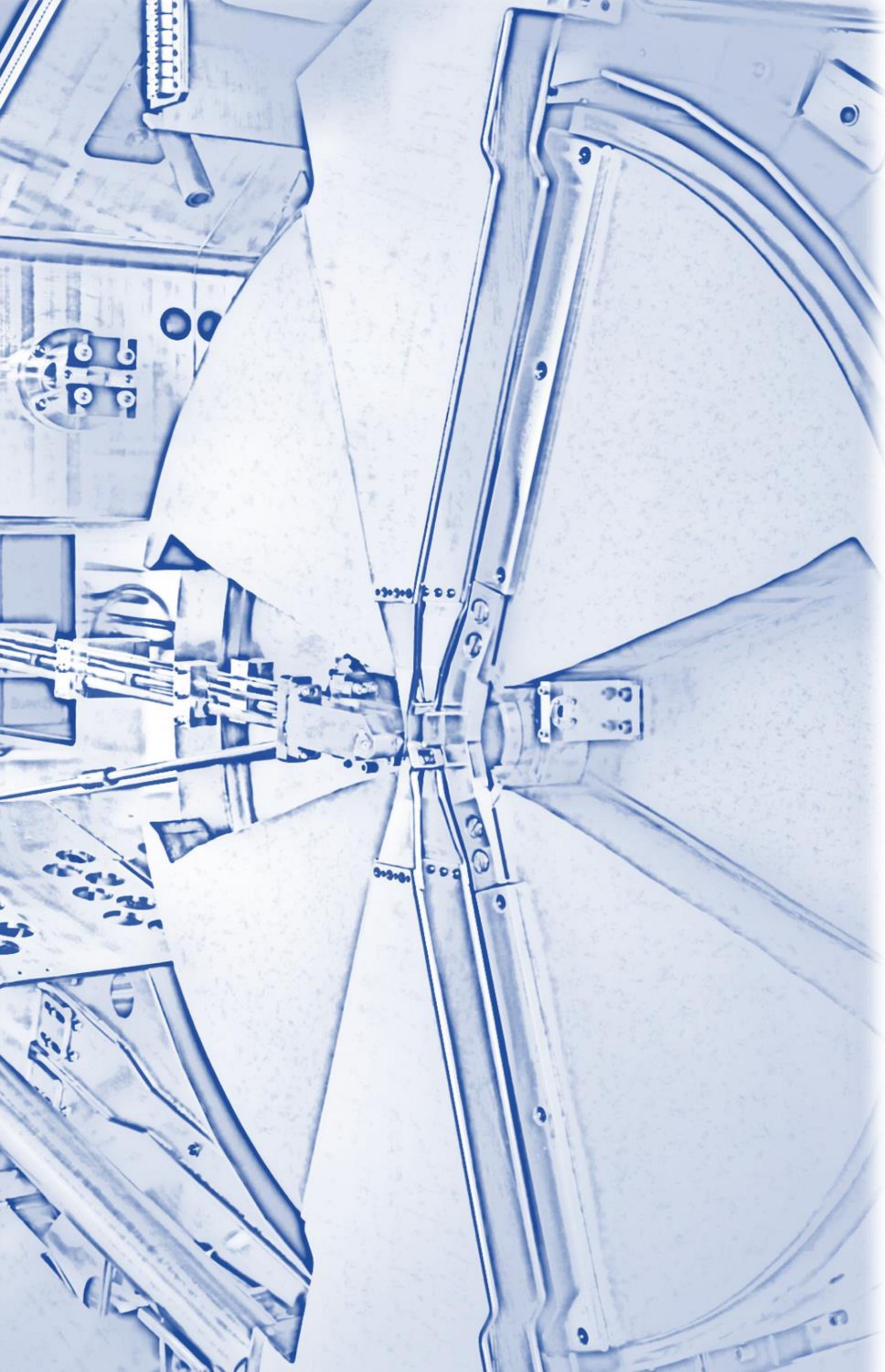


BNCT and Proton Therapy Systems of Sumitomo Heavy Industries

MAY 15, 2023 @ PSI

Medical & Advanced Equipment Unit,
Industrial Equipment Division,
Sumitomo Heavy Industries, Ltd.

Table of Contents

Sumitomo Heavy Industries: Company Profile

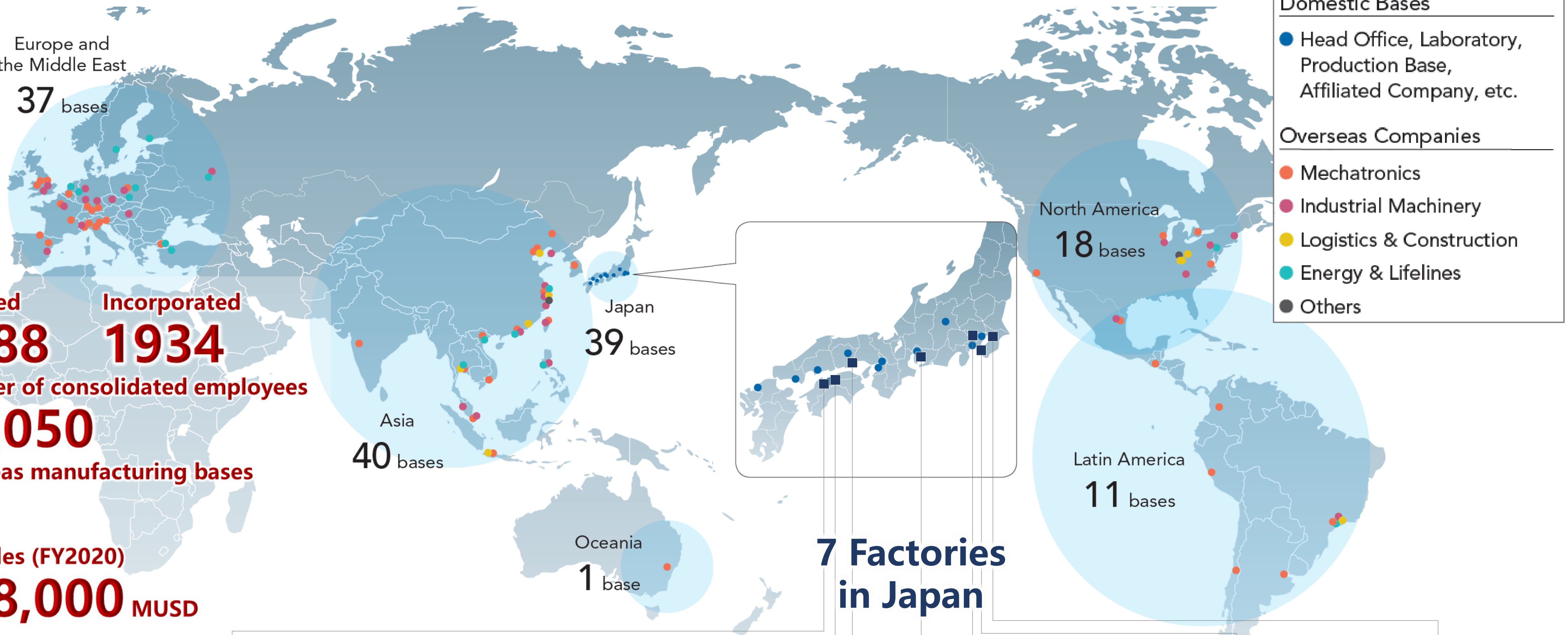
Founded
1888

Incorporated
1934

Number of consolidated employees
24,050

Overseas manufacturing bases
28

Net sales (FY2020)
Approx. **8,000** MUSD



7 Factories in Japan


Saijo


Niihama


Okayama


Nagoya


Tanashi

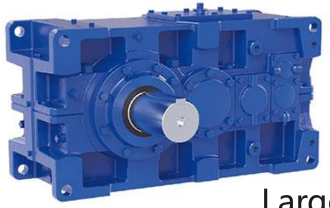

Yokosuka


Chiba

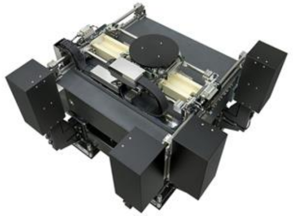
Sumitomo Heavy Industries: Business Portfolio

Mechatronics


Gearmotors
(CYCLO® DRIVE)


Large Gearbox


High Precision Gearboxes


Precision Positioning
Equipment

Industrial Machinery

Injection
Molding Machine

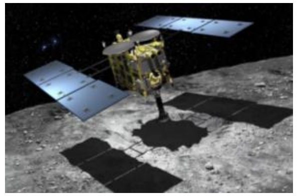

Cryocooler


Cryopumps

Used in MRI & accelerators.


PET Cyclotron


Proton Therapy
System

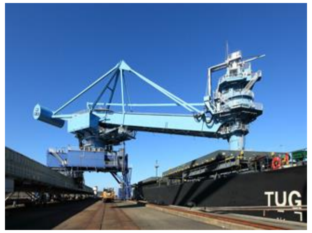

Space Equipment
(Hayabusa 2)

Logistic & Construction

Hydraulic
Excavators


Crawler Cranes


Bridge Type
Unloader



Continuous
Ship Unloader


Parking System

Energy & Lifelines


Circulating
Fluidized
Bed Boilers


Recycling
Facilities

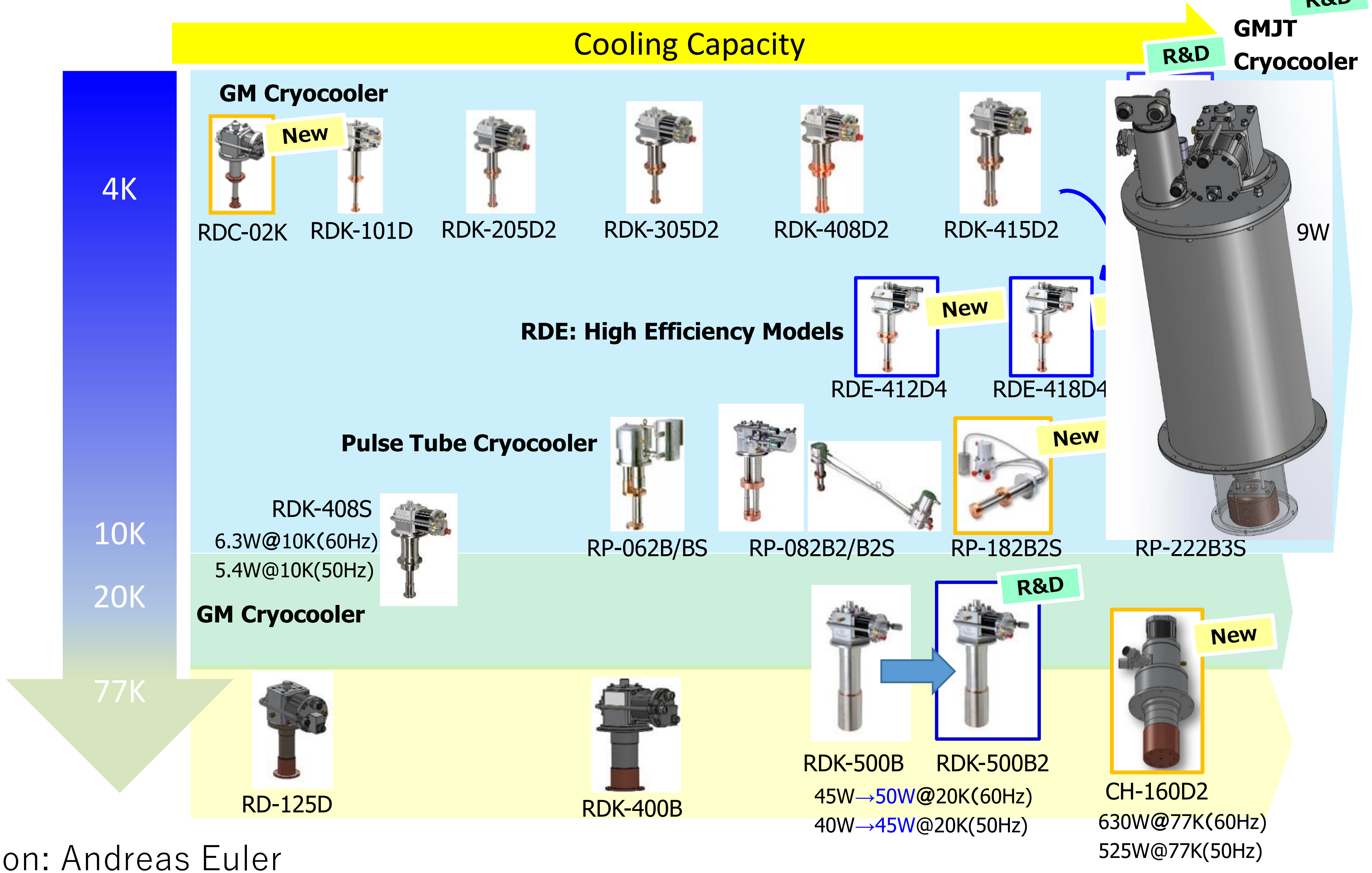

Reactor Vessel

Oil Tanker

CryoPumps

Confidential

Sumitomo Heavy Industries, Ltd.



Contact Person: Andreas Euler
andreas.euler@shi-g.com

History of Accelerator Business

Approx. 50 years' business history

1972
Cyclotron for Research
(Osaka Univ.)

1981
PET Cyclotron
(Kyoto Univ.)

1988
Injector for Carbon Therapy
(NIRS)

1997
Proton Therapy System
(National Cancer Center)

2009
BNCT System
(Kyoto Univ.)

2015
Cyclotron for Radionuclide Therapy
(Fukushima Medical Univ.)

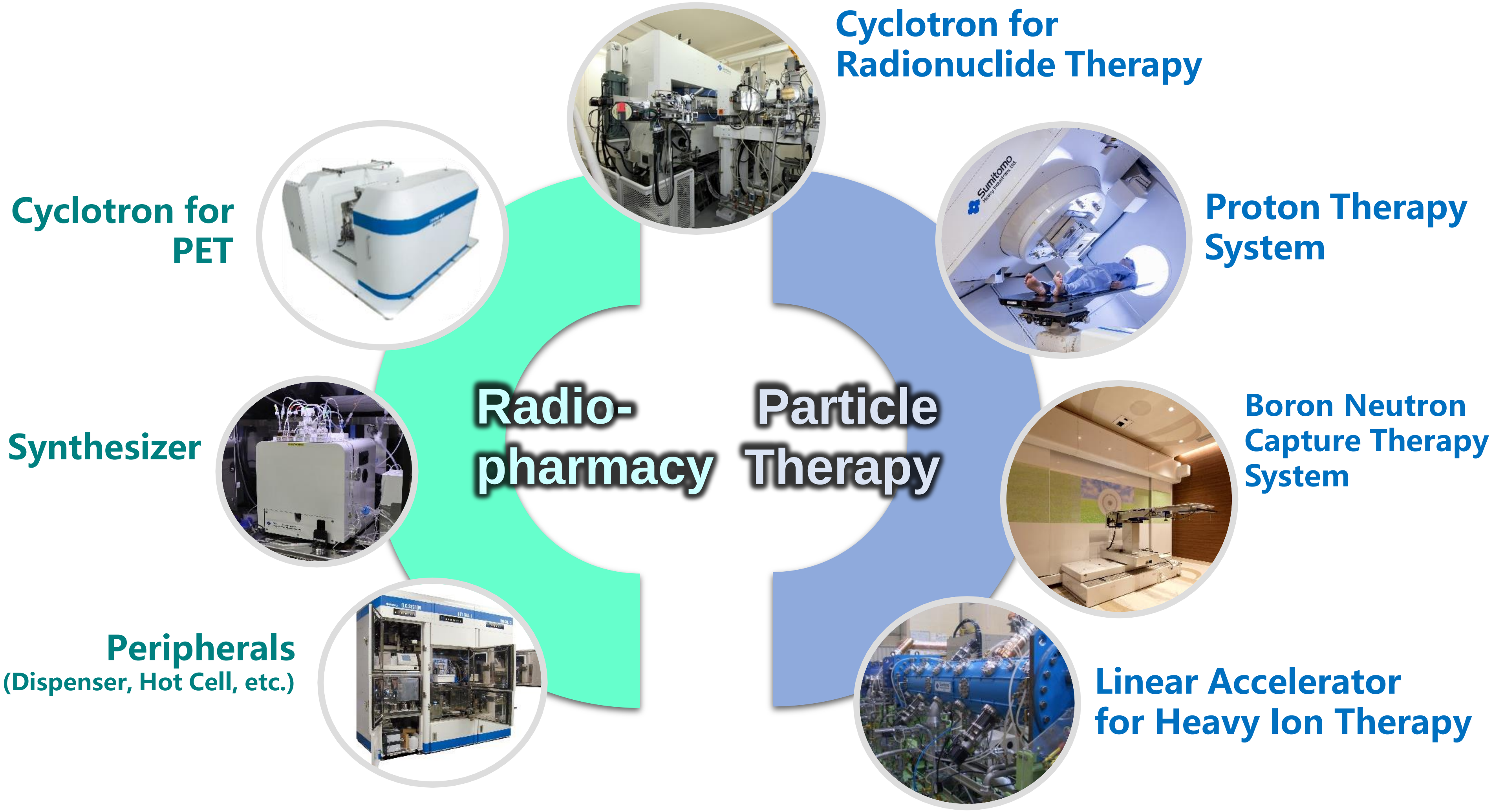
2020
World's First Medical Device Approval for BNCT System in Japan

Accelerator Business

Medical Business

Sumitomo Medical Equipment

Sumitomo provide accelerators for radio pharmacy and particle therapy.



Sumitomo PET Radio-Tracer Production System

PET Radio-Tracer Production Facility layout

- Compact and efficient facility design
- Total solution* complied with GMP and local regulations

* Incl. design, setting-up, training and maintenance.

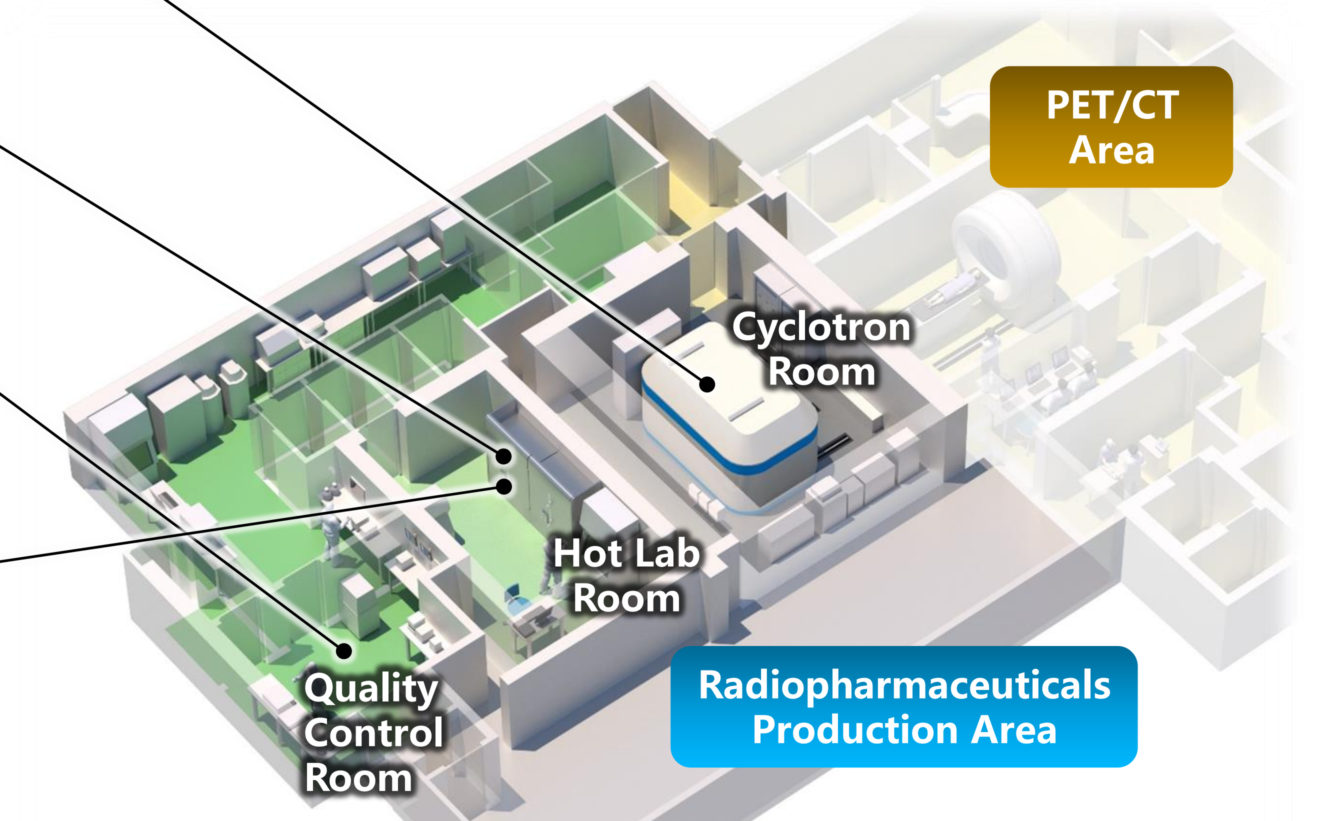
Radioisotope production (Cyclotron)

Synthesis (Synthesizer)

Quality Check

Dispensing

Injection



Cyclotron Facilities of Dpt. of Diagnostic Radiology, The University of Hong Kong

Sumitomo PET Radio-Tracer Production System

Radioisotope production (Cyclotron)

Synthesis (Synthesizer)

Quality Check

Dispensing

Injection

<Sumitomo's CYPRIS® Cyclotrons>

- MP-30 (30 MeV)
- HM-20 (20 MeV)
- HM-18HC (18 MeV)
- HM-12 (12 MeV)
- HM-12SPC (12 MeV)

Target solutions

- ^{18}F
- ^{11}C
- ^{13}N
- ^{15}O
- ^{68}Ga Liquid Target
- ^{68}Ga, ^{64}Cu, ^{89}Zr by Solid Target LT*
- ^{68}Ga, ^{64}Cu, ^{89}Zr, ^{123}I, ^{124}I by Solid Target PT*

* LT: Liquid Transfer
PT: Plate Transfer

Synthesizer

- SmartPharm (For FDG)
- MPS200 (For CFN)

Purification system

- STP-MPP200 (For ^{68}Ga, ^{64}Cu, ^{89}Zr)

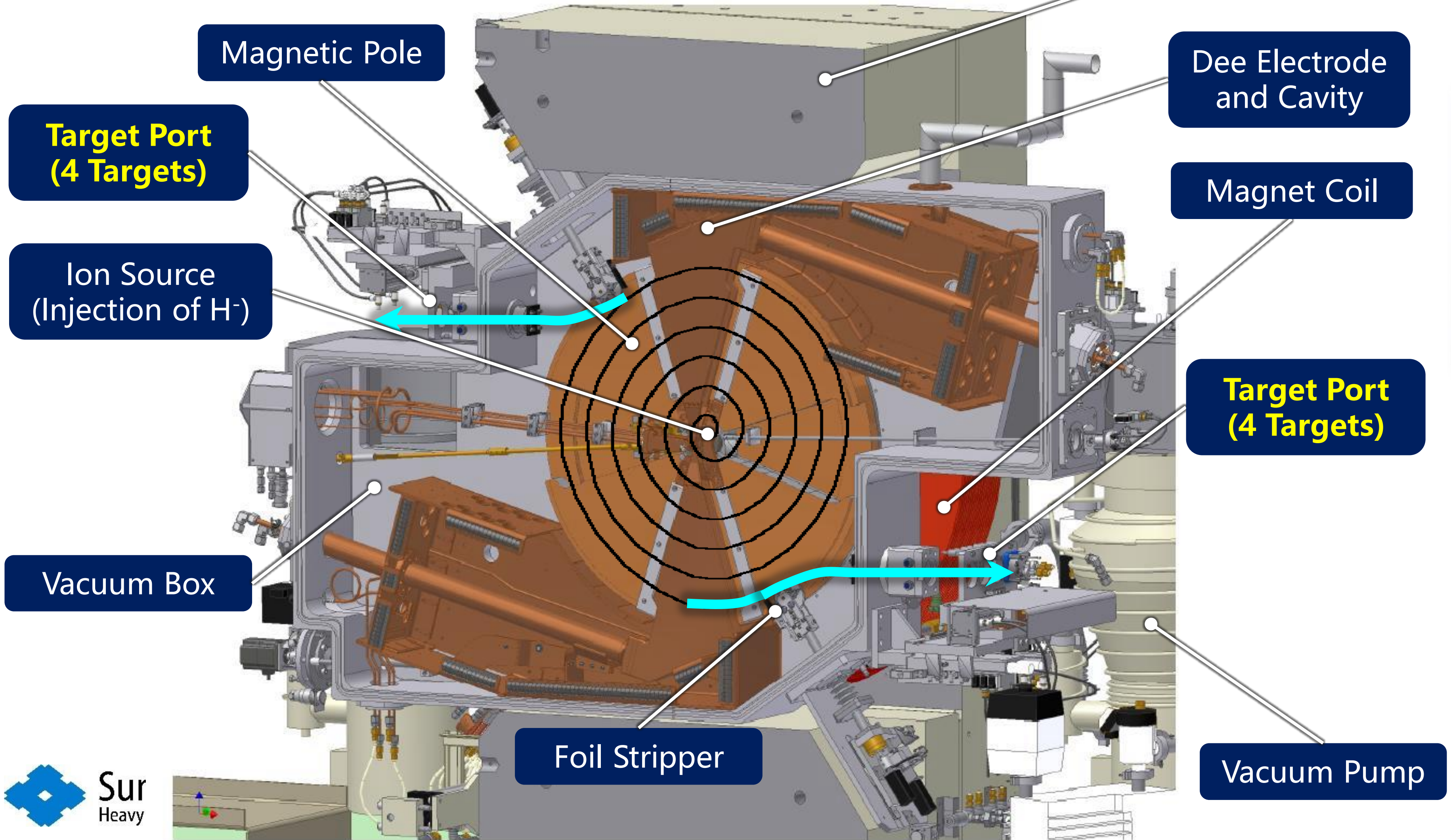
Peripheral equipment

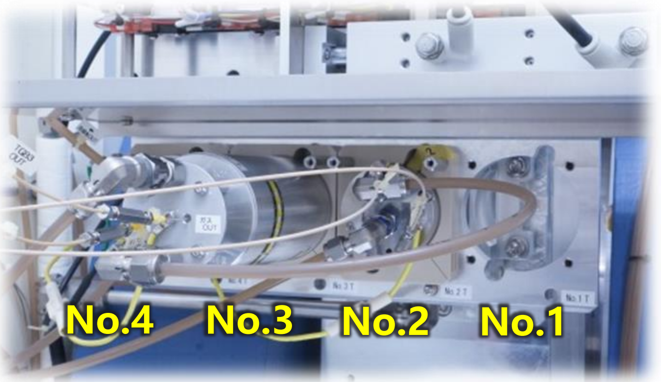
- D200 (Dispensing)
- Hot cell

Provide efficient workflow with the products designed and manufactured in own factory.

Internal Structure of CYPRIS® HM-12/20

- Vertical acceleration: Easy and less radiation exposure for maintenance
- 2 Ports Simultaneous Irradiation is possible.
- Total 8 targets (4 targets x 2 ports) for various isotopes





Target Port
(Max. 4 targets can be mounted on each target port.)

Sample target configuration

<A port>	<B port>
● ^{18}F liquid	● ^{13}N liquid
● ^{11}C gas	● ^{15}O gas
● Solid TG	● $^{18}F_2$ gas
● (Dummy)	● (Dummy)

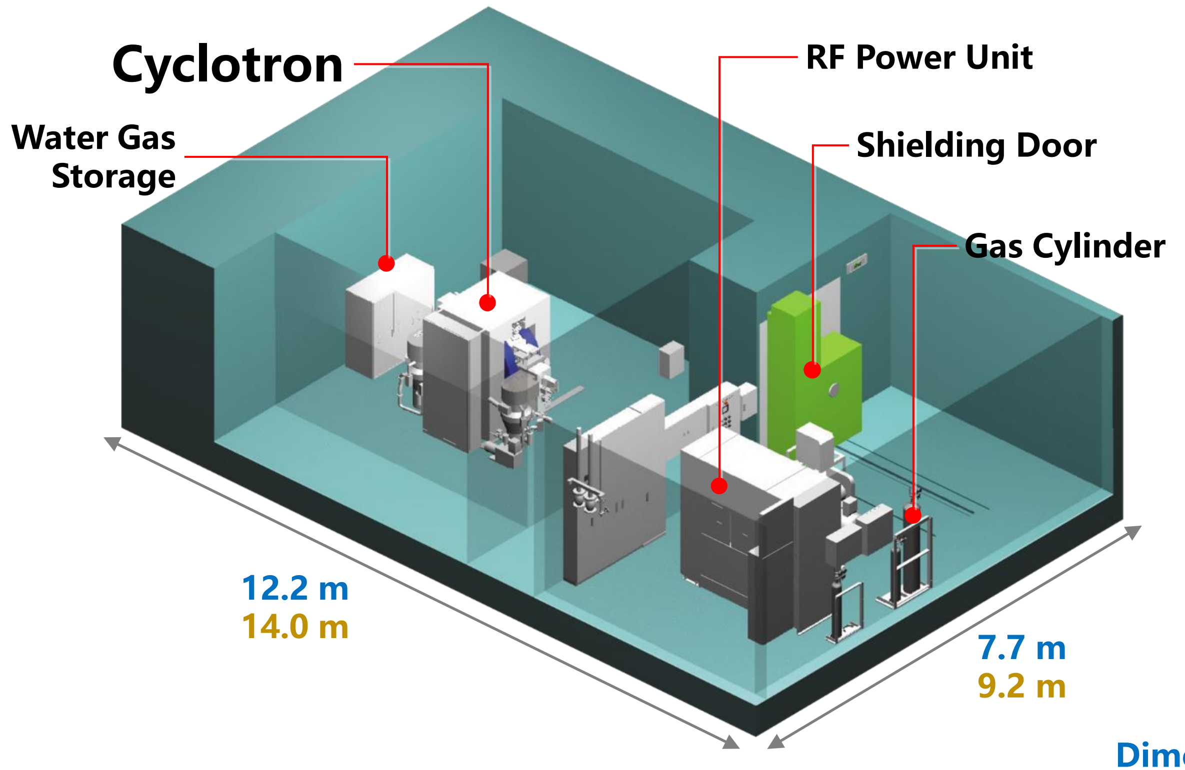
Sumitomo Heavy

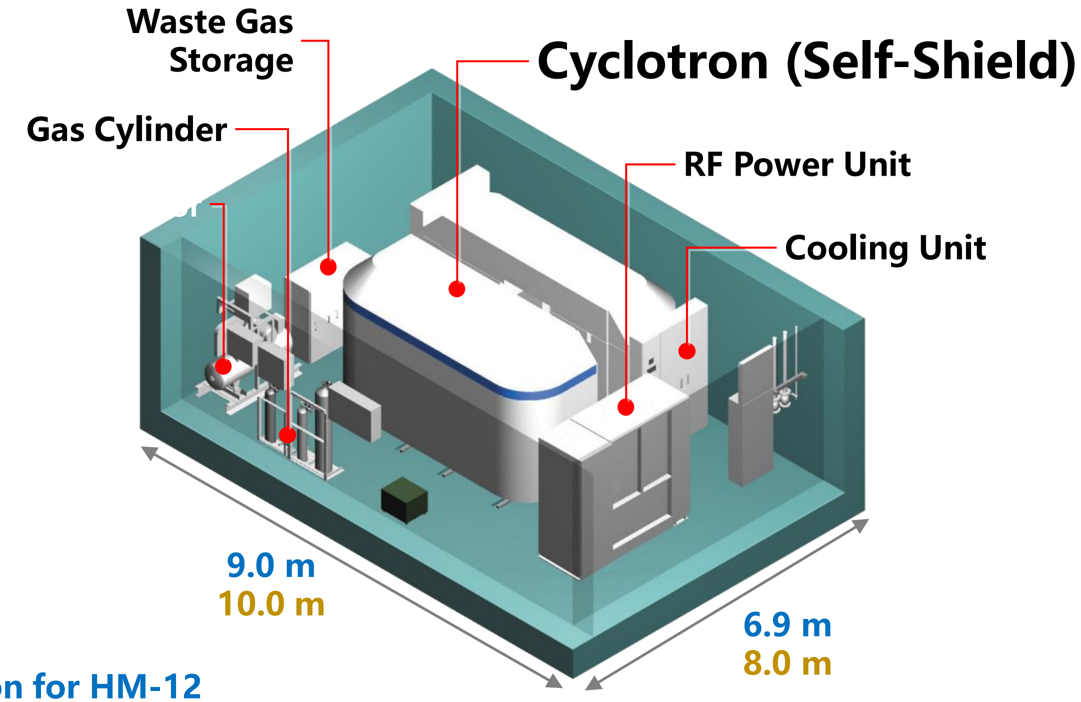
Space and Cost Saving with Self-shielded Cyclotron

Wall-shielded Cyclotron

Self-shielded Cyclotron

- > 30% Down of necessary space
- Simple layout
- No expensive shielding door
- Less radioactive for building





Dimension for HM-12
Dimension for HM-20

Sumitomo PET Cyclotrons in the world

Japan **132** units — **70% Market share**

China **82** units — **>30% Market share**

Others **22** units — **Expansion to Asian Countries**

Total: 236 units

as of April,2023

BNCT

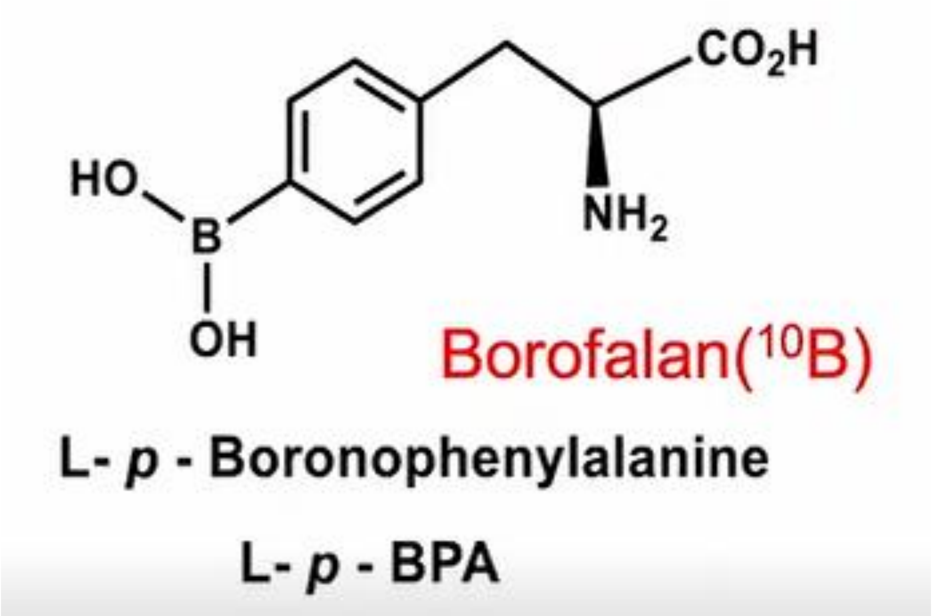
Introducing Sumitomo Accelerator-Based BNCT System NeuCure

Confidential

Sumitomo Heavy Industries, Ltd.

Table of contents

1.How BNCT works (biology)



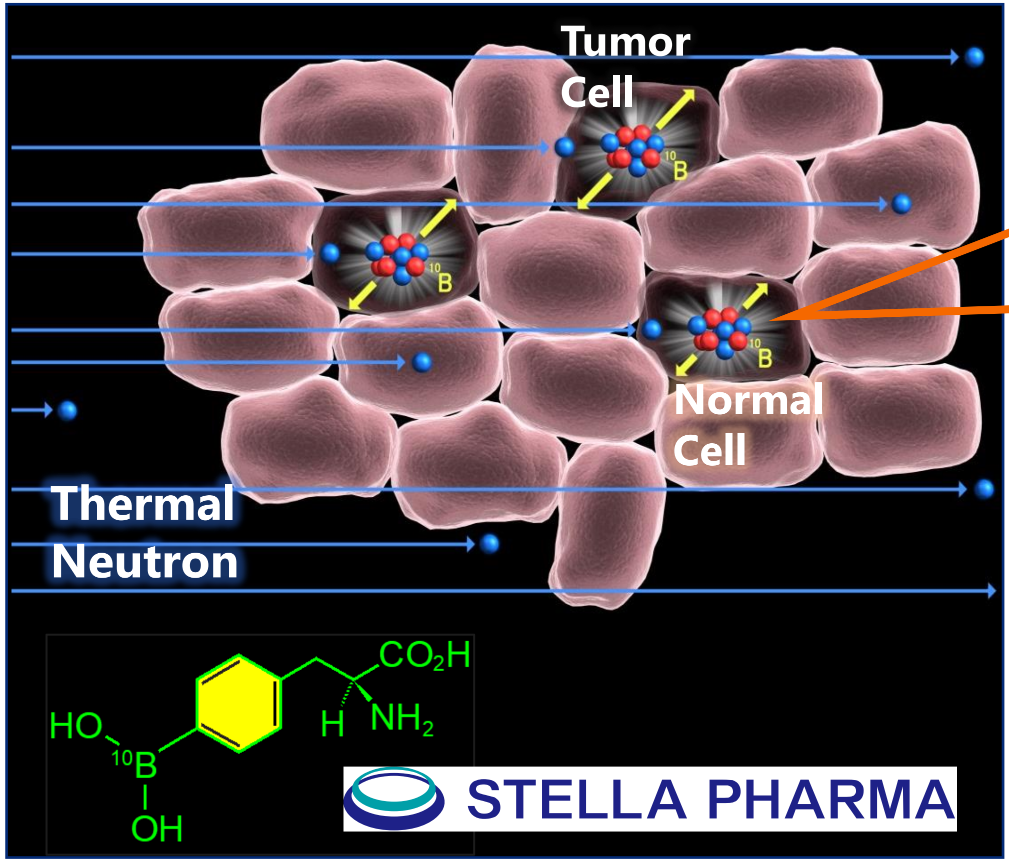
STELLA PHARMA

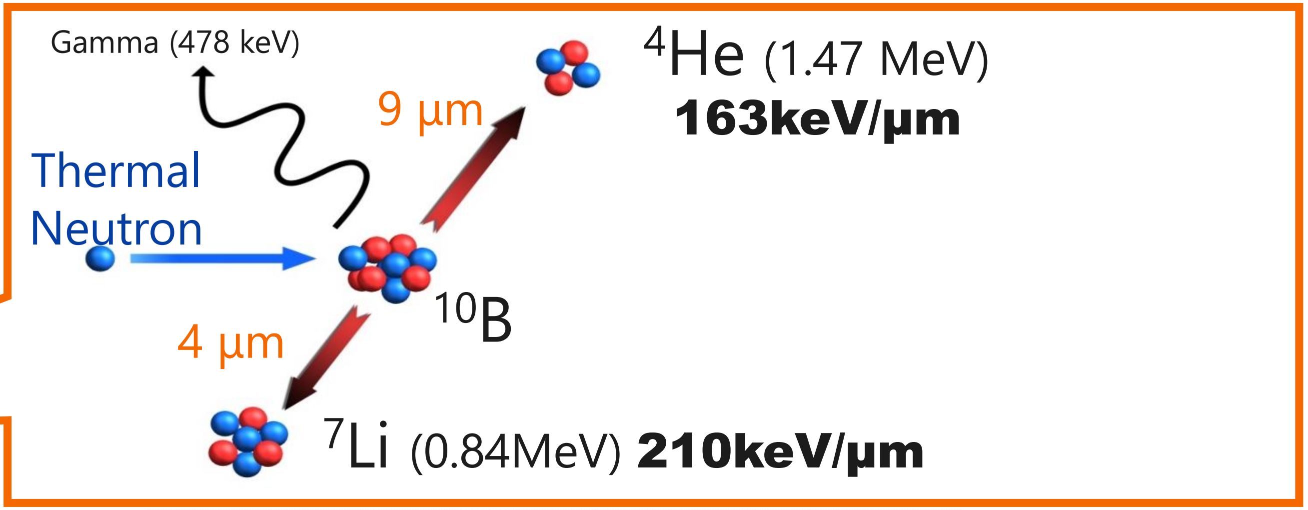
Boron drug BPA is taken into tumor cells selectively
via LAT1 transporter, which appears at proliferating tumor cells.

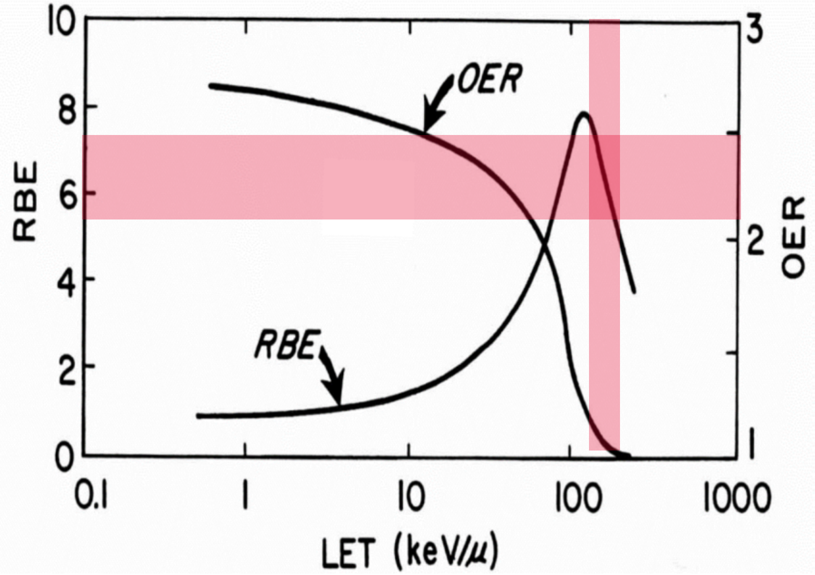
1.How BNCT works (physics)

^{10}B reacts with thermal neutron.

Short-range ^{4}He and ^{7}Li are generated.







1.How BNCT works (Neutron Source)

Accelerator-based neutron source

Lithium
- Low melting point
- ^{7}Be production

Beryllium
- High melting point
- High heat conductivity

Heavy material (Tantalum etc.)
- High melting point
- High heat conductivity
- Activation of target

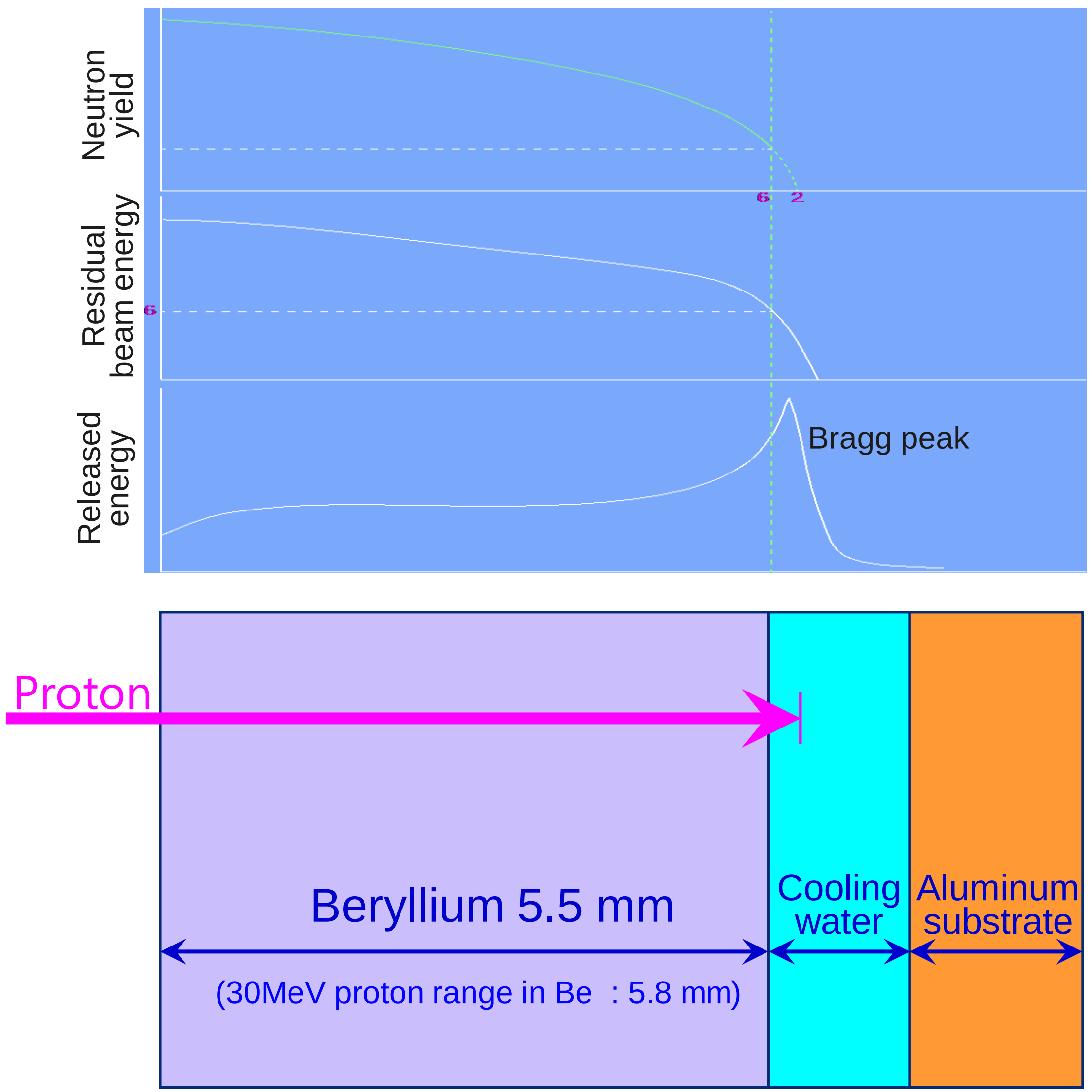
Low energy proton < 3 MeV
- Neutron production yield ： low
- Activation ：low
- Moderator ：small
- Blistering
- High current～20mA

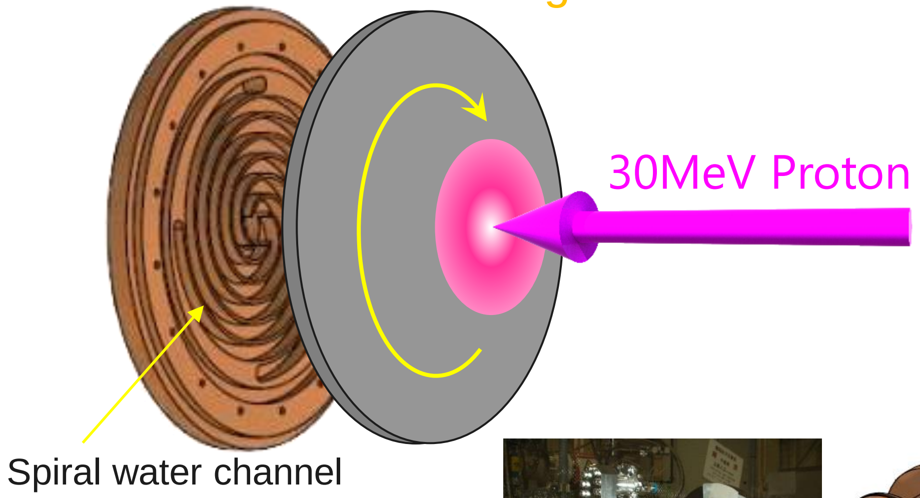
3 MeV < Middle energy < 8MeV
- Neutron production ：middle
- Activation ：Low
- Moderator ：Middle
- Blistering
- High current～5mA

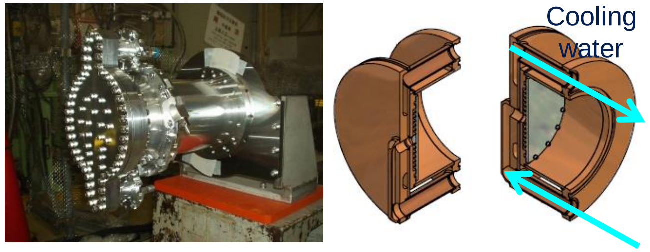
8 MeV < High energy proton
- Neutron production yield ：High
- Activation ：High
- Moderator ：Large
- No blistering
- Small current～1mA

30 MeV and 1mA proton beam

1.How BNCT works (Neutron Source)







✓The heat load from the Bragg peak is released in the cooling water.

✓Circularly wobbled beam reduces the local heat load on the target surface.

2.Experience of BNCT systems

3	180+	2020
Systems operating	Patient treated*	Device approved since

Two systems are for clinical use,
one system is for non-clinical use.

* After device approval

2.References of Sumitomo BNCT systems

Osaka Medical & Pharmaceutical Univ. (Takatsuki, 2018)

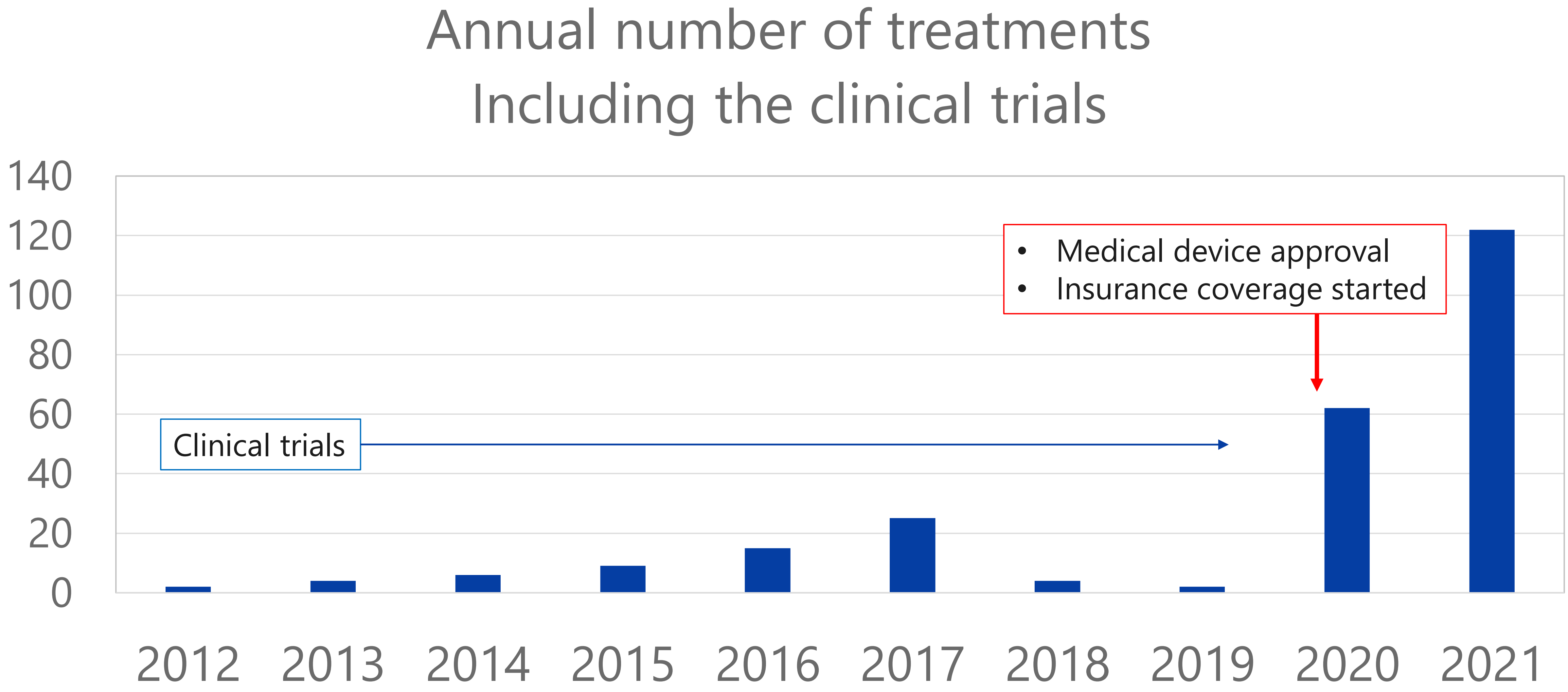
Pengbo (Hainan) Medical Technology
(Boao, under construction)

4 AB-BNCT Systems

Southern Tohoku General Hospital
(Koriyama, 2016)

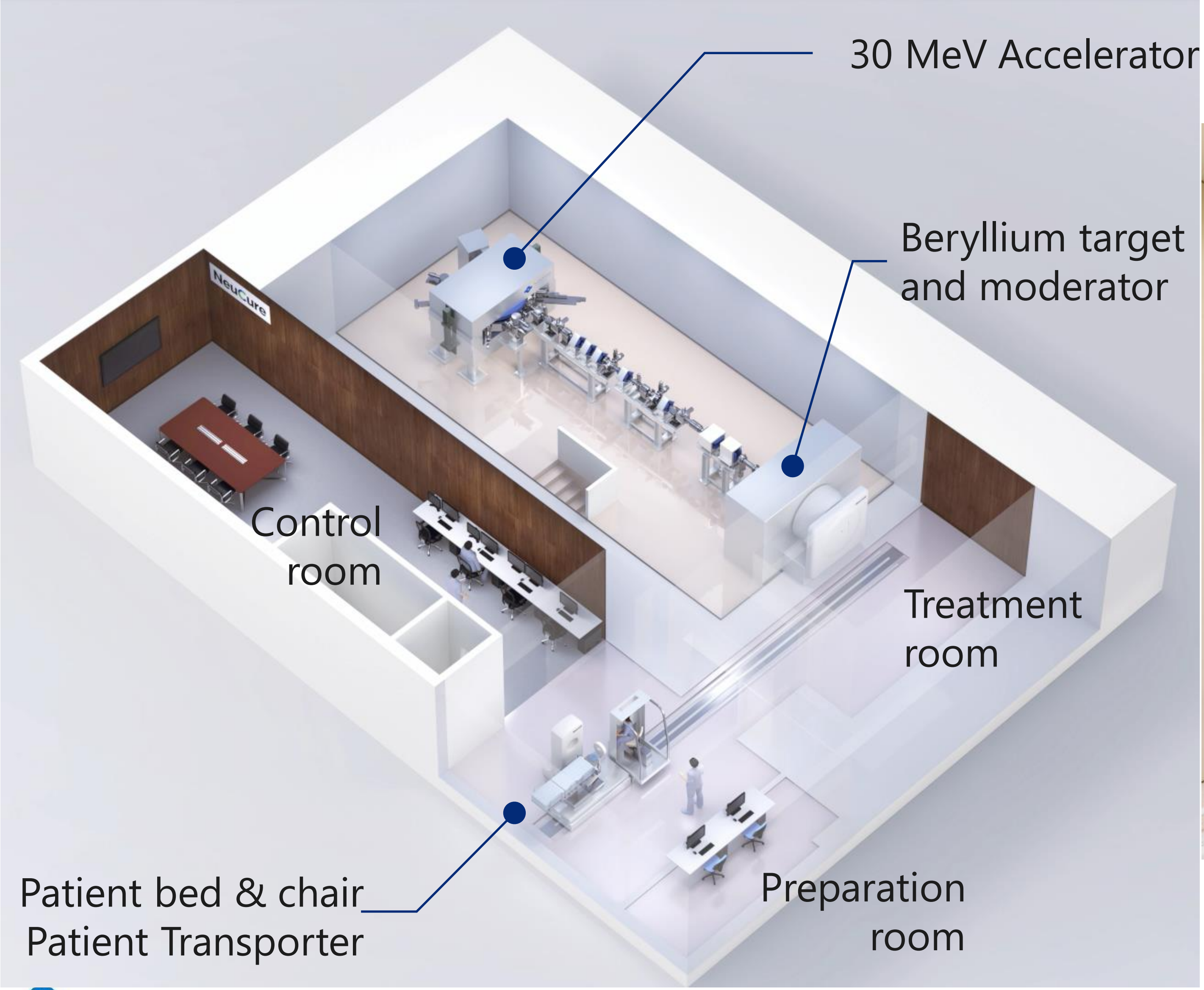
Kyoto University
(Kumatori, 2013)

2.Patients treated with SHI BNCT systems



Total +250 cases

3.NeuCure BNCT System

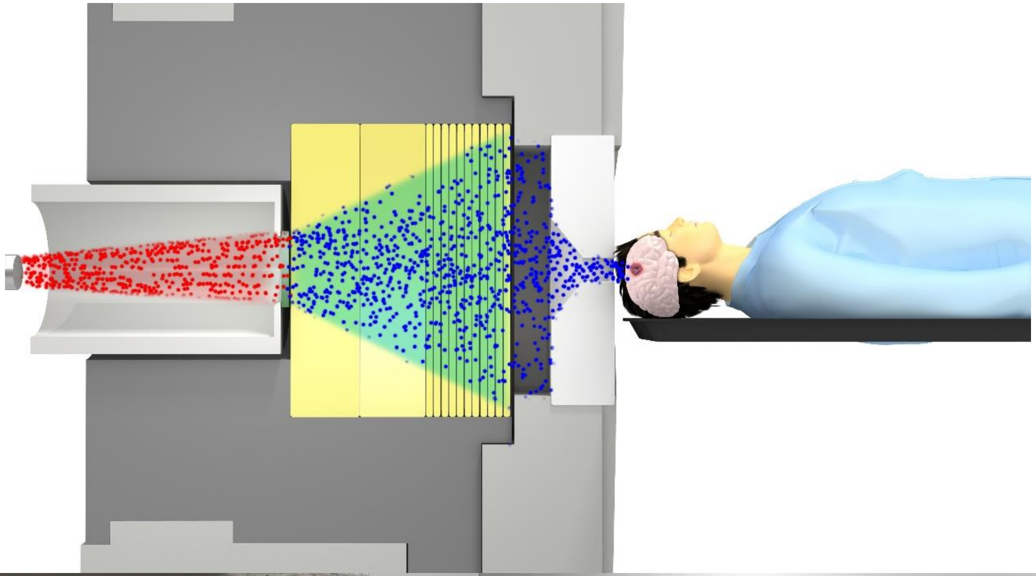


3.Cyclotron

- 200+ installations in hospitals for PET and proton therapy.
- 30 MeV, 1 mA proton beam

3.Target and BSA

- Beryllium target produces neutrons with high stability, and safety.
- Patented neutron dose control by proton current monitors for accurate dose delivery.
- > 1.0 x 10^9 / cm^2 / s epi-thermal neutron flux.

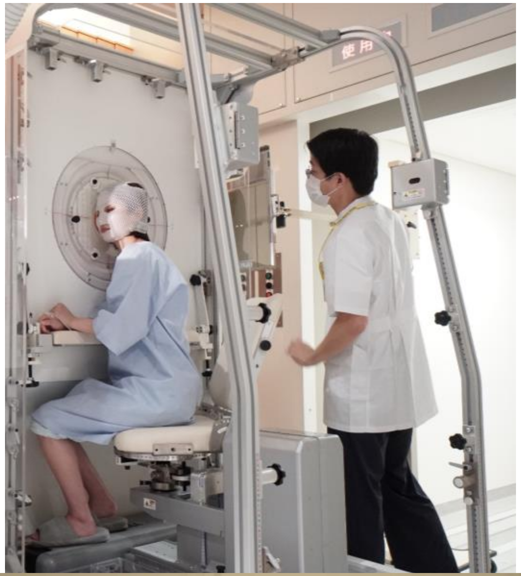


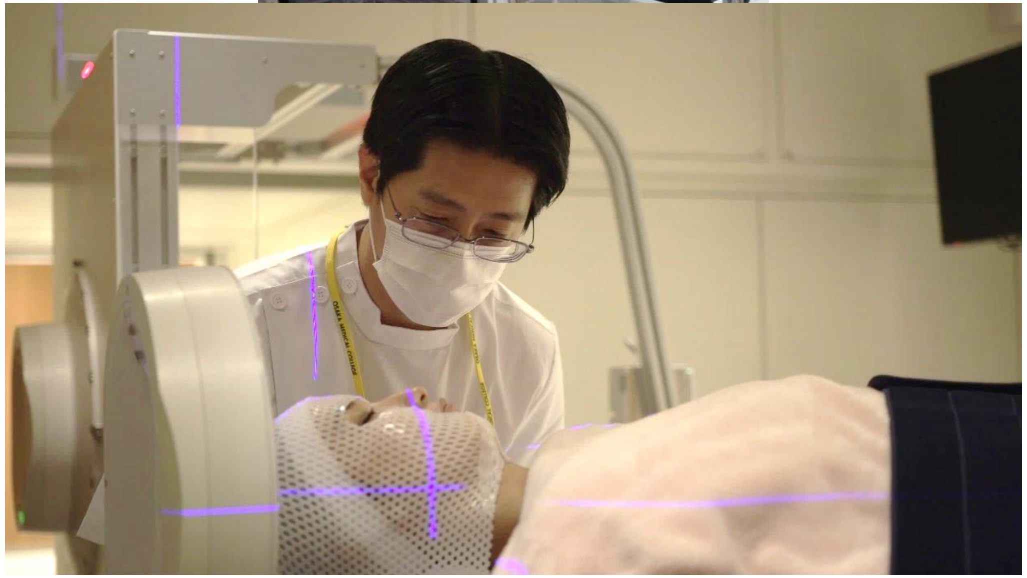
3.Patient transport system

- Transport patients safely from the preparation room, reducing exposure of medical personnel.

3.Seated and supine treatment table

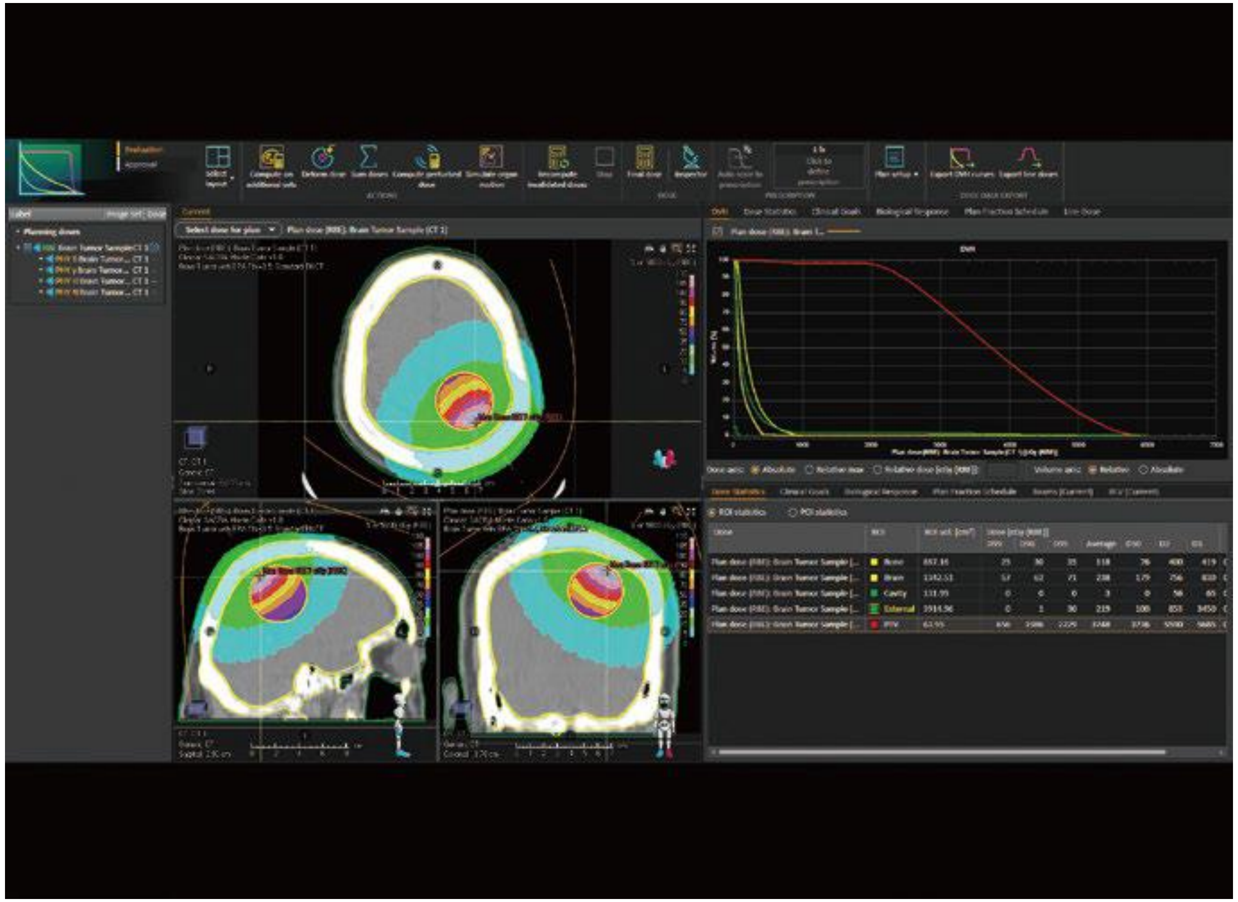
- Applicable to various regions.
  - Seated for head & neck
  - Supine for brain
- Minimize air gap to make the most of neutron flux.





3.Treatment planning system

- PHITS based dose engine by Sumitomo
- Intuitive GUI by Raysearch Raystation
- Validated in combination with the machine
- NeuCure dose engine approved in Japan as medical device, March 2020



3.New extended collimators approved

- New extended collimators approved in 2022
- +5cm and +10cm extension
- For easy patient posture
- While keeping neutron flux

3.Pipeline

Head & Neck Cancer

- Unresectable locally recurrent or locally advanced
- Approved for the world’s first medical device and drug
- Approved for public insurance coverage

Malignant Glioma

- Recurrent
- P2 Completed, Discussing with PMDA

Malignant Meningioma

- Recurrent
- P2 Recruited

3.Head and neck Phase 2 clinical trial

- Unresectable recurrent or locally advanced head and neck cancer
- SHI machine + SP BPA
- Response rate 71%
- No grade 4 or 5 serious adverse events, except for hyperamylasemia
- K. Hirose et.al., Radiotherapy and Oncology 155 (2021) 182–187

Response	SCC (*n* = 8)	nSCC (*n* = 13)	Total (*n* = 21)
Response, No. (%)			
Complete response	4 (50)	1 (8)	5 (24)
Partial response	2 (25)	8 (62)	10 (48)
Stable disease	1 (13)	4 (31)	5 (24)
Progression	0 (0)	0 (0)	0 (0)
Not evaluable	1 (13)	0 (0)	1 (5)
ORR, % (95% CI)	75 (35–97)	69 (39–91)	71 (48–89)
DCR, % (95% CI)	88 (47–100)	100 (79–100)	95 (76–100)
Proportion OS at 2 years, % (95% CI)	58 (18–84)	100 (79–100)	85 (61–95)

Treatment-related adverse event	Grade 1 or 2 (≥10%) *N* (%)	Grade 3 (any occurrence) *N* (%)	Grade 4 (any occurrence) *N* (%)
Alopecia	20 (95)	–	–
Hyperamylasemia	2 (10)	1 (5)	15 (71)
Nausea	17 (81)	0	–
Dysgeusia	15 (71)	–	–
Parotitis	14 (67)	0	0
Loss of appetite	14 (67)	0	0
Oral mucositis	12 (57)	1 (5)	0
Hyperprolactinemia	12 (57)	0	0
Vomiting	10 (48)	0	0
Dry mouth	9 (43)	0	–

Proton Therapy

Sumitomo Particle Therapy Systems in Asia

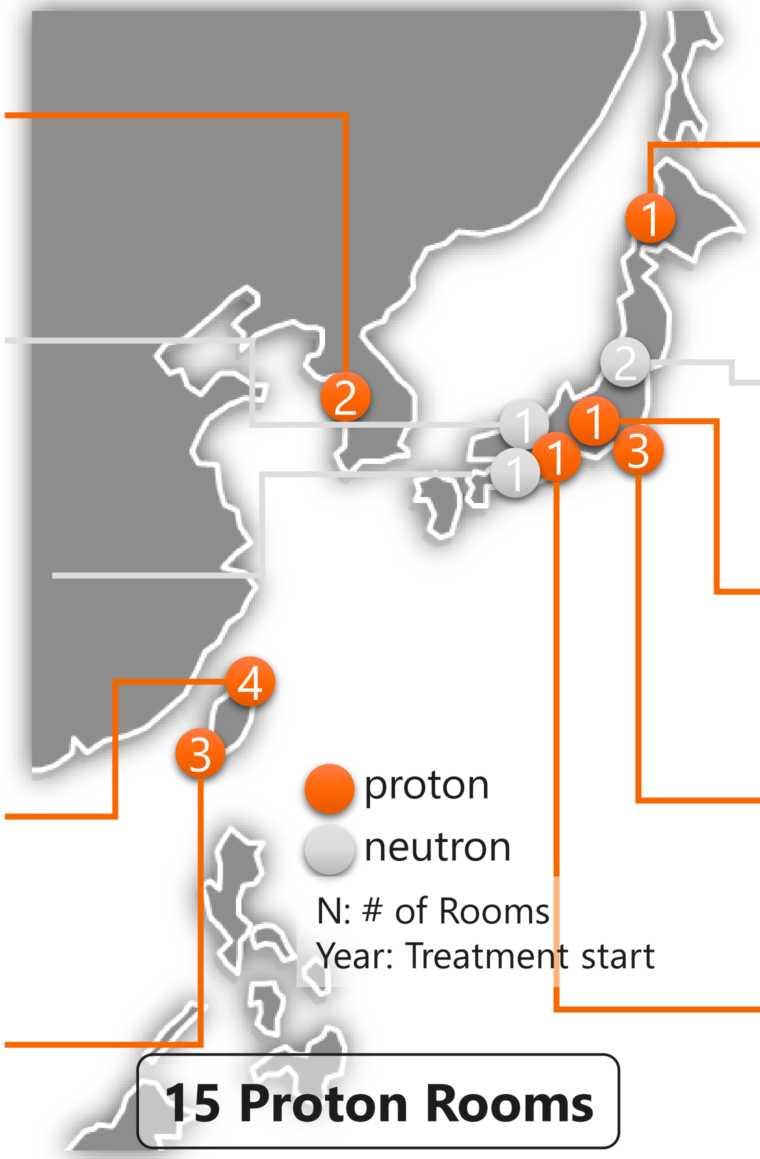
Samsung Medical Center
(Seoul, 2015)

Osaka Medical College
(Takatsuki, 2018)

Kyoto University
(Kumatori, 2013)

Chang Gung Memorial Hospital, Linkou
(Taoyuan, 2015)

Chang Gung Memorial Hospital, Kaohsiung
(Kaohsiung, 2018)



Sapporo Teishinkai Hospital
(Sapporo, 2016)

Southern Tohoku General Hospital
(Koriyama, 2016)

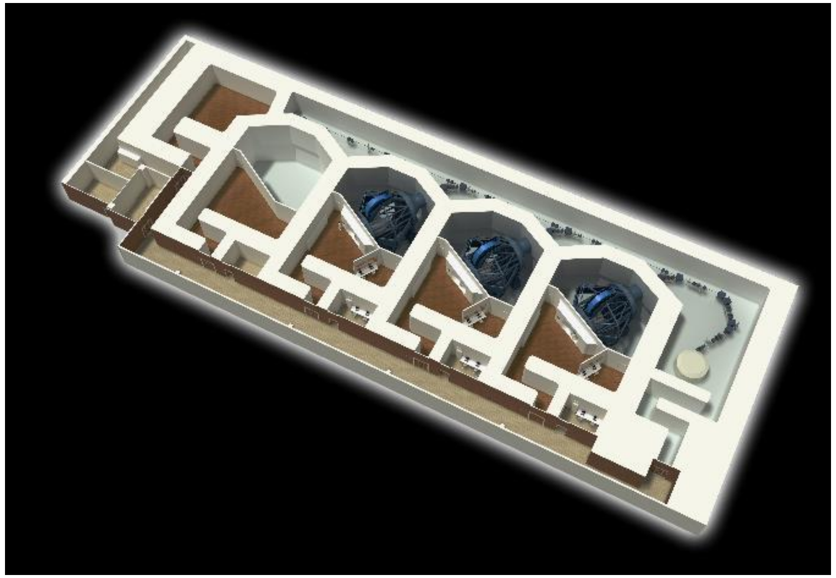
Aizawa Hospital
(Matsumoto, 2014)

National Cancer Center
(Kashiwa, 1998)

Takai Hospital
(Tenri, 2018)

Latest Proton Project: CGMH Kaohsiung, Taiwan

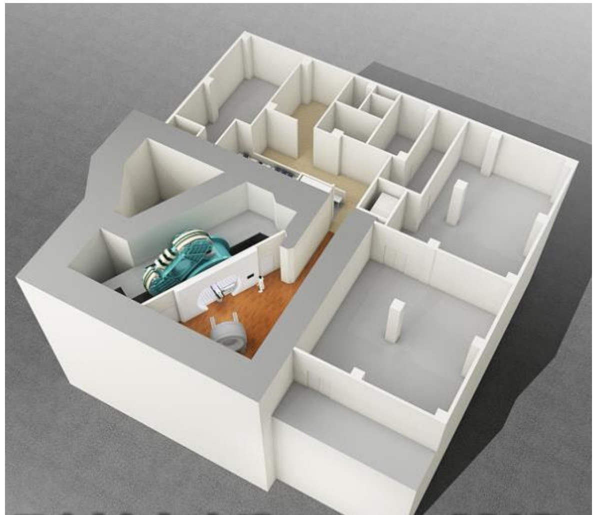
- Chang Gung Memorial Hospital, Kaohsiung, Taiwan
- 3 Gantries + 1 Room for future Expansion + 1 Research Room
- Treatment started in 2018
- Latest technology is installed
  - **Continuous Line Scanning**
  - **Fast Layer Switching**
  - CBCT

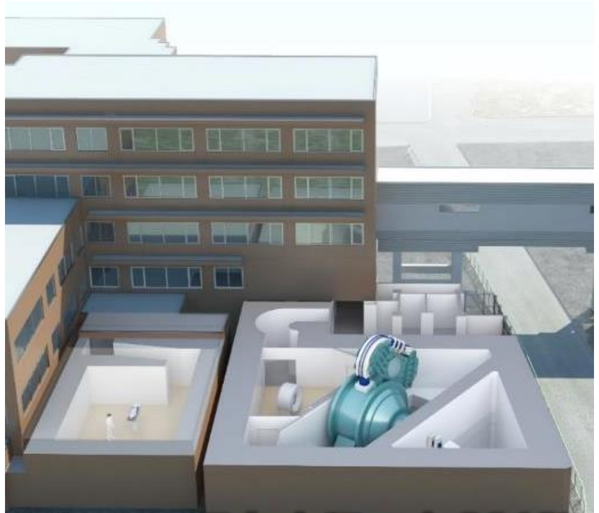


Single-Room Projects in Japan

- Vertical Layout + Compact 360 Gantry to minimize the footprint
- Smooth integration with existing photon vaults


Aizawa (Matsumoto, 2014)


Teishinkai (Sapporo, 2016)


Takai (Tenri, 2018)

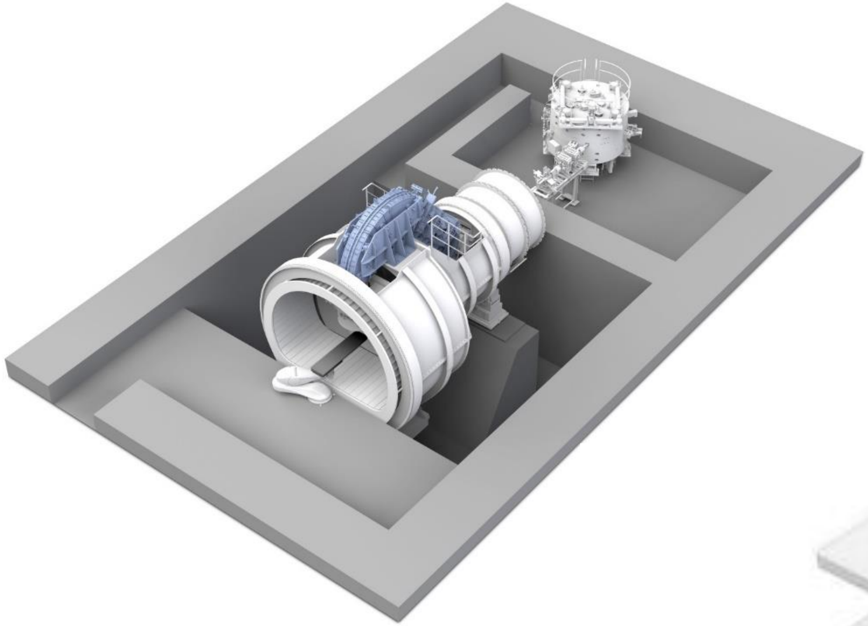
Next Generation PTS CyBeam™

Aug., 2022

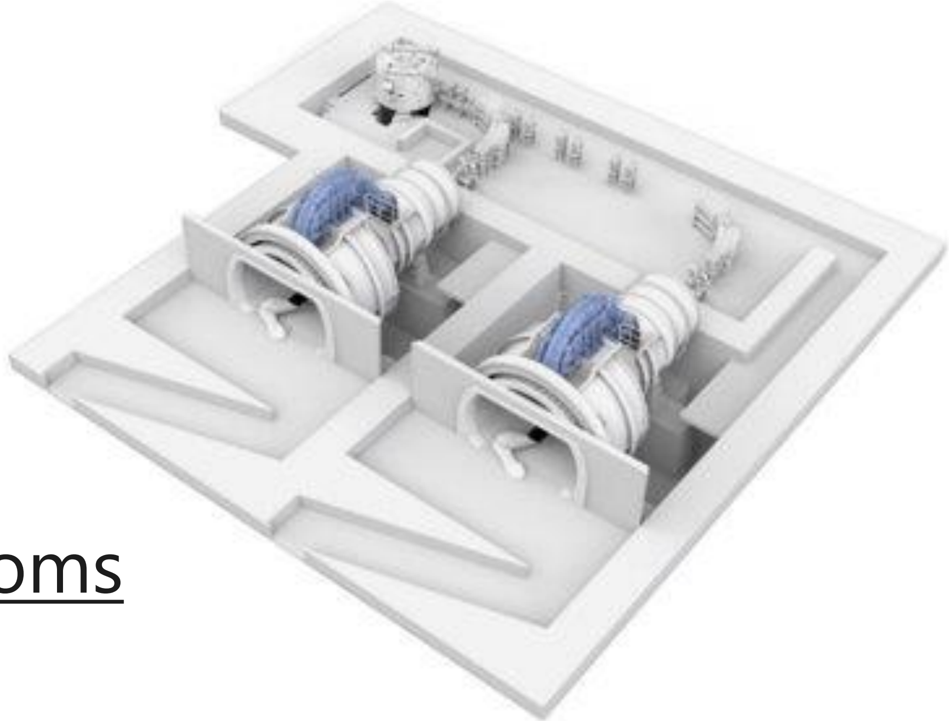
Sumitomo Heavy Industries, Ltd.

Introducing proton therapy easily

- Smaller building volume
- Shorter installation period
- Flexible room plan



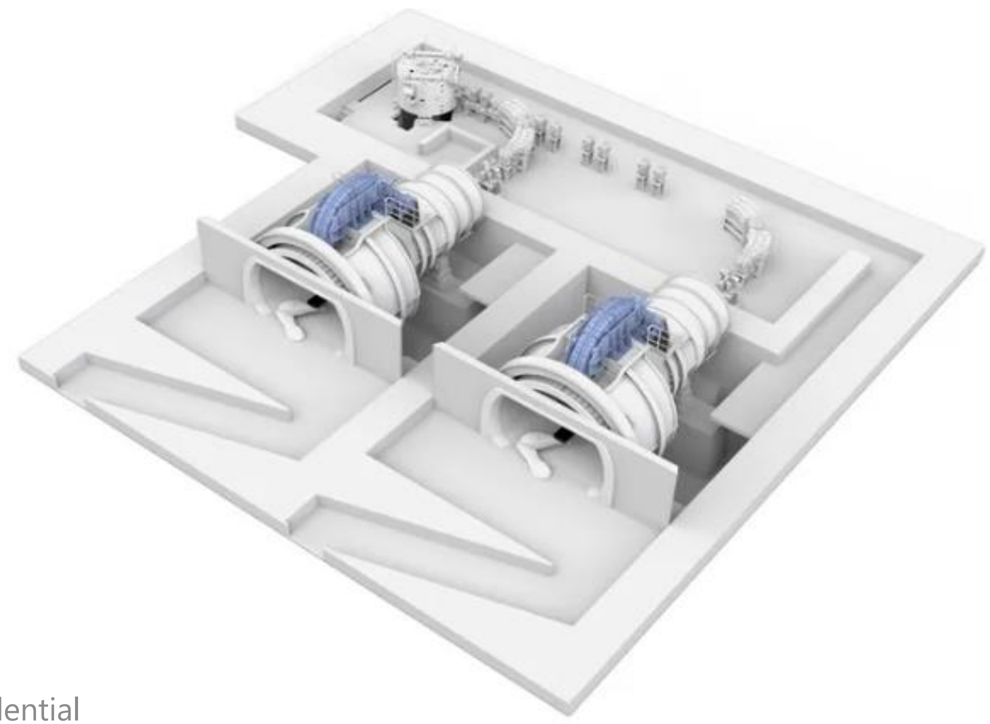
Single room



Multi rooms

First order for next-generation proton therapy system from Taichung Veterans General Hospital

- SHI has received an order from Taichung Veterans General Hospital (Taiwan) for a next-generation proton therapy system.
- The next-generation system will be installed at a new proton therapy center to be established in Taichung City, Taiwan, and proton therapy is scheduled to begin in 2026. This is the first order for SHI's next-generation system.



【台中栄民総医院（Taichung Veterans General Hospital）】

Taichung Veterans General Hospital is a national hospital located in central Taiwan and provides safe and high-quality medical services with new medical technologies and outstanding talents.

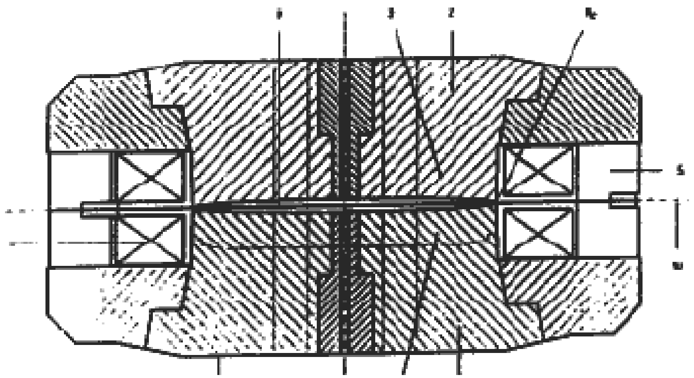
Superconducting cyclotron

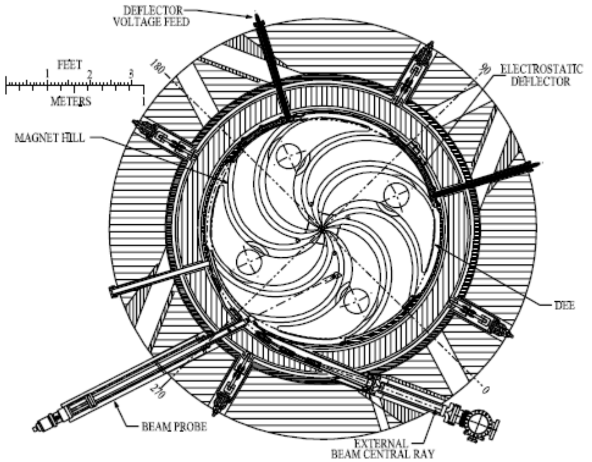
	Normal conducting cyclotron (Existing model)	Superconducting cyclotron (Latest model)	
Energy	230 MeV	230 MeV	
Beam current	300 nA	1000 nA	**>3 times Higher The highest in the world**
Power consumption	450 kW	250 kW	**>44% Saving**
Size	D 4.4 m, H 2.1 m	D 2.8 m, H 1.7 m	**>30% Smaller**
Weight	220 t	70 t	**>60% Lighter**
Other feature		**Liquid-helium free**	**Sumitomo's original technology**

Normal conducting cyclotron

Superconducting cyclotron

Two Types of AVF Cyclotron Design



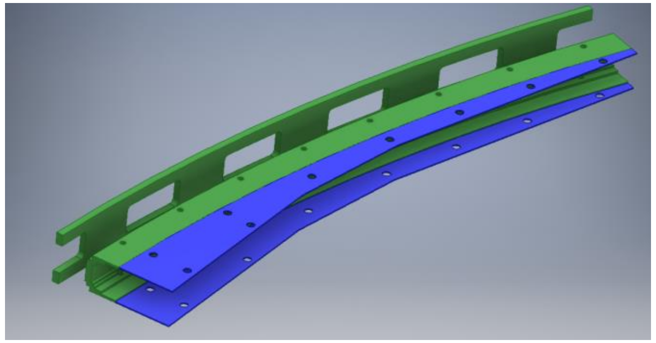


	A. Laisne	Prof. H. Blosser
Hill gap	Narrow (~10 mm)	Wide (> 60 mm)
Advantages	Compact Low magnetic field in extraction beam line	Enough space to set extraction components in hill gaps
Example	P235 / C235 (SHI/IBA) SHI SC230	MSU K500, K1200 Varian 250MeV

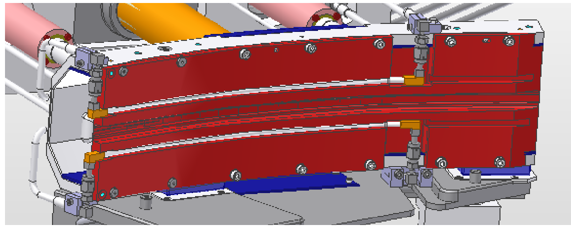
Sumitomo Heavy Industries, Ltd.

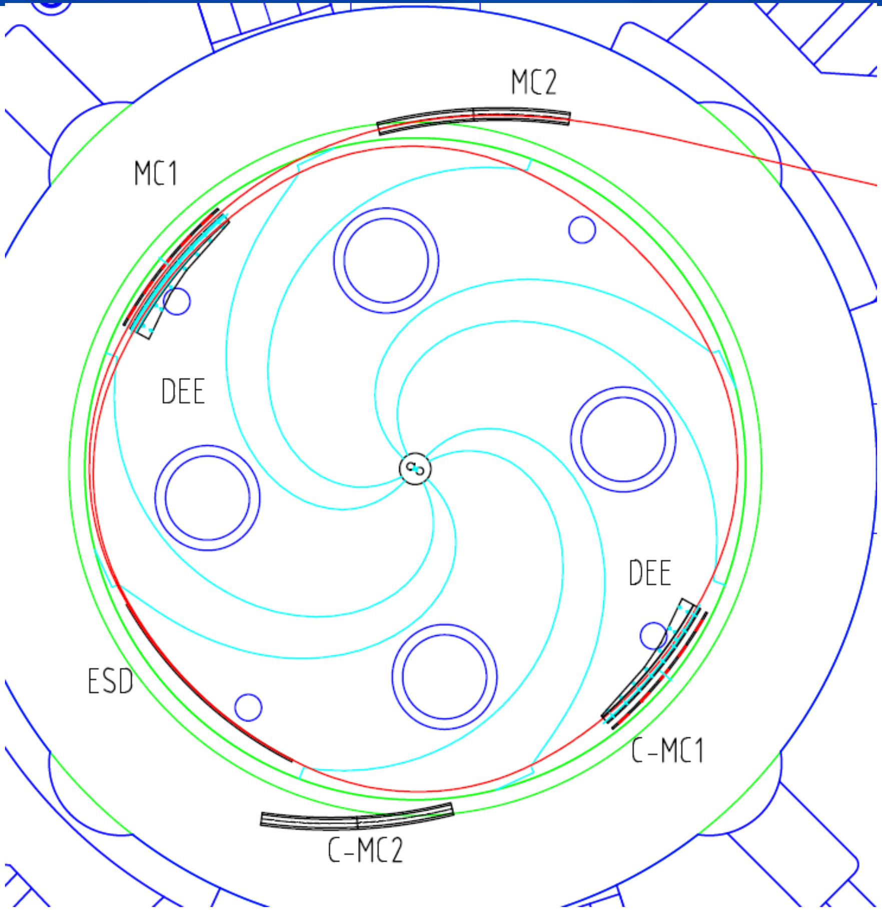
Beam Extraction Scheme

MC1

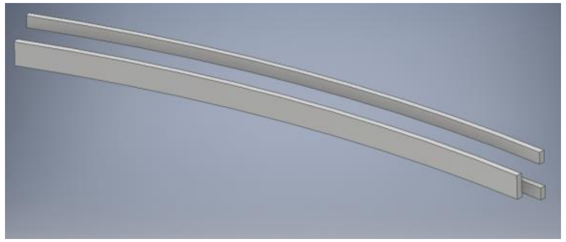


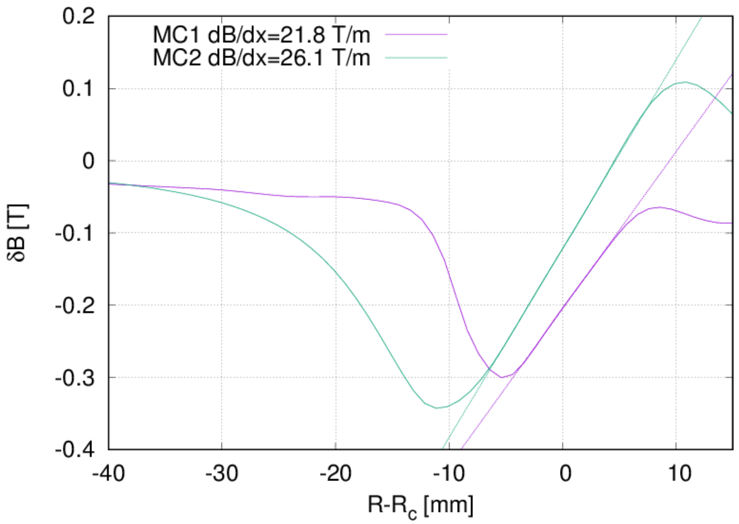
ESD -54 kV, 4mm gap





MC2

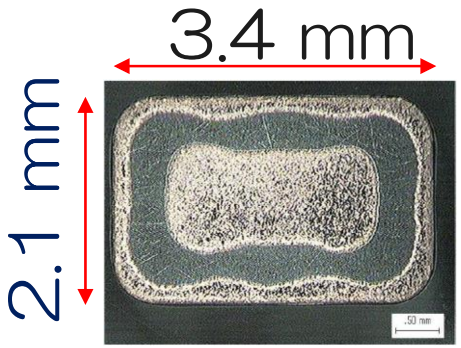




- Beam extraction is made by ESD + MC1 + MC2
- C-MC1, C-MC2 for reducing B1 component.

SC Coil and Cryostat

NbTi wire

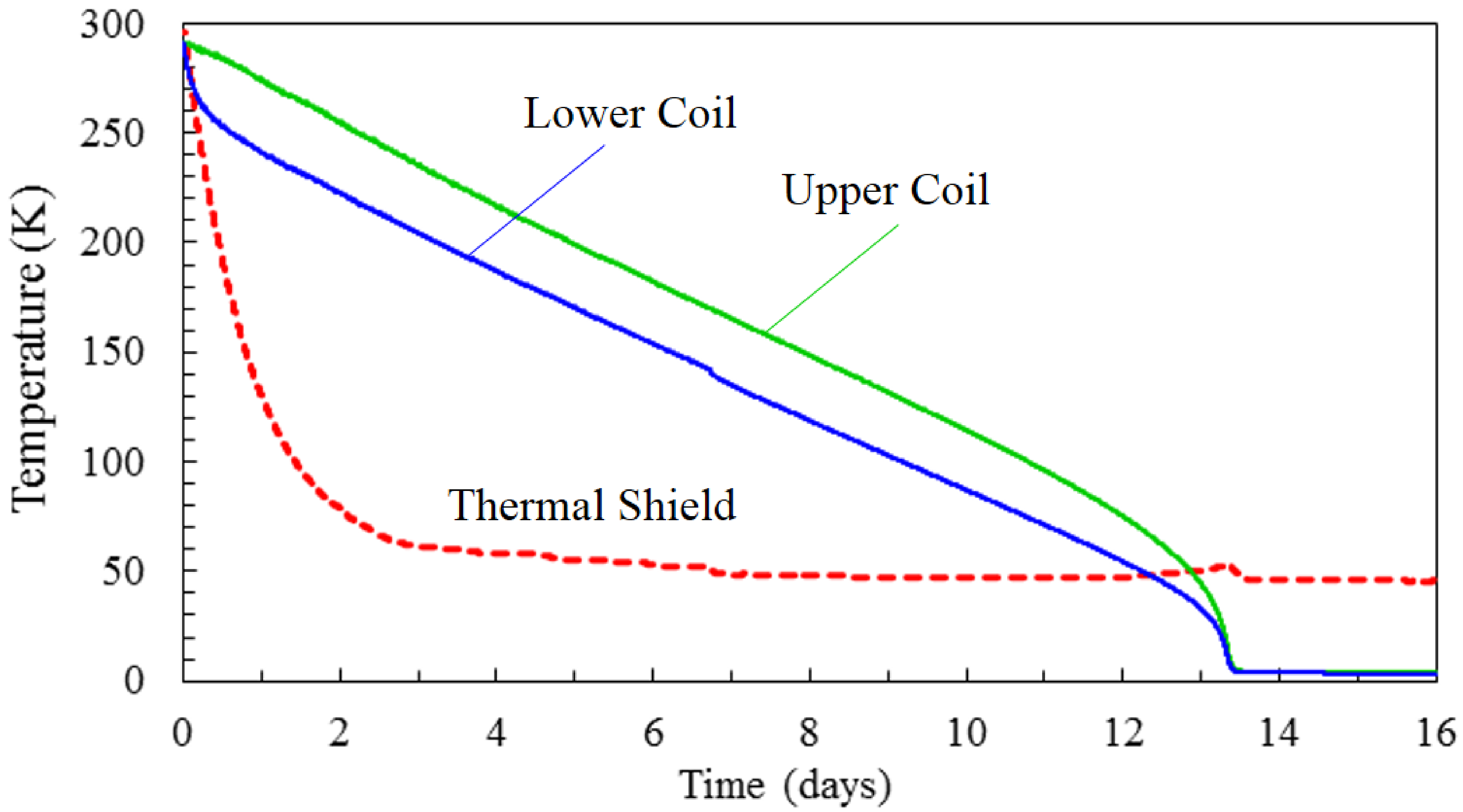


Conductor	Material	NbTi/OFC
	Size	2.1 mm ×3.4 mm
Coil	Structure	Two solenoids
	# of Turn	2208 Turns/coil
Cooling	Type	Conduction cooling
	Cooler	Four 4 K-GM coolers
Rated current		442 A
Maximum current		488 A
Peak B in coil @Imax		4.4 T
Critical temp. @ Imax		7.4 K
Nominal temperature		4.7 K
Initial cooling time		14 days

J. Yoshida et al., in Proc. MT26, 2019.
T. Tsurudome et al., in EUCAS 2019.

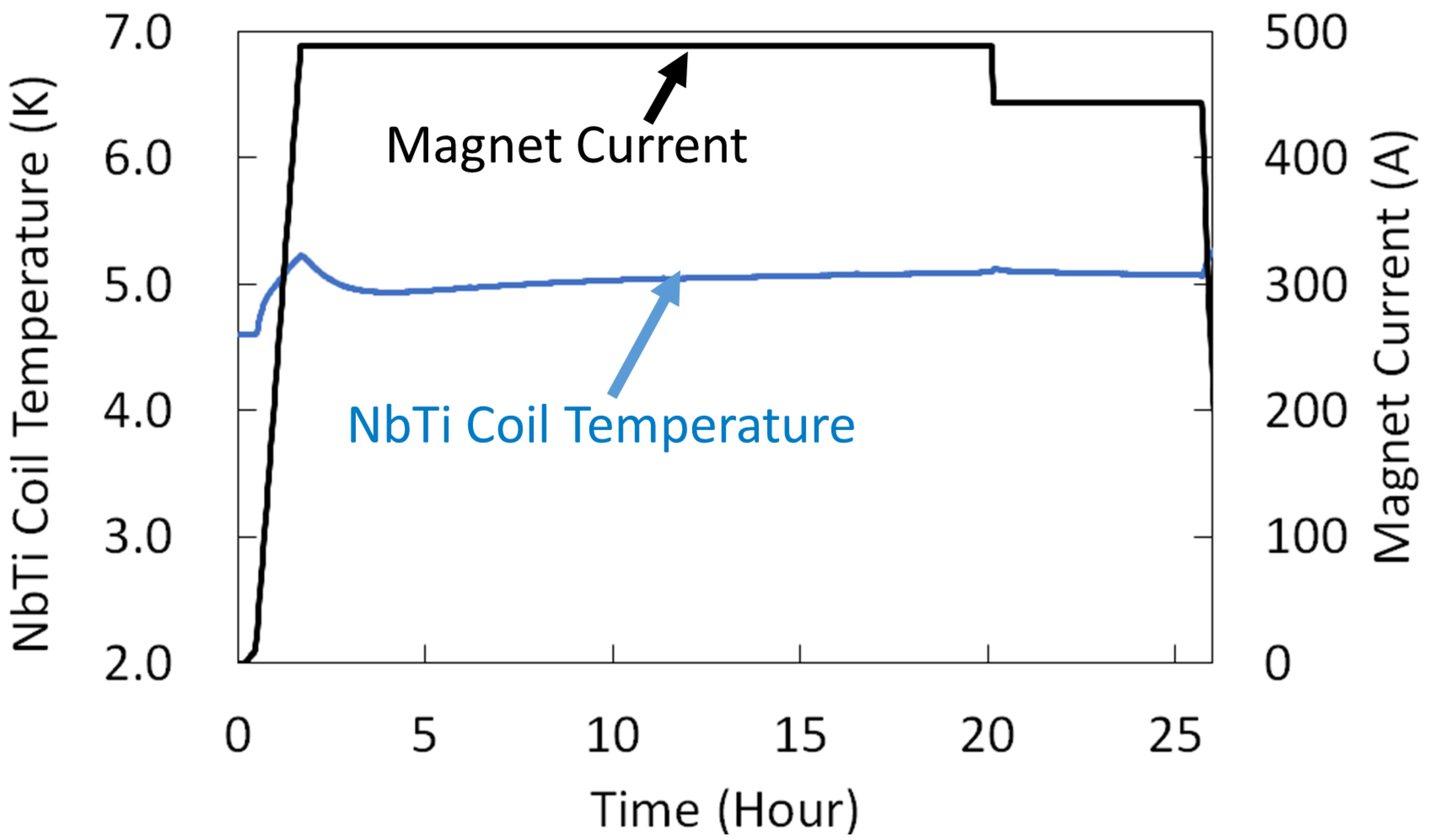
Probe Port
Heavy Industries, Ltd.

Cryostat Cooling Test



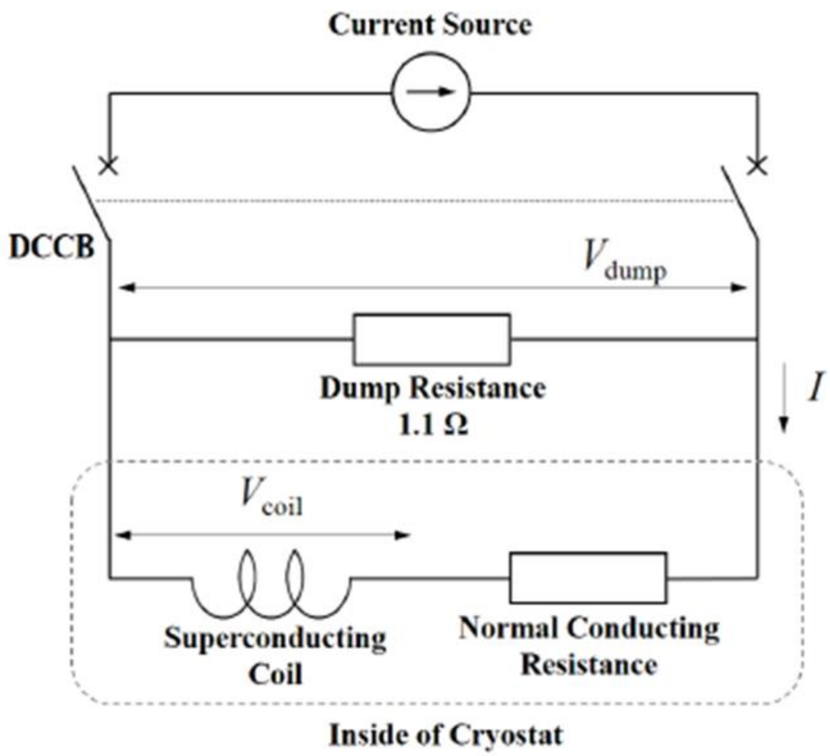
Initial cooling time was 14 days

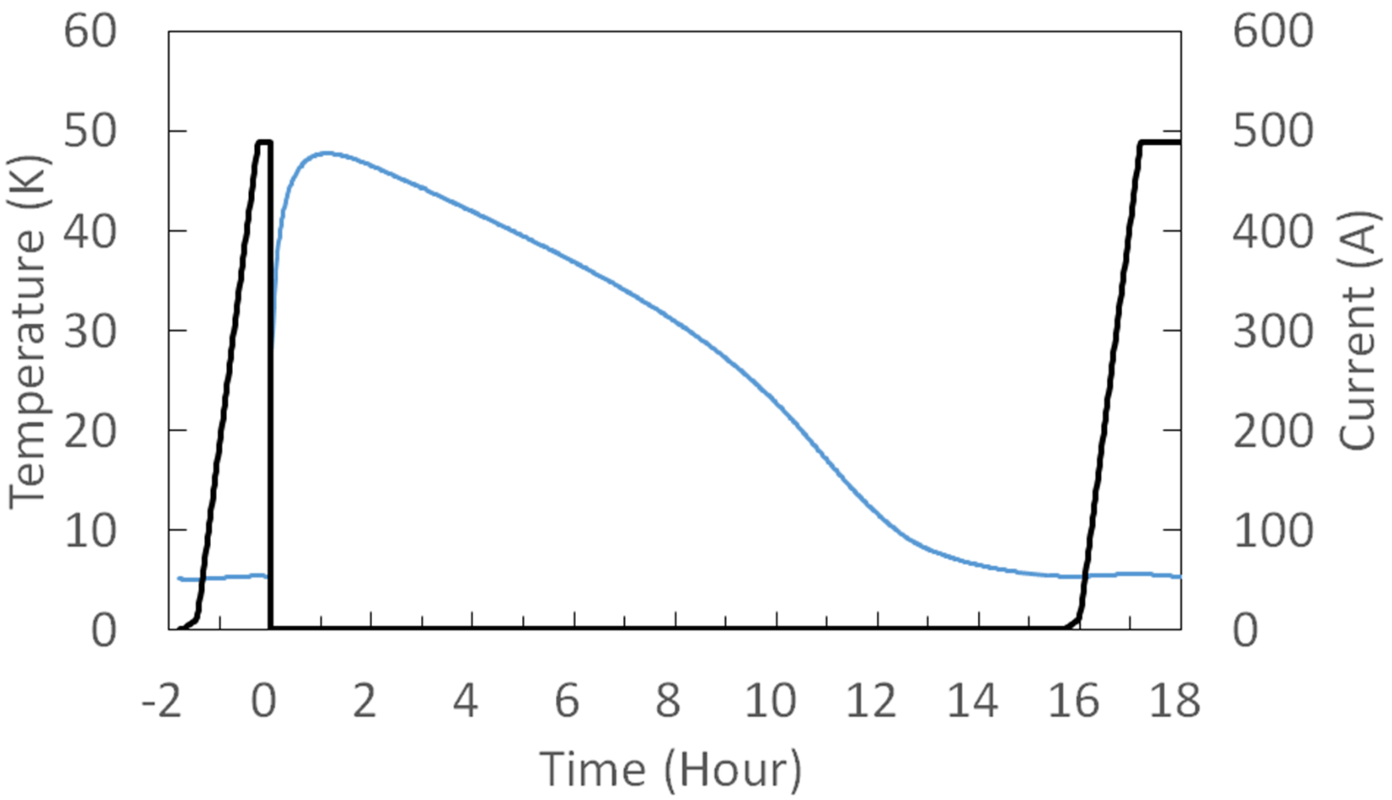
Coil Excitation Test



Ramping up time to 488 A was 1.5 h.
We did not experience quench except during scheduled quench tests.

Quench Recovery Test

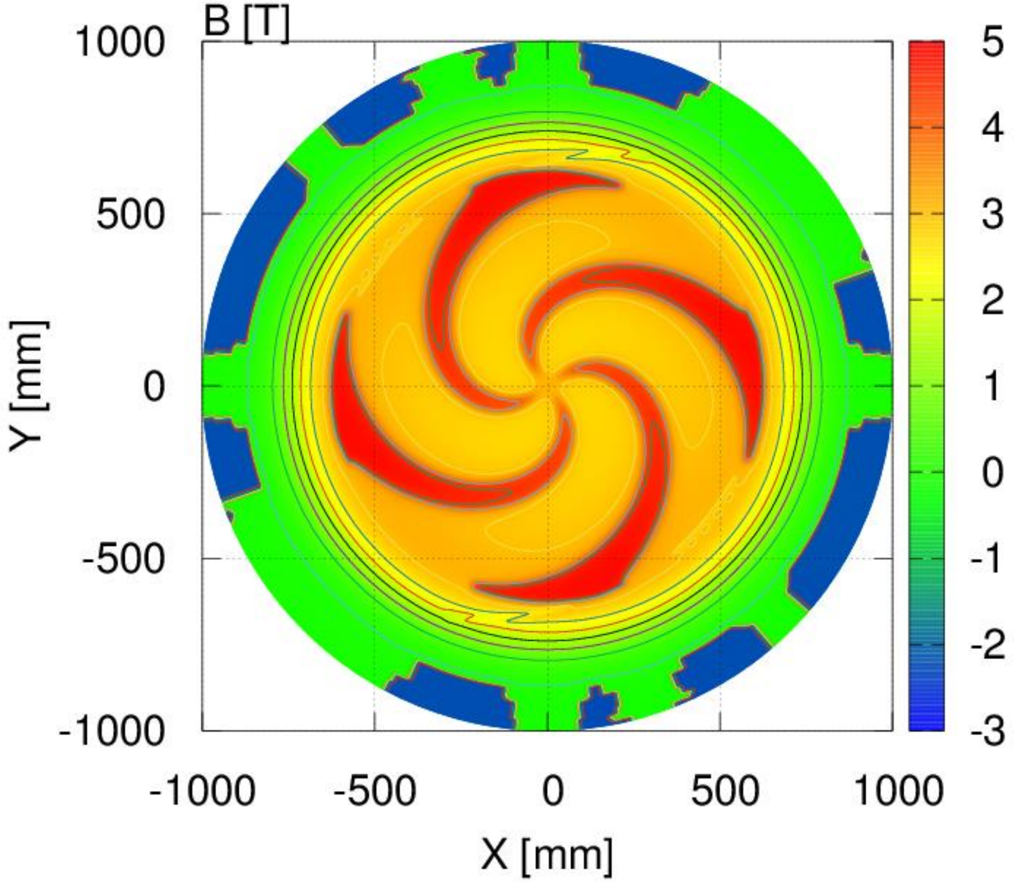




- Stored energy(=5.1 MJ) was consumed by SC coil and dump resistor.
- Quench recovery time was 17 h.

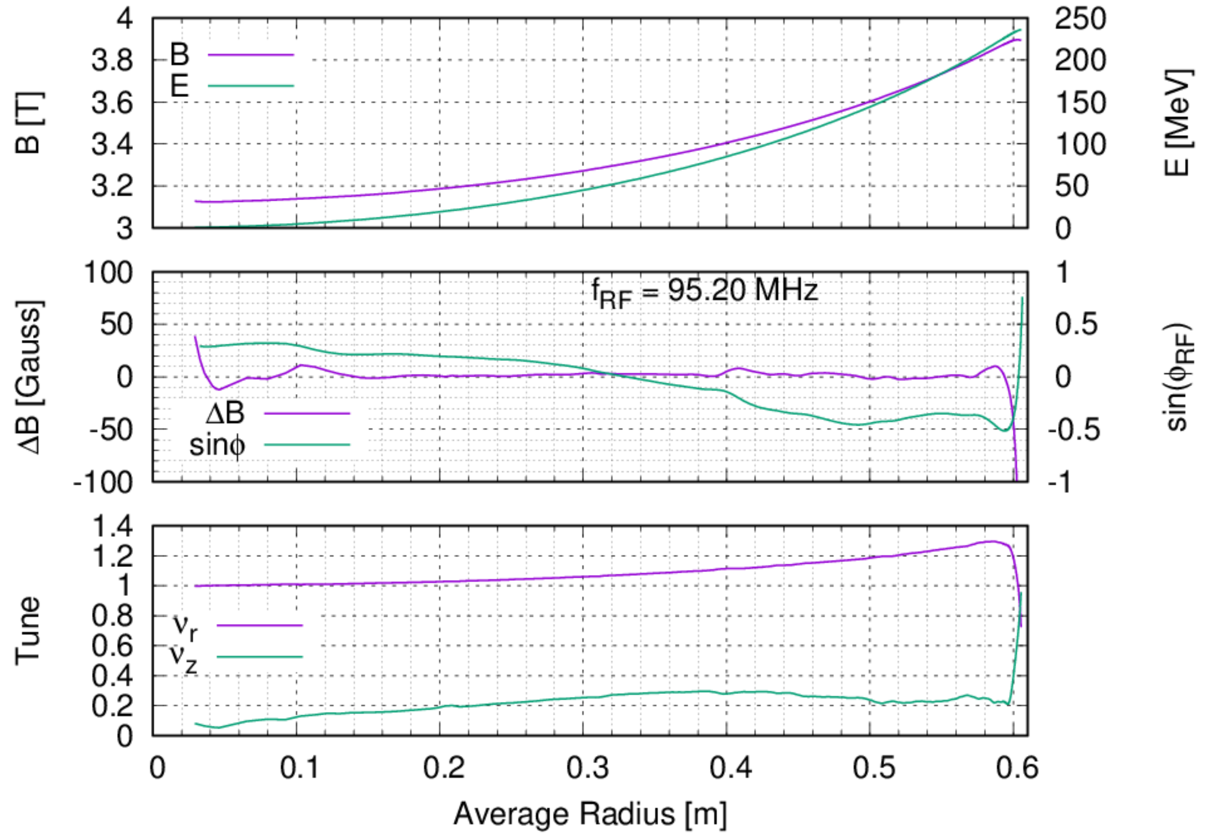
Field Mapping System

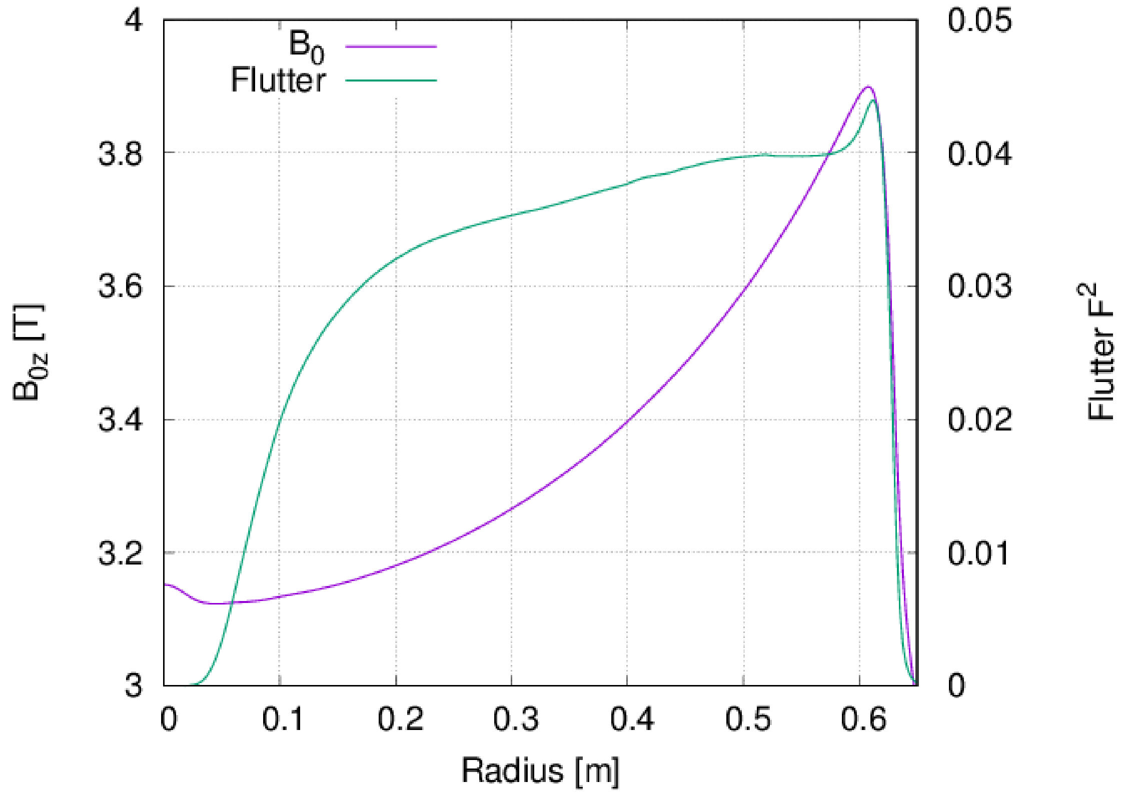
Y. Ebara et al., in Cyclotrons 2019



- It took 2.5 h to obtain a full field map by 6 Hall probes

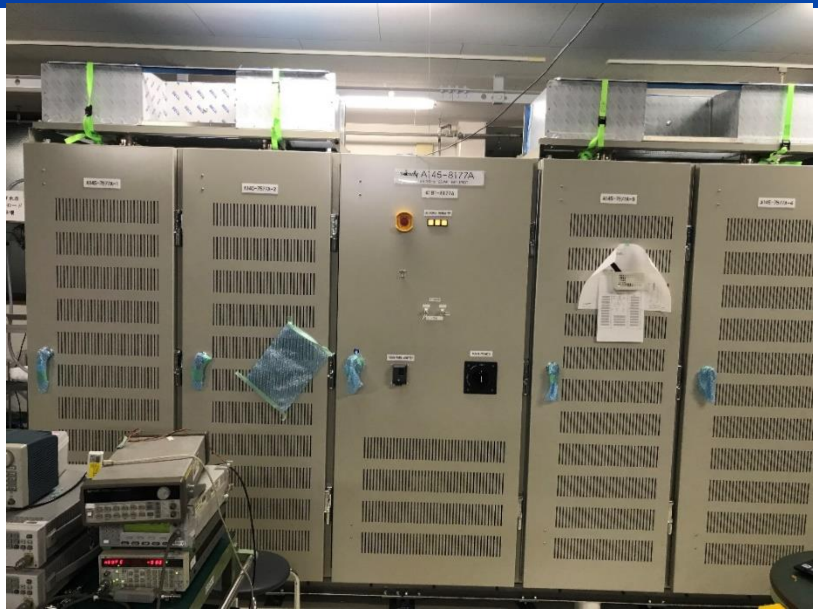
Isochronous Field





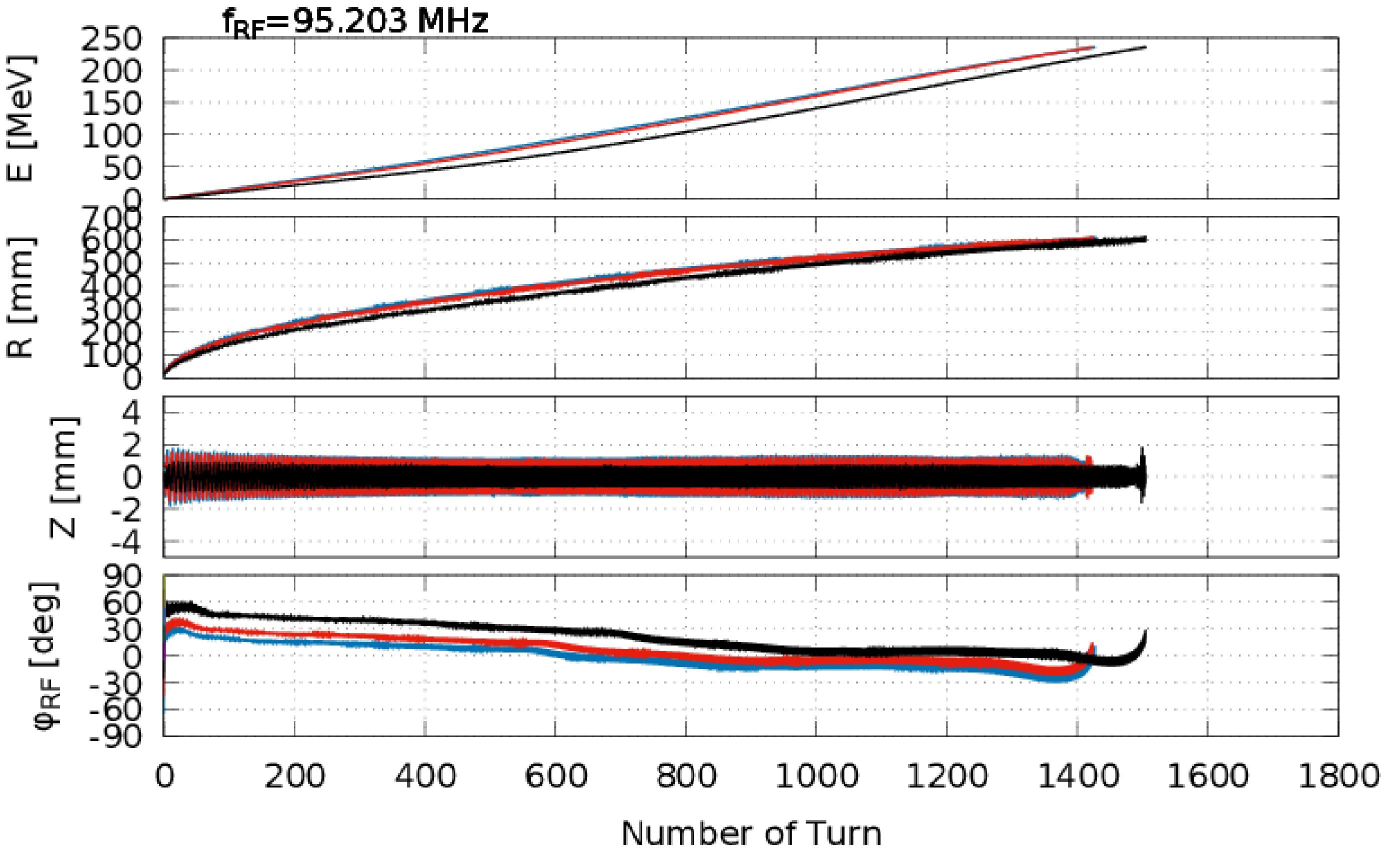
- Sectors were machined three times to obtain isochronous field

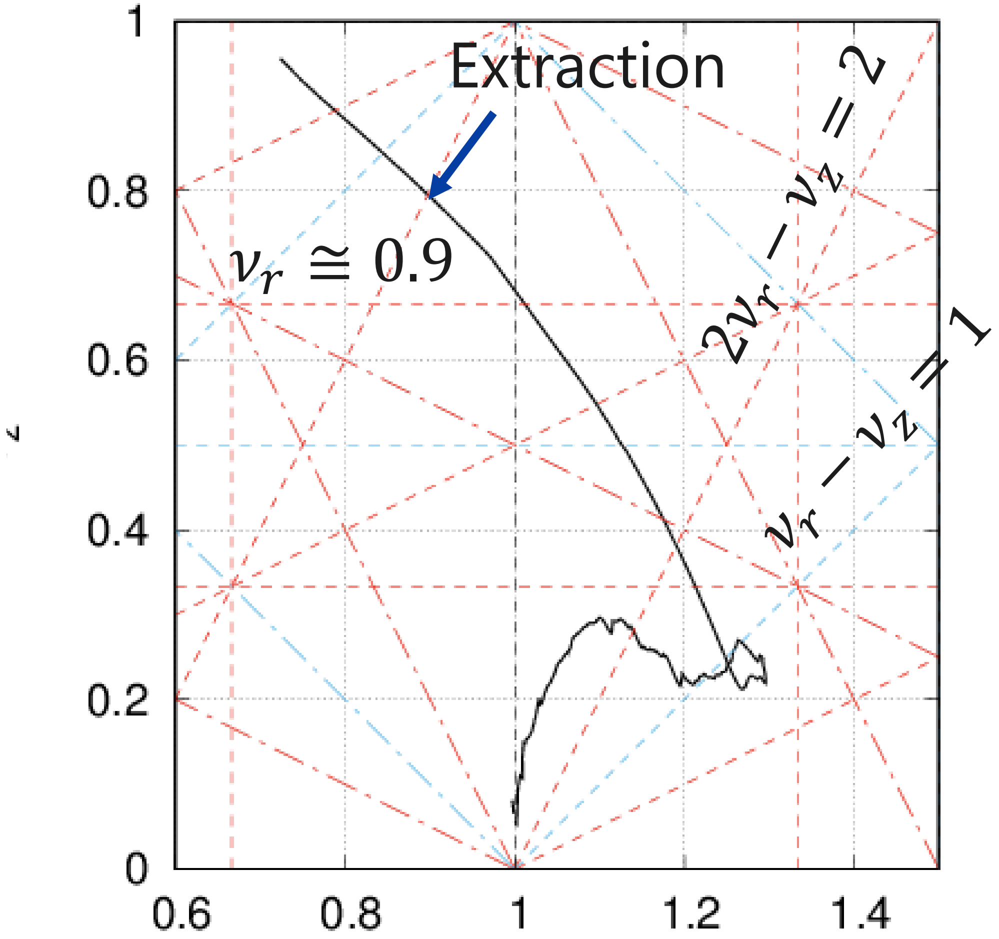
RF System



Type	120 kW solid state
Frequency	95.2 MHz
Cavity Wall Loss	70 kW
Dimension	W3,704 x H2,000 x D1,110

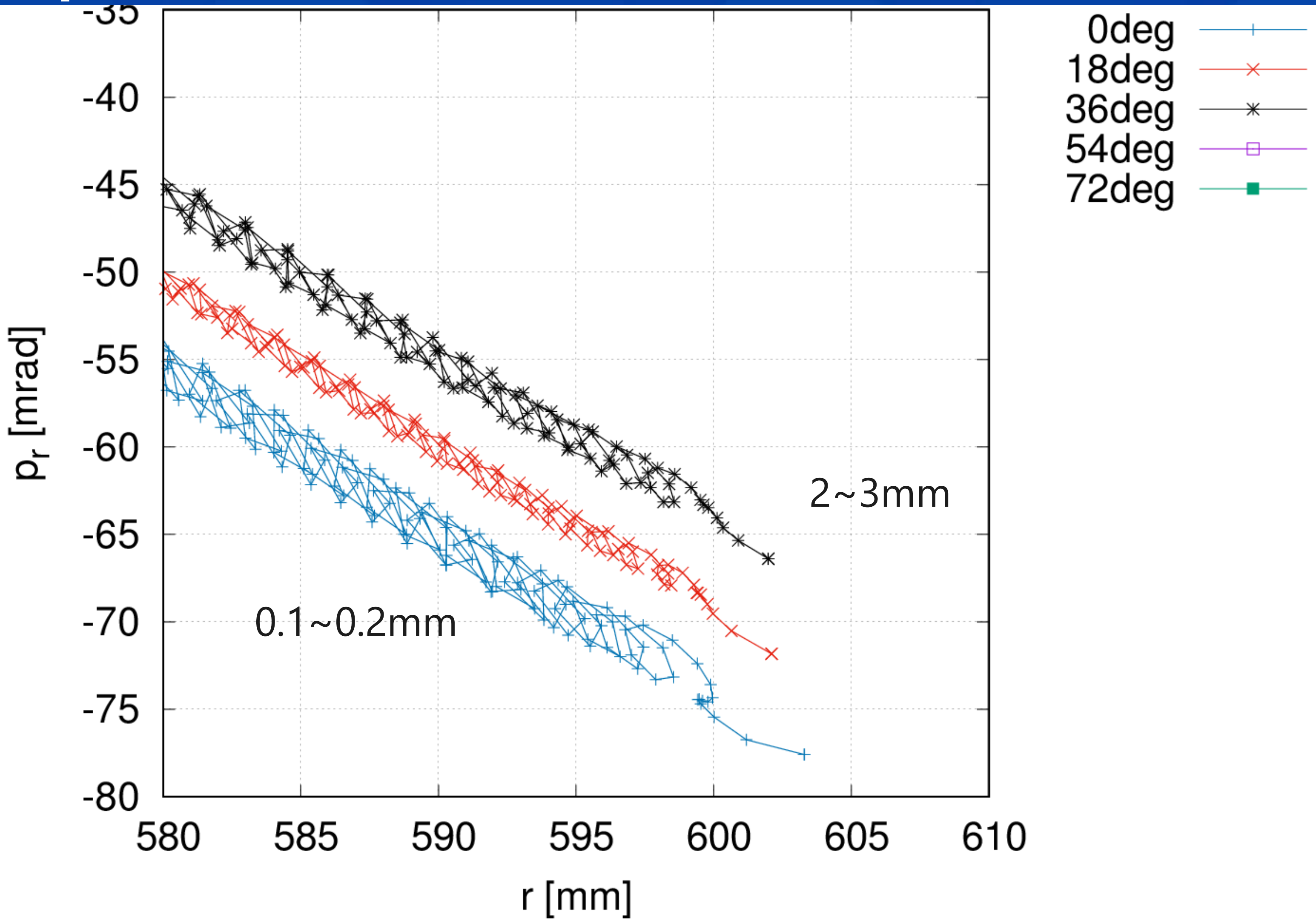
Beam Acceleration Simulation





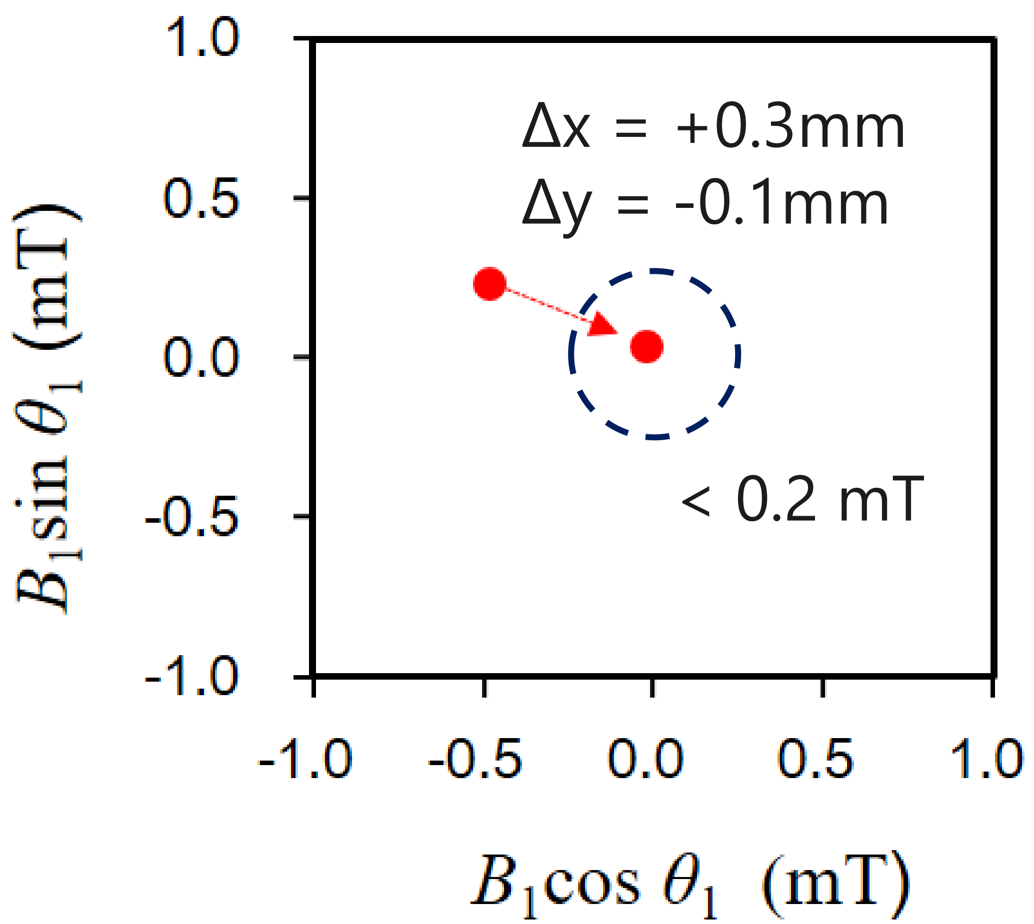
- No apparent beam blow up during acceleration.
- Precessional extraction should be used to get large turn separation.

Turn Separation around Extraction



Sumitomo Heavy Industries, Ltd.

B1 correction



B1 at R=600 was corrected by manually moving SC coils horizontally.

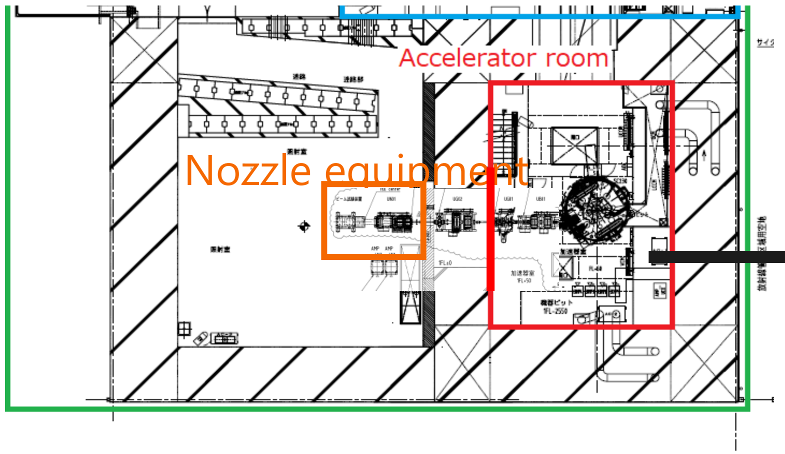
Cyclotron transferred to Saijo Plant

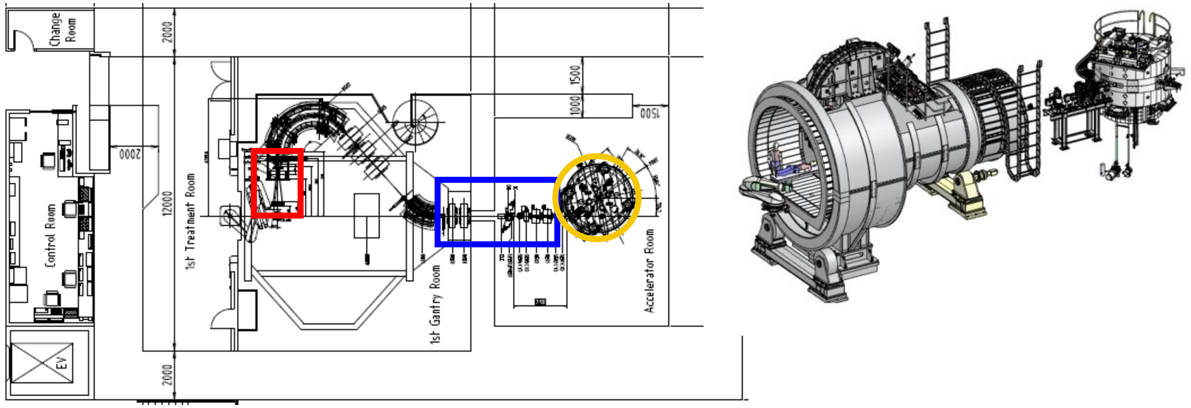
Sumitomo Heavy Industries, Ltd.

CyBeam test system

Confidential

- Cyclotron, ESS, and Nozzle system

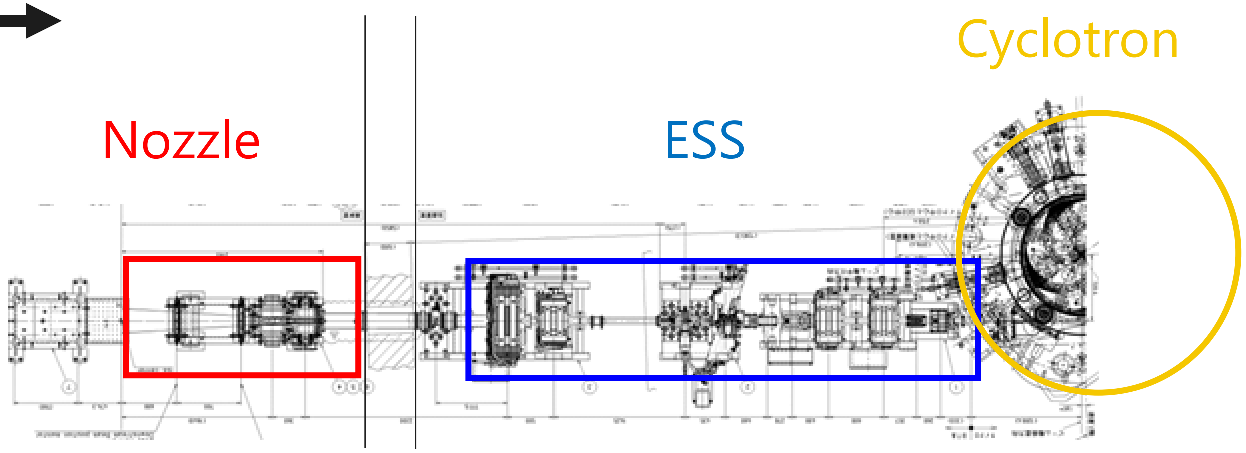




Next generation proton therapy system

<u>Test items</u>

- ✓ Cyclotron
  - ✓ Energy, Maximum beam current
- ✓ ESS
  - ✓ Energy switching time
- ✓ Nozzle
  - ✓ Field size, Beam position accuracy
  - ✓ Scanning speed
  - ✓ Dose rate

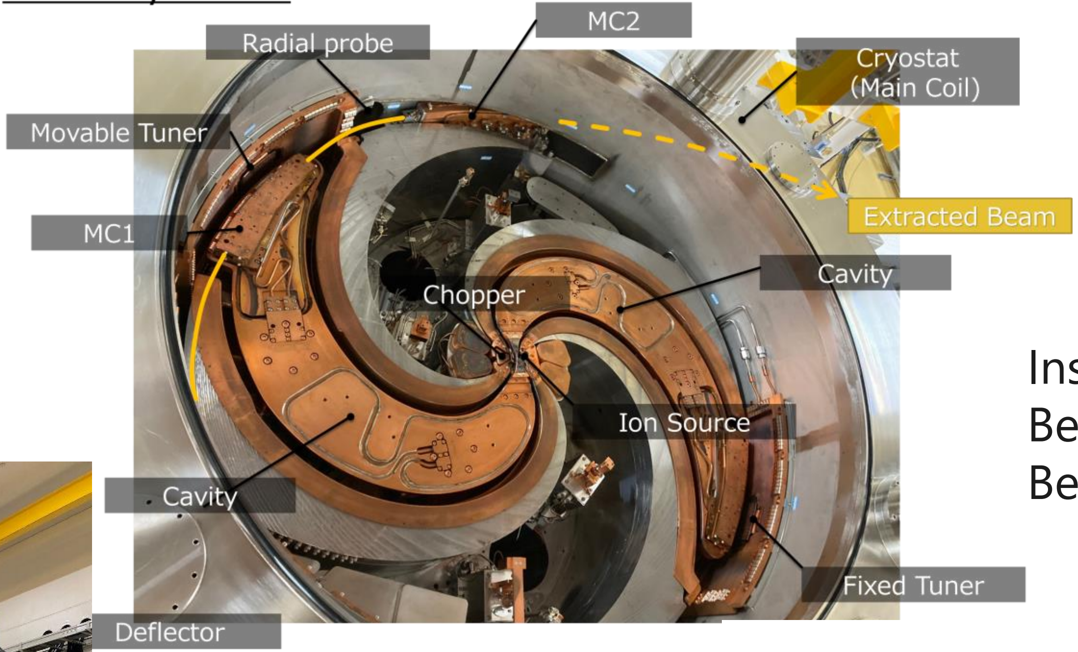


Saijo APDC layout

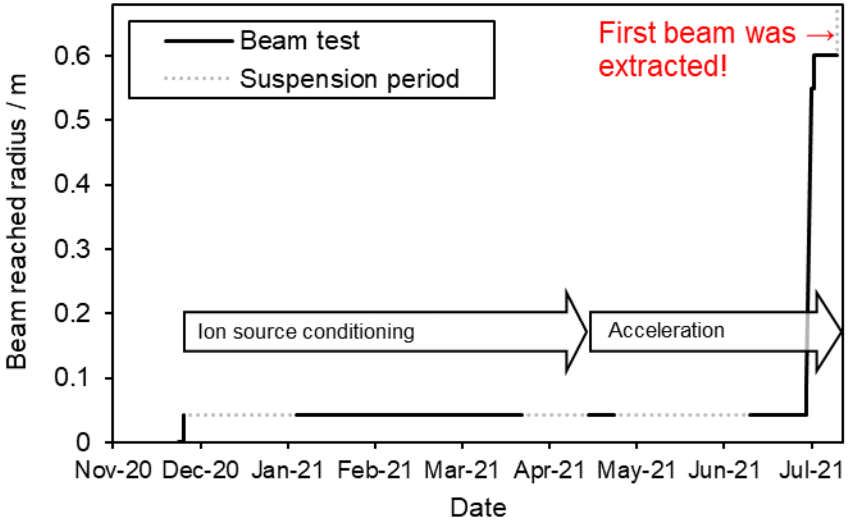
Superconducting cyclotron 1

Confidential

Inside cyclotron

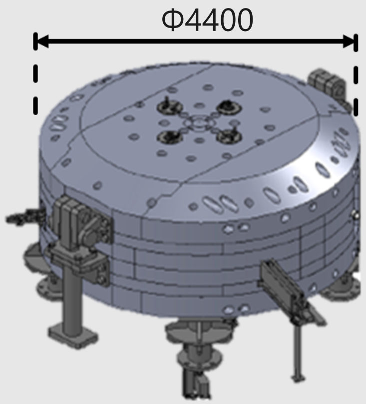
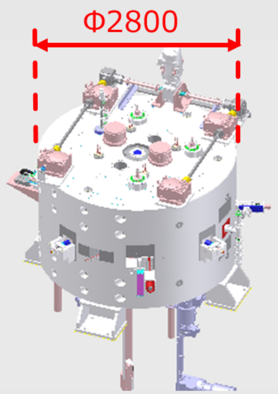


Install start: May 2020
Beam test start: Apr. 2021
Beam extracted: Jul. 2021

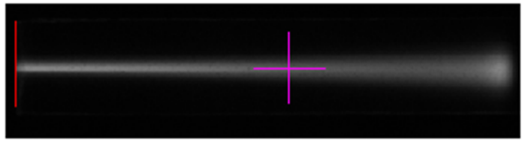


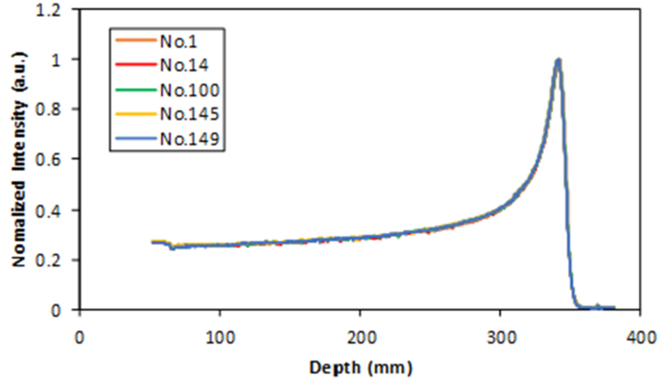
Superconducting cyclotron 2

Comparison with existing model

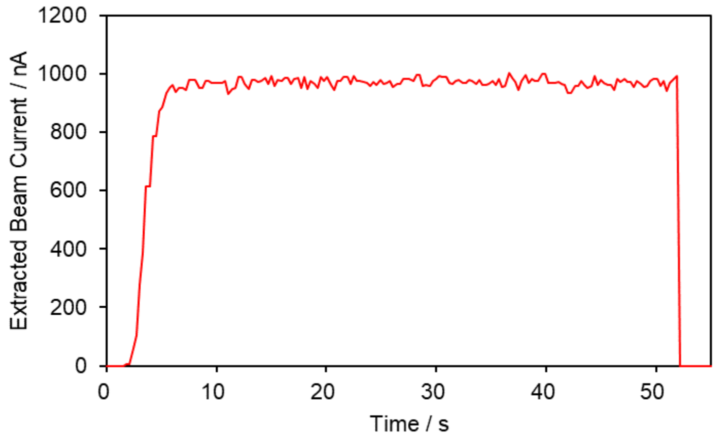
Item	Existing model P235	New model SC230	Comparison
Energy	230 MeV	230 MeV	-
Max. Beam current	300 nA　CW	1,000 nA　CW	X 3.3⤴
Footprint	Φ4.4	Φ2.8	60% Down
Weight	220 t	70 t	68% Down
Power Consumption	450 kW	250kW	44% Down
Image			

☑Energy 236MeV　> 230MeV



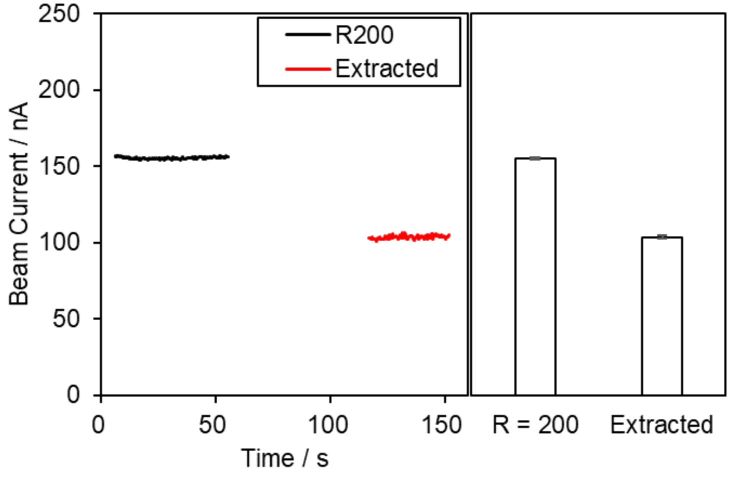


☑ 1,000nA beam extraction.

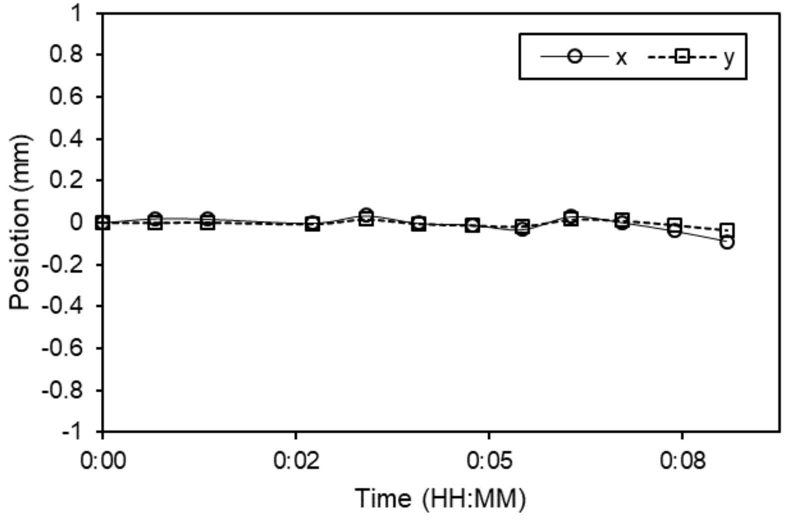


Superconducting cyclotron 3

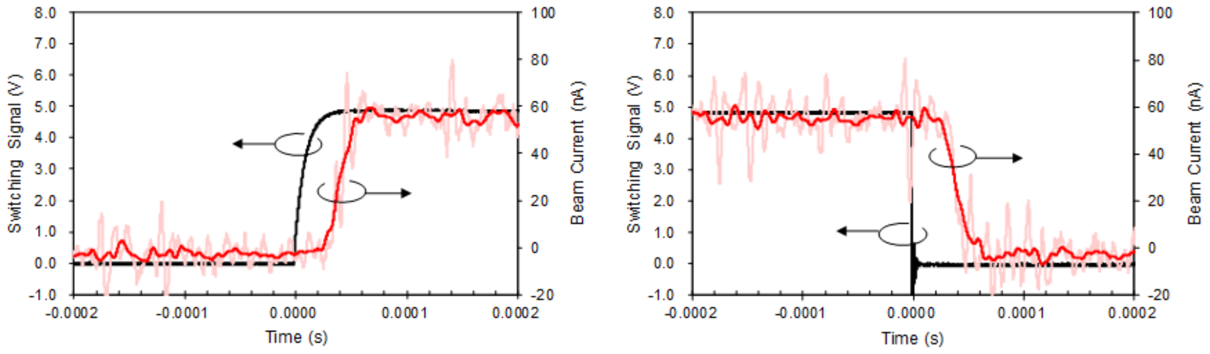
☑Extraction efficiency: Extracted / R200 = 67%



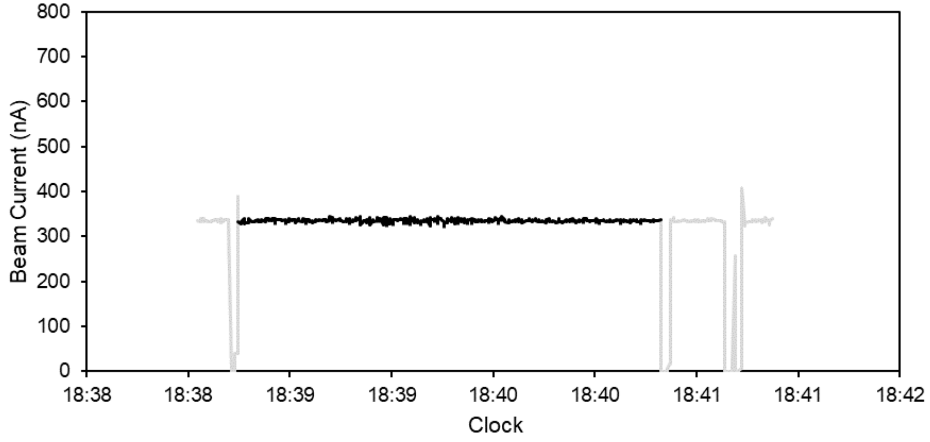
☑ Beam position stability < 0.1mm



☑Beam on/off < 50us



☑ Beam Current stability (1sigma) < 2%



Thank you for your attention!