Status of the short-lived radioisotope supplying platform in Japan

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Demand for radio isotopes

- Industry: non-destructive testing,
- Chemistry: tracer, nuclear chemistry, synthesis of nuclear chemicals/medicine
- Biology, Agriculture: tracer, radiobiology
- Medicine: probes for diagnosis, cancer therapy

Increasing demand especially in the field of nuclear medicine

Xofigo® radium Ra 223 dichloride SOLUTION FOR INJECTION

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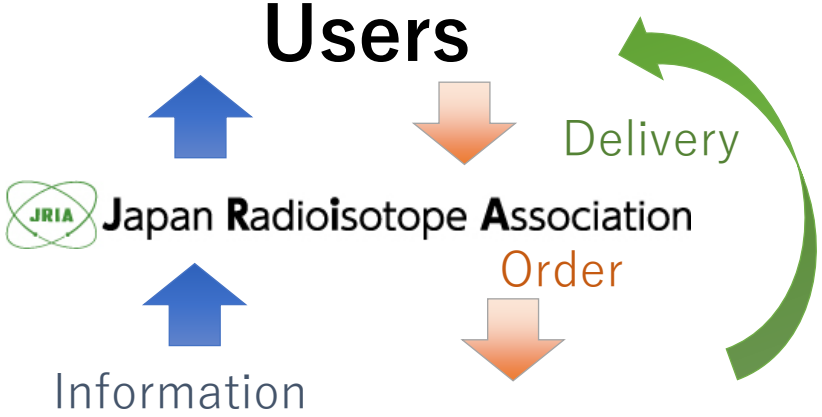
LUTATHERA® (lutetium Lu 177 dotatate) injection, for intravenous use

www.hcp.novartis.com

Supply of radioisotopes in Japan

- Commercial supply
  - Unified trades via JRIA



- Private communications / Self production

JRAM

- JRIA RadioActive Material
  - portal site for scientific/safety information and supply of radioactive materials
  - promotion of the use of radioactive materials

- Information
  - Usage/Guides for experiments
  - Liaison with experts of experiments
  - News
- Supply
  - 6 importers/4 domestic manufacturers
  - Agent for ready-made and order-made RIs to manufacturers

71 Nuclides

shortest life: F-18 109 minutes

longest life: I-129 1.57×10^7 years

H-3	Se-75	I-129
C-14	Rb-81/Kr-81m	I-131
F-18	Rb-86	Cs-134
Na-22	Sr-85	Cs-137
P-32	Sr-89	Ba-133
P-33	Sr-90	Ce-139
S-35	Y-88	Ce-144
Cl-36	Y-90	Pm-147
Ca-45	Zr-89	Eu-152
Cr-51	Zr-95	Eu-154
Mn-54	Nb-95	Gd-153
Fe-55	Mo-99	Lu-177
Fe-59	Tc-99	Hg-203
Co-56	Ru-106	Tl-201
Co-57	Ag-110m	Tl-204
Co-58	Cd-109	Pb-210
Co-60	In-111	Bi-207
Ni-63	In-114m	Po-210
Cu-64	Sn-113	Np-237
Cu-67	Sb-124	Am-241
Zn-65	Sb-125	Am-243
Ga-67	I-123	Cm-244
Ge-68	I-124	Cf-252
Ge-68/Ga-68	I-125	

Commercial RI supply

Advantage

- Market mechanism
  - Widely used RIs can be easily procured (ex. F-18)
  - Import from the whole world
- Many kinds of chemical forms
  - RI materials are tools for the science
    ← Easiness of use of RIs

Disadvantage

- Market mechanism
  - Less frequently used RIs are difficult to be purchased (e.g. Co-56, very high price!)
  - Supply depends on the world situation (e.g. Ru-103 from Russia or Mo-99 due to the eruption of the volcano)

Our aim

The short-lived-RI supplying platform was organized to assist the research subjects supported by MEXT/JSPS KAKENHI by supplying short-lived RIs regularly and stably, and by giving technical assistance for safe RI treatment.

- Supply of short-lived RIs which cannot be purchased from JRIA.
- Stable supply of RIs by all-Japan accelerator consortium consisting of high-performance accelerator facilities.
- Unification of contact office at RCNP as a core of collaborative use and research to improve convenience and to increase users.
- Supporting basic research in a various field, based on the peer-review system on the scientific merit and impact

The platform started from FY2016 supported by Grants-in-Aid for Scientific Research on Innovative area 16H02678
It continued after FY2022 supported by Grants-in-Aid for Transformative Research Area 22H03924

RCNP 大阪大学 核物理研究センター　RIKEN NISHINA CENTER　CYRIC TOHOKU UNIVERSITY　TOHOKU UNIVERSITY　QST

Accelerator Facilities for RI production

- 6 accelerator facilities in Japan
  - Almost all the cyclotron facilities for external scientific use: RCNP, RIBF, CYRIC, and QST
  - The most intense electron linac in ELPH

→ Covering many kinds of nuclides and stable supply

Supply of	RCNP	RIBF	CYRIC	ELPH	QST-QMS	QST-Takasaki
Positron-emitting RIs	Possible	Possible	OK	Possible	OK	OK
Single-photon emitting RIs	OK	Possible	-	OK	OK	-
Beta-emitting RIs	Possible	Possible	Possible	Possible	OK	-
Alpha-emitting RIs	OK	OK	Possible	-	OK	OK
Neutron-rich RIs	-	-	-	OK	-	-
Heavy-element RIs	-	OK	-	-	-	-

Process of RI supply

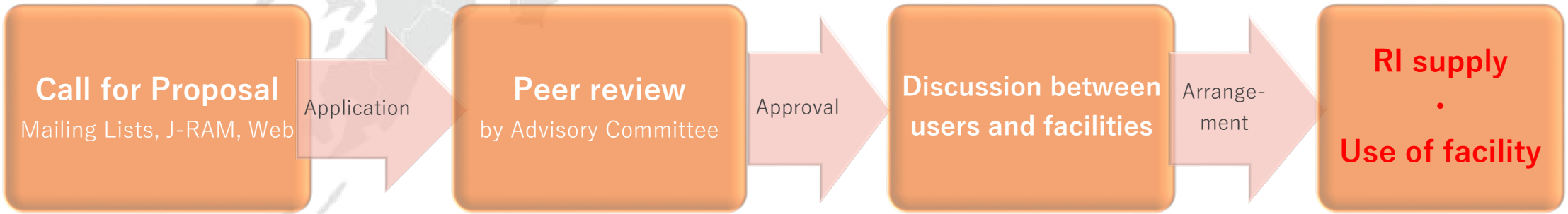
Example of available RIs

Nuclide	Chemical form	Facility
Be-7	Chloride	RIKEN
C-11	Various compounds	CYRIC
O-15	H_2O	CYRIC
F-18	F-(NaF), FDG, etc.	CYRIC
Mg-28	In metal, Chloride	RIKEN
K-42	Any form	ELPH
K-42, 43	Mixed solution	ELPH
K-43	Any form	ELPH
Sc-44m	In metal	RCNP
Co-56	In metal, Chloride	RCNP, RIKEN

Nuclide	Chemical form	Facility
Cu-67	Chloride	RIKEN, ELPH
Zr-88	In Yttrium metal	RIKEN, RCNP
Y-90	Any form	RCNP
Mo-99	Any form	RCNP
Ag-111	In metal	RIBF
Cs-136	Any form	ELPH
Lu-177	Any form	RCNP
Pt-191	Any form	RCNP
Au-195	Any form	RCNP
At-211	Any form	RCNP, RIKEN, QST Takasaki

Other nuclides can be supplied upon consultation

Flow chart of application to supply

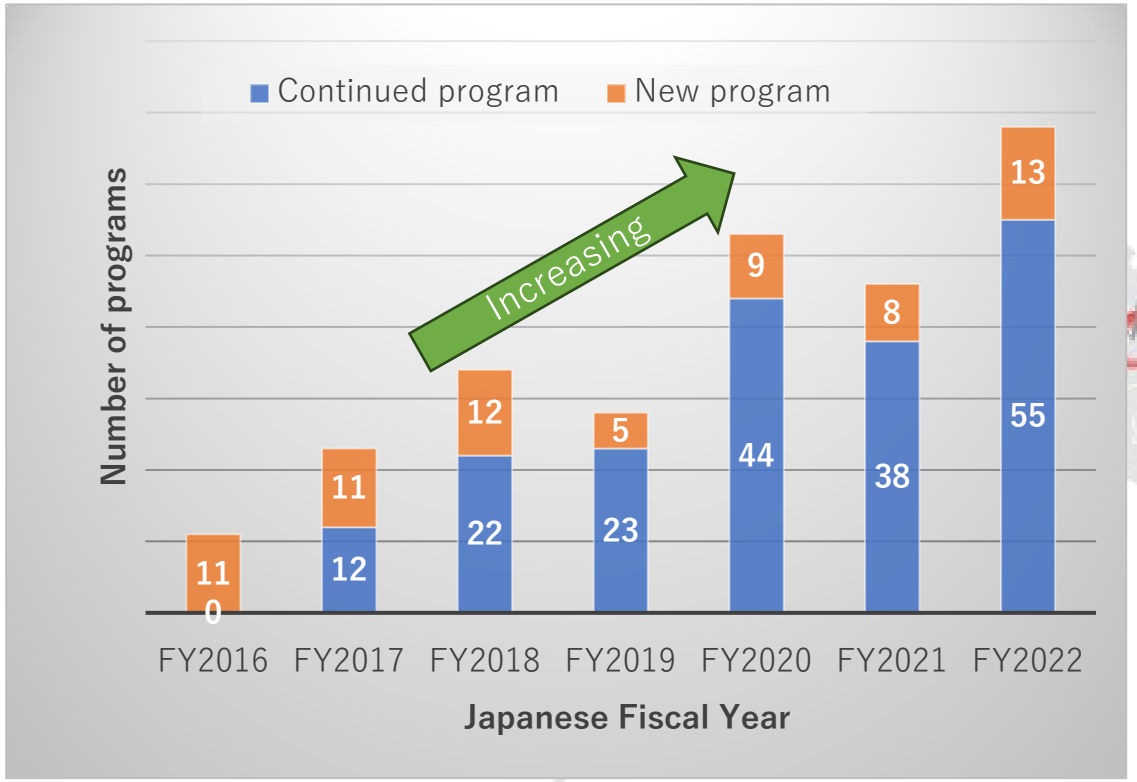


Technical Training Course

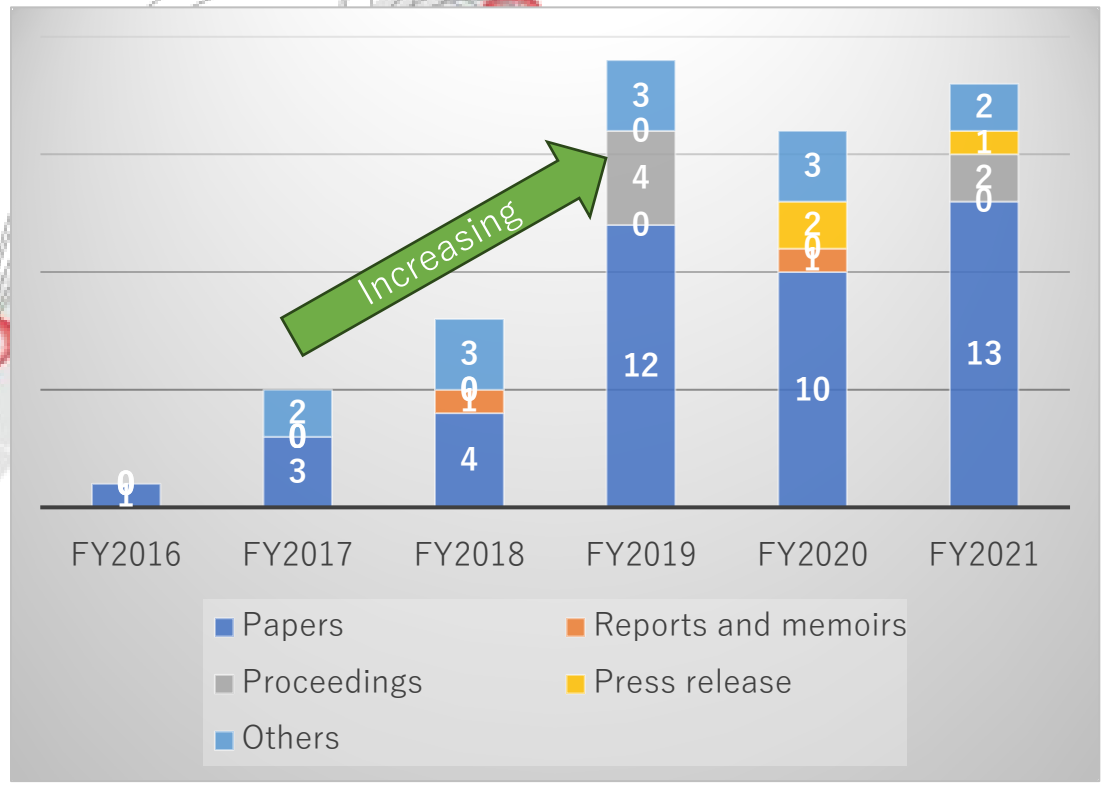
- Opened twice a year at CYRIC and RCNP
- Lectures on the basic and the state-of-the-art research with RIs
- Technique of treatment of the non-sealed RIs and measurement of the radiation

Stats

Number of approved research programs



Number of publications



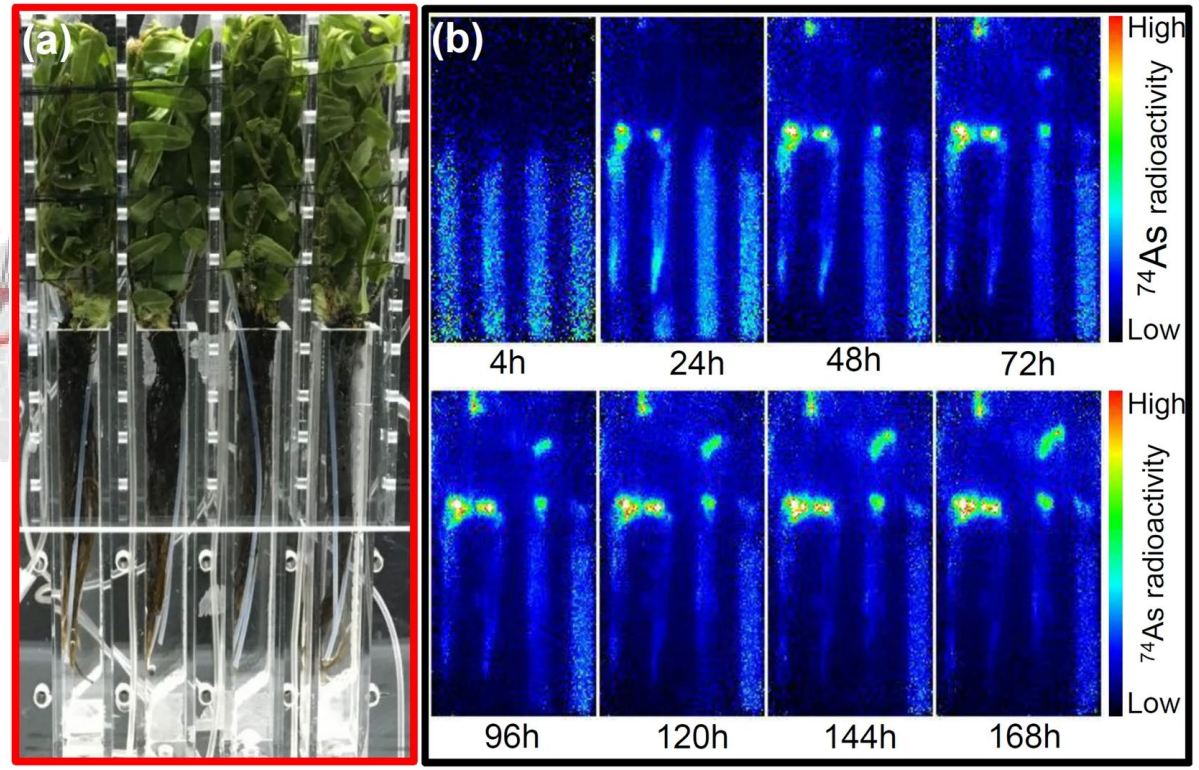
Many “Repeaters”

Significant result: PETIS for analysis of arsenic dynamics in plant

- A kind of plant can accumulate the toxic element arsenic
- Positron emitting As-74 supplied from our platform and PETIS revealed the mechanism of Arsenic accumulation in Pteris vittata

→ Phytoremediation of Arsenic contaminated soil and water by Pteris vittata

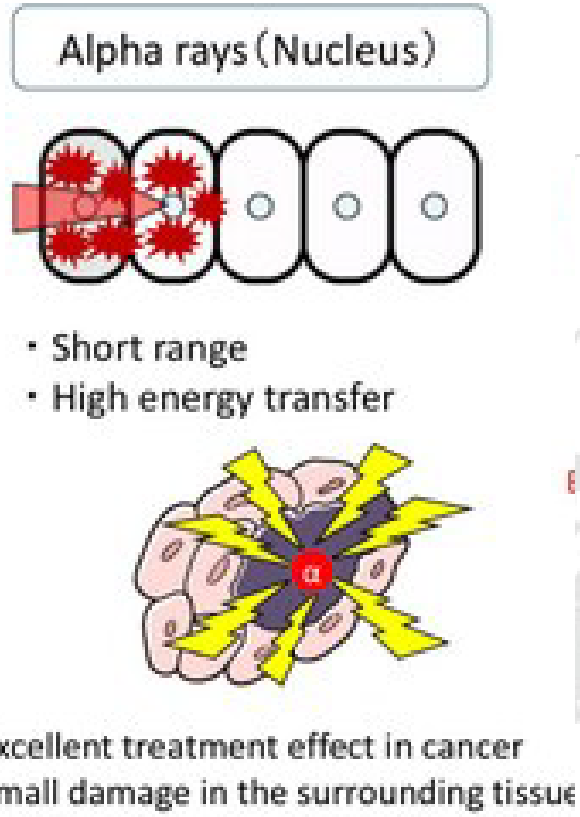
https://www.tohoku.ac.jp/japanese/2021/07/press20210709-01-moeji.html



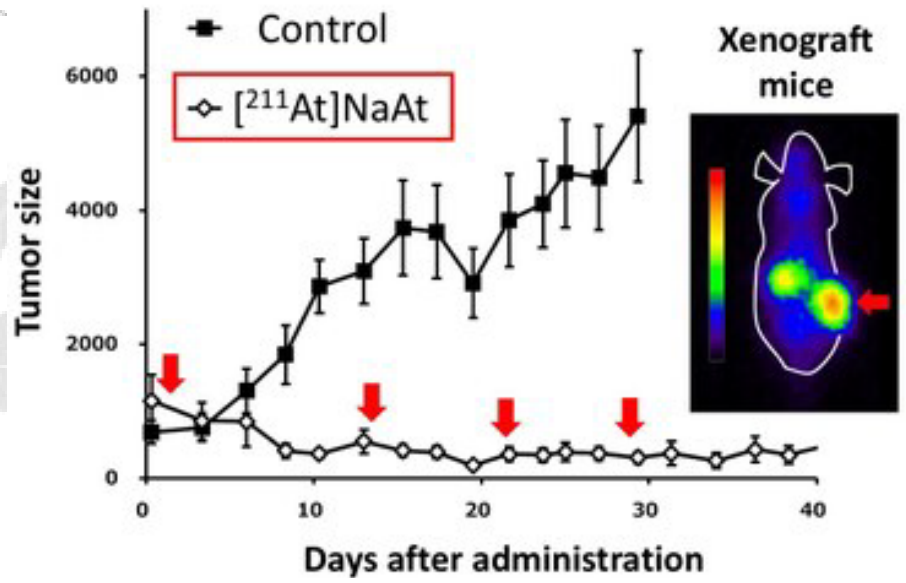
DOI:10.1038/s41598-021-91374-1

Significant result: Astatine-211 for TAT

- Targeted Alpha Therapy (TAT) is emerging as the next generation cancer treatment



- Sodium Astatide [At-211] works as sodium iodide symporter to thyroid cancer
- It showed significant reduction of the tumor site for iodine-refractory thyroid cancer

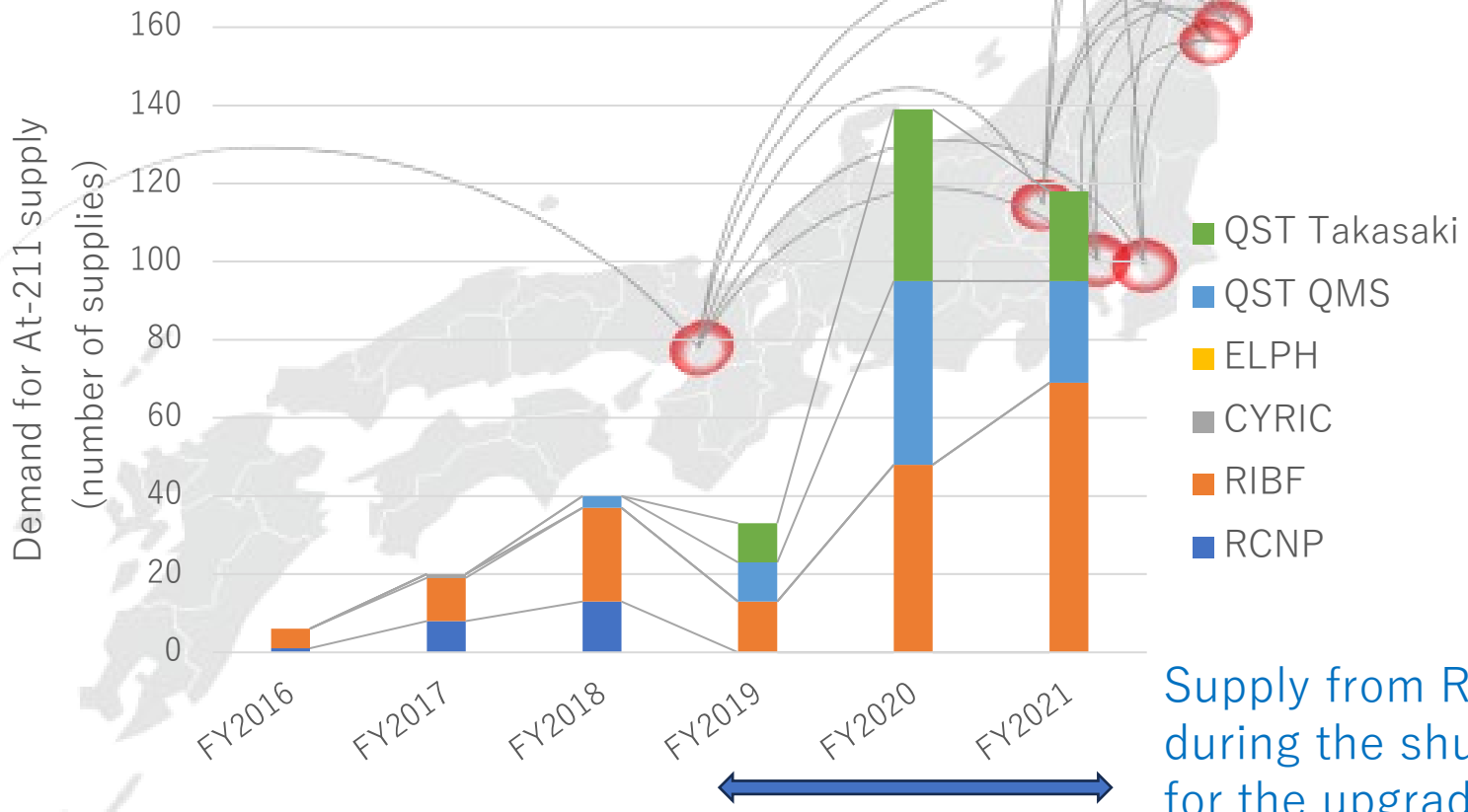


doi.org/10.2967/jnumed.118.222638

Clinical test of [^{211}At]NaAt (TAH-1005) for human is underway at Osaka University Hospital with At-211 supplied by RIBF, RIKEN.

Emerging demand for At-211

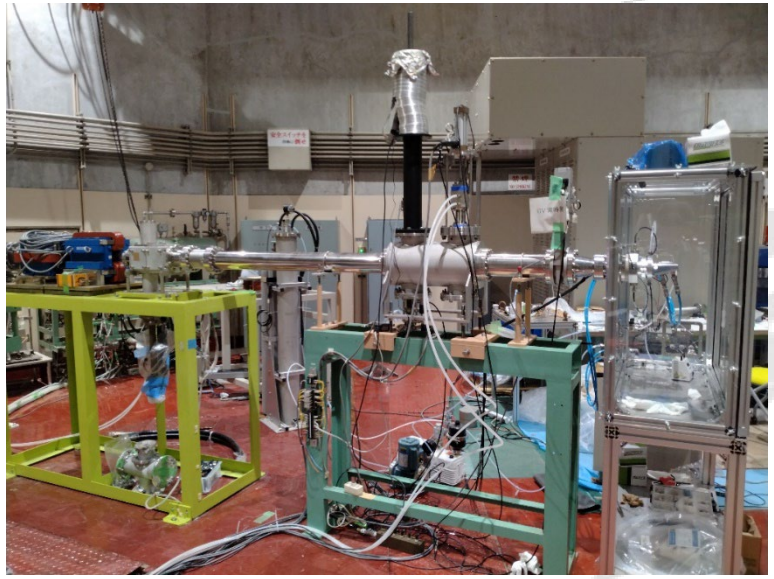
- Demand for At-211 is increasing
- Other facilities, mainly RIBF, backed up the At-211 production and supply during the shutdown period of RCNP
- Increasing supplying capacity is urgent matter of importance



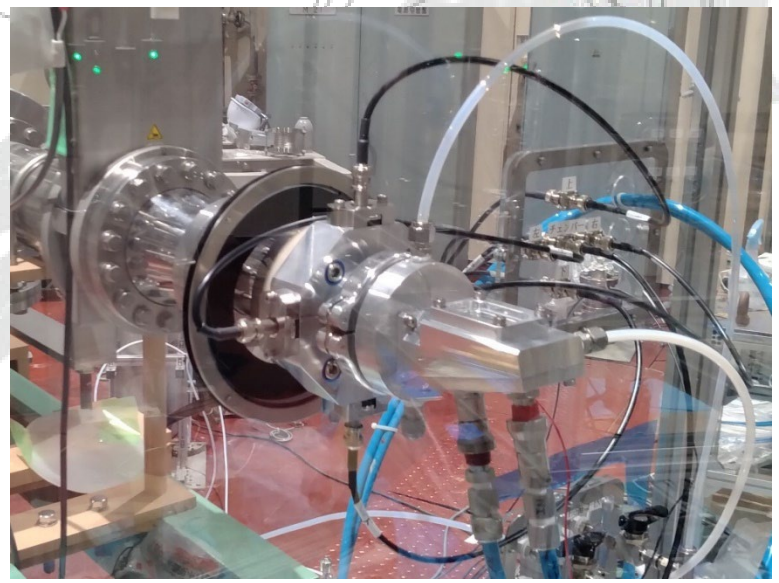
Supply from RCNP was stopped during the shutdown period for the upgrade of the facility and the AVF cyclotron

At-211 production at RCNP

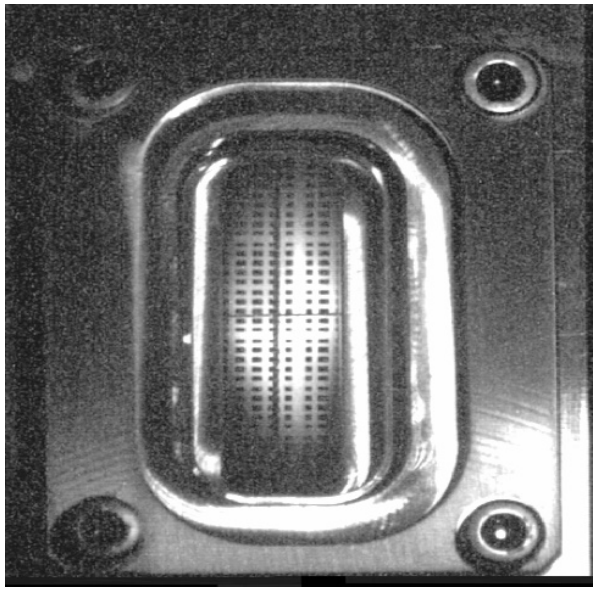
- The upgrade of AVF cyclotron and the beam irradiation system for increasing the beam intensity was completed and the beam commissioning started in FY2022
- A slant target and beam wobbler moderate heat dissipation to accept intense beams
- The current of the $^{4}He^{2+}$ beam reached 8 eμA by June 2023
- **Stable production and supply of At-211 is expected for the clinical test at Osaka University Hospital**



Beam course for RI production



Target station



Beam spot at the target position

Summary

- Six accelerator facilities: RCNP, RIBF, CYRIC, ELPH, QST-QMS, and QST-Takasaki formed “Supply platform for short-lived RI” in order to support the basic research in a various research field using RIs
- We have continued supporting scientific research with RI supply and technical assistance from FY2016
- Significant results to be published are increasing in recent years
- Demand for At-211 is greatly increasing. We attempt to increase our supplying capacity.
- [^{211}At]NaAt (TAH-1005) is one of the most significant results and it is under clinical test at Osaka University Hospital.