Production of astatine-211 for targeted α-particle therapy at RIBF

Nishina Center for Accelerator-Based Science, RIKEN

Hiromitsu Haba

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1. Production of radioisotopes for application studies at RIBF
2. Astatine-211 for targeted α-particle therapy
3. Summary

1. Production of radioisotopes for application studies at RIBF

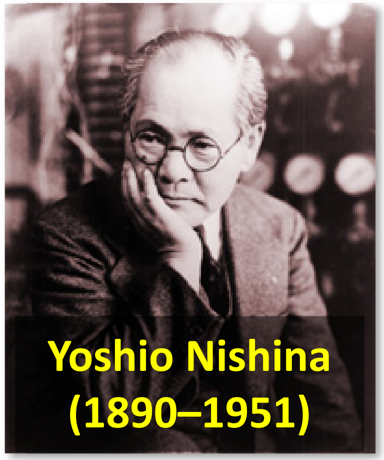
RIKEN accelerators and radioisotope (RI) applications

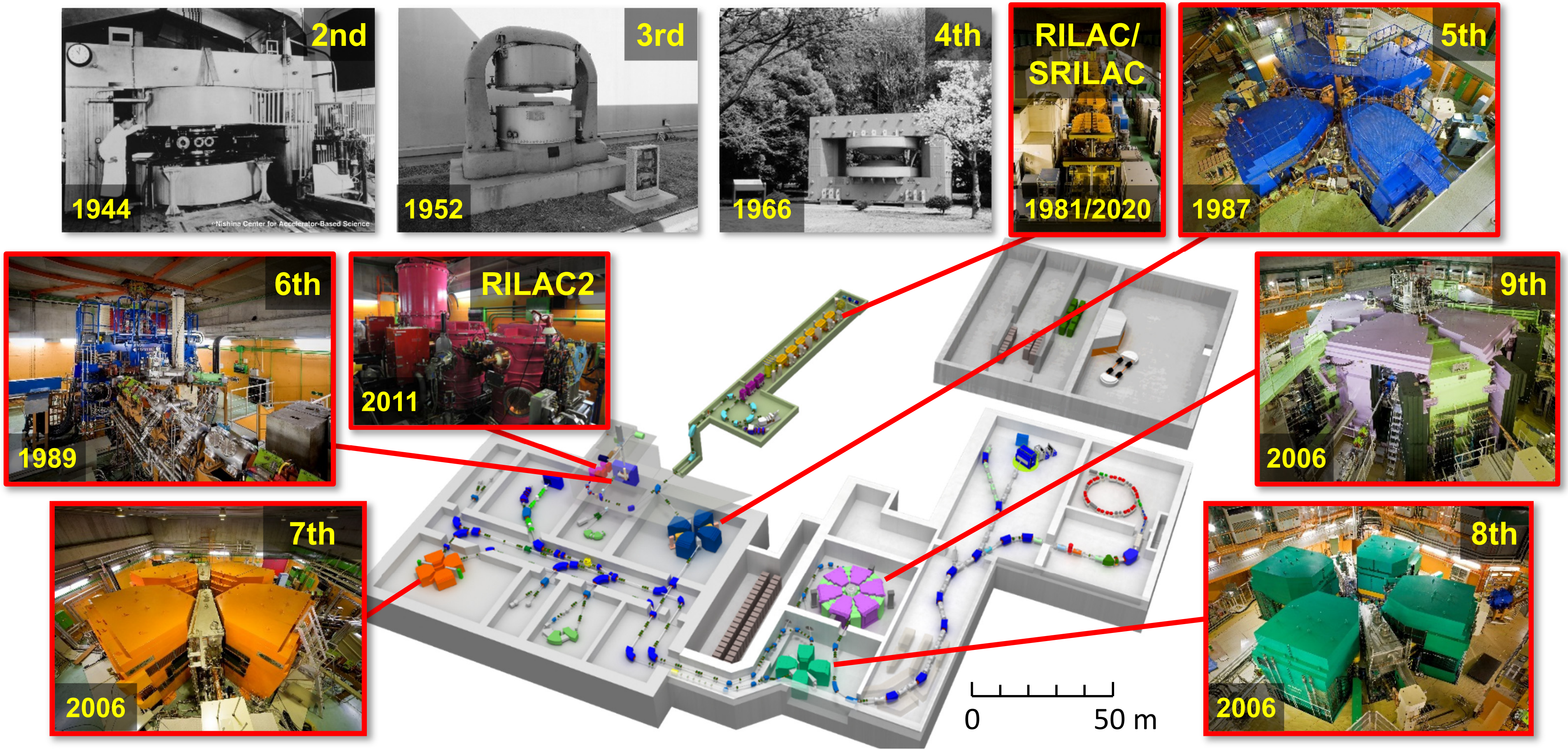
1937 Construction of 1st cyclotron

1938 Application of RIs as tracers for chemistry and biology

...

2006 Construction of 7th – 9th cyclotrons → RIBF





Production of radioisotopes for applications at RIBF

Development of RI production technologies

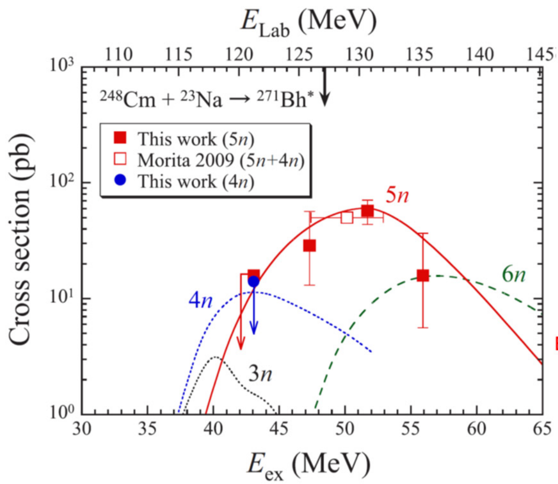
(a) Nuclear reaction

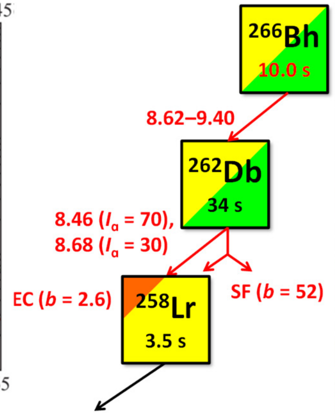
Precision measurements of excitation functions

→ • Effective and quantitative RI production

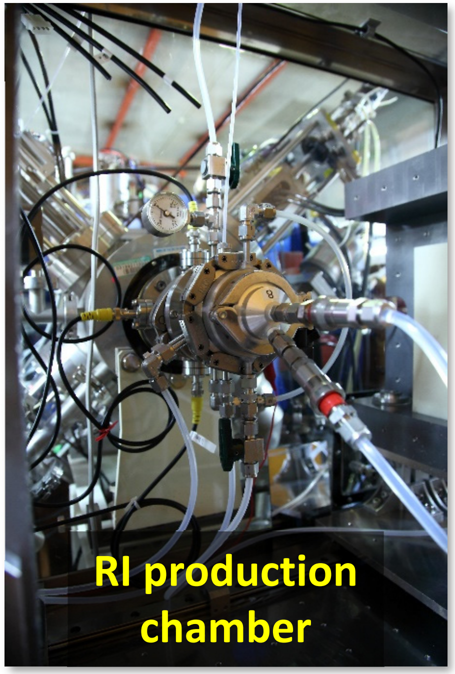
• Reduction of by-product

• Verification of theoretical code





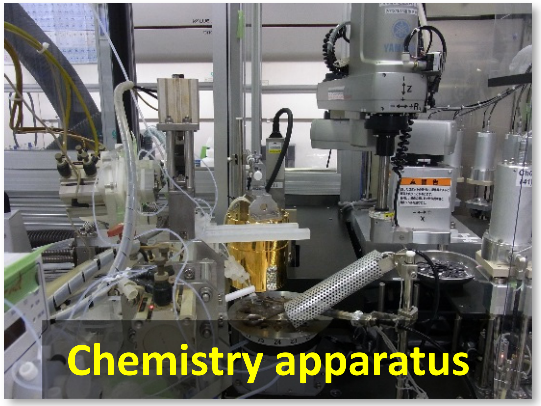
H. Haba et al., Phys. Rev. C **102**, 024625 (2020).



(b) Irradiation

• Irradiation apparatus

• Target (form, cooling, and chemistry)



(c) Chemical separation

• Yield, separation time, and radiation exposure

• Radionuclidic purity

• Specific radioactivity

• Chemical purity

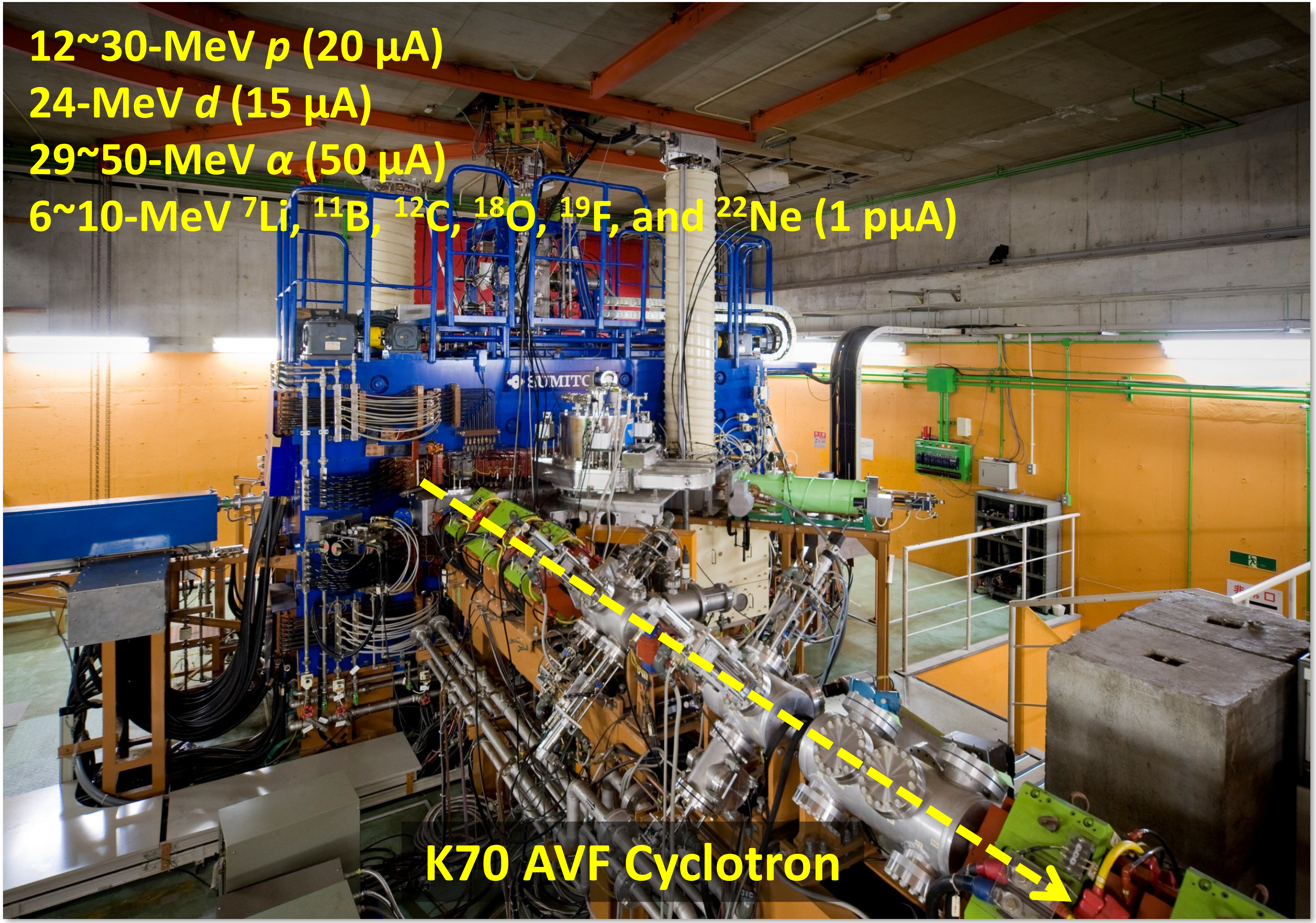
(d) Specification

• γ/α spectrometry

• Chemical analysis with ICP-MS

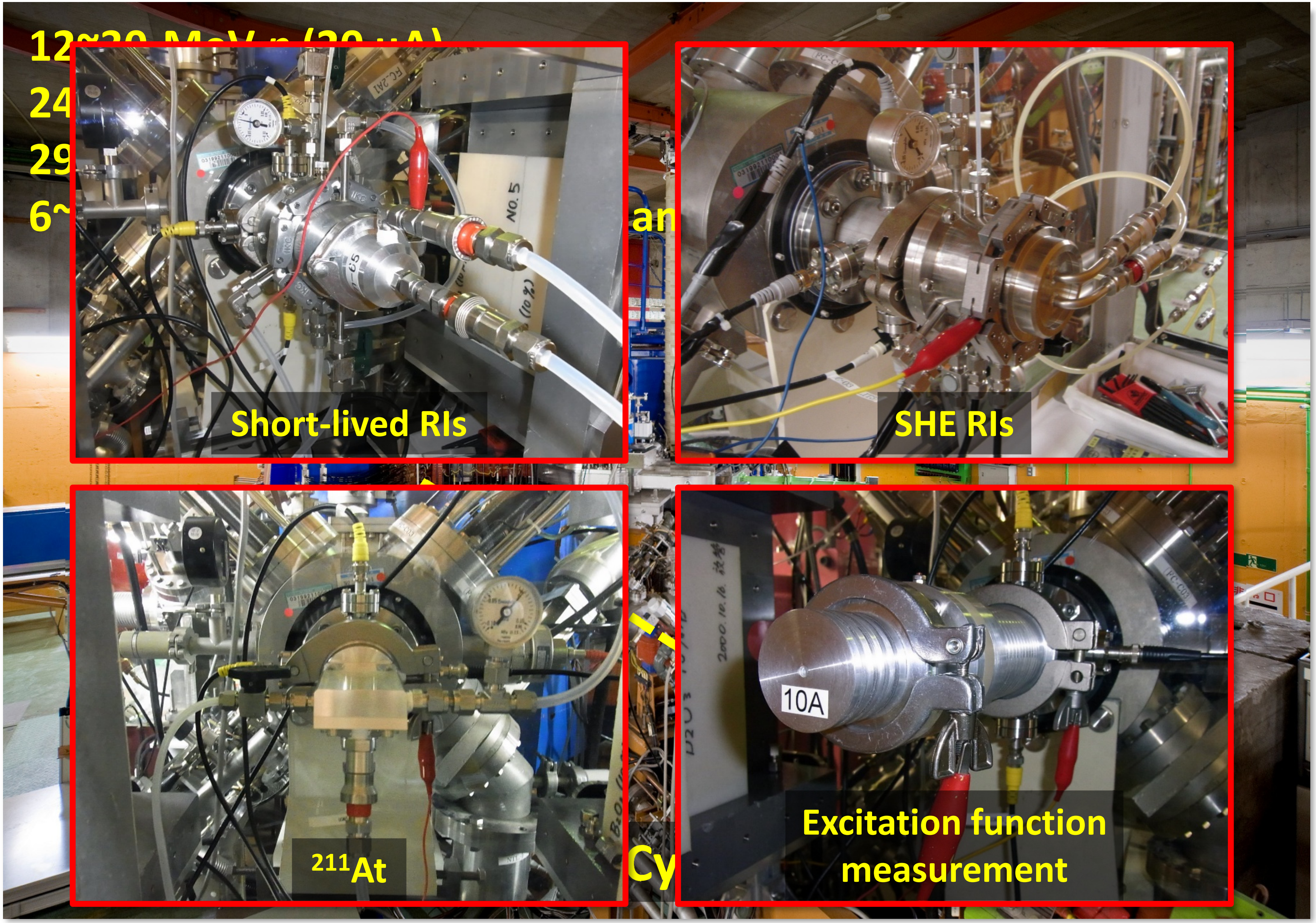
(a) AVF Cyclotron

Production of ^{7}Be (Z = 4) – ^{262}Db (Z = 105)



(a) AVF Cyclotron

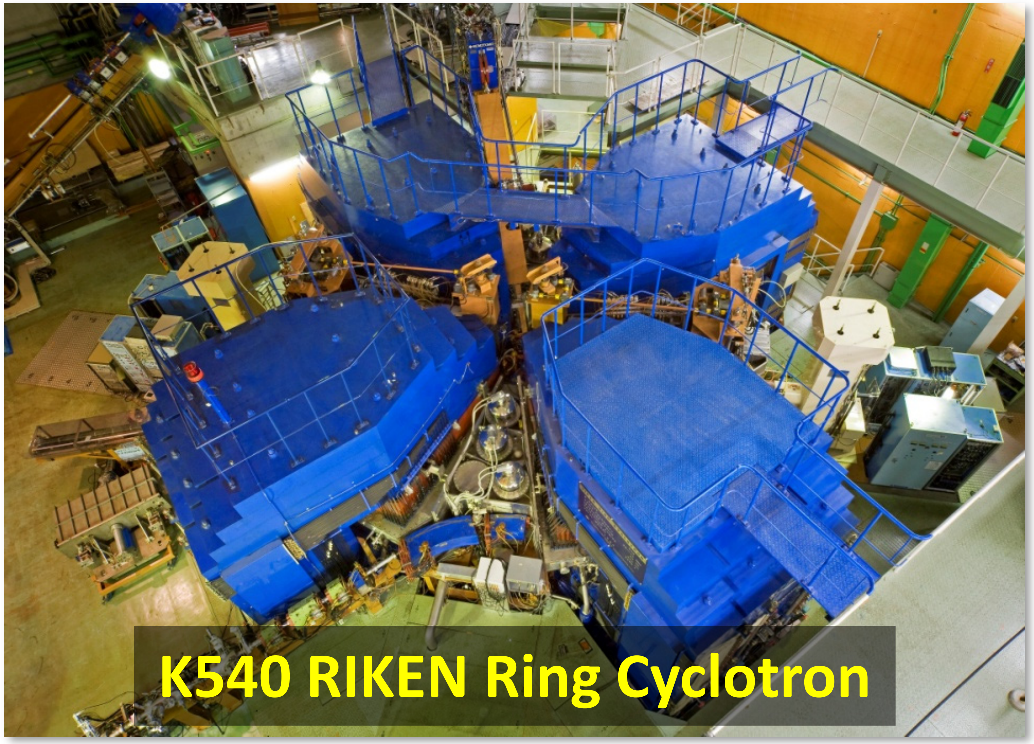
Production of ^{7}Be (Z = 4) – ^{262}Db (Z = 105)

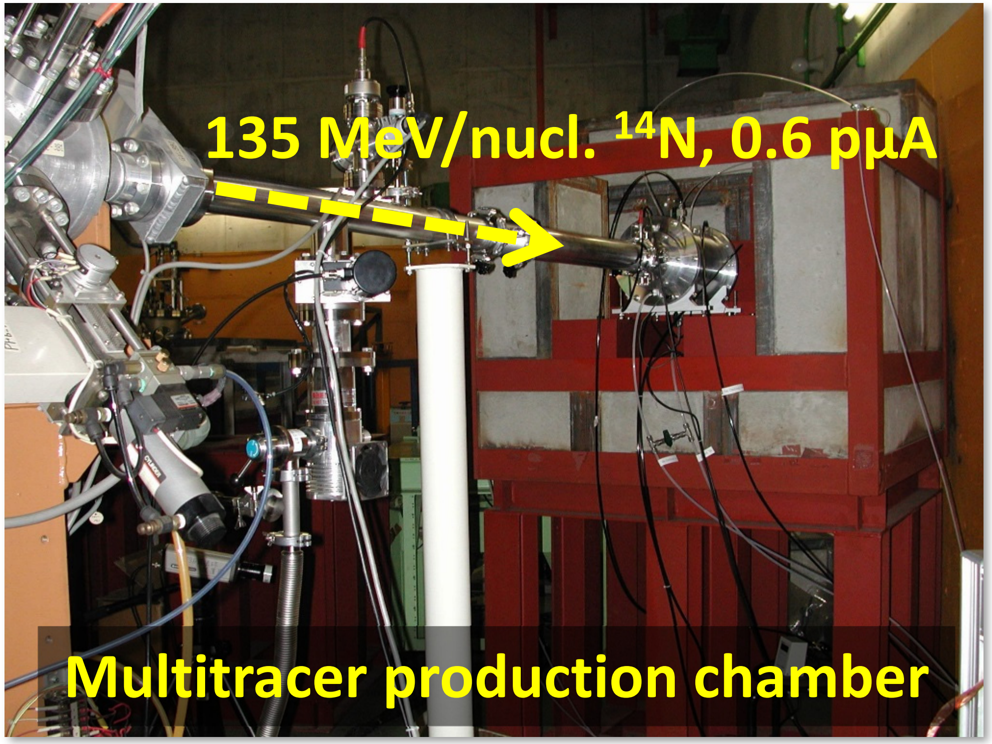


(b) RIKEN Ring Cyclotron (RRC)

Multitracer technology

RIs of a large number of elements are simultaneously produced from targets such as Ti, Ag, and Au irradiated with a 135 MeV/nucl. ^{14}N (or ^{12}C, ^{16}O) beam from RRC [Ambe et al., Chem. Lett. **1991**, 149 (1991).]





H. Haba *et al.*, Radiochim. Acta **93**, 539 (2005).

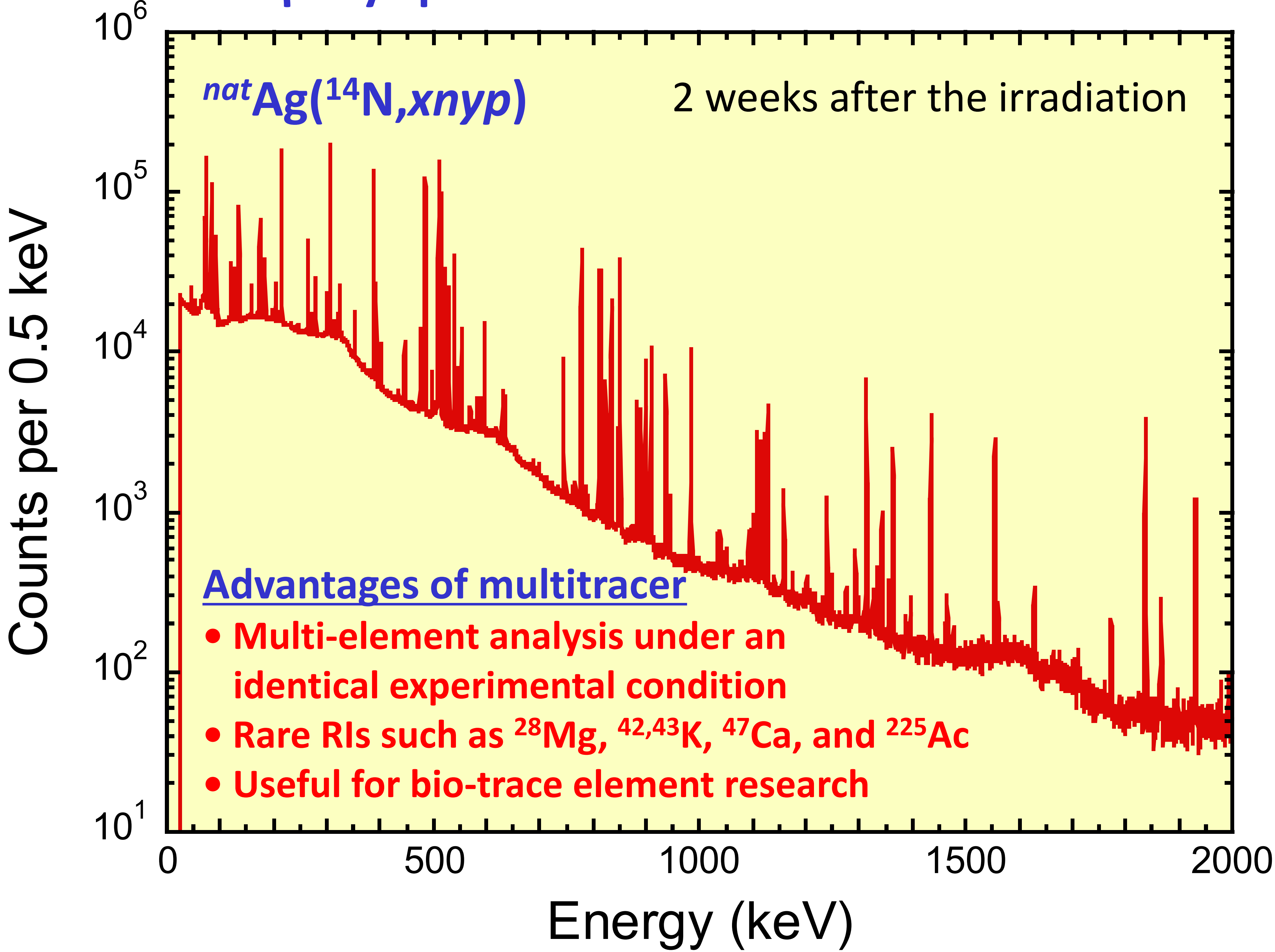
- **Long-lived RIs**

  ^{nat}Ti, ^{nat}Ag, ^{nat}Hf, ^{197}Au, and $^{232}ThO_2$ (1–5 g/cm^2) → Chemical separation

- **Short-lived RIs**

  ^{nat}Cu, ^{nat}Ag, ^{197}Au, ^{nat}Ta, and ^{nat}Pb (1–5 μm x 30) → Gas-jet transport

γ-ray spectrum of the multitracer

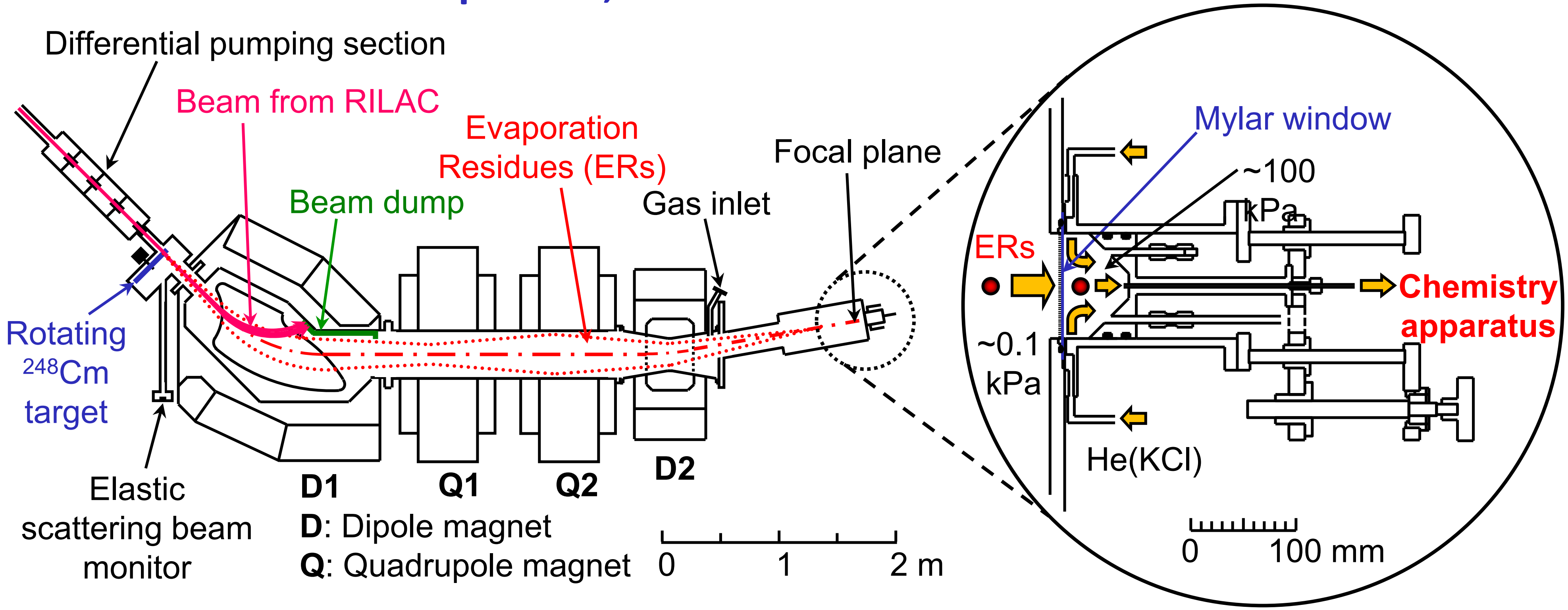


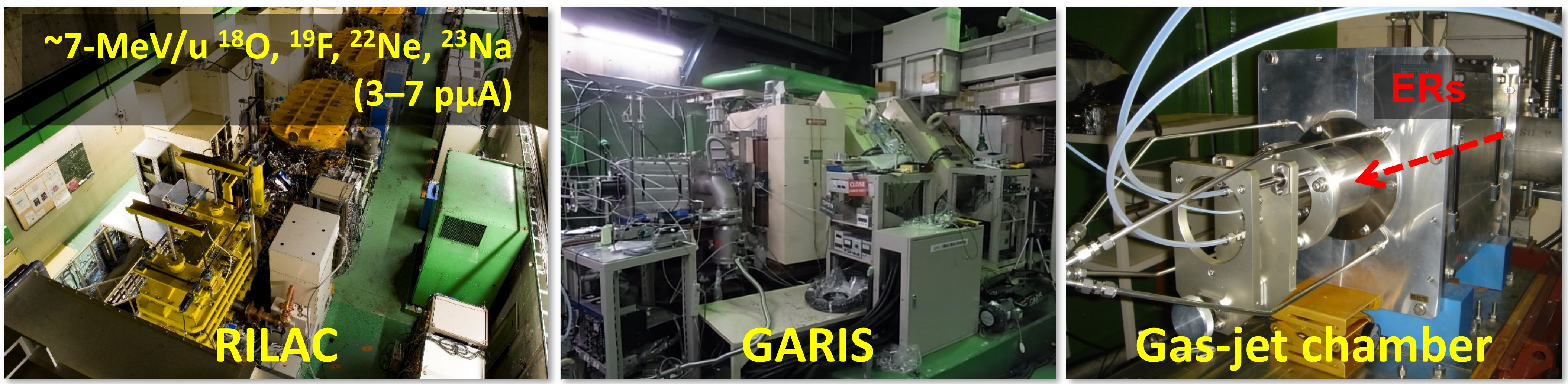
(c) RIKEN Liner Accelerator (RILAC)

Superheavy elements ($Z \geq 104$) for chemistry studies

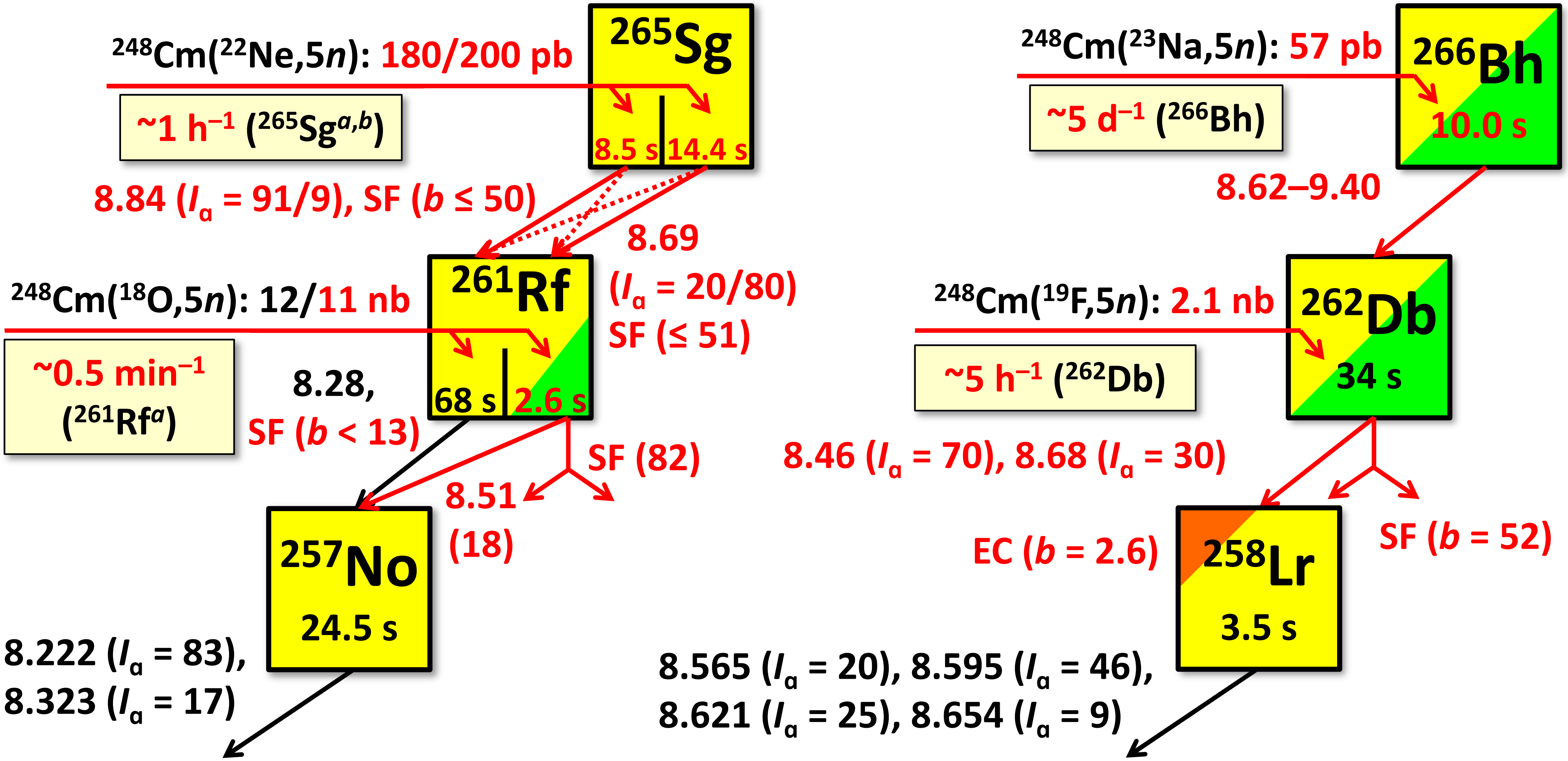
GAs-filled Recoil Ion Separator, GARIS

Gas-jet Transport System





Production and decay studies of ^{261}Rf, ^{262}Db, ^{265}Sg, and ^{266}Bh



H. Haba et al., Chem. Lett. **38**, 426 (2009).
H. Haba et al., Phys. Rev. C **83**, 034602 (2011).
H. Haba et al., Phys. Rev. C **85**, 024611 (2012).
H. Haba et al., Phys. Rev. C **89**, 024618 (2014).
H. Haba et al., EPJ Web Conf. **131**, 07006 (2016).
H. Haba et al., Phys. Rev. C **102**, 024625 (2020).

Pre-separated SHE RIs are ready for chemistry experiments.

RIKEN radioisotopes for application studies

Nuclides	*Z*	*T* 1/2	Accel.	Reactions	Research fields
^{7}Be	4	53.29 d	AVF	^{nat}Li(p,xn) ^{nat}Li(d,xn)	Ind.
^{24}Na	11	14.9590 h	AVF	^{nat}Mg(d,x)	Ind., Med.
^{28}Mg	12	20.91 h	AVF	^{27}Al(α,3p)	Chem.
^{42,43}K	19	12.360 h, 22.3 h	AVF	^{nat,43,44}Ca(d,x)	Ind., Med.
^{44m,g}Sc	21	58.6 h, 3.927 h	AVF	^{nat}Ti(d,x) ^{nat,44}Ca(d,x)	Ind., Med.
^{44}Ti	22	49 y	AVF	^{45}Sc(d,3n)	Ind.
^{48}V	23	15.9735 d	AVF	^{nat}Ti(p,xn)	Pharm. sci., Med.
^{48,51}Cr	24	21.56 h, 27.702 d	AVF	^{nat}Ti(α,xn)	Phys., Chem.
^{48}Cr	24	21.56 h	AVF	^{46}Ti(α,2n)	Ind.
^{52g,54}Mn	25	5.591 d, 312.3 d	AVF	^{nat}Cr(p,xn)	Pharm. sci., Med.
^{56,57,58}Co	27	77.27 d, 271.79 d, 70.82 d	AVF	^{nat}Fe(d,xn)	Med.
^{61}Cu	29	3.333 h	AVF	^{nat}Zn(d,x)	Chem.
^{65}Zn	30	244.26 d	AVF	^{nat}Cu(p,xn) ^{nat}Cu(d,xn)	Phys., Chem., Biol., Med., Pharm. sci., Ind., Environ. sci.
^{66,67}Ga	31	9.49 h, 3.2612 d	AVF	^{nat}Zn(d,xn)	Chem., Ind.
^{67}Cu	29	61.83 h	AVF	^{70}Zn(p,α) ^{70}Zn(d,αn)	Pharm. sci., Med.
^{69m}Zn	30	13.76 h	AVF	^{nat}Zn(d,x)	Chem.
^{74}As	33	17.77 d	AVF	^{nat}Ga(α,x)	Biol.
^{75}Se	34	119.779 d	AVF	^{75}As(p,n) ^{75}As(d,2n) ^{nat}Ge(α,xn)	Biol., Med., Pharm. sci., Environ. sci.
^{85}Sr	38	64.84 d	AVF	^{nat}Rb(p,xn) ^{nat}Rb(d,xn)	Environ. sci., Chem.
^{85g}Zr*	40	7.86 min	AVF/RILAC	^{nat}Ge(^{18}O,xn)	Chem.
^{86,88}Y	39	14.74 h/106.65 d	AVF	^{nat}Sr(p,xn) ^{nat}Sr(d,xn) ^{nat}Rb(α,xn)	Chem., Biol., Med., Pharm. sci., Ind.
^{88,89}Zr	40	83.4 d, 78.41 h	AVF	^{89}Y(p,xn) ^{89}Y(d,xn)	Chem., Ind., Pharm. sci., Med., Environ. sci.
^{89m}Zr*	40	4.18 min	AVF	^{89}Y(p,n) ^{89}Y(d,2n) ^{nat}Sr(α,xn)	Chem.
^{88m,88g}Nb*	41	7.8, 14.5 min	AVF/RILAC	^{nat}Ge(^{19}F,xn)	Chem.
^{90m,90g}Nb*	41	18.81 s, 14.60 h	AVF	^{nat}Zr(p,xn) ^{nat}Zr(d,xn)	Phys., Chem.
^{90}Mo*	42	5.67 h	AVF/RILAC	^{nat}Ge(^{22}Ne,xn)	Chem.
^{92m,95}Nb	41	10.15 d, 34.975 d	AVF	^{nat}Zr(p,xn) ^{nat}Zr(d,xn)	Chem., Environ. sci.
^{92,94}Tc*	43	4.23 min, 293 min	AVF	^{nat}Mo(d,xn)	Chem.
^{93m}Mo*	42	6.85 h	AVF	^{93}Nb(p,n) ^{93}Nb(d,2n) ^{nat}Zr(α,xn)	Chem.
^{93g,94}Tc*	43	2.75 h, 293 min	AVF	^{93}Nb(α,xn)	Chem.
^{95,96}Tc	43	20.0 h, 4.28 d	AVF	^{nat}Mo(d,xn)	Phys.
^{95m}Tc	43	61 d	AVF	^{95}Mo(p,n) ^{nat}Mo(d,xn) ^{93}Nb(α,2n)	Environ. sci., Chem. Chem.
^{99}Mo	42	65.94 h	AVF	^{nat}Zr(α,xn)	Chem.
^{99}Rh	45	16.1 d	AVF	^{99}Ru(p,n)	Chem.
^{109m}Pd*	46	4.696 min	AVF	^{nat}Pd(d,x)	Chem.
^{104m,g}Ag*	47	33.5 min, 69.2 min	AVF	^{nat}Pd(d,xn)	Chem.
^{111}Ag	47	7.45 d	AVF	^{nat}Pd(d,xn)	Chem., Med.
^{109}Cd	48	462.6 d	AVF	^{nat}Ag(p,xn) ^{nat}Ag(d,xn)	Biol., Med., Pharm. sci., Ind., Environ. sci.
^{124}Sb	51	60.20 d	AVF	^{nat}Sn(d,x)	Chem.
^{121m}Te	52	154 d	AVF	^{nat}Sn(α,xn) ^{nat}Sb(d,xn)	Environ. sci.
^{124}I	53	4.1760 d	AVF	^{124}Te(d,2n)	Ind., Pharm. sci., Med.
^{133}Ba	56	10.551 y	AVF	^{133}Cs(d,2n)	Chem.
^{135m}Ba	56	28.7 h	AVF	^{133}Cs(α,x) ^{nat}La(d,x)	Med.
^{135}La	57	19.4 h	AVF	^{nat}Ba(p,x)	Chem.
^{139}Ce	58	137.640 d	AVF	^{nat}La(p,xn) ^{nat}La(d,xn)	Chem.
^{141}Ce	58	32.501 d	AVF	^{nat}Ba(α,x)	Chem., Med.

Nuclides	*Z*	*T* 1/2	Accel.	Reactions	Research fields
^{141m}Nd*	60	62.0 s	AVF	^{141}Pr(d,2n)	Chem.
^{143}Pm	61	265 d	AVF	^{141}Pr(α,x)	Chem.
^{143}Sm*	62	66 s	AVF	^{144}Sm(d,p2n)	Chem.
^{143,144}Eu*	63	2.63 min, 10.2 s	AVF	^{144}Sm(d,xn)	Chem.
^{146}Gd	64	48.27 d	AVF	^{144}Sm(α,2n)	Chem.
^{149}Eu	63	93.1d	AVF	^{nat}Sm(α,xn)	Chem.
^{155}Tb	65	5.32 d	AVF	^{nat}Eu(α,xn)	Med., Ind.
^{162,163}Yb*	70	18.87 min, 11.05 min	AVF	^{nat}Gd(^{12}C,xn)	Phys.
^{163,164}W*	74	2.75 s, 6.0 s	RILAC	^{144}Sm(^{24}Mg,xn)	Chem.
^{165}Er	68	10.36 h	AVF	^{165}Ho(d,2n)	Med.
^{169}Yb	70	32.018 d	AVF	^{169}Tm(d,2n)	Ind.
^{169}Hf*	72	3.24 min	AVF/RILAC	^{nat}Gd(^{18}O,xn)	Chem.
^{170}Ta*	73	6.76 min	AVF/RILAC	^{nat}Gd(^{19}F,xn)	Chem.
^{170}Re*	75	9.2 s	RILAC	^{152}Gd(^{23}Na,5n)	Chem.
^{173}Hf*	72	23.6 h	AVF	^{nat}Yb(α,xn)	Chem.
^{173}W*	74	7.6 min	AVF/RILAC	^{nat}Gd(^{22}Ne,xn)	Chem.
^{174}Re*	75	2.40 min	RILAC	^{nat}Gd(^{23}Na,xn)	Chem.
^{175}Hf	72	70 d	AVF	^{nat}Lu(p,xn) ^{nat}Lu(d,xn)	Chem., Environ. sci.
^{177,178a,179}Ta	73	56.56 h, 2.36 h, 1.82 y	AVF	^{nat}Hf(p,xn) ^{nat}Hf(d,xn)	Chem., Environ. sci.
^{177}W*	74	135 min	AVF	^{nat}Hf(α,xn)	Chem.
^{178a}Ta*	73	2.36 h	AVF	^{nat}Hf(d,xn)	Chem.
^{179m}W*	74	6.40 min	AVF	^{nat}Ta(d,xn)	Chem.
^{180}Re*	75	2.44 min	AVF	^{nat}Ta(α,xn)	Chem.
^{181}W	74	121.2 d	AVF	^{nat}Ta(p,xn) ^{nat}Ta(d,xn)	Chem.
^{181}Re*	75	19.9 h	AVF	^{nat}W(d,xn)	Chem.
^{182}Ta	73	114.43 d	AVF	^{nat}Hf(α,x)	Chem.
^{182a,183,184m,184g}Re	75	12.7 h, 70.0 d, 169 d, 38.0 d	AVF	^{nat}W(d,xn)	Phys., Chem.
^{183}Re	75	70.0 d	AVF	^{nat}Ta(α,xn)	Chem.
^{185}Os	76	93.6 d	AVF	^{nat}Re(p,xn)	Chem.
^{186}Re	75	90.64 h	AVF	^{186}W(p,n) ^{186}W(d,2n)	Med., Ind.
^{188,189,191}Pt	78	10.2 d, 10.87 h, 2.802 d	AVF	^{nat}Os(α,xn) ^{nat}Ir(d,xn)	Med. Phys.
^{195,196}Au	79	186.01 d/6.1669 d	AVF	^{nat}Ir(α,xn)	Med., Ind.
^{203}Pb	82	51.873 h	AVF	^{203}Tl(p,n)	Med.
^{206}Bi	83	6.243 d	AVF	^{nat}Pb(p,xn) ^{nat}Pb(d,xn)	Pharm. sci., Med. Chem.
^{206}Fr*	87	15.9 s	RILAC	^{169}Tm(^{40}Ar,3n)	Phys.
^{209}Fr*	87	50.0 s	RILAC	^{197}Au(^{18}O,6n)	Phys.
^{211}At	85	7.214 h	AVF/RRC	^{209}Bi(α,2n)	Pharm. sci., Med.
^{212}Fr*	87	20.0 min	AVF	^{206,207,208,nat}Pb(^{11}B,x)	Chem.
^{214}Ac*	89	8.2 s	RILAC	^{197}Au(^{22}Ne,5n)	Phys.
^{225}Ac	89	10.0 d	RRC	^{232}Th(^{14}N,xnyp)	Chem., Med.
^{229}Pa	91	1.50 d	AVF	^{232}Th(p,4n)	Chem.
^{230}Pa	91	17.4 d	AVF	^{232}Th(d,4n)	Chem.
^{236}Np	93	1.54×10^{5} y	AVF	^{232}Th(^{7}Li,3n)	Environ. sci.
^{245}Fm*	100	4.2 s	RILAC	^{208}Pb(^{40}Ar,3n)	Phys.
^{255}No*	102	3.1 min	AVF/RILAC AVF	^{238}U(^{22}Ne,5n) ^{248}Cm(^{12}C,5n)	Phys., Chem.
^{255}Lr*	103	22 s	RILAC	^{209}Bi(^{48}Ca,2n)	Phys.
^{257}Lr*	103	0.646 s	AVF	^{248}Cm(^{14}N,5n)	Phys.
^{259}Lr*	103	6.3 s	AVF	^{248}Cm(^{15}N,4n)	Phys.
^{261a,b}Rf*	104	68, 1.9 s	AVF/RILAC	^{248}Cm(^{18}O,5n)	Phys., Chem.
^{262}Db*	105	34 s	AVF/RILAC	^{248}Cm(^{19}F,5n)	Phys., Chem.
^{265a,b}Sg*	106	8.5, 14.4 s	RILAC	^{248}Cm(^{22}Ne,5n)	Phys., Chem.
^{266}Bh*	107	10.0 s	RILAC	^{248}Cm(^{23}Na,5n)	Phys.
Multitracer	<22		RRC	^{nat}Ti(^{14}N,xnyp)	Chem., Biol., Med., Pharm. sci., Ind., Environ. sci.
Multitracer*	<29		RRC	^{nat}Cu(^{14}N,xnyp)	
Multitracer	<47		RRC	^{nat}Ag(^{14}N,xnyp)	
Multitracer	<72		RRC	^{nat}Hf(^{14}N,xnyp)	
Multitracer*	<73		RRC	^{nat}Ta(^{14}N,xnyp)	
Multitracer	<79		RRC	^{197}Au(^{14}N,xnyp)	
Multitracer*	<83		RRC	^{209}Bi(^{14}N,xnyp)	
Multitracer	<90		RRC	^{232}Th(^{14}N,xnyp)	

* RIs produced with the gas-jet system.

20-Jul-23

RIKEN radioisotopes for application studies

Nuclides	Z	$T_{1/2}$	Accel.	Reactions	Research fields
^{7}Be	4	53.29 d	AVF	^{nat}Li(p,xn) ^{nat}Li(d,xn)	Ind.
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^{28}Mg	12	20.91 h	AVF	^{27}Al(α,3p)	Chem.
^{42,43}K	19	12.360 h, 22.3 h	AVF	^{nat,43,44}Ca(d,x)	Ind., Med.
^{44m,g}Sc				^{nat}Ti(d,x)	
^{44}Ti					
^{48}V					
^{48,51}Cr					
^{48}Cr					
^{52g,54}Mn					
^{56,57,58}Co					
^{61}Cu					
^{65}Zn					
^{66,67}Ga					
^{67}Cu					
^{69m}Zn					
^{74}As					
^{75}Se	34	119.779 d	AVF	^{75}As(p,n) ^{75}As(d,2n)	Biol., Med., Pharm. sci., Environ. sci.
^{85}Sr					
^{85g}Zr*					
^{86,88}Y					
^{88,89}Zr					
^{89m}Zr*					
^{88m,88g}Nb*					
^{90m,90g}Nb*					
^{90}Mo*					
$^{…,95}$Nb					
…*					
$^{…,94}$Tc*					
^{95,96}Tc					
^{95m}Tc					
^{99}Mo					
^{99}Rh					
^{109m}Pd*					
^{104m,g}Ag*					
^{111}Ag					
^{109}Cd					
^{124}Sb					
^{121m}Te					
^{124}I					
^{133}Ba					
^{135m}Ba	56	28.7 h	AVF	^{133}Cs(α,x) ^{nat}La(d,x)	Med.
^{135}La	57	19.4 h	AVF	^{nat}Ba(p,x)	Chem.
^{139}Ce	58	137.640 d	AVF	^{nat}La(p,xn) ^{nat}La(d,xn)	Chem.
^{141}Ce	58	32.501 d	AVF	^{nat}Ba(α,x)	Chem., Med.

Nuclides	Z	$T_{1/2}$	Accel.	Reactions	Research fields
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^{143}Pm	61	265 d	AVF	^{141}Pr(α,x)	Chem.
^{143}Sm*	62	66 s	AVF	^{144}Sm(d,p2n)	Chem.
^{143,144}Eu*	63	2.63 min, 10.2 s	AVF	^{144}Sm(d,xn)	Chem.
^{146}Gd	64	48.27 d	AVF	^{144}Sm(α,2n)	Chem.
^{149}Eu	63	93.1d	AVF	^{nat}Sm(α,xn)	Chem.
^{177}W*	74	135 min	AVF	^{nat}Hf(α,xn)	Chem.
^{178a}Ta*	73	2.36 h	AVF	^{nat}Hf(d,xn)	Chem.
Multitracer	<72		RRC	^{nat}Hf(^{14}N,xnyp)	Chem., Biol., Med., Pharm. sci., Ind., Environ. sci.
Multitracer*	<73		RRC	^{nat}Ta(^{14}N,xnyp)	
Multitracer	<79		RRC	^{197}Au(^{14}N,xnyp)	
Multitracer*	<83		RRC	^{209}Bi(^{14}N,xnyp)	
Multitracer	<90		RRC	^{232}Th(^{14}N,xnyp)	

* RIs produced with the gas-jet system.

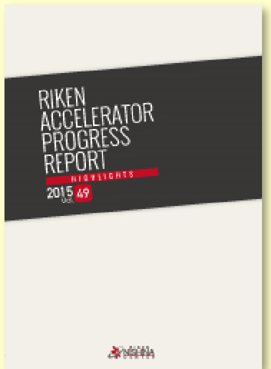
20-Jul-23

AVF: Single radioisotopes (^{7}Be – ^{262}Db)

RRC: Multitracer (^{7}Be – ^{225}Ac)

SRILAC: Superheavy elements (^{85}Zr – ^{266}Bh)

RI application studies in the fields of physics, chemistry, biology, engineering, medicine, pharmaceutical and environmental sciences



RIKEN Accelerator Progress Report (APR)

Sect. “Radiochemistry and Nuclear Chemistry”

http://www.rarf.riken.go.jp/researcher/APR/

Search **RIKEN APR**

Contribution to society through distribution of RIKEN RIs

(i) Material Transfer Agreement (MTA)

公益社団法人 日本アイソトープ協会 Japan Radioisotope Association

FY2007 – FY2022

RIs	Orders	Users	Activity (MBq)
^{65}Zn	110	28	586.8
^{67}Cu	2	1	15
^{85}Sr	19	12	55.8
^{88}Y	16	3	14.13
^{109}Cd	37	16	219.15
Total	184	60	890.88

大阪大学 OSAKA UNIVERSITY 東京大学

FY	RI	Orders	Activity (MBq)
2019	^{211}At	12	2,400
2020	^{211}At	16	3,200
2021	^{211}At	16	4,600
2022	^{211}At	18	6,550
Total		62	16,750

(ii) JSPS Grants-in-Aid for Scientific Research

Supply platform of short-lived radioisotopes

科研費 KAKENHI

FY2016 – FY2022 from RIBF

RIs	Orders	Users	Activity (MBq)
^{7}Be	1	1	0.45
^{28}Mg	3	3	4
^{44m}Sc	7	4	30
^{67}Cu	5	4	230
^{86}Y	2	1	5
^{88}Zr	17	13	25
^{95}Nb	12	8	20
^{111}Ag	5	3	2.72
^{121m}Te	5	4	10
^{124}Sb	2	2	4
^{141}Ce	5	2	1.002
^{175}Hf	12	9	16
^{179}Ta	7	6	7.5
^{211}At	107	26	6,251
Total	190	86	6,606.7

RIKEN radioisotopes for application studies

Nuclides	Z	$T_{1/2}$	Accel.	Reactions	Research fields
^{7}Be	4	53.29 d	AVF	^{nat}Li(p,xn) ^{nat}Li(d,xn)	Ind.
^{24}Na	11	14.9590 h	AVF	^{nat}Mg(d,x)	Ind., Med.
^{28}Mg	12	20.91 h	AVF	^{27}Al(α,3p)	Chem.
^{42,43}K	19	12.360 h, 22.3 h	AVF	^{nat,43,44}Ca(d,x)	Ind., Med.
^{44m,g}Sc	21	58.6 h, 3.927 h	AVF	^{nat}Ti(d,x) ^{nat,44}Ca(d,x)	Ind., Med.
^{44}Ti	22	49 y	AVF	^{45}Sc(d,3n)	Ind.
^{48}V	23	15.9735 d	AVF	^{nat}Ti(p,xn)	Pharm. sci., Med.
^{48,51}Cr	24	21.56 h, 27.702 d	AVF	^{nat}Ti(α,xn)	Phys., Chem.
^{48}Cr	24	21.56 h	AVF	^{46}Ti(α,2n)	Ind.
^{52g,54}Mn	25	5.591 d, 312.3 d	AVF	^{nat}Cr(p,xn)	Pharm. sci., Med.
^{56,57,58}Co	27	77.27 d, 271.79 d, 70.82 d	AVF	^{nat}Fe(d,xn)	Med.
^{61}Cu	29	3.333 h	AVF	^{nat}Zn(d,x)	Chem.
^{65}Zn	30	244.26 d	AVF	^{nat}Cu(p,xn) ^{nat}Cu(d,xn)	Phys., Chem., Biol., Med., Pharm. sci., Ind., Environ. sci.
^{66,67}Ga	31	9.49 h, 3.2612 d	AVF	^{nat}Zn(d,xn)	Chem., Ind.
^{67}Cu	29	61.83 h	AVF	^{70}Zn(p,α) ^{70}Zn(d,αn)	Pharm. sci., Med.
^{69m}Zn	30	13.76 h	AVF	^{nat}Zn(d,x)	Chem.
^{74}As	33	17.77 d	AVF	^{nat}Ga(α,x)	Biol.
^{75}Se	34	119.779 d	AVF	^{75}As(p,n) ^{75}As(d,2n) ^{nat}Ge(α,xn)	Biol., Med., Pharm. sci., Environ. sci.
^{85}Sr	38	64.84 d	AVF	^{nat}Rb(p,xn) ^{nat}Rb(d,xn)	Environ. sci., Chem.
^{85g}Zr*	40	7.86 min	AVF/RILAC	^{nat}Ge(^{18}O,xn)	Chem.
^{86,88}Y	39	14.74 h/106.65 d	AVF	^{nat}Sr(p,xn) ^{nat}Sr(d,xn) ^{nat}Rb(α,xn)	Chem., Biol., Med., Pharm. sci., Ind.
^{88,89}Zr	40	83.4 d, 78.41 h	AVF	^{89}Y(p,xn) ^{89}Y(d,xn)	Chem., Ind., Pharm. sci., Med., Environ. sci.
^{89m}Zr*	40	4.18 min	AVF	^{89}Y(p,n) ^{89}Y(d,2n) ^{nat}Sr(α,xn)	Chem.
^{88m,89g}Nb*	41	7.8, 14.5 min	AVF/RILAC	^{nat}Ge(^{19}F,xn)	Chem.
^{90m,90g}Nb*	41	18.81 s, 14.60 h	AVF	^{nat}Zr(p,xn) ^{nat}Zr(d,xn)	Phys., Chem.
^{90}Mo*	42	5.67 h	AVF/RILAC	^{nat}Ge(^{22}Ne,xn)	Chem.
^{92m,95}Nb	41	10.15 d, 34.975 d	AVF	^{nat}Zr(p,xn) ^{nat}Zr(d,xn)	Chem., Environ. sci.
^{92,94}Tc*	43	4.23 min, 293 min	AVF	^{nat}Mo(d,xn)	Chem.
^{93m}Mo*	42	6.85 h	AVF	^{93}Nb(p,n) ^{93}Nb(d,2n) ^{nat}Zr(α,xn)	Chem.
^{93g,94}Tc*	43	2.75 h, 293 min	AVF	^{93}Nb(α,xn)	Chem.
^{95,96}Tc	43	20.0 h, 4.28 d	AVF	^{nat}Mo(d,xn)	Phys.
^{95m}Tc	43	61 d	AVF	^{95}Mo(p,n) ^{nat}Mo(d,xn) ^{93}Nb(α,2n)	Environ. sci., Chem. Chem.
^{99}Mo	42	65.94 h	AVF	^{nat}Zr(α,xn)	Chem.
^{99}Rh	45	16.1 d	AVF	^{99}Ru(p,n)	Chem.
^{109m}Pd*	46	4.696 min	AVF	^{nat}Pd(d,x)	Chem.
^{104m,g}Ag*	47	33.5 min, 69.2 min	AVF	^{nat}Pd(d,xn)	Chem.
^{111}Ag	47	7.45 d	AVF	^{nat}Pd(d,xn)	Chem., Med.
^{109}Cd	48	462.6 d	AVF	^{nat}Ag(p,xn) ^{nat}Ag(d,xn)	Biol., Med., Pharm. sci., Ind., Environ. sci.
^{124}Sb	51	60.20 d	AVF	^{nat}Sn(d,x)	Chem.
^{121m}Te	52	154 d	AVF	^{nat}Sn(α,xn) ^{nat}Sb(d,xn)	Environ. sci.
^{124}I	53	4.1760 d	AVF	^{124}Te(d,2n)	Ind., Pharm. sci., Med.
^{133}Ba	56	10.551 y	AVF	^{133}Cs(d,2n)	Chem.
^{135m}Ba	56	28.7 h	AVF	^{133}Cs(α,x) ^{nat}La(d,x)	Med.
^{135}La	57	19.4 h	AVF	^{nat}Ba(p,x)	Chem.
^{139}Ce	58	137.640 d	AVF	^{nat}La(p,xn) ^{nat}La(d,xn)	Chem.
^{141}Ce	58	32.501 d	AVF	^{nat}Ba(α,x)	Chem., Med.

Nuclides	Z	$T_{1/2}$	Accel.	Reactions	Research fields
^{141m}Nd*	60	62.0 s	AVF	^{141}Pr(d,2n)	Chem.
^{143}Pm	61	265 d	AVF	^{141}Pr(α,x)	Chem.
^{143}Sm*	62	66 s	AVF	^{144}Sm(d,p2n)	Chem.
^{143,144}Eu*	63	2.63 min, 10.2 s	AVF	^{144}Sm(d,xn)	Chem.
^{146}Gd	64	48.27 d	AVF	^{144}Sm(α,2n)	Chem.
^{149}Eu	63	93.1d	AVF	^{nat}Sm(α,xn)	Chem.
^{155}Tb	65	5.32 d	AVF	^{nat}Eu(α,xn)	Med., Ind.
^{162,163}Yb*	70	18.87 min, 11.05 min	AVF	^{nat}Gd(^{12}C,xn)	Phys.
^{163,164}W*	74	2.75 s, 6.0 s	RILAC	^{144}Sm(^{24}Mg,xn)	Chem.
^{165}Er	68	10.36 h	AVF	^{165}Ho(d,2n)	Med.
^{169}Yb	70	32.018 d	AVF	^{169}Tm(d,2n)	Ind.
^{169}Hf*	72	3.24 min	AVF/RILAC	^{nat}Gd(^{18}O,xn)	Chem.
^{170}Ta*	73	6.76 min	AVF/RILAC	^{nat}Gd(^{19}F,xn)	Chem.
^{170}Re*	75	9.2 s	RILAC	^{152}Gd(^{23}Na,5n)	Chem.
^{173}Hf*	72	23.6 h	AVF	^{nat}Yb(α,xn)	Chem.
^{173}W*	74	7.6 min	AVF/RILAC	^{nat}Gd(^{22}Ne,xn)	Chem.
^{174}Re*	75	2.40 min	RILAC	^{nat}Gd(^{23}Na,xn)	Chem.
^{175}Hf	72	70 d	AVF	^{nat}Lu(p,xn) ^{nat}Lu(d,xn)	Chem., Environ. sci.
^{177,178a,179}Ta	73	56.56 h, 2.36 h, 1.82 y	AVF	^{nat}Hf(p,xn) ^{nat}Hf(d,xn)	Chem., Environ. sci.
^{177}W*	74	135 min	AVF	^{nat}Hf(α,xn)	Chem.
^{178a}Ta*	73	2.36 h	AVF	^{nat}Hf(d,xn)	Chem.
^{179m}W*	74	6.40 min	AVF	^{nat}Ta(d,xn)	Chem.
^{180}Re*	75	2.44 min	AVF	^{nat}Ta(α,xn)	Chem.
^{181}W	74	121.2 d	AVF	^{nat}Ta(p,xn) ^{nat}Ta(d,xn)	Chem.
^{181}Re*	75	19.9 h	AVF	^{nat}W(d,xn)	Chem.
^{182}Ta	73	114.43 d	AVF	^{nat}Hf(α,x)	Chem.
^{182a,183,184m,184g}Re	75	12.7 h, 70.0 d, 169 d, 38.0 d	AVF	^{nat}W(d,xn)	Phys., Chem.
^{183}Re	75	70.0 d	AVF	^{nat}Ta(α,xn)	Chem.
^{185}Os	76	93.6 d	AVF	^{nat}Re(p,xn)	Chem.
^{186}Re	75	90.64 h	AVF	^{186}W(p,n) ^{186}W(d,2n)	Med., Ind.
^{188,189,191}Pt	78	10.2 d, 10.87 h, 2.802 d	AVF	^{nat}Os(α,xn) ^{nat}Ir(d,xn)	Med. Phys.
^{195,196}Au	79	186.01 d/6.1669 d	AVF	^{nat}Ir(α,xn)	Med., Ind.
^{203}Pb	82	51.873 h	AVF	^{203}Tl(p,n)	Med.
^{206}Bi	83	6.243 d	AVF	^{nat}Pb(p,xn) ^{nat}Pb(d,xn)	Pharm. sci., Med. Chem.
[illegible]Fr	87	15.9 s	RILAC	^{169}Tm(^{40}Ar,3n)	Phys.
^{209}Fr*	87	[illegible]	RILAC	^{197}Au(^{18}O,6n)	Phys.
^{211}At	85	[illegible]	AVF/RRC	^{209}Bi(α,2n)	Pharm. sci., Med.
^{212}Fr*	87	20.0 min	AVF	^{206,207,208,nat}Pb(^{11}B,x)	Chem.
^{214}Ac*	89	8.2 s	RILAC	^{197}Au(^{22}Ne,5n)	Phys.
^{225}Ac	89	10.0 d	RRC	^{232}Th(^{14}N,xnyp)	Chem., Med.
^{229}Pa	91	1.50 d	AVF	^{232}Th(p,4n)	Chem.
^{230}Pa	91	17.4 d	AVF	^{232}Th(d,4n)	Chem.
^{236}Np	93	1.54×10^{5} y	AVF	^{232}Th(^{7}Li,3n)	Environ. sci.
^{245}Fm*	100	4.2 s	RILAC	^{208}Pb(^{40}Ar,3n)	Phys.
^{255}No*	102	3.1 min	AVF/RILAC AVF	^{238}U(^{22}Ne,5n) ^{248}Cm(^{12}C,5n)	Phys., Chem.
^{255}Lr*	103	22 s	RILAC	^{209}Bi(^{48}Ca,2n)	Phys.
^{257}Lr*	103	0.646 s	AVF	^{248}Cm(^{14}N,5n)	Phys.
^{259}Lr*	103	6.3 s	AVF	^{248}Cm(^{15}N,4n)	Phys.
^{261a,b}Rf*	104	68, 1.9 s	AVF/RILAC	^{248}Cm(^{18}O,5n)	Phys., Chem.
^{262}Db*	105	34 s	AVF/RILAC	^{248}Cm(^{19}F,5n)	Phys., Chem.
^{265a,b}Sg*	106	8.5, 14.4 s	RILAC	^{248}Cm(^{22}Ne,5n)	Phys., Chem.
^{266}Bh*	107	10.0 s	RILAC	^{248}Cm(^{23}Na,5n)	Phys.
Multitracer	<22		RRC	^{nat}Ti(^{14}N,xnyp)	Chem., Biol., Med., Pharm. sci., Ind., Environ. sci.
Multitracer*	<29		RRC	^{nat}Cu(^{14}N,xnyp)	
Multitracer	<47		RRC	^{nat}Ag(^{14}N,xnyp)	
Multitracer	<72		RRC	^{nat}Hf(^{14}N,xnyp)	
Multitracer*	<73		RRC	^{nat}Ta(^{14}N,xnyp)	
Multitracer	<79		RRC	^{197}Au(^{14}N,xnyp)	
Multitracer*	<83		RRC	^{209}Bi(^{14}N,xnyp)	
Multitracer	<90		RRC	^{232}Th(^{14}N,xnyp)	

211 At

* RIs produced with the gas-jet system.

20-Jul-23

2. Astatine-211 for targeted α-particle therapy

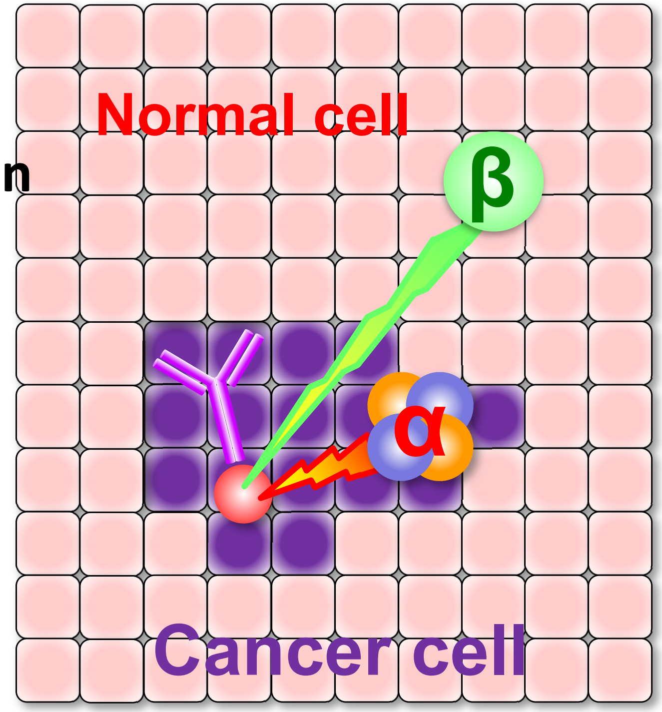
Astatine-211

Promising therapeutic RI for disseminated cancer, blood cancer, micro-metastatic cancer, …

- **Shorter range of α particle in tissue and higher LET than those of β particle**

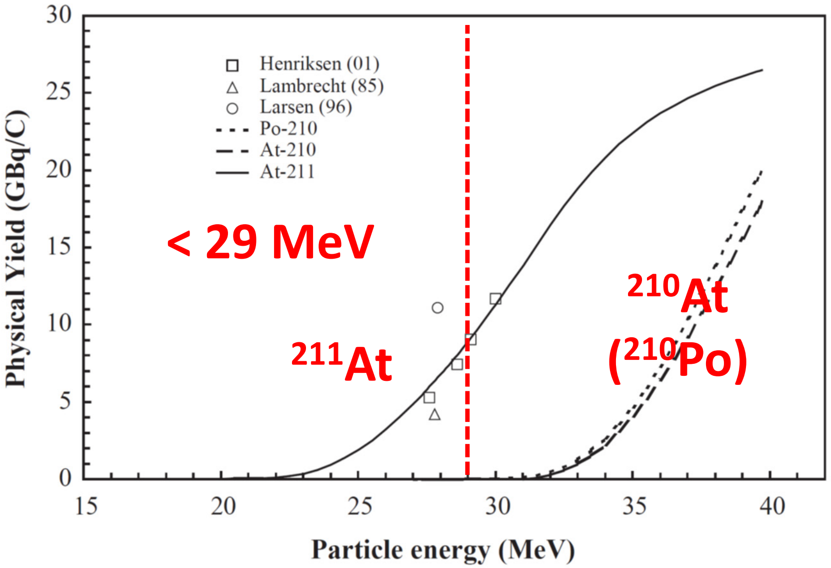
Particle	Energy (MeV)	Range in tissue (μm)	LET (keV/μm)
α	5–9	40–100	80
β	0.05–2.3	50–12000	0.2

K. Washiyama, Drug Delivery System **35**, 102 (2020).

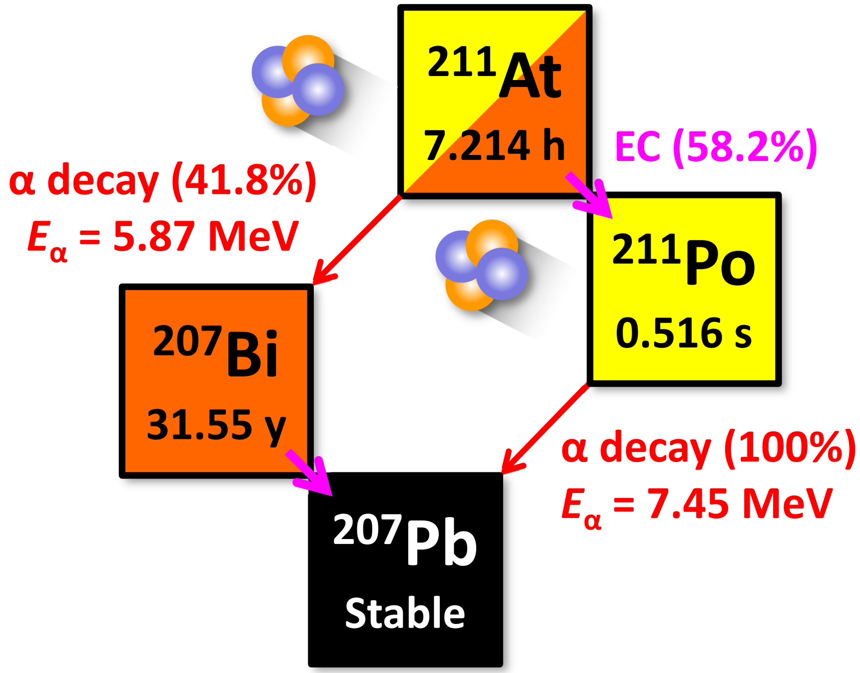


- **High cytotoxicity and small influence for normal cell**

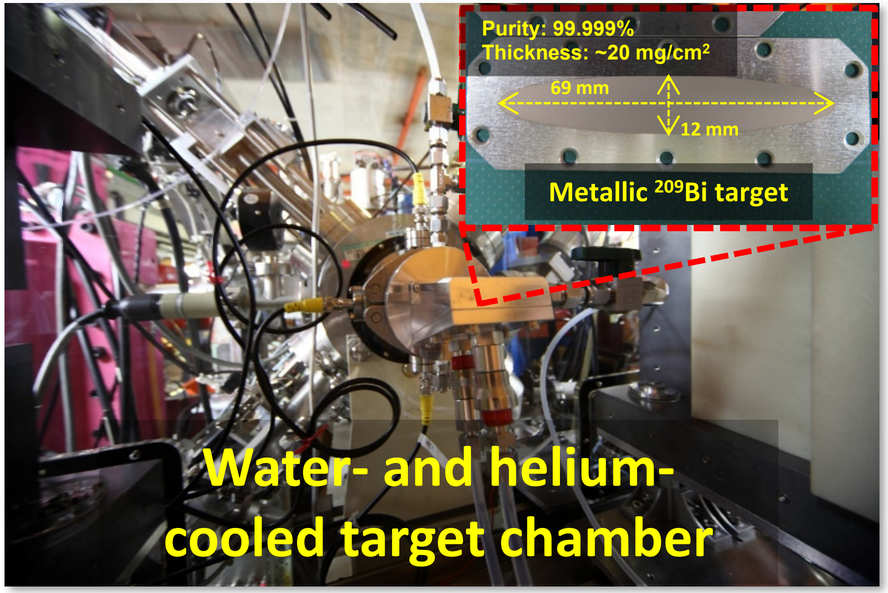
$^{209}Bi(^{4}He,2n)^{211}At$

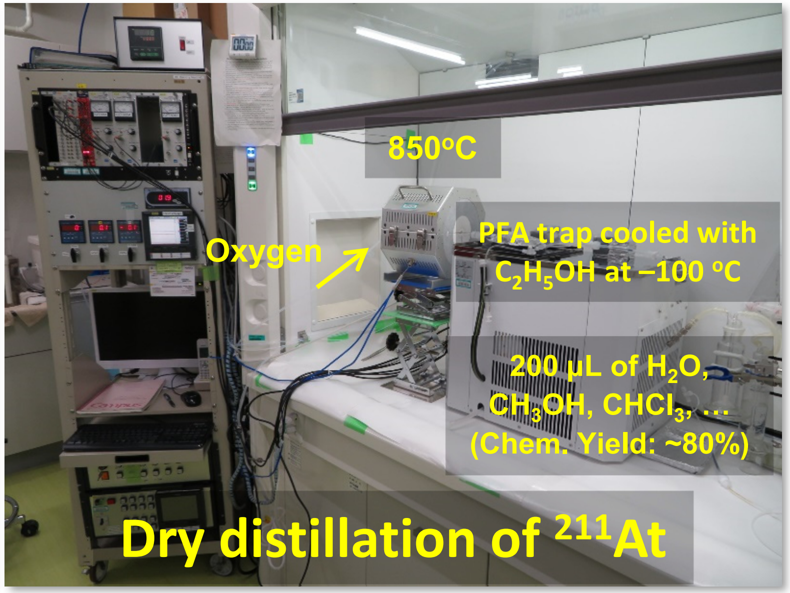


Hermanne et al., Appl. Radiat. Isot. **63** (2005) 1.



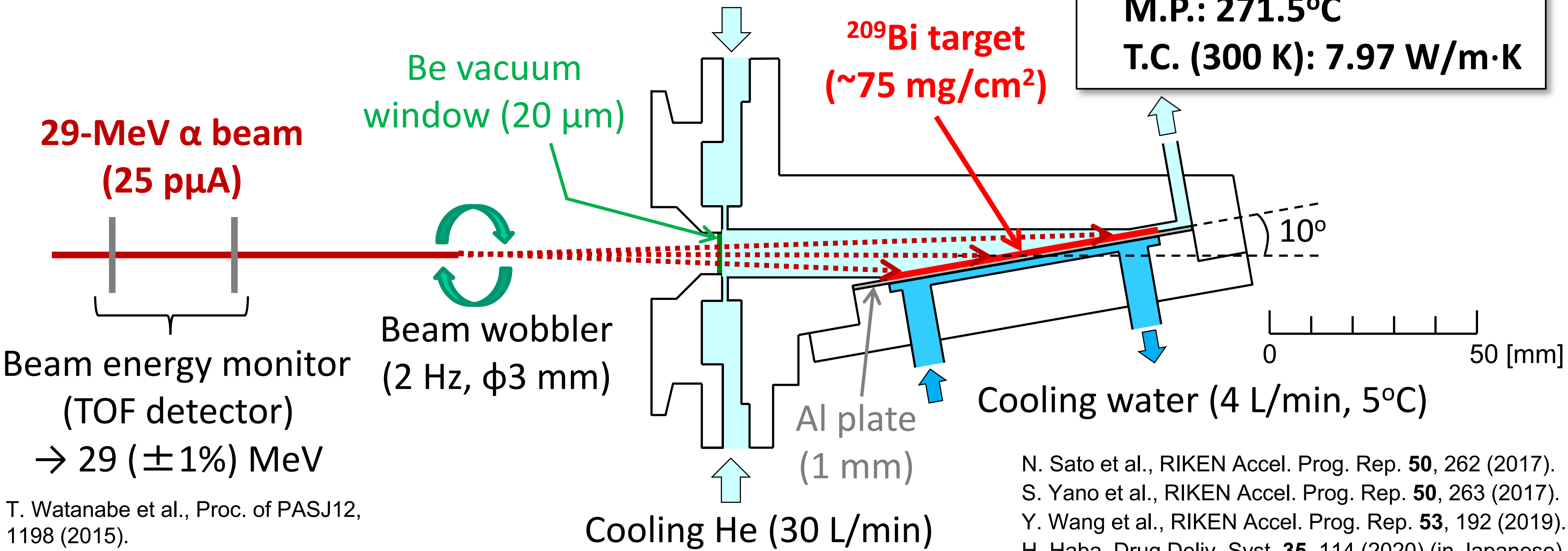
Development of production technology of ^{211}At at AVF





25 pμA × 1 h → 1.2 GBq of ^{211}At (EOB)

Metallic Bi
M.P.: 271.5°C
T.C. (300 K): 7.97 W/m·K



T. Watanabe et al., Proc. of PASJ12, 1198 (2015).

N. Sato et al., RIKEN Accel. Prog. Rep. **50**, 262 (2017).
S. Yano et al., RIKEN Accel. Prog. Rep. **50**, 263 (2017).
Y. Wang et al., RIKEN Accel. Prog. Rep. **53**, 192 (2019).
H. Haba, Drug Deliv. Syst. **35**, 114 (2020) (in Japanese).

RIKEN RI platform for α-particle therapy

Distribution of ^{211}At (2016–)

21 groups (FY2023, increasing)

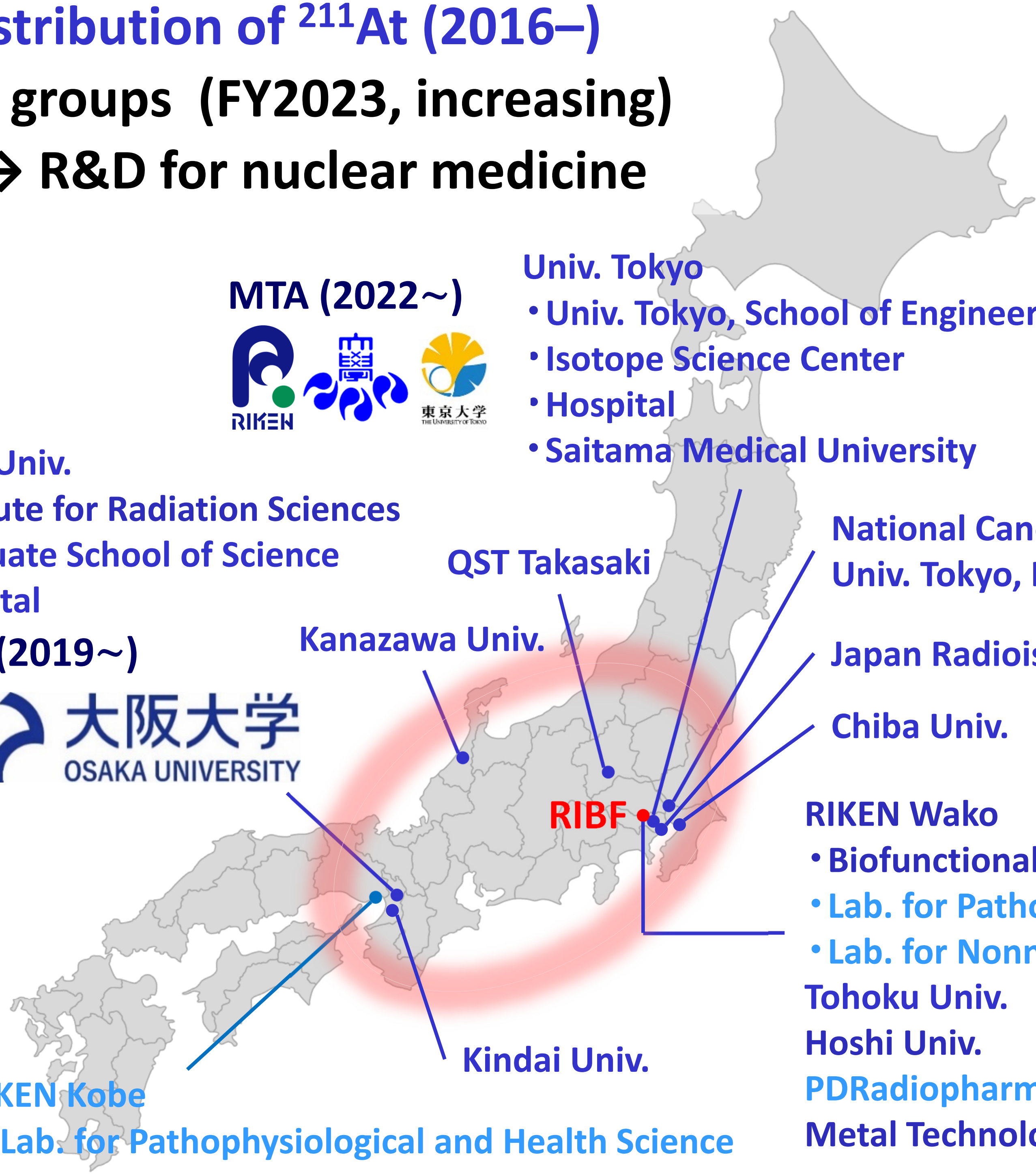
→ R&D for nuclear medicine

平成28年度「新学術領域研究（研究領域提案型）
『学術研究支援基盤形成』」リソース支援プログラム
短寿命RI
供給プラットフォーム

JSPS Grants-in-Aid for Scientific Research
Supply platform of short-lived radioisotopes
(2016~)

P-PROMOTE
AMED 次世代がん医療加速化研究事業

Project for Promotion of Cancer Research and Therapeutic Evolution
(2023~)



MTA (2022~)

Univ. Tokyo
- Univ. Tokyo, School of Engineering
- Isotope Science Center
- Hospital
- Saitama Medical University

Osaka Univ.
- Institute for Radiation Sciences
- Graduate School of Science
- Hospital

MTA (2019~)

大阪大学 OSAKA UNIVERSITY

QST Takasaki

Kanazawa Univ.

National Cancer Center Japan
Univ. Tokyo, Kavli IPMU

Japan Radioisotope Association

Chiba Univ.

RIKEN Wako
- Biofunctional Synthetic Chemistry Lab.
- Lab. for Pathophysiological and Health Science
- Lab. for Nonnatural Amino Acid Technology

Tohoku Univ.
Hoshi Univ.
PDRadiopharma Inc.
Metal Technology Co. Ltd.

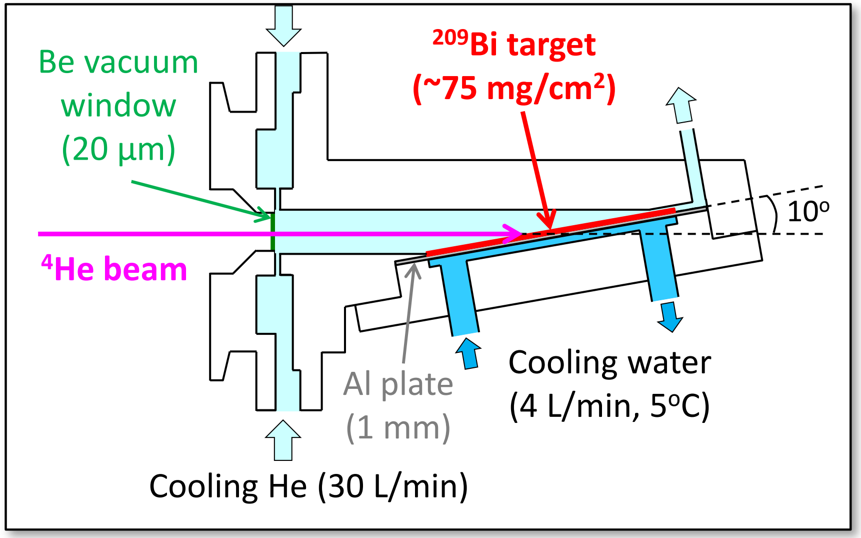
Kindai Univ.

RIKEN Kobe
- Lab. for Pathophysiological and Health Science

^{211}At production challenges

Rapidly increasing demand of ^{211}At

Increase of beam intensity to increase production yield: 1.2 GBq/h (25 pμA) →



Metallic Bi

Low melting points: 271.5°C

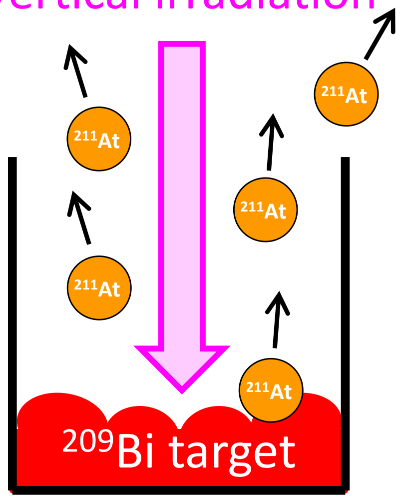
Low thermal conductivity (300 K): 7.97 W/m·K

→ The Bi target melts due to heat and the amount of ^{211}At produced is not proportional to the beam intensity at > 25 pμA.

Vertical irradiation of the Bi target ?

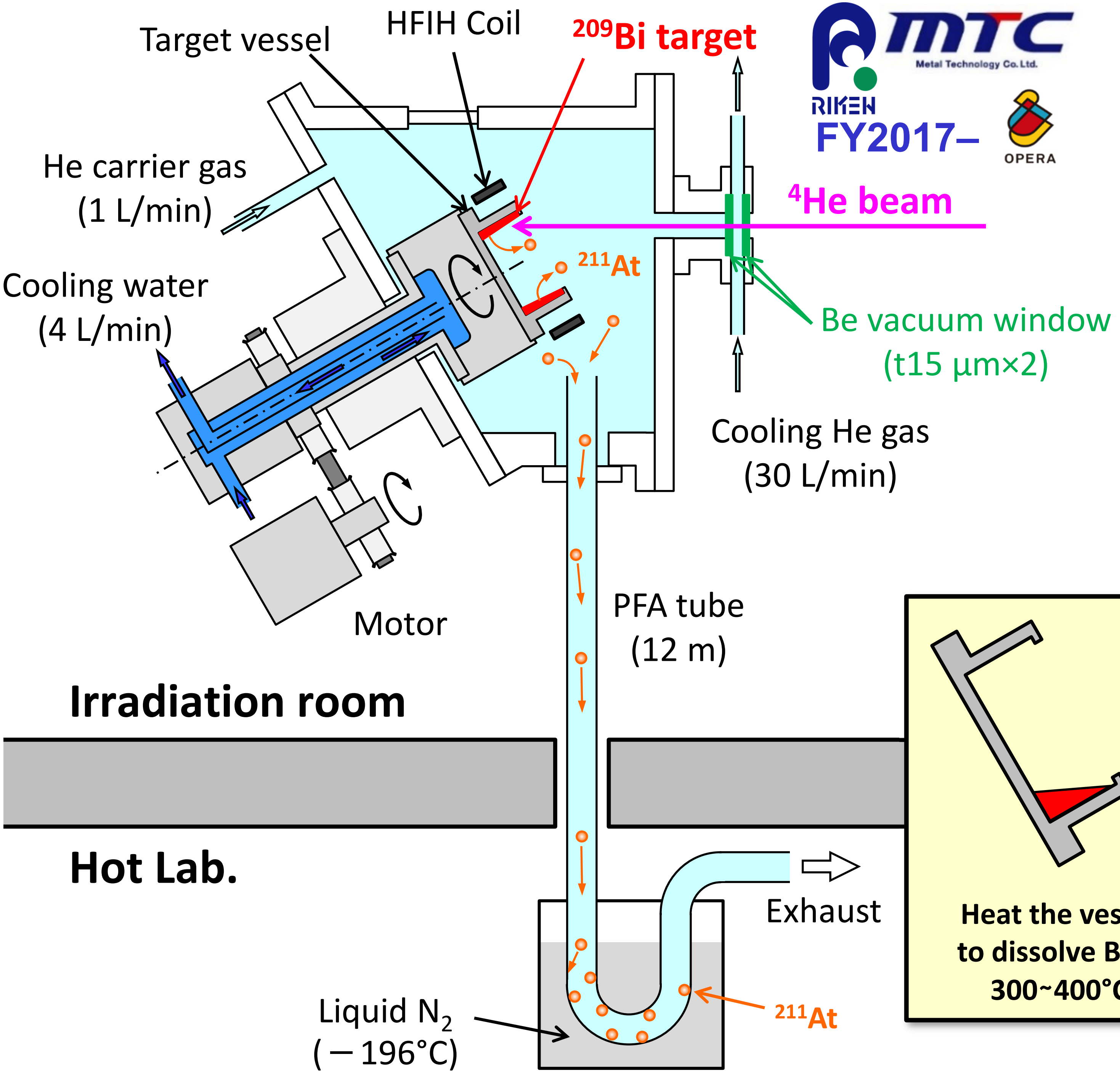
→ The ^{211}At is vaporized and lost from the target when the beam is irradiated on the melted and hot Bi target.

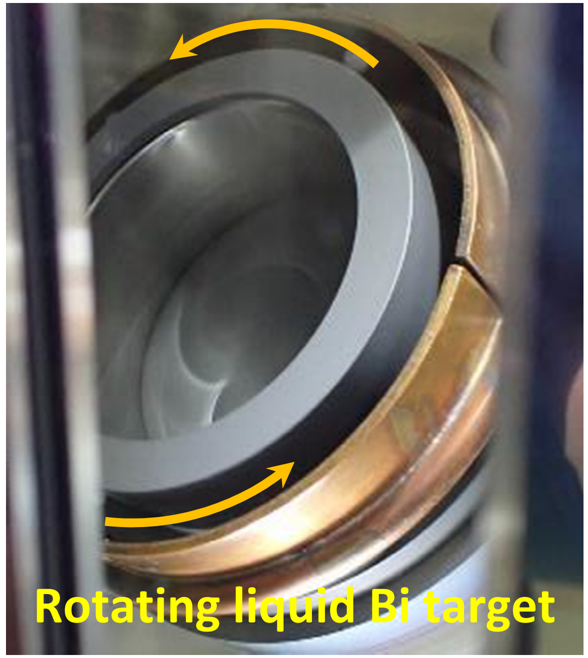
Vertical irradiation

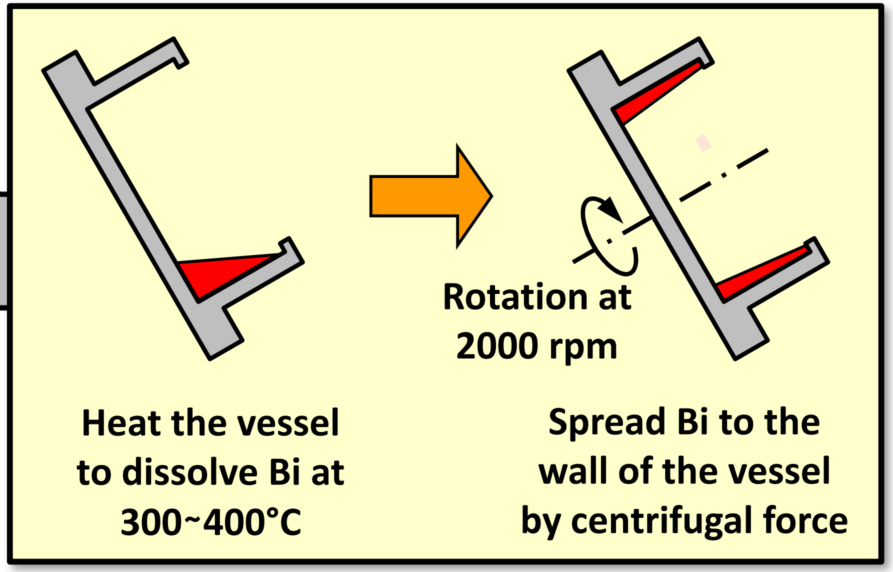


Breakthroughs in the production technology are needed to quantitatively produce ^{211}At with beams of > 25 pμA.

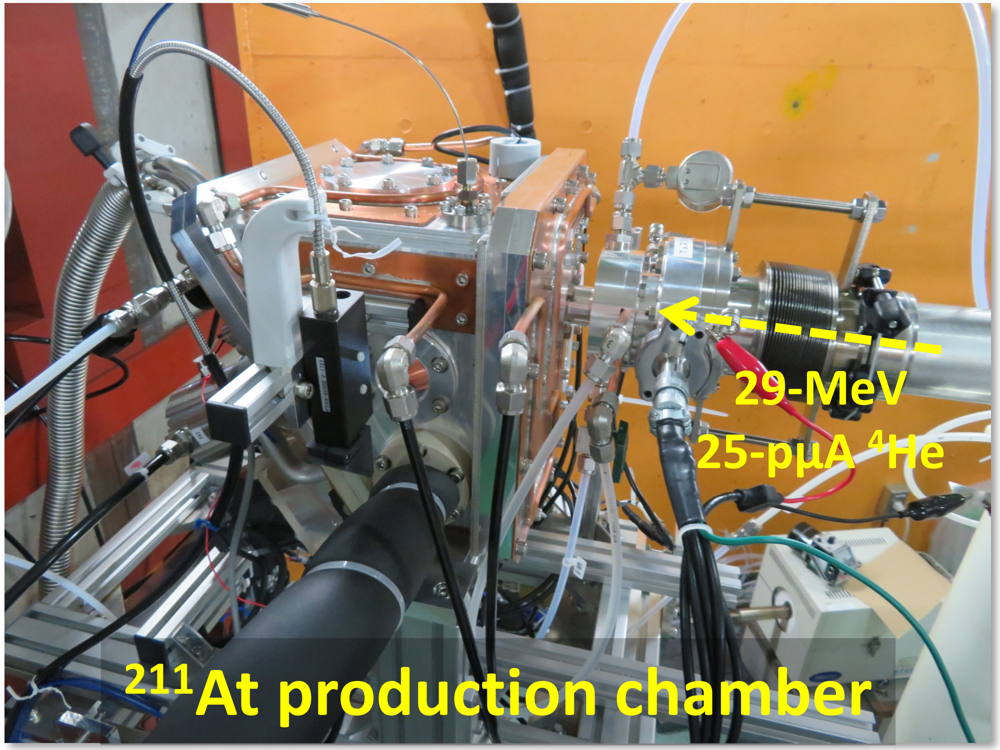
Development of a large-scale ^{211}At production apparatus





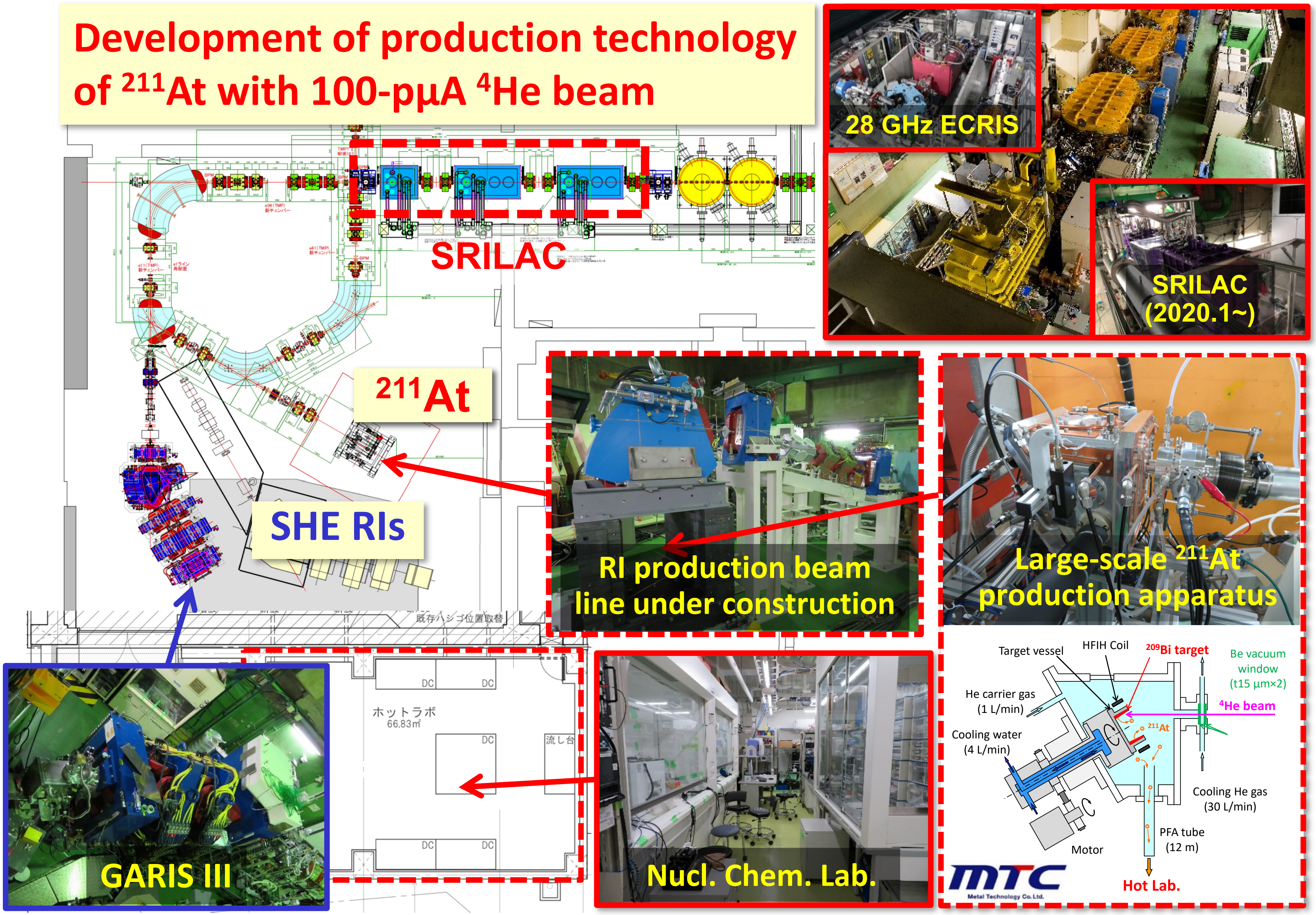


Commissioning of the large-scale ^{211}At production apparatus



- Irradiation with 28-MeV × 25-pμA ^{4}He beam
- High recovery yield (~80%), comparable to that of conventional apparatus
- Production of ~200 MBq of purified ^{211}At required for a typical use after 1.5-h irradiation

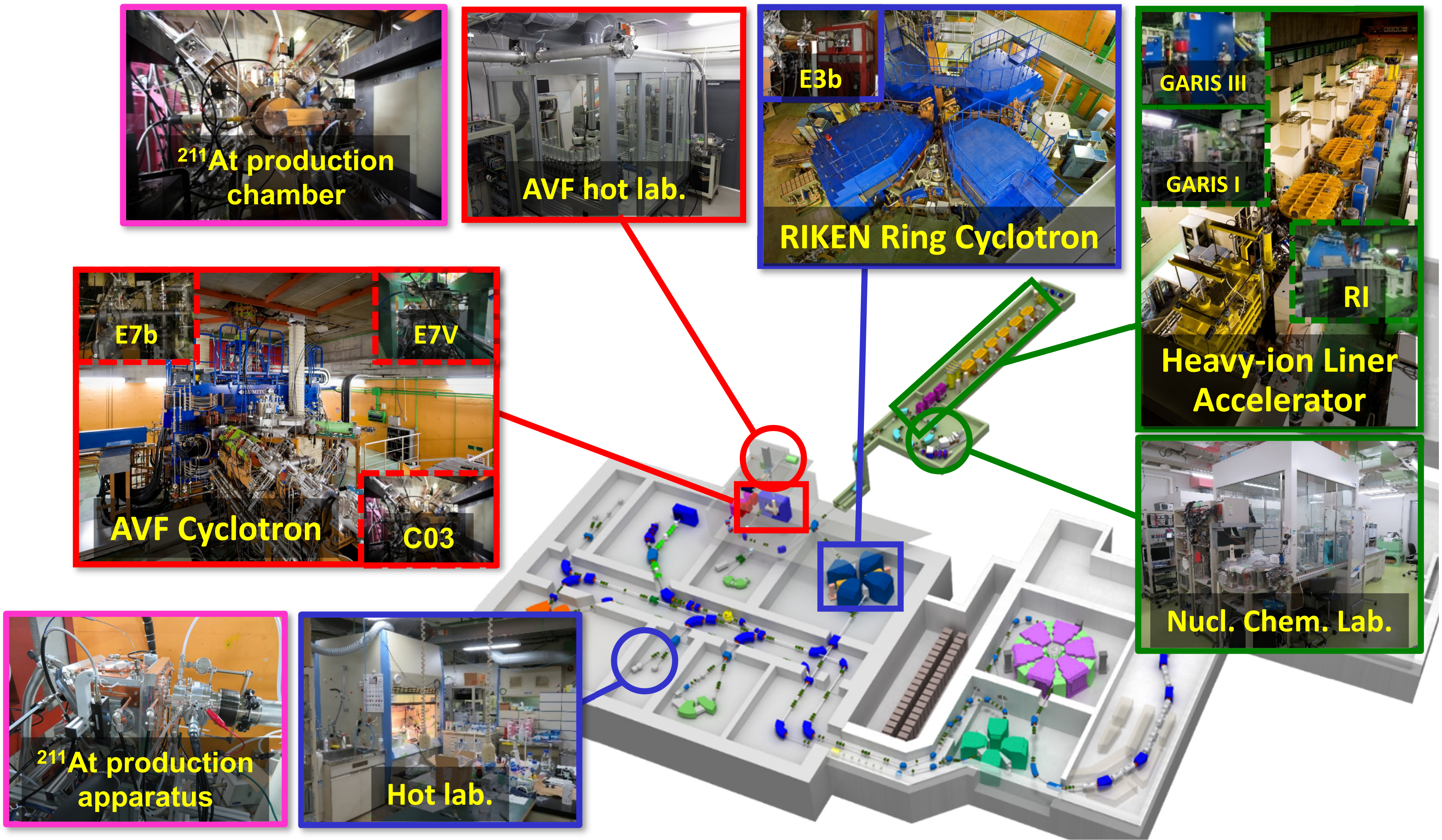
Future plan: large-scale production of ^{211}At at SRILAC



3. Summary

Production of > 100 radioisotopes for application studies at RIBF

Production of ^{211}At for targeted α-particle therapy



Collaboration through RIKEN Radioisotopes

RIKEN Laboratories

Accelerator Group
Radioactive Isotope Physics Group
Nuclear Dynamics Research Group
Nuclear Structure Research Group
Superheavy Element Research Group
Safety Management Group
Biofunctional Synthetic Chemistry Laboratory
Quantum Metrology Laboratory

Domestic Universities and Institutes

Osaka University
Niigata University
Kanazawa University
Tohoku University
University of Tsukuba
Kyoto University
Okayama University
Hokkaido University
University of Tokyo
Saitama University
Saitama Medical University
Tokyo Institute of Technology
Tokyo Metropolitan University
International University of Health and Welfare
Hamamatsu Univ. School of Medicine
Suzuka University of Medical Science
Hoshi University
Kindai University
Japan Atomic Energy Agency
National Institutes for Quantum and Radiological Science
Institute of Particle and Nuclear Studies, KEK
National Cancer Center Japan

Oversea Universities and Institutes

Institute of Modern Physics, CAS, China
Sunway University, Malaysia
ATOMKI, Hungary
Johannes Gutenberg University Mainz, Germany
Helmholtzzentrum für Schwerionenforschung GmbH, Germany
Helmholtz-Institut Mainz, Germany
Bern University, Switzerland
Paul Scherrer Institut, Switzerland
Umaru Musa Yar'adua University, Katsina, Nigeria
International Atomic Energy Agency, Austria
Australian National University, Australia

Public Interest Incorporated Association

Japan Radioisotope Association

Companies

PDRadiopharma Inc.
Metal Technology Co., Ltd.
ATOX Co., Ltd.
Chiyoda Technol Co., Ltd.
RIN Institute Inc.