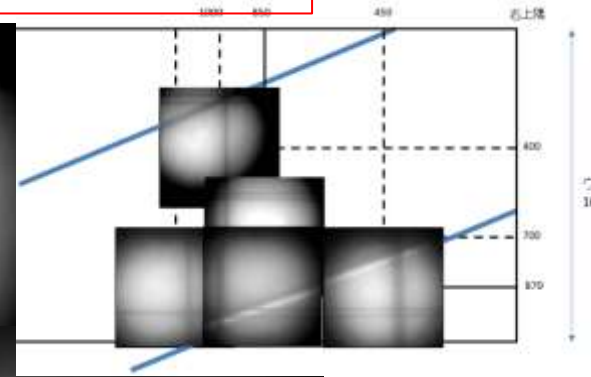
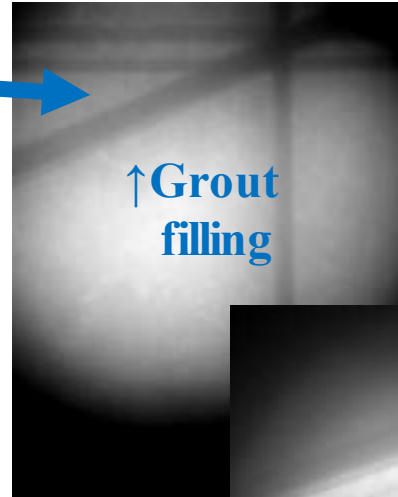
Parameters of Accelerator	
Operating frequency	9.3 [GHz]
RF source	Magnetron
RF Power	250kW
Width and number of repetitive of pulse	2[μ s], 280[PPS]
Length of acceleration tube	25[cm]
Form of acceleration tube	Side coupled structure
Number of accelerating cell	Half1 + full8
Coupling between cells	3 %
Filling time	0.18 μ s
Shunt impedance	110-130M Ω /m Regular part
Beam current	64mA or more
Focusing fashion	RF focusing
Intensity of X-ray	50[mGy/min] or more at 1[m]
Voltage of electron gun	20KV
Electron gun	Triode

On-site X-ray Inspection by 950 keV system for PC (Prestressed Concrete) bridges of up to ~50 cm thickness

Crack



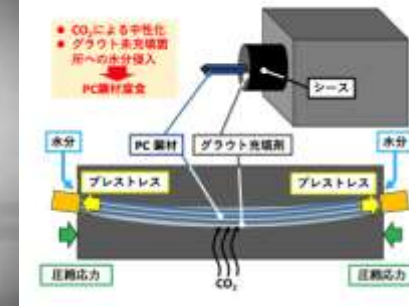
↑ **Grout filling**



↑ **No grout**



↑ **Cracks and leak of Ca components**



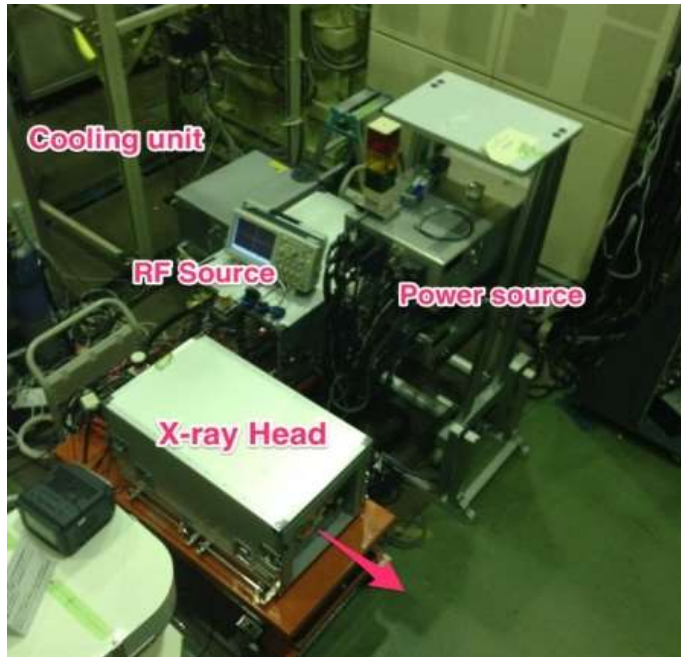
↑ **Grout filling**

↑ **No grout**



X-ray transmission images indicate reinforced iron rods and grout filling and not-filling around the PC wires in the PC sheath clearly

Portable 3.95MeV X-band linac X-ray source of University of Tokyo

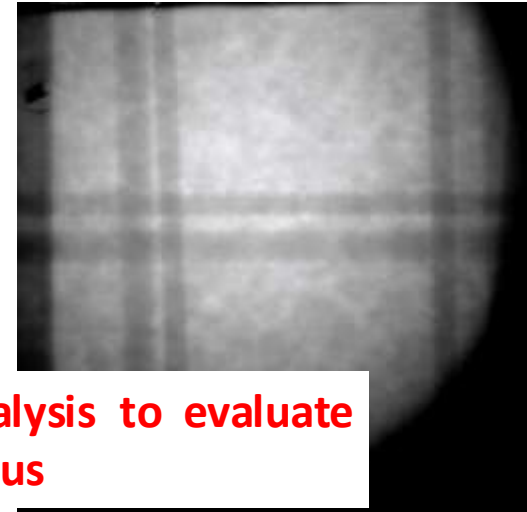


Main unit	Accelerating tube	RF Source	HVPS Control
Weight (kg)	80+62 (Collimator + Accelerating tube)	62	116
Parameters	Electron gun output current 300mA	Frequency 9.3GHz	
	Electron gun voltage 20kV	Pulse width 4μs	
	Beam current 100mA	Repetition rate 200pps	
		RF power output 15 MW	

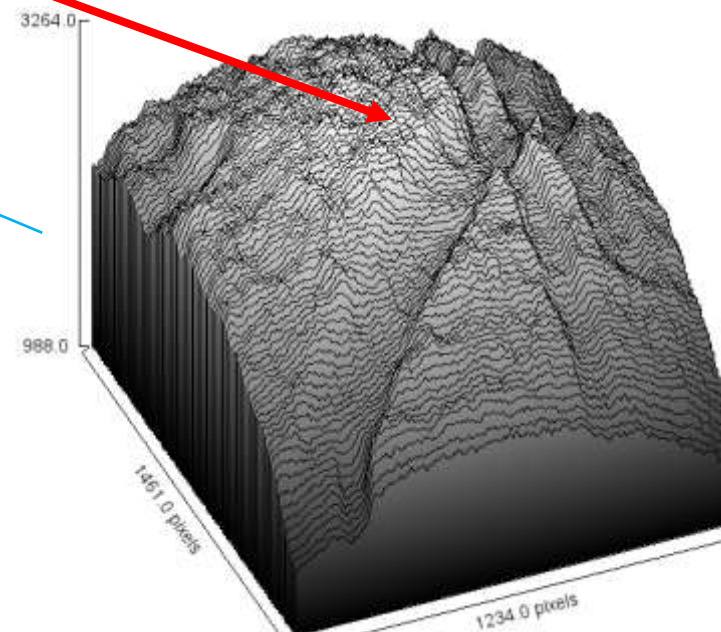
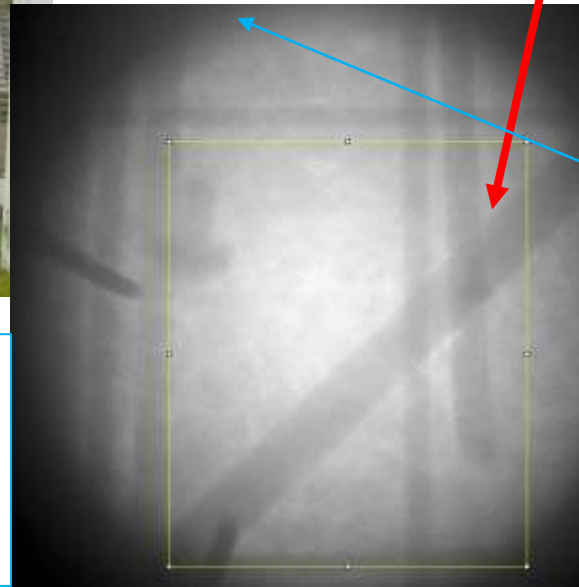
Amendment of the law that allows use of accelerators below 4 MeV accelerator for only for on-site bridge inspection was implemented in Japan in 2005. That is why we set its energy 3.95 MeV just below 4 MeV.

This machine can be also used as a neutron source with 10^7 neutrons / sec by using a solid Be target

On-site X-ray Inspection by 3.95 MeV system for PC (Prestressed Concrete) bridges of up to ~1 m thickness



Gray value image processing analysis to evaluate
the grout filling and not-filling status



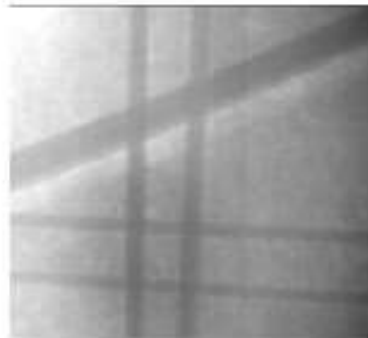
More than 10 real bridges
and one highway bridge
under the Japanese national
project

Formation of Technical Guideline for On-site X-ray Bridge Inspection

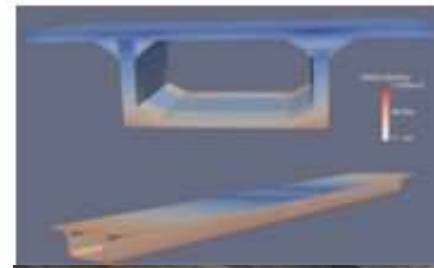
**Visual and
hammering-
sound
inspections**



X-ray inspection



**Structural
analysis**



**Repair and
reinforcement**



We hope to apply this guidelines to all aged bridges soon in Japan and finally in the world

Fighting with Rains and Salty Sea Breeze in Japan



Dedicated Car with Power Source

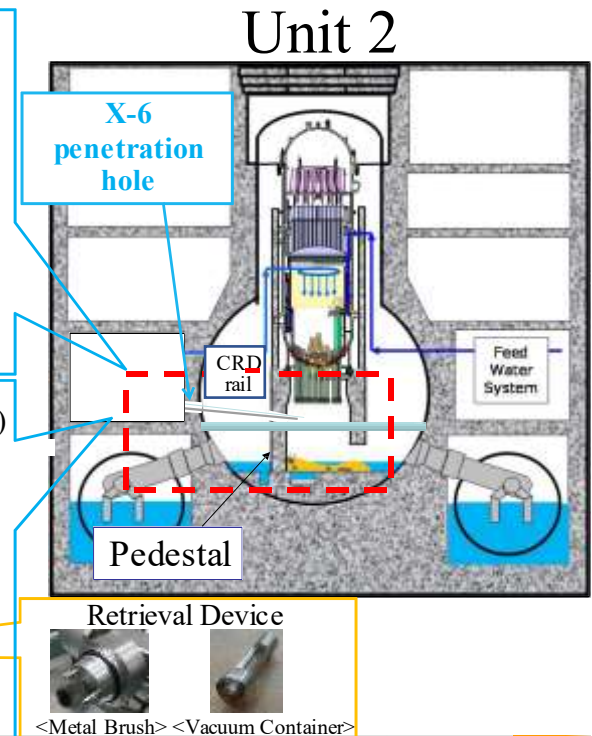
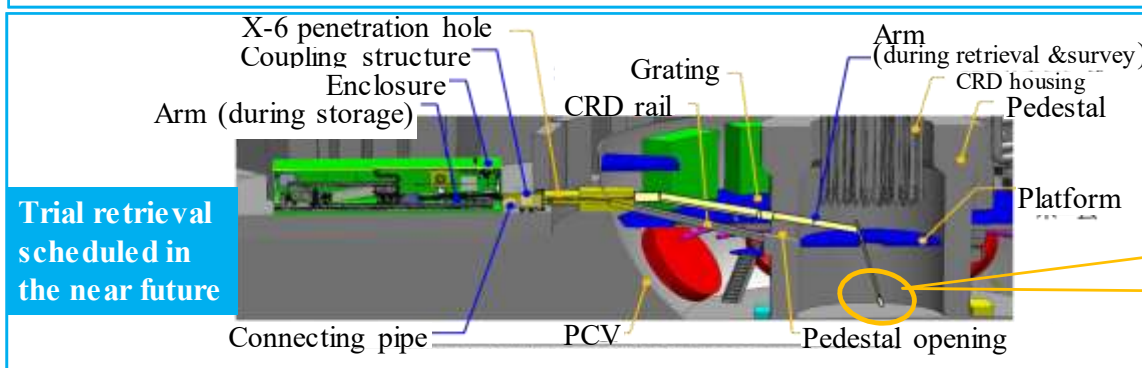
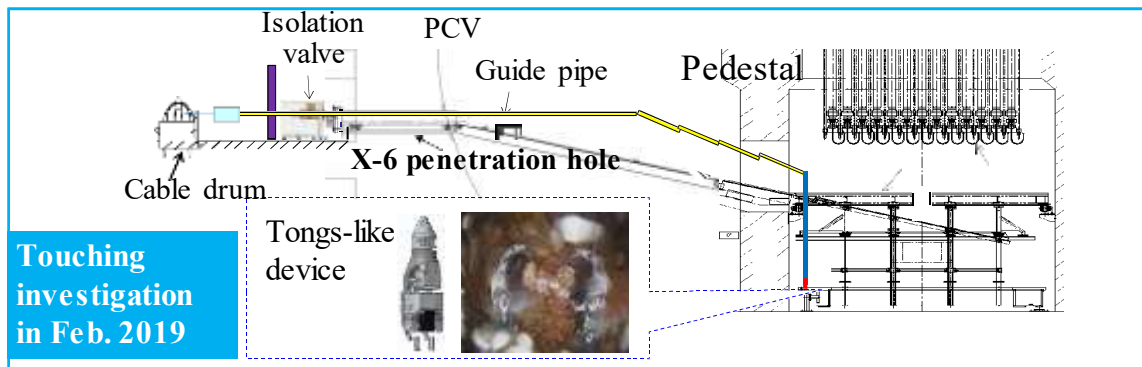
Japanese carefulness and endurance

Waterproof electric housing



- **Downsizing of Accelerators**
- **Medical RI Production by Best Mix of Research Reactors and Accelerators**
- **Sustainable Social Infrastructure**
- **Decommission of TEPCO Fukushima Daiichi Nuclear Power Station (FDNPS)**
- **Summary**

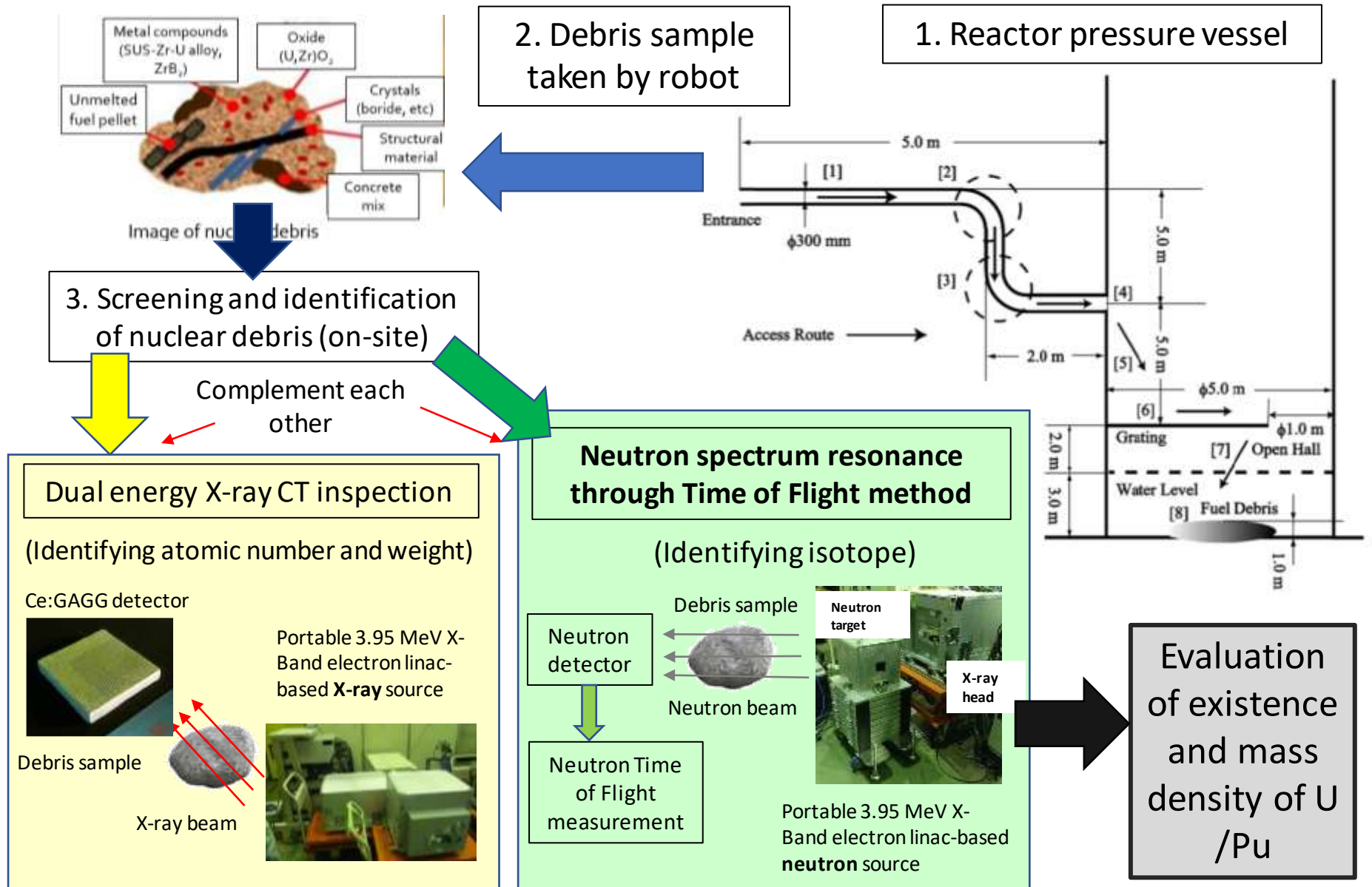
- We will insert an arm-type device through the same access route as the investigation in 2019.
- A metal brush or vacuum container will be attached to the device to collect the grain debris we observed in a touching investigation.



Source: Materials for Meeting of Secretariat of the Team for Countermeasures for Decommissioning, Contaminated Water and Treated Water held in Jan. 2019, Feb. 2019 & May 2022 provided by TEPCO HD & IRID

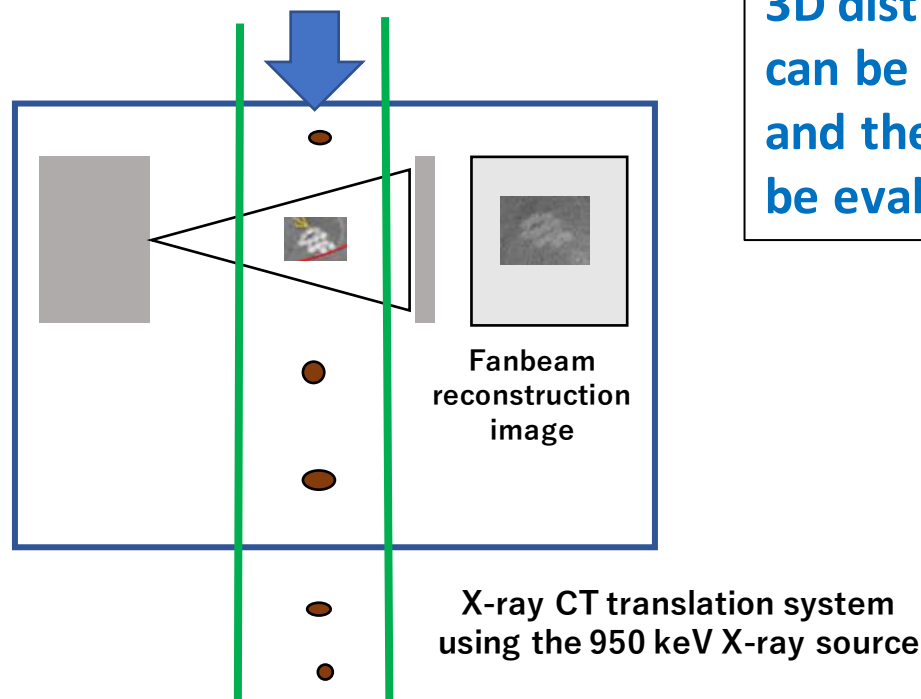
Ref) M. Ishikawa, "Fukushima Dai-ichi Nuclear Power Plant's Decommissioning -Current Status and Challenges-", Asian Youth Nuclear Symposium 2022, July 10, 2022 in Remote.

Proposal of Component Identification for Fuel Debris

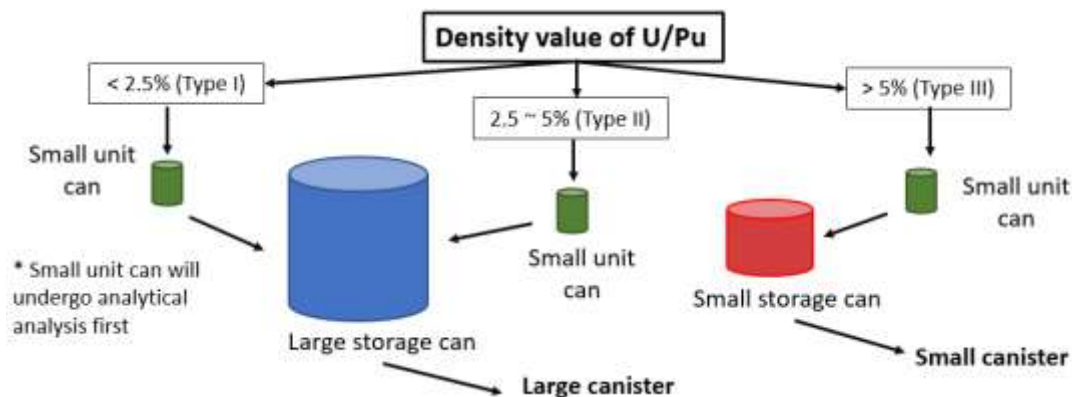


Schematic scenario of the screening process by the prompt X-ray CT for mass-extraction of nuclear debris

3D distribution of atomic number
can be estimated by the X-ray CT
and the mass density of U/Pu can
be evaluated

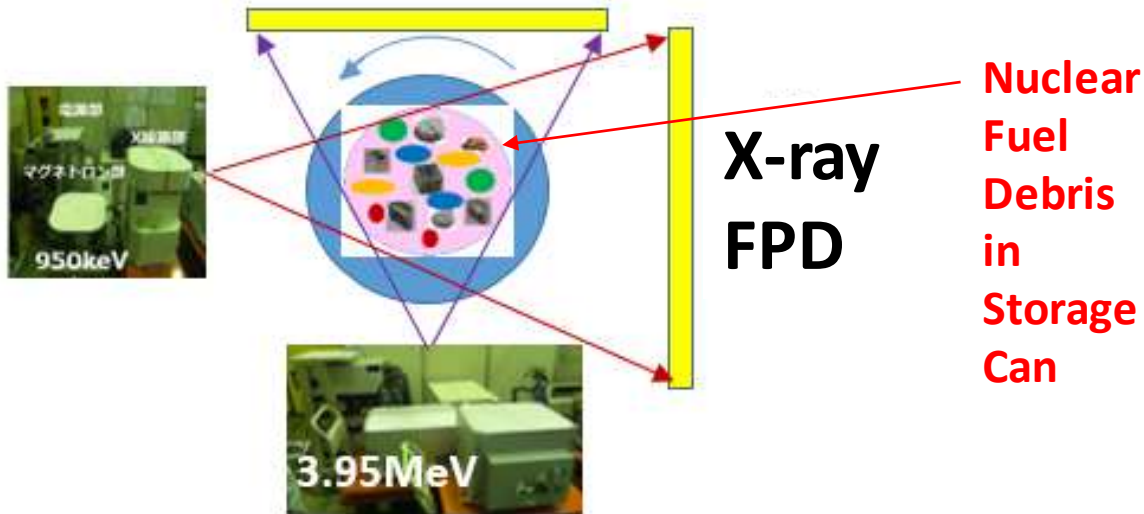


With the acquired information of existence and mass density of U / Pu, the debris is discriminated into the two storage systems for spent nuclear fuel with U / Pu with criticality control and normal radioactive wastes without U / Pu



Practical and Reasonable
Storage System

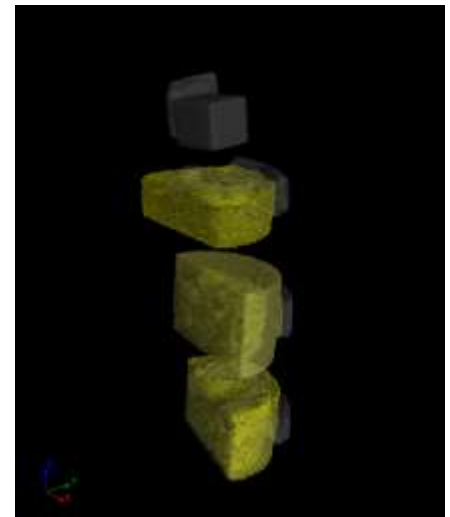
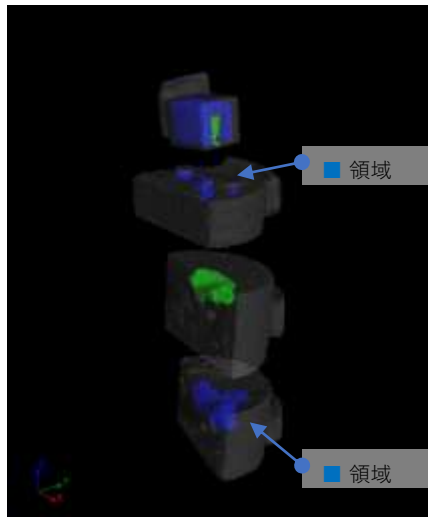
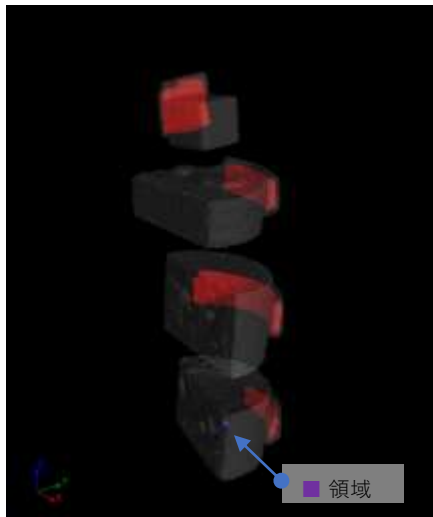
Proof-of-principle X-ray CT Results for Model Melt Nuclear Fuel Debris



3D component data are obtained and the mass density of U / Pu is estimated within mins.

The trial by using the real nuclear fuel debris will be carried out soon.

Results by 3.95 MeV X-ray Source



■ Pb
■ Gd+PGM

U / Pu

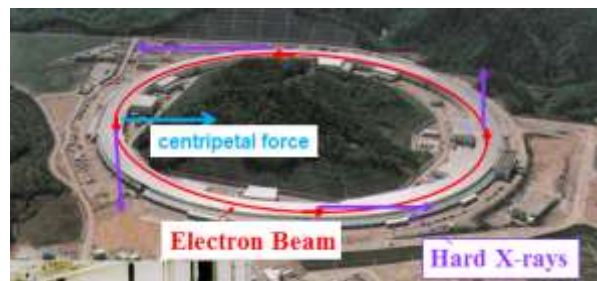
■ Fe
■ Zr

■ Concrete

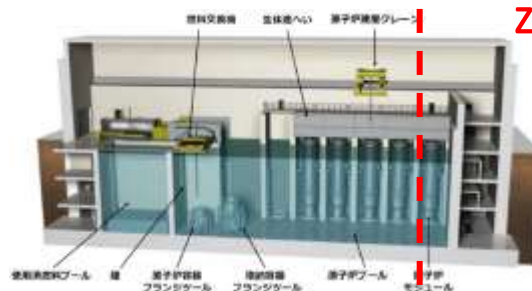
■ Polymer

Three major components

Downsizing of Accelerator and Nuclear Reactor



Smart city for
zero-emission/contamination



SUMMARY

- **Downsizing of big accelerators enables portable accelerators for a variety of applications.**
- **Medical RI production is shifting to the best mix of accelerators and low enriched U research reactors.**
- **Portable X-ray and neutron sources are expected to be applied to infrastructure maintenance and nuclear power plant decommissioning.**
- **Proposal of smart city with micro-reactor and small accelerators for zero-emission/contamination.**

Thanks for the collaboration to KEK, JAEA, JASRI/SPring-8, QST, MEXT, METI, MLIT, DOE, SLAC, LANL, Element Aero and the Center for Bright Beams, TRIUMF, JRC, etc.