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RI production using s-band high power electron linac (WG3)

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- **Introduction**
 - ELPH : Research Center for ELeCtron PHoton Science
 - Accelerator complex in ELPH
 - High power s-band electron linac

- **RI production using electron linac
via photonuclear reaction**
 - Photonuclear reaction
 - Bremsstrahlung gamma-ray
 - S-band electron linac (power efficiency)

- **Medical isotope production
(Collaborative research @ELPH)**
 - ^{99}Mo production
 - ^{225}Ac production

- **Summary**

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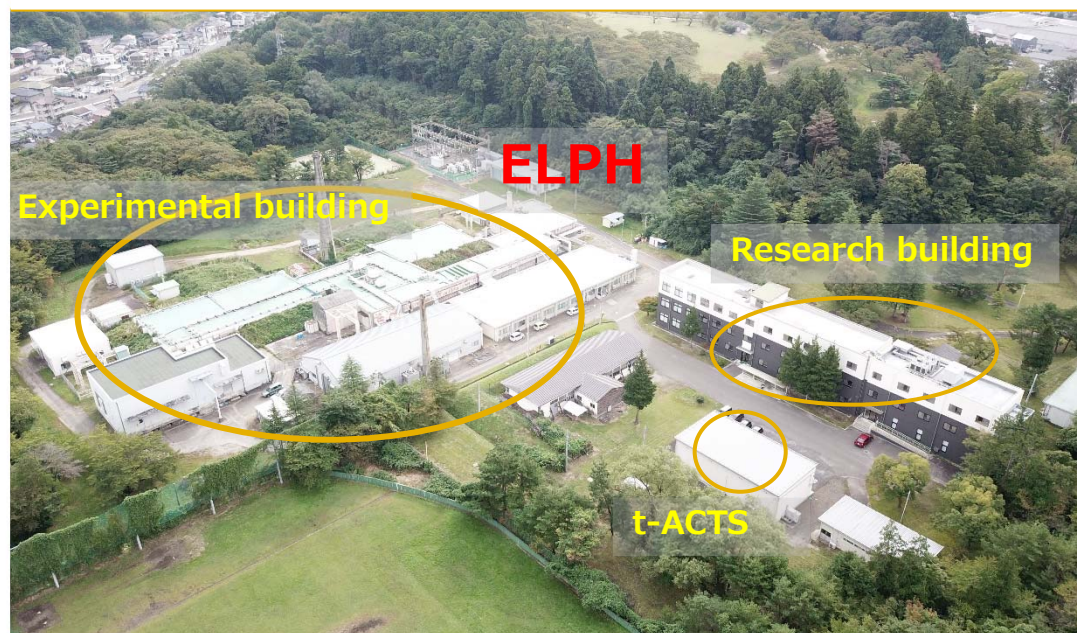
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■ Summary

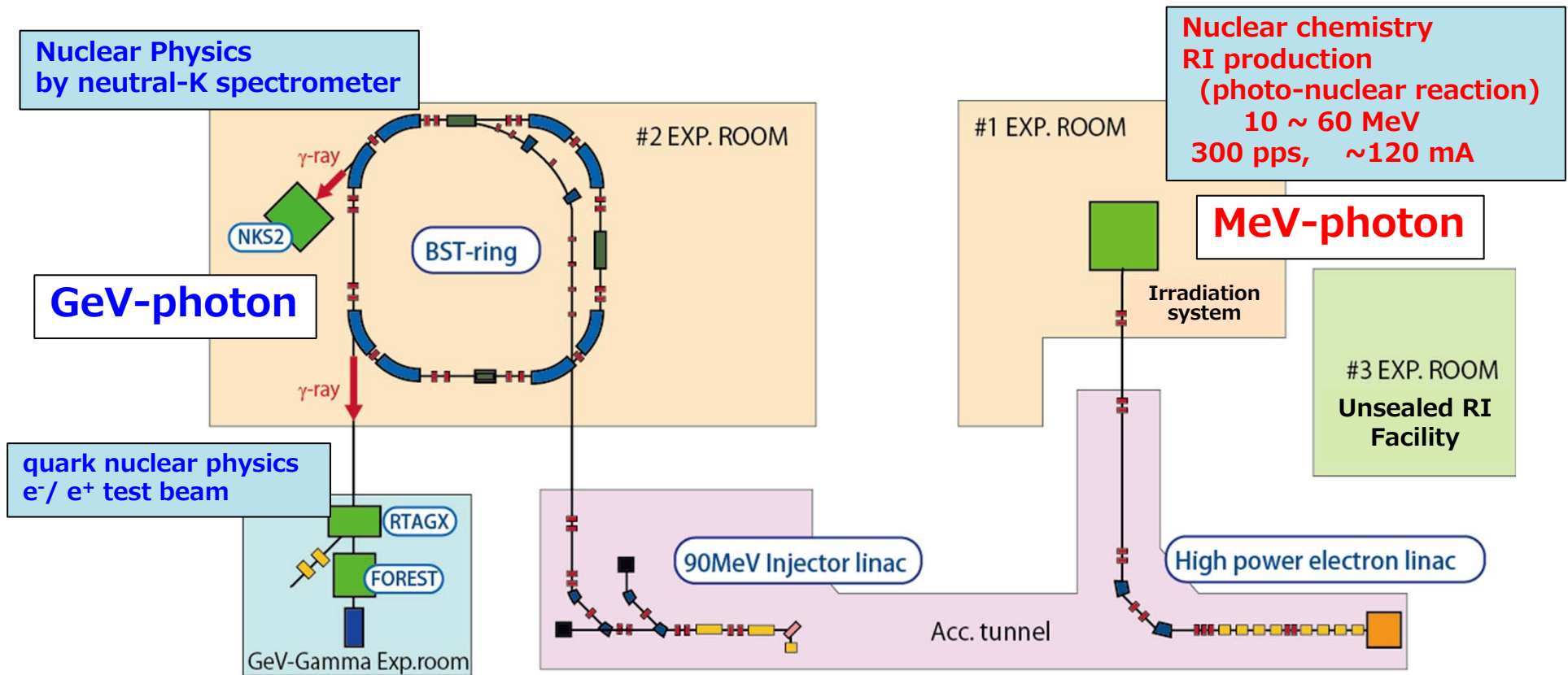


1966 Laboratory of Nuclear Science (LNS) established
2009 LNS =>ELPH

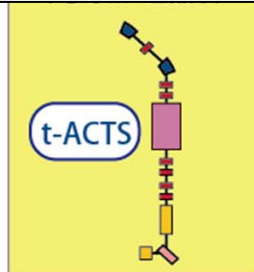


- Beam Physics and Accelerator Science
- Quark Nuclear Physics
- **Radioactive-isotope Science**
- Condensed Matter Nuclear Reaction

Physicist: 14
 Professor: 4
 Associate Prof.: 5
 Assistant Prof.: 5
 Engineer: 5,
 Officer: 4
 Student: 20



meV-photon



test-Accelerator as Coherent THz Source (50 MeV electron linac)
 # Generation of short pulse e-beam
 # THz light source

Research Center for **EL**ectron **PH**oton Science

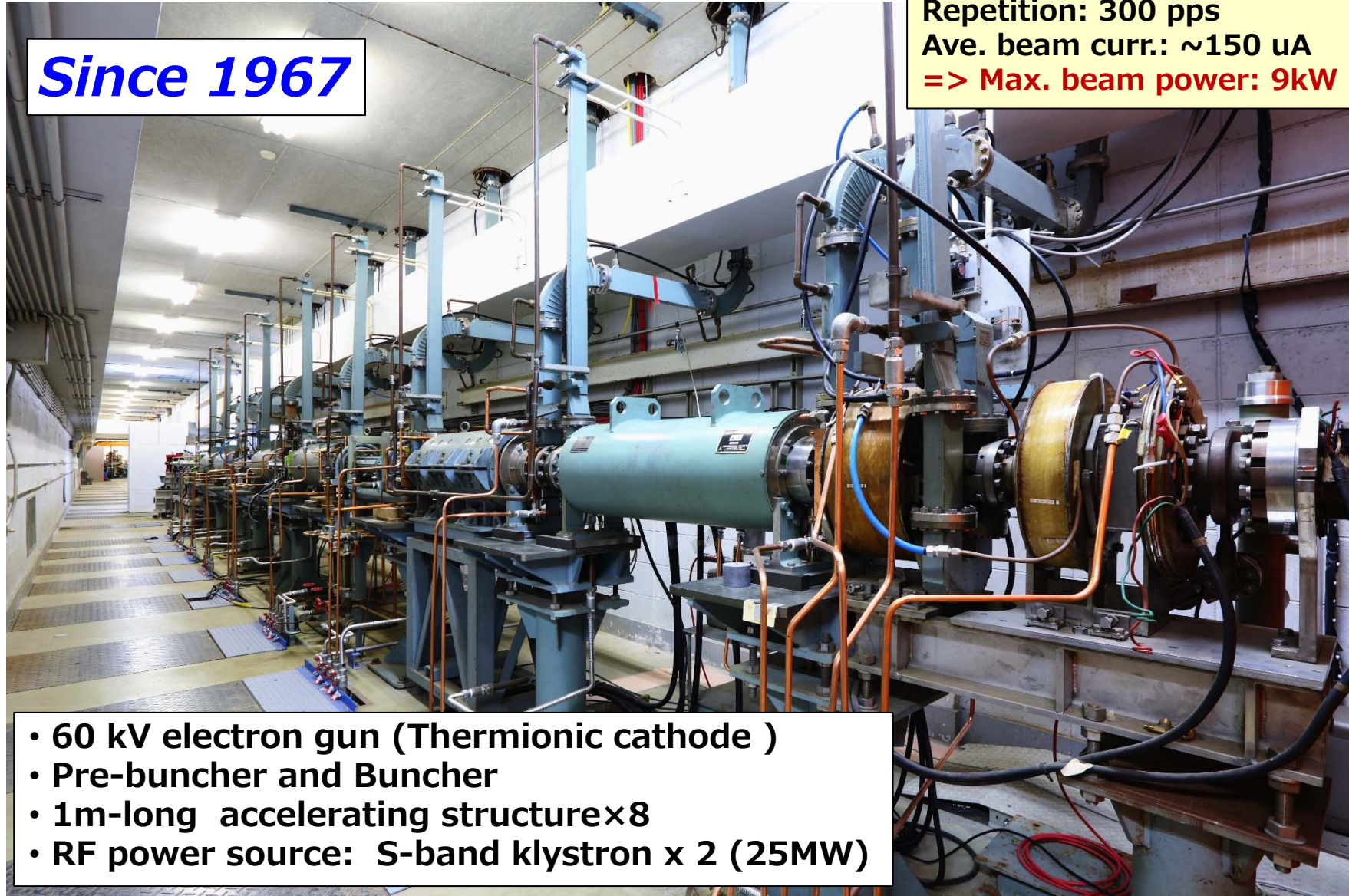


GeV
MeV
meV (THz)

Since 1967

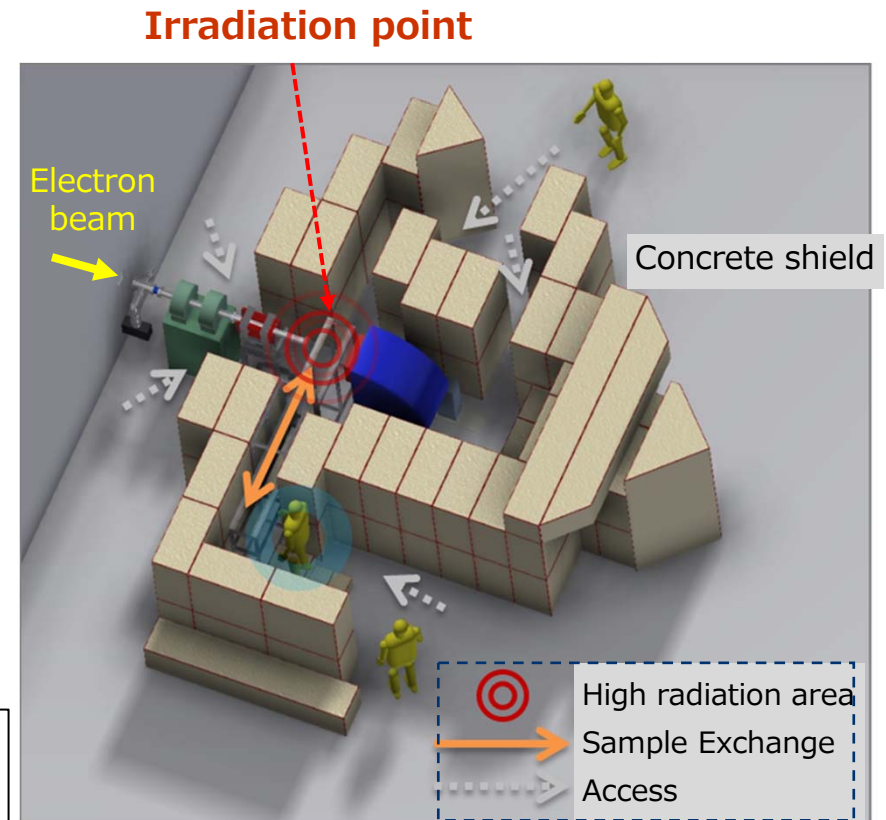
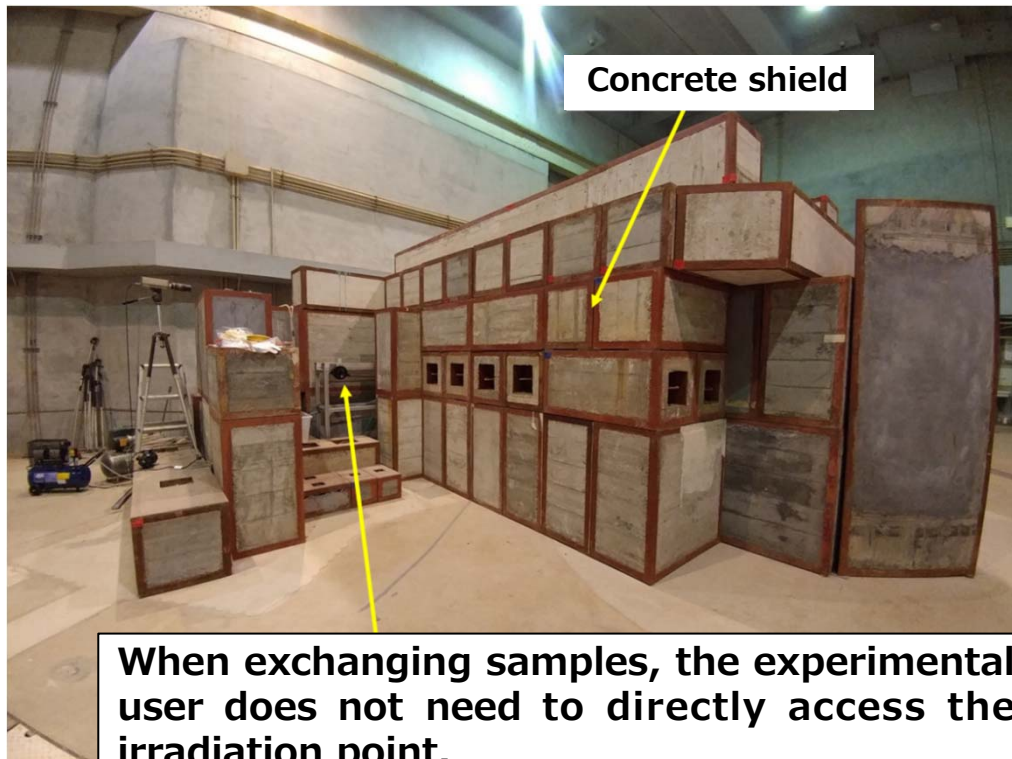
Beam energy: 10~60 MeV
Repetition: 300 pps
Ave. beam curr.: ~150 μ A
=> Max. beam power: 9kW

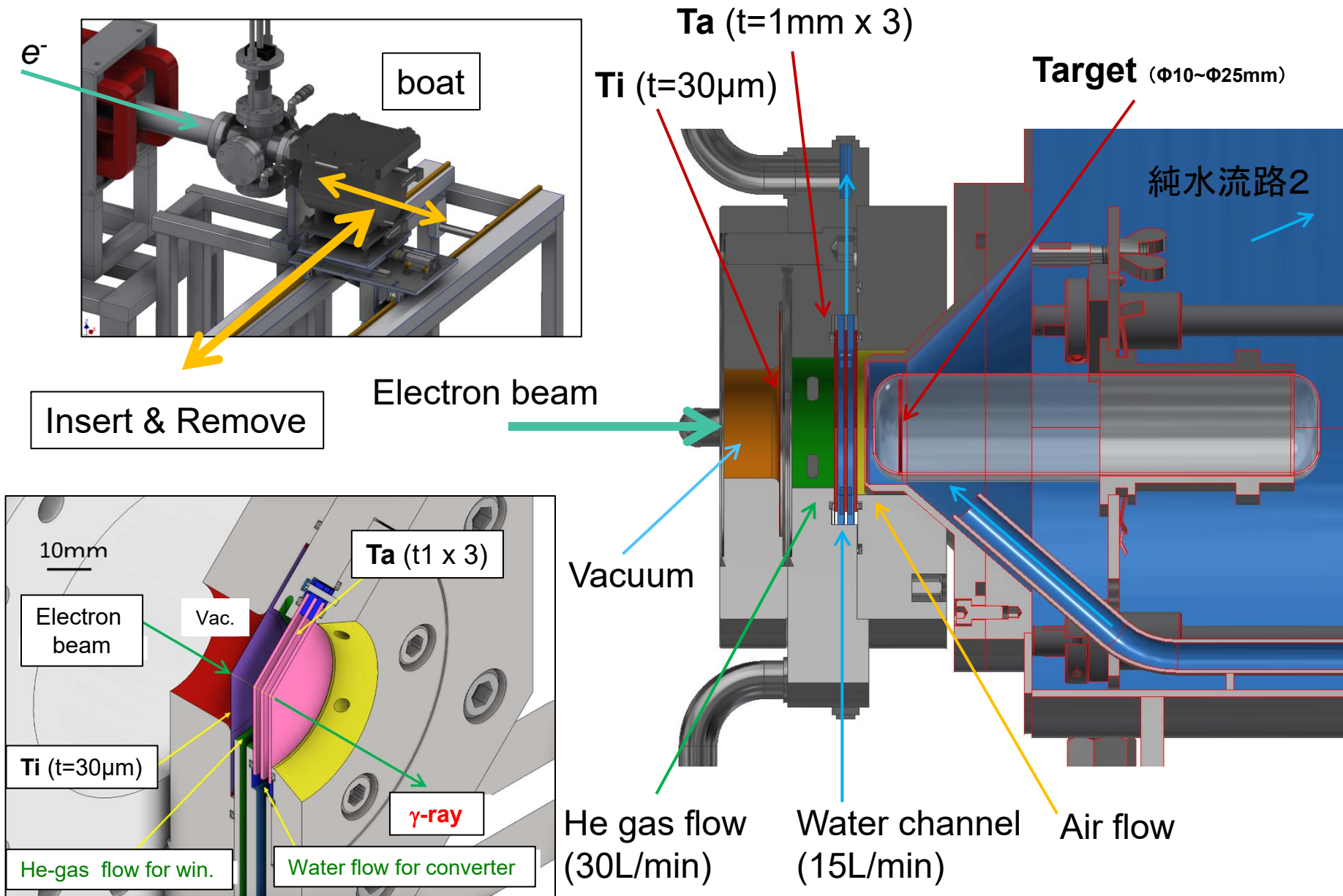
- 60 kV electron gun (Thermionic cathode)
- Pre-buncher and Buncher
- 1m-long accelerating structure \times 8
- RF power source: S-band klystron \times 2 (25MW)



- The irradiation point is surrounded by a concrete blocks, since strong radiation is generated at the irradiation point (about 10^{12} neutron/s).

Irradiation room (Experimental Hall 1)





Radioisotopes Hot Lab.



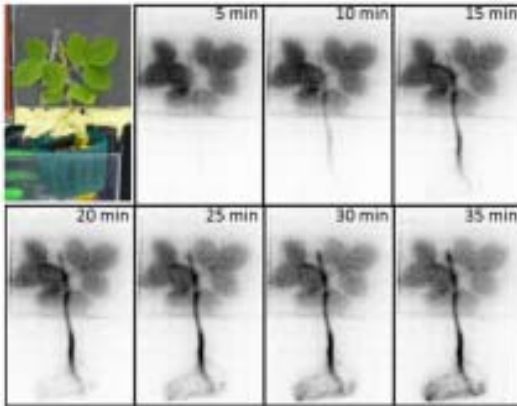
Unsealed Radio-Isotope Facility (376 nuclides)



- International controlled material use facility (U, Th)
- The genetic modification experiment facility (P1P level)
- Chemistry Laboratory
- Radiation measurement room (Ge detector etc.)

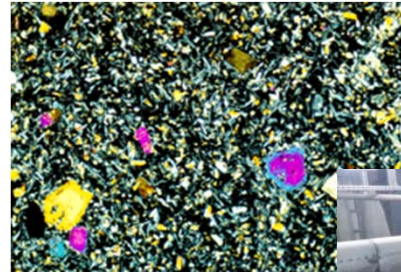
- RI are useful for various basic research.

Tracer



Imaging of water absorption

Nuclide Identification

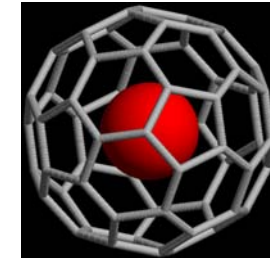


Materials
in Igneous rock



Metals in Household waste

Exploring Chemical properties



Endohedral
promethium-fullerene

- RI are applied to Nuclear Medicine & Therapy

- ✓ **Diagnostics**

γ emitter -> SPECT ^{99m}Tc

β^+ emitter -> PET ^{18}F , ^{68}Ga

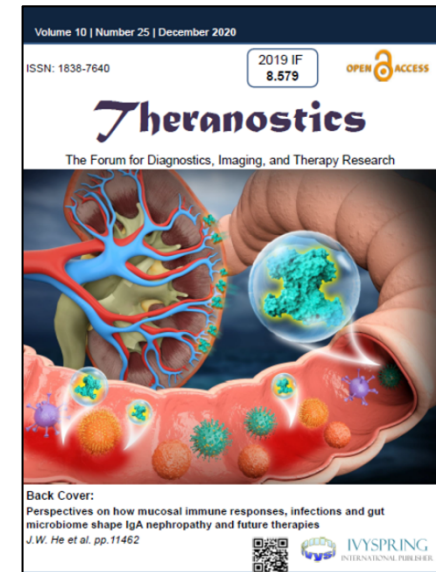
- ✓ **Therapy (Therapeutics)**

β emitter

α emitter

Auger electron

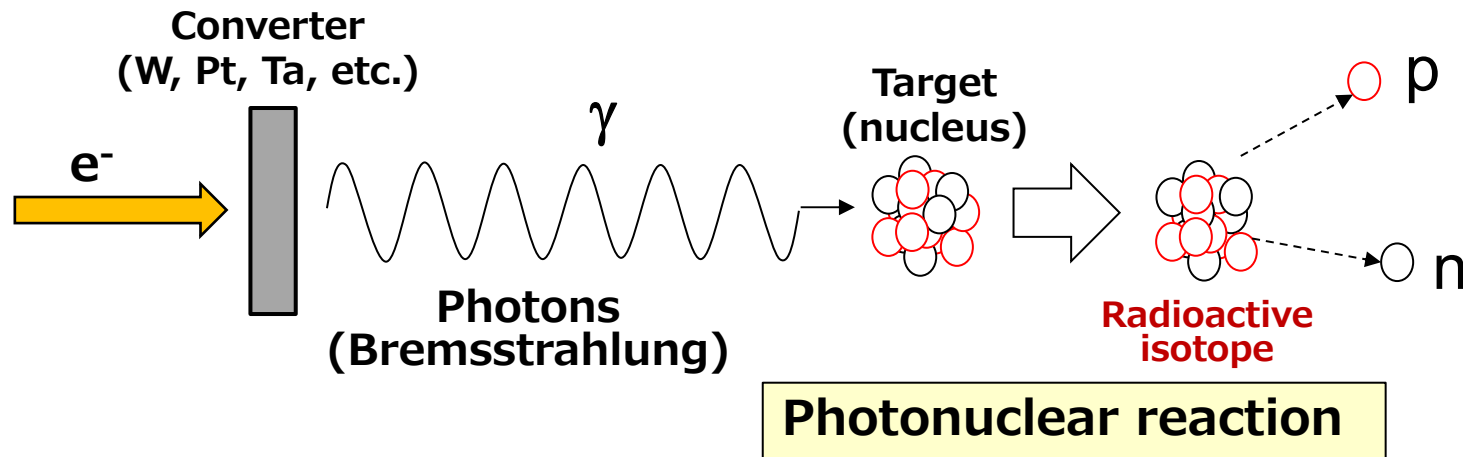
“Theranostics”



<https://www.thno.org/>

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- RIs can be produced using **nuclear reactor** or **accelerator**.
- **Bremsstrahlung gamma-ray** is used in **electron accelerator**.



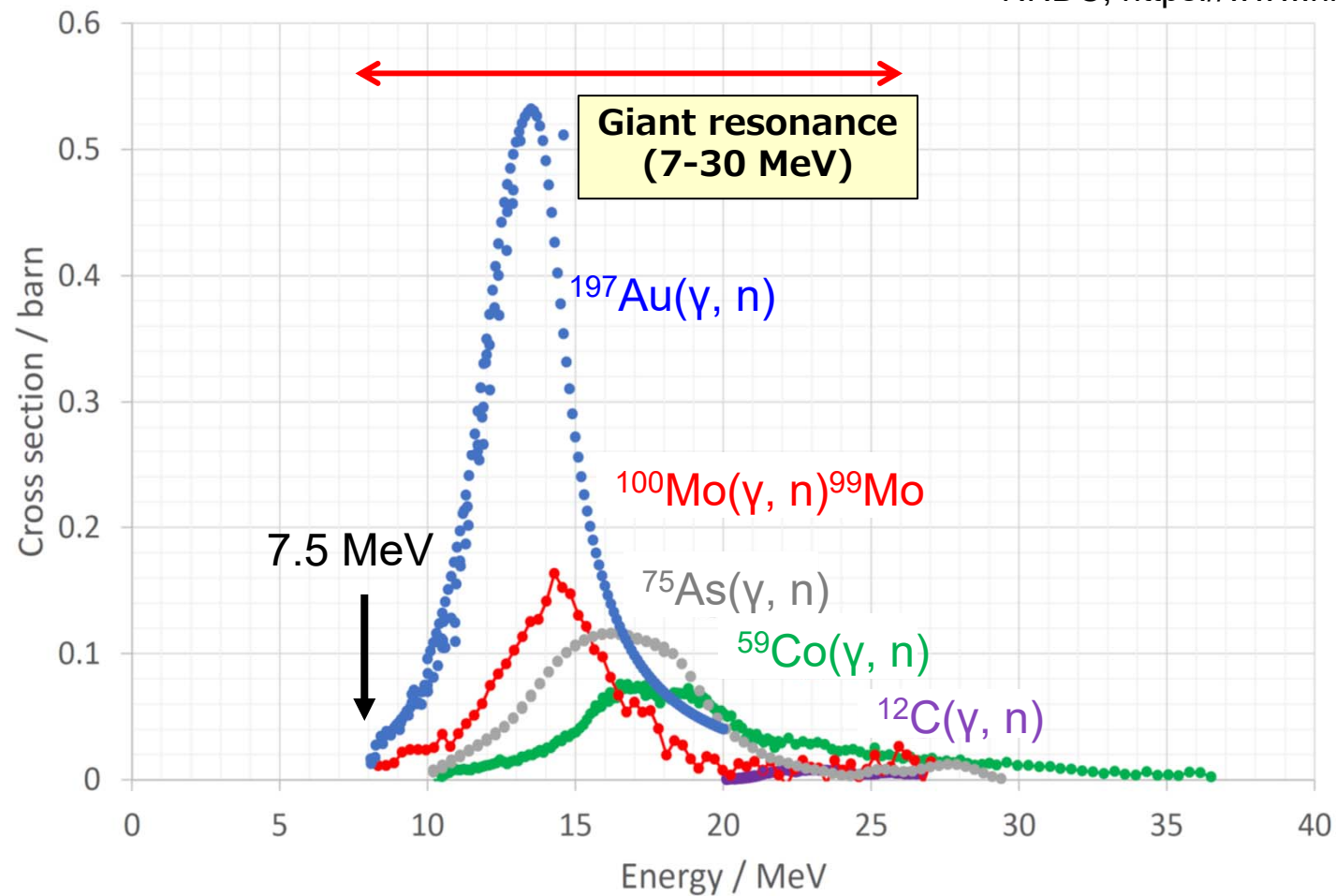
□ Main reaction using 60 MeV electron linac

1. (γ , xn) reaction: ex. $^{100}\text{Mo}(\gamma, n)^{99}\text{Mo}$
2. (γ , xpyn) reaction : ex. $^{\text{nat}}\text{Ru}(\gamma, X)^{99}\text{Mo}$, $^{66}\text{Zn}(\gamma, pn)^{64}\text{Cu}$
3. (γ , f) reaction : ex. $^{238}\text{U}(\gamma, f)^{99}\text{Mo}$

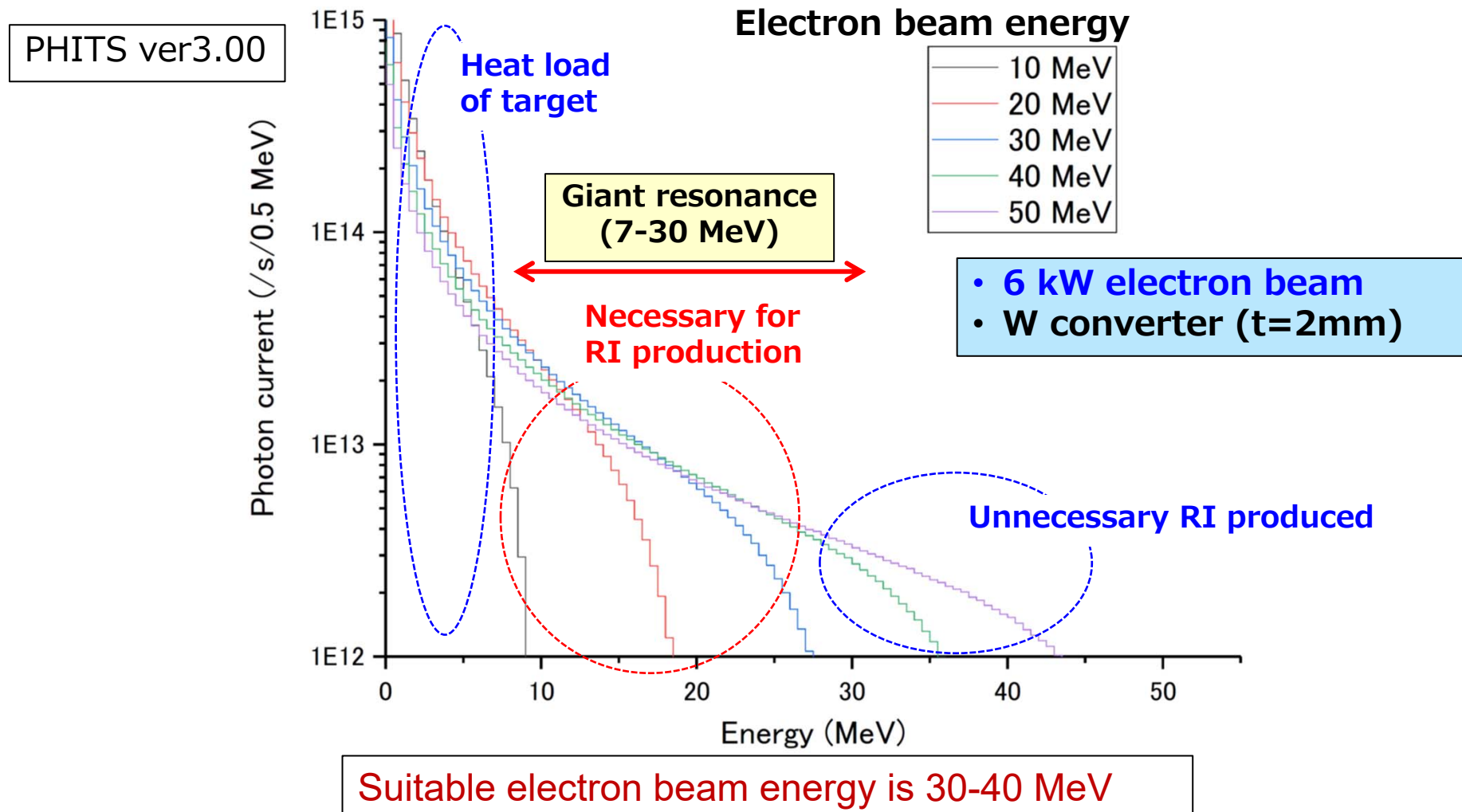
- The nucleus absorbs photons and causes a reaction.

-> Photonuclear reaction

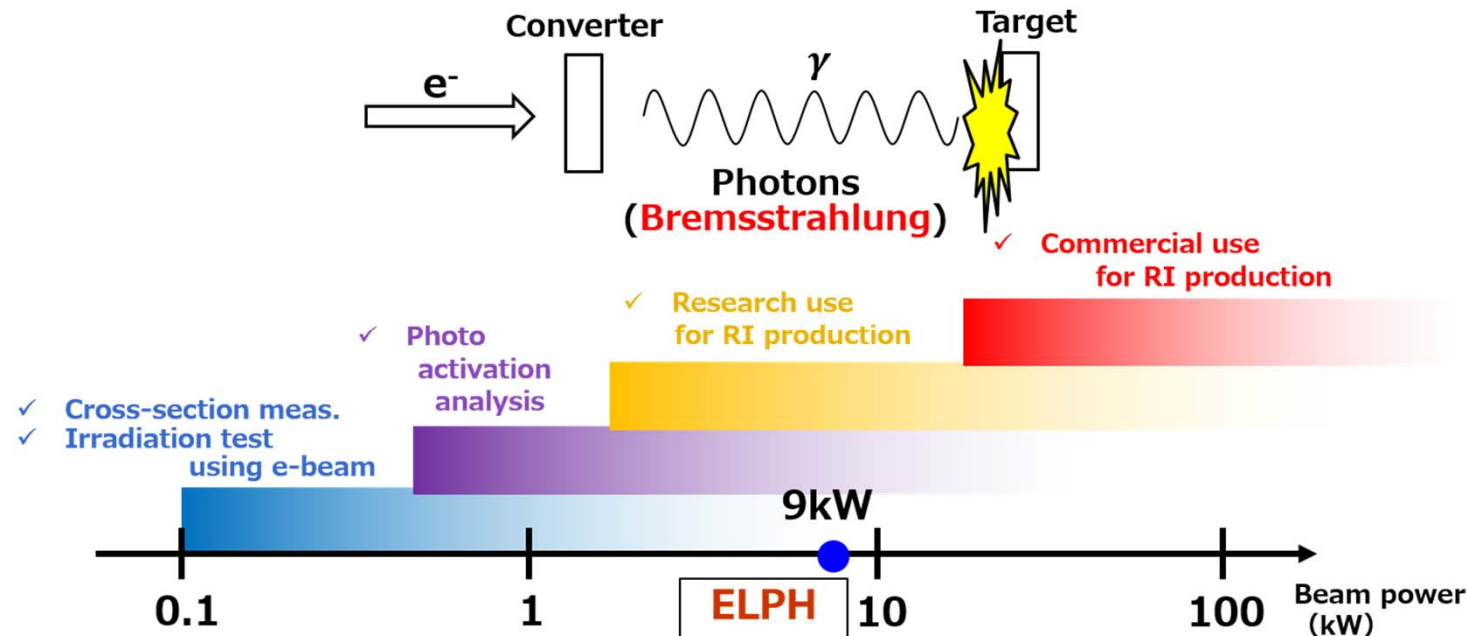
NNDC, <https://www.nndc.bnl.gov/>



- The spectrum of bremsstrahlung depends on the electron beam energy.
- Most nuclei have a large cross-section in **Giant resonance**.
- To generate radioisotope, many photons is required in this energy region.



- Application of electron linac depends on the beam power.



Requirements for accelerator

Reliability (Stable and high operation rate, Robust, Easy maintenance)

Profitability (Low Initial & Running cost, Compact (including shield))

Specification (High beam power, Easy operation)

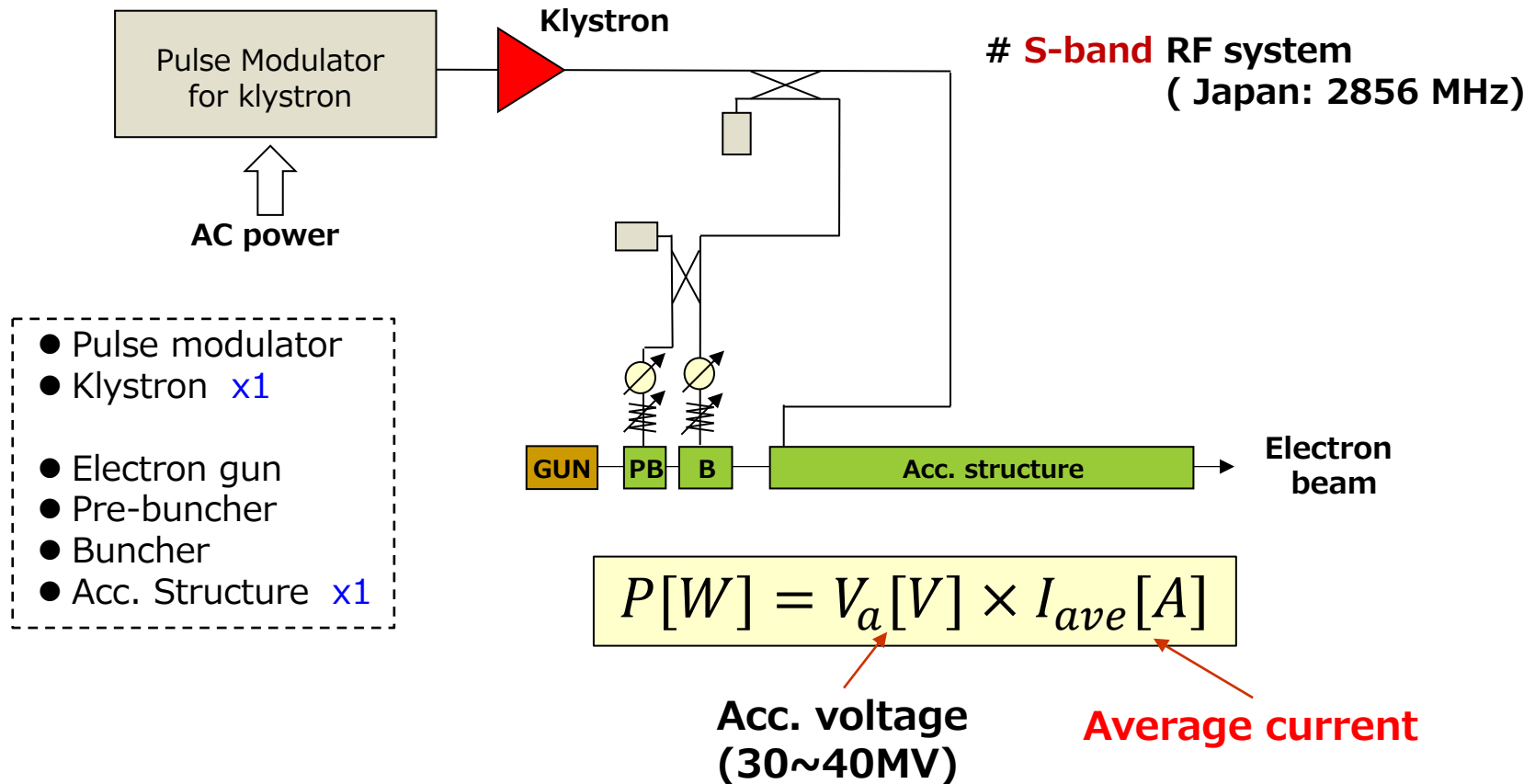
◆ Advantages of electron beam (compare with proton beam)

- ✓ Neutron generation is small => Radiation shield and activation will be small.
 - ✓ Thick target can be used (proton beam has short range, thick target ×)
 - ✓ Small heat-load of target => Cooling system of target will be easy.
- Mass production of RI is possible

- ❑ For RI production, **high beam power is required.**
- ❑ Appropriate electron beam energy is **30~40MeV.**

We don't need
Large accelerator!

Basic configuration



✓ **Average beam current** should be high !

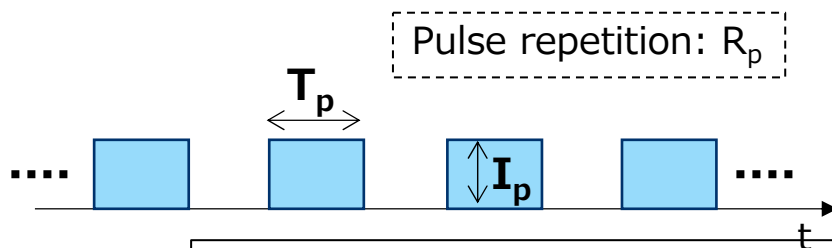
Beam power:

$$P[W] = V_a[V] \times I_{ave}[A]$$

- ✓ **Accelerating voltage (30~40MeV): Size of accelerator**
 - Number of accelerator tubes (E_a)
 - Number of RF unit (Klystron & Modulator)
- ✓ **Average beam current: (Duty cycle of beam)**
 - Peak current (I_p)
 - Pulse width (T_p), Pulse repetition (R_p)

$$I_{ave}[A] = I_p[A] \times T_p[s] \times R_p[Hz]$$

Normal-conducting: PULSE operation
Super-conducting: PULSE, CW operation

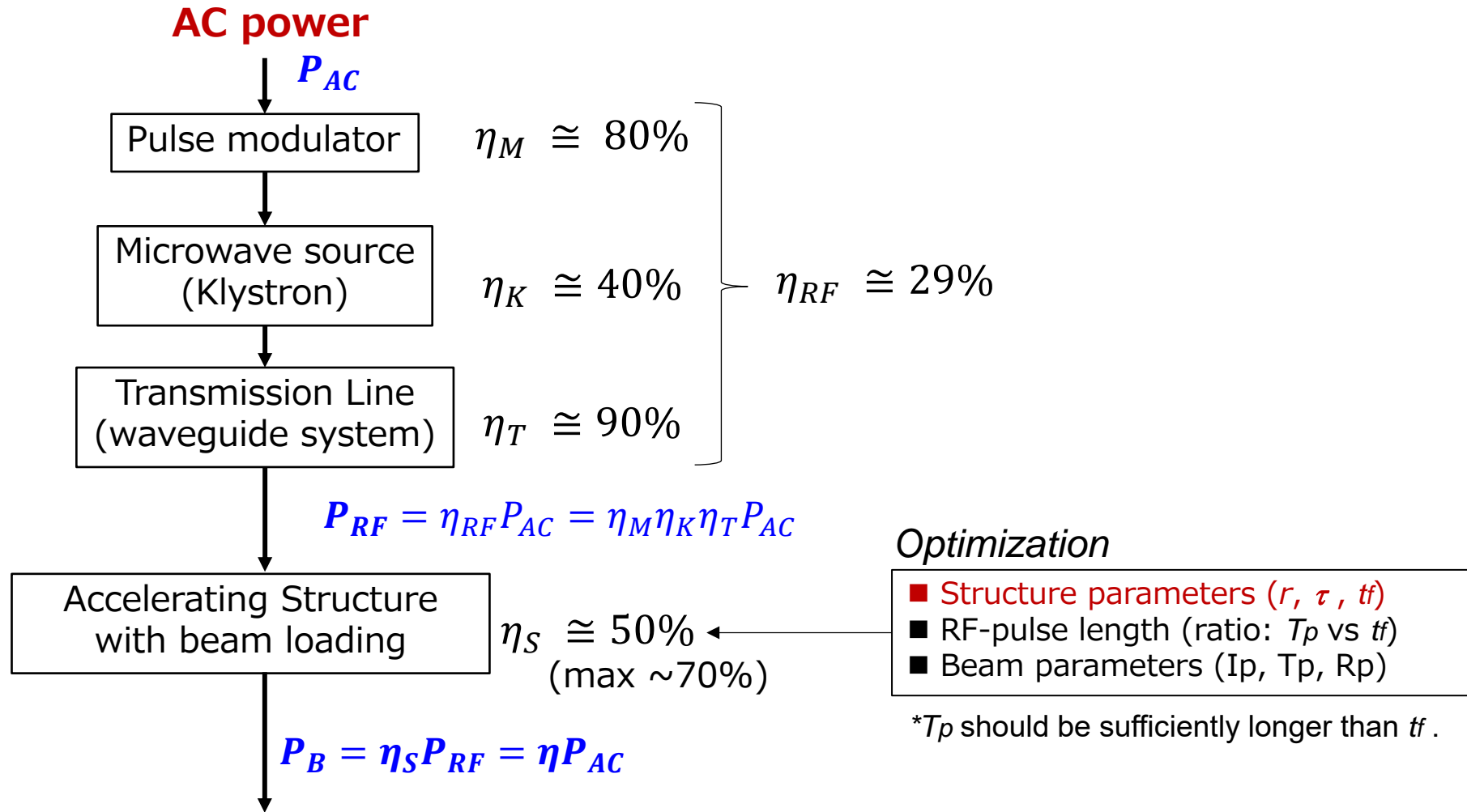


CW operation

$$T_p[s] \times R_p[Hz] \Rightarrow 1$$

- ✓ In the case of **normal conducting RF linac**, the beam duty is limited by the RF source. (maximum ~12%, peak power = 5MW)
- ✓ **Superconducting RF linac** can be operated in CW mode.
 (Operated in several national laboratories. Still difficult for commercial use)

Power flow & efficiency (ex. S-band linear accelerator)



Efficiency(η): $\sim 15\%$ (ELPH $\sim 6\%$)

Total efficiency: 10~12% (*Cyclotron: 8~13%)

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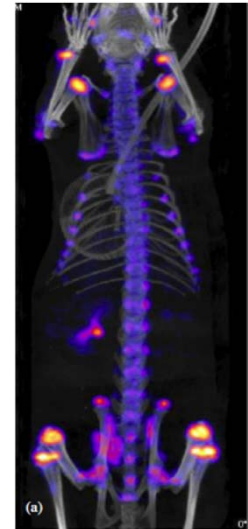
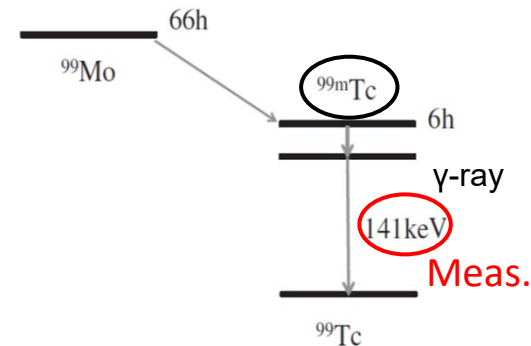
- ^{99}Mo production
- ^{225}Ac production

■ Summary

- Basic studies of RI production for Nuclear Medicine (diagnostics & Therapy) using **Electron Linac**.

1) Production of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ for SPECT.

SPECT (Single Photon Emission Computed Tomography)

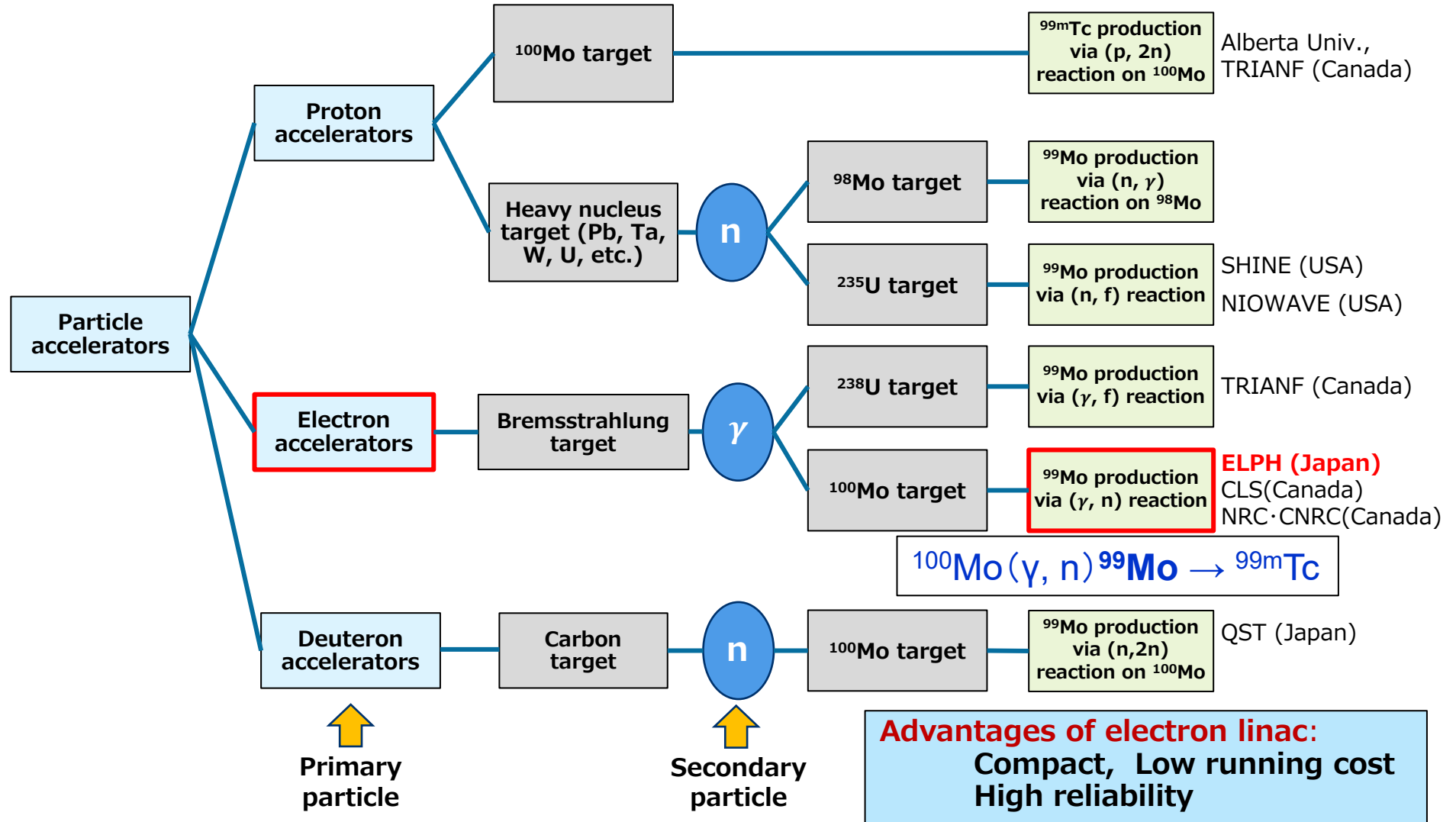


2) Production of ^{225}Ac for Targeted Radionuclide/Alpha Therapy.



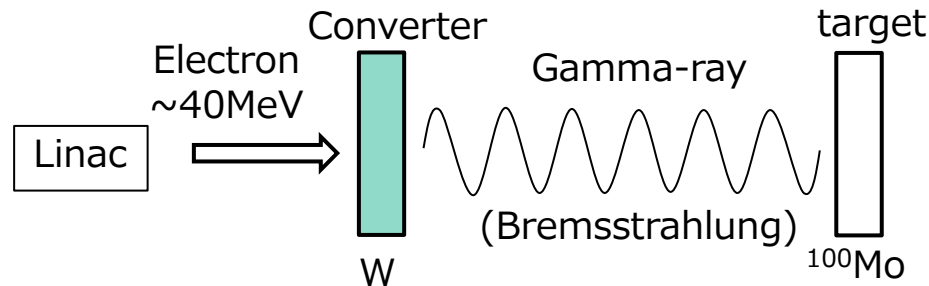
^{99}Mo production

- ✓ ^{99}Mo is the most widely used medical RI in the world.
- ✓ Most of ^{99}Mo is currently produced in **nuclear reactors**.
- ✓ Global shortage of $^{99\text{m}}\text{Tc}$ occurred around 2008, RI production using accelerator was proposed for stable supply.



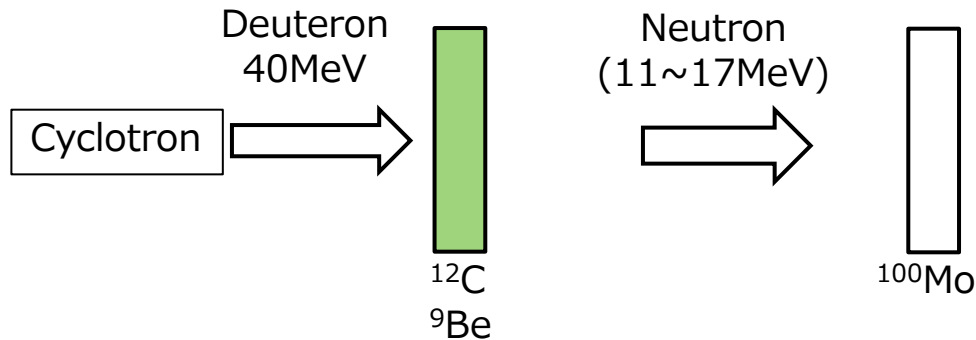
Comparison of ^{99}Mo production by primary beam (e^- , d) :[kBq/mg/uA/h]

Depend on the arrangement of the converter and target.



- E-beam energy: 40 MeV
 - Beam power: 0.4 kW
- Armenian Journal of Physics, 2013, 6, pp35-44*

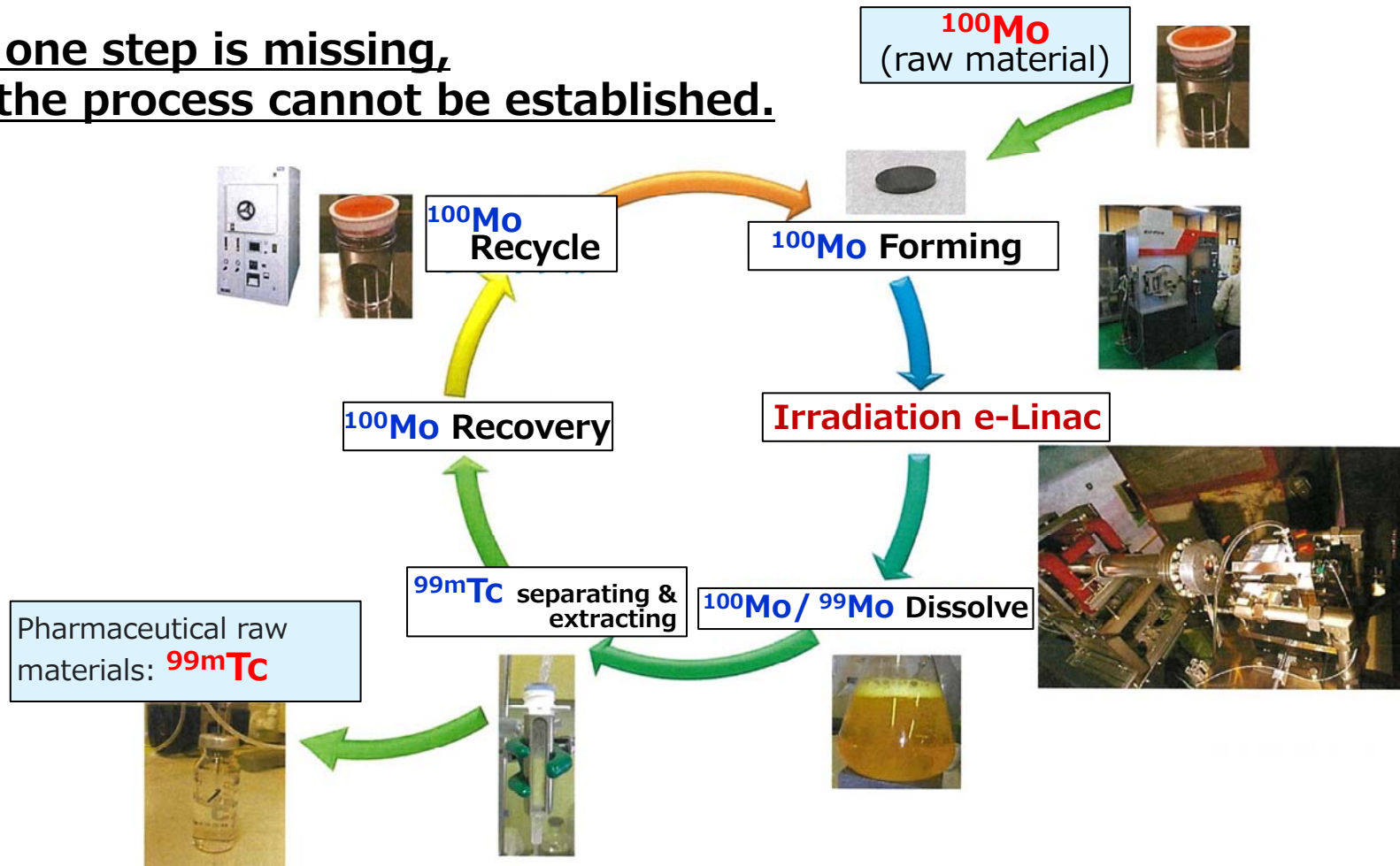
0.09~3.2k [Bq/mg/uA/h] (Exp.)
 $\sim 3\text{k}$ [Bq/mg/uA/h] (Exp.@ELPH)



- Deuteron beam: 40MeV, 100nA
 - MoO_3 : 0.5g
- $\sim 1.8\text{k}$ [Bq/mg/uA/h] (Exp. ^9Be)

Y. Nagai et al., J. Phys. Soc. Jpn. 82 (2013) 06420
 GRAND project: 40MeV, 2mA (cyclotron)

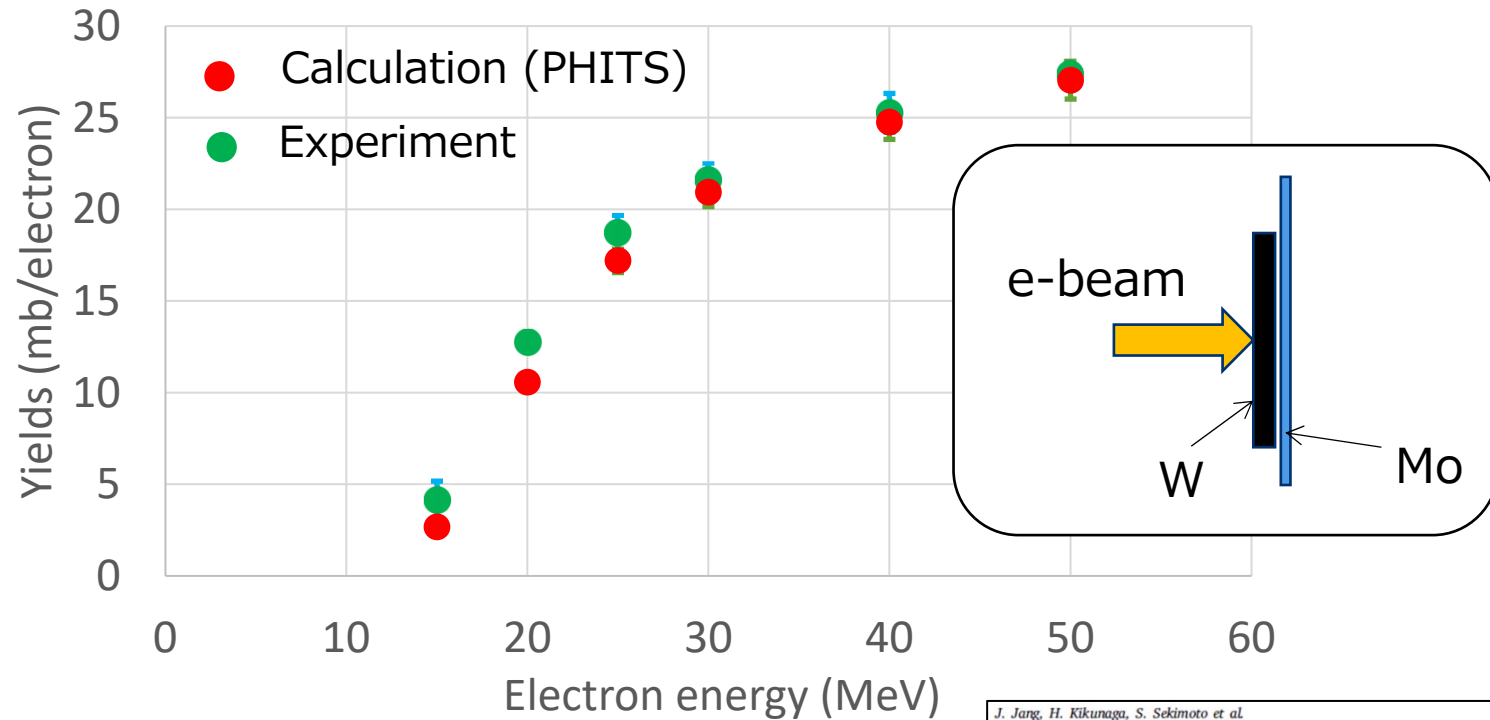
Even if one step is missing,
the process cannot be established.



Study items

- ✓ Estimation of ^{99}Mo yield and comparison with beam experiment.
- ✓ Target system: material (^{100}Mo or MoO_3 etc.) and structure design.
- ✓ Development of Chemical process (dissolve, separation, recycle,,,,,)

□ Production test: Yields on the Mo-100(γ,n)Mo-99 reaction



□ Target design studies (MoO₃)

Nuclear Inst. and Methods in Physics Research, A 987 (2021) 164815

Contents lists available at ScienceDirect

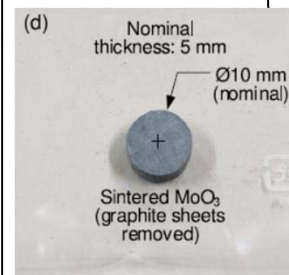
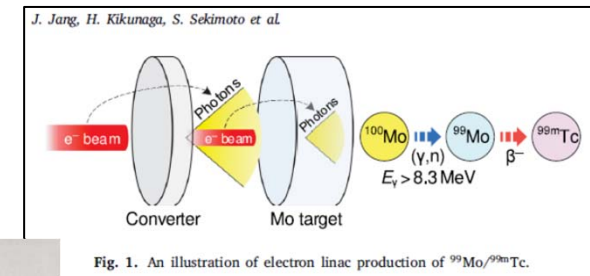
Nuclear Inst. and Methods in Physics Research, A

ELSEVIER journal homepage: www.elsevier.com/locate/nima

Design and testing of a W-MoO₃ target system for electron linac production of ⁹⁹Mo/^{99m}Tc

Jaewoong Jang^{a,1,*}, Hidetoshi Kikunaga^b, Shun Sekimoto^c, Makoto Inagaki^c, Tomohiko Kawakami^d, Tsutomu Ohtsuki^c, Shigeru Kashiwagi^b, Ken Takahashi^b, Kyo Tsukada^b, Katsuyoshi Tatenuma^d, Mitsuru Uesaka^{a,e}

^a Department of Bioengineering, University of Tokyo, Bunkyo, Tokyo 113-8656, Japan
^b Research Center for Electron Photon Science, Tohoku University, Sendai, Miyagi 982-0826, Japan
^c Institute for Integrated Radiation and Nuclear Science, Kyoto University, Soraku, Osaka 590-0494, Japan
^d Koken Inc., Mito, Ibaraki 310-0903, Japan
^e Nuclear Professional School, University of Tokyo, Naka, Ibaraki 319-1188, Japan





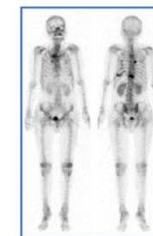
**S-band electron linac
(two RF unit and two Acc. tube)
40 MeV, 1 mA -> 40kW**

Nihon Medi-Physics Launches In-house Production of Molybdenum-99

October 8, 2019, Tokyo, Japan. Nihon Medi-Physics (NMP), the leading radiopharmaceutical company in Japan, announced the in-house production of Molybdenum-99 (^{99}Mo), the critical raw material for Technetium-99m ($^{99\text{m}}\text{Tc}$).

NMP launched a project for the in-house production of ^{99}Mo by investing about JPY1.3Bn and plans to start commercial production of ^{99}Mo in 2023. They have developed a new manufacturing process that uses an accelerator instead of a nuclear reactor. It is an environment-friendly procedure without generating nuclear waste.

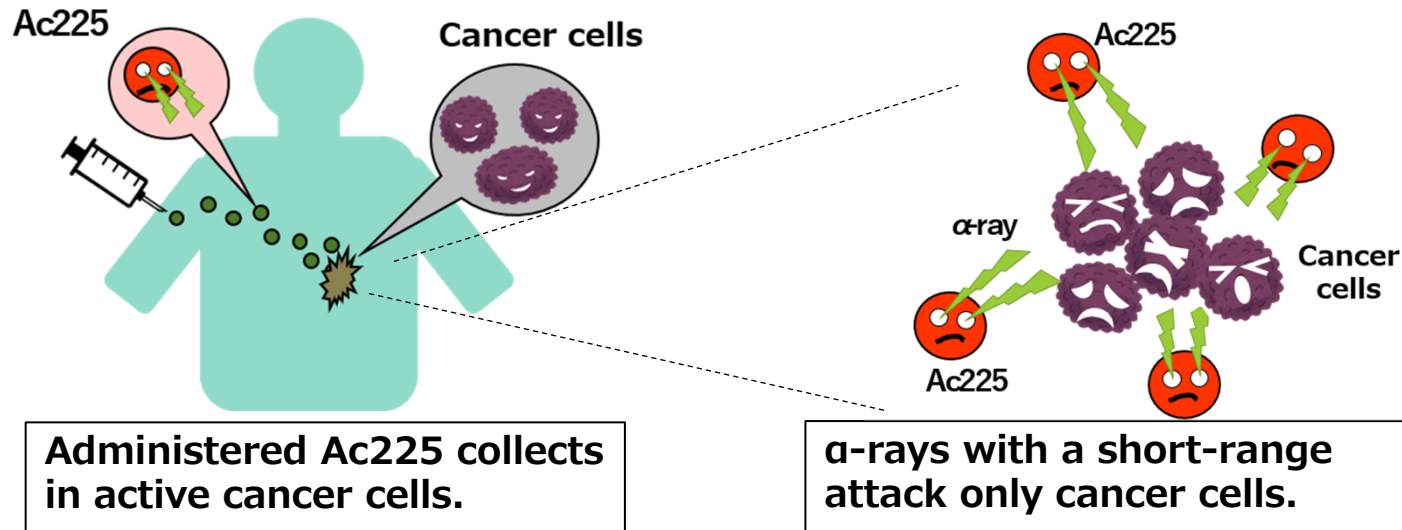
A stable supply of pharmaceutical products is the most important mission for a pharmaceutical manufacturer. Stable procurement of ^{99}Mo is an essential factor for fulfilling this mission sustainably. Therefore, NMP has been collaborating with the Research Center for Electron Photon Science, Tohoku University, since 2016 to develop a new ^{99}Mo manufacturing process using an electron accelerator. NMP has successfully conquered various issues such as ^{99}Mo quality as a raw material for $^{99\text{m}}\text{Tc}$ radiopharmaceutical products as well as its productivity. NMP has confirmed the suitability of the manufacturing process for commercial production.



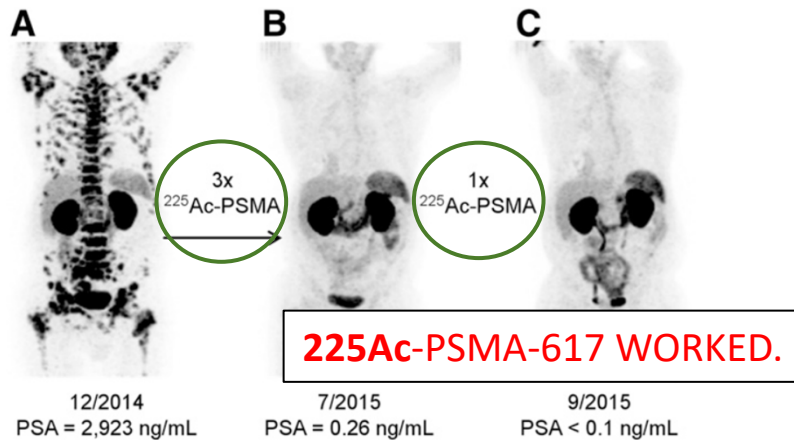
Nuclear medicine scan
by Technetium-99m
radiopharmaceutical.

**The 40kW electron linac can produce 10~15%
of Japan's domestic demand for ^{99}Mo .**

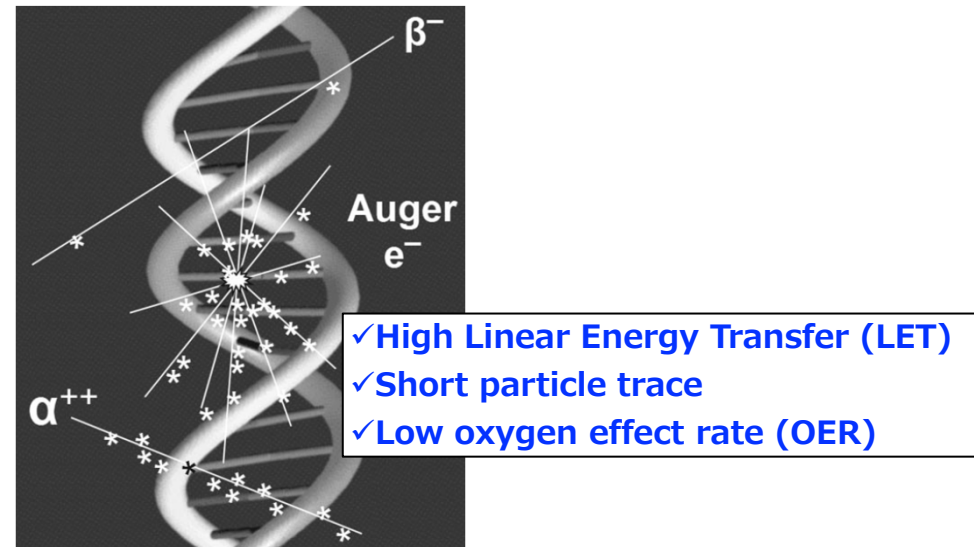
Targeted Radionuclide Therapy (TRT) using Alpha-emitter



Reported by Heidelberg University, Germany (prostate cancer)



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



Kassis, AI et al., J Nucl. Med., 2005, 46:4S-125S

Requirements for α -emitter RI in clinical use

1. Appropriate **Half-life** (neither too short nor long)
2. Able to be labeled by ligands (for TAT/TRT)

~400 RIs emitting α -ray in ($> Z=82$)
Only 10 candidates
 (^{149}Tb , ^{211}At , ^{224}Ra , ^{225}Ac , ^{213}Bi etc)
 for clinical development

The most promising alpha-emitter RIs

^{211}At

$T_{1/2} = 7 \text{ h}$

✓ $^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$ * α -beam (30MeV)

^{225}Ac

$T_{1/2} = 10 \text{ days}$

✓ ^{229}Th generator \leftarrow "present"

JRC Karlsruhe:Germany

ONL (Oak Ridge National Lab) :USA

IPPE (Institute of Phys. and Power Eng.) :Russia

Total (3 institutes) $< 100\text{GBq/year}$

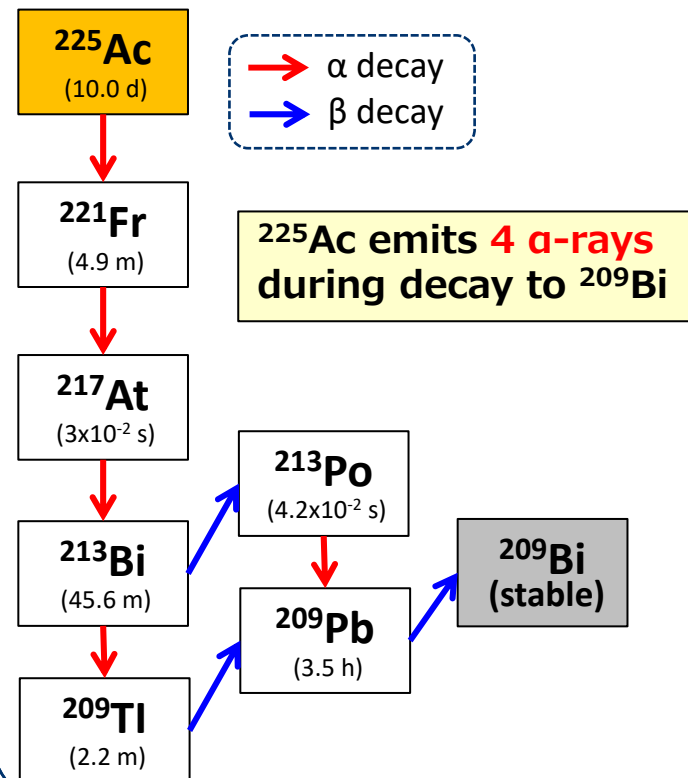
✓ $^{232}\text{Th}(p, \text{spall})^{225}\text{Ac}$ *cyclotron \leftarrow Large cyclotron ($> 100\text{MeV}$)

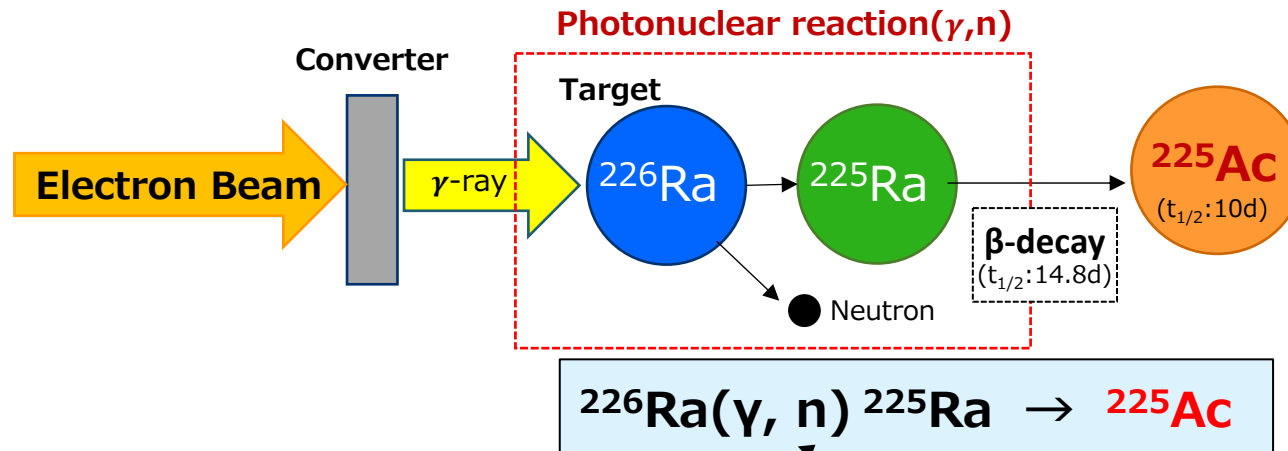
✓ $^{226}\text{Ra}(p, 2n)^{225}\text{Ac}$ *cyclotron ($< 25\text{MeV}$)

impurity nuclides are produced

✓ $^{226}\text{Ra}(\gamma, n)^{225}\text{Ra} \rightarrow ^{225}\text{Ac}$
 *Electron linac ($\sim 35 \text{ MeV}$)

^{225}Ac Decay chain





No experimental data of cross-section, only theoretical calculation

< Advantages >

- Cost-effectiveness, Compact
- Can be scaled up by **the electron beam power & amount of ^{226}Ra .**
- **No ^{226}Ac or ^{227}Ac are produced by photonuclear reaction.**
(Impurity nuclide)

< Challenges >

- Handling of ^{226}Ra target which decays to ^{222}Rn .
- Separation of ^{225}Ac from ^{226}Ra and ^{225}Ra .

Study Items

- ✓ ^{225}Ac production test with different electron beam energy. (Cross-section)
- ✓ Target studies (^{226}Ra handling).
- ✓ Establish the chemical process of ^{225}Ac separation.
- ✓ **“Scale studies” of ^{225}Ac production.**

(In actual ^{225}Ac production, it is necessary to irradiate “GBq” order of ^{226}Ra at one time.) 10 [kBq] => 10 [MBq] ----> 10 [GBq]

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- ❑ We are conducting the basic research for RI production using electron linac, such as optimization of target system and improvement of chemical process.
- ❑ **High power electron linac** is powerful tool and very useful for RI production. Suitable beam energy is about **30~40MeV**, therefore **the accelerator system will be compact and total electric power efficiency is more than 10%** by optimizing the beam and RF parameters.
- ❑ Production of radiopharmaceuticals using accelerator have been attracting attention. **We are developing medical RI ($^{99}\text{Mo}/^{99\text{m}}\text{Tc}$, ^{225}Ac) manufacturing process using an electron linac.**
- ❑ **In ^{99}Mo production process**, an electron beam can generate RI more efficiently than the deuteron beam. **Nihon Medi-Physics Co., Ltd. decided to build the 40kW electron linac for producing of ^{99}Mo .** (*Collaboration achievement)
- ❑ **In ^{225}Ac production, electron beam has some advantages over proton beam.** **No ^{226}Ac or ^{227}Ac** (impurity nuclide) are produced by photonuclear reaction and the electron linac will be compact than proton cyclotron.

Acknowledgement

We would like to thank all the collaborators. This work is supported by the Program on Open Innovation Platform with Enterprises, Research Institute and Academia(OPERA) from Japan Science and Technology Agency (JST).