QST

NIRS HIMAC

PRESENT STATUS AND FUTURE PROSPECT OF HEAVY ION RADIOTHERAPY

Contents:

1. Introduction
2. Facilities and contribution from ECRISs
3. Clinical result
4. Present status under the Japanese national health insurance
5. Future prospect of heavy ion radiotherapy

A. Kitagawa, T. Fujita, M. Muramatsu

National Institute of Radiological Sciences,

National Institutes for Quantum and Radiological Science and Technology (QST-NIRS), Chiba, Japan

1. Introduction

QST NIRS HIMAC

Advantage of charged particles

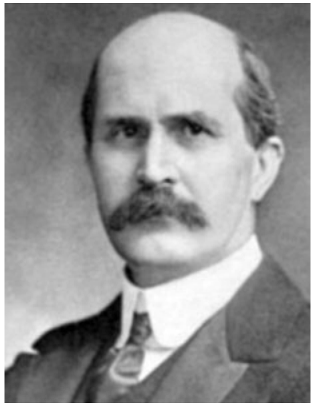
Charged particle

Particles' movement
in a straight line

Particles' energy is slowly decreasing
through the interaction

High dose distribution
near the stopping position

Low dose distribution
at high energy region



William Henry Bragg
(1862-1942)

Robert Rathbun Wilson
(1914-2000)

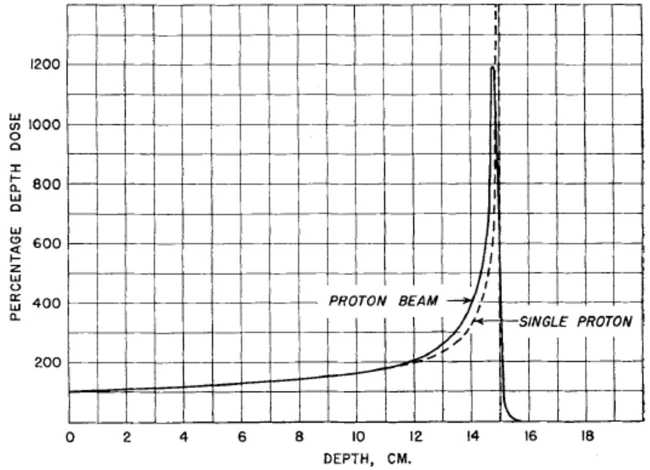


Fig. 2. The dotted curve shows the relative dose due to a single 140 Mev proton. The full curve shows qualitatively the depth dose curve for a beam of 140 Mev protons in tissue.

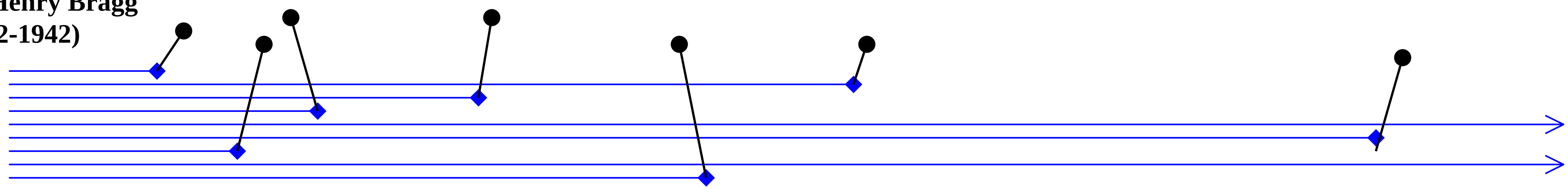
"If a depth of 15 cm were required, then 140 MeV protons would be needed.

…

Heavier nuclei, such as very energetic carbon atoms, may eventually become therapeutically practical. "

Robert R. Wilson, Radiology. 47 (5): 487, 1946.

photons



High dose distribution
due to amount of photons

Photons' amount and energy
are steadily decreasing

Low dose distribution,
and a few photons penetrate deep

1. Introduction

Biological effectiveness of heavy ions

Heavy ions

Particles' movement in a straight line

Particles' energy is slowly decreasing through the interaction

High dose distribution near the stopping position

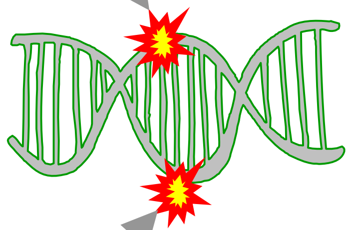
Low dose distribution at high energy region

Robert Rathbun Wilson (1914-2000)

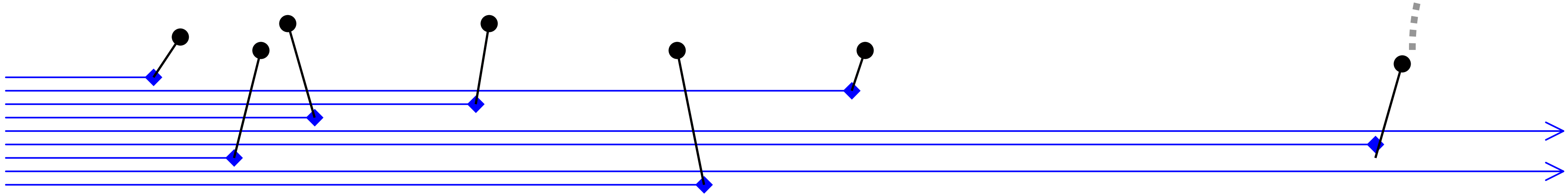
"the biological damage depends not only on the number of ions produced in a cell, but also upon the density of ionization. Thus the biological effects near the end of the range will be considerably enhanced due to greater specific ionization, the degree of enhancement depending critically upon the type of cell irradiated."

Robert R. Wilson, Radiology. 47 (5): 487, 1946.

Secondary electrons or radicals affect DNA in cells



photons



High dose distribution due to amount of photons

Photons' amount and energy are steadily decreasing

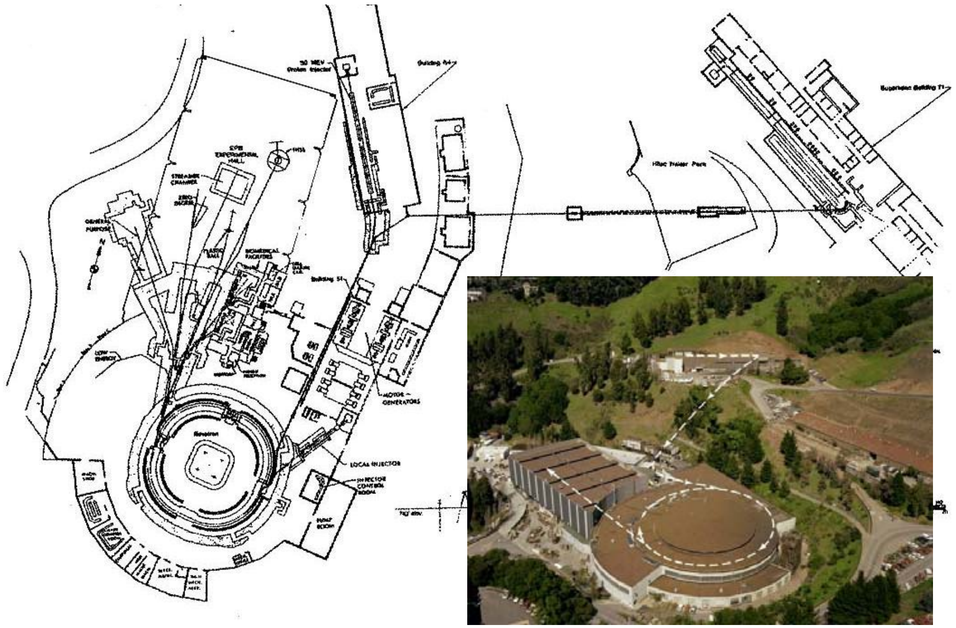
Low dose distribution, and a few photons penetrate deep

Pioneer work at Lawrence Berkeley Laboratory

1940‘s R. Willson proposed the medical application of heavy ion.

↓

1975 LBL start clinical trials (mainly Ne). 440 patients has been treated.
1992 The research had been aborted



The facility was dedicated for physics.
The institute had no hospital.

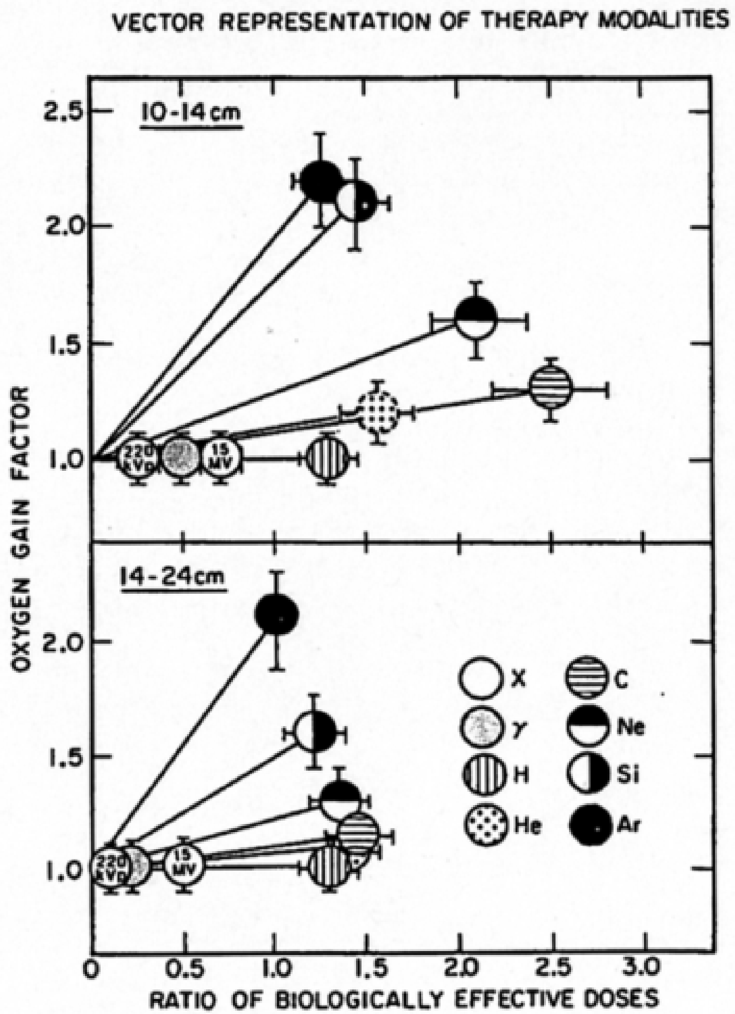


FIG. 31. Vector representation of low LET and high LET particle therapy modalities (as discussed in Section V in the text) for treatment of a small, shallow field (upper panel) and a large, deep field (lower panel).

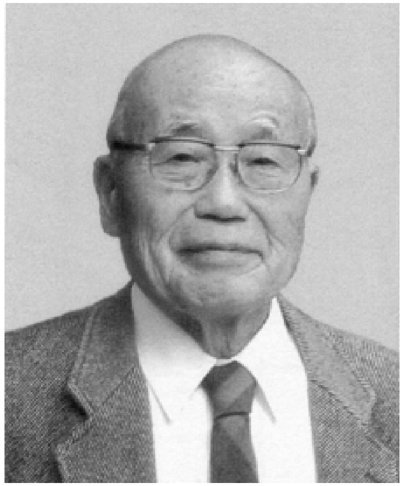
E.A. Blakely, et al., Adv. Radiat. Biol. 11, 295 (1984).

HIMAC project

1980's Feasibility study at NIRS

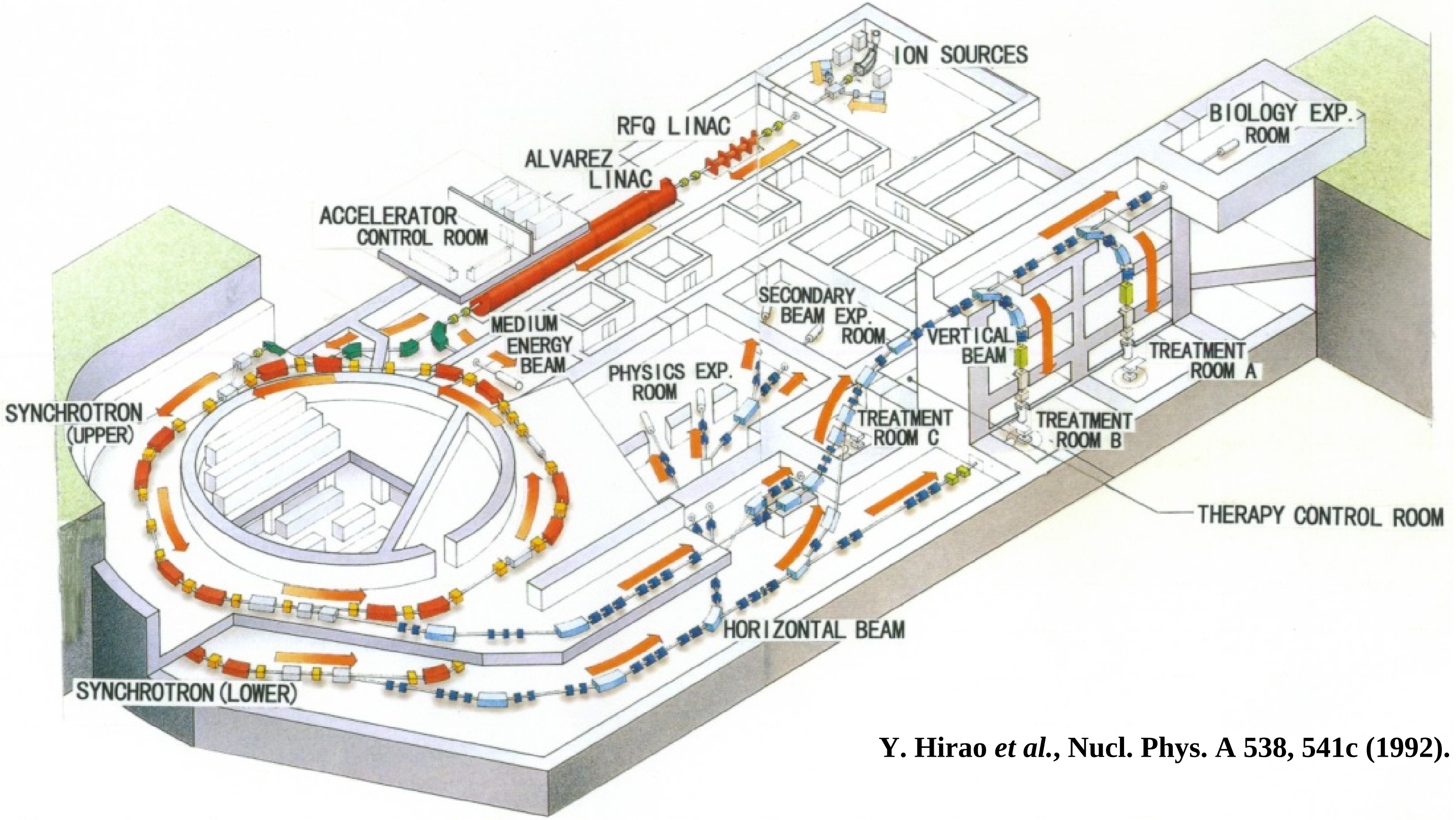
1984 Start of Heavy Ion Medical Accelerator in Chiba Project

1994 Clinical research was started



Youichiro Umegaki
(1922-2010)

Yasuo Hirao
(1930-2016)



Y. Hirao *et al.*, Nucl. Phys. A 538, 541c (1992).

The facility was designed for medical use and it has own hospital.

NIRS

HIMAC

He ← C → Ne

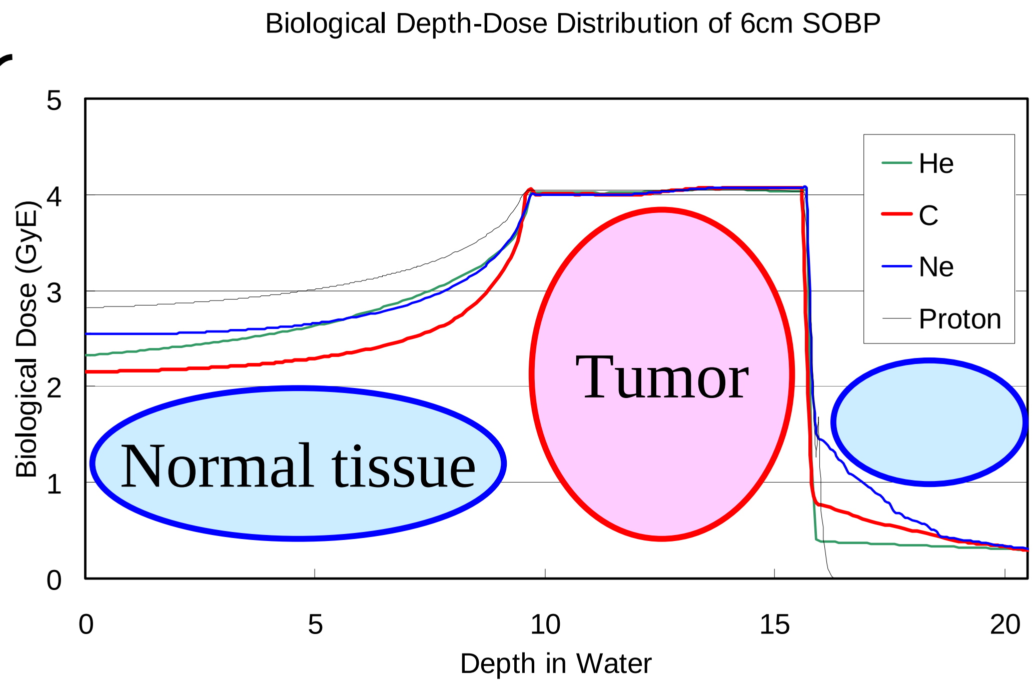
Why Carbon?

<Physical>

Logitudinal Distribution
- **Bragg peak**
- **Projectile fragmentation**

Lateral Distribution
- **Multiple scattering**

<Biological>
- **Relative Biological Effectiveness**
- **Oxygen Enhancement Ratio**
- **Cold spot problem**



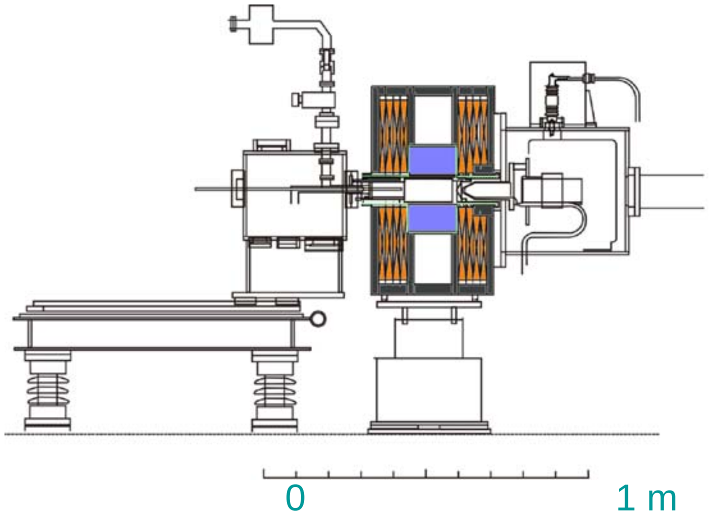
Thickness: ~ 6 cm

Depth: ~ 16 cm

2. Facilities and contribution from ECRISs

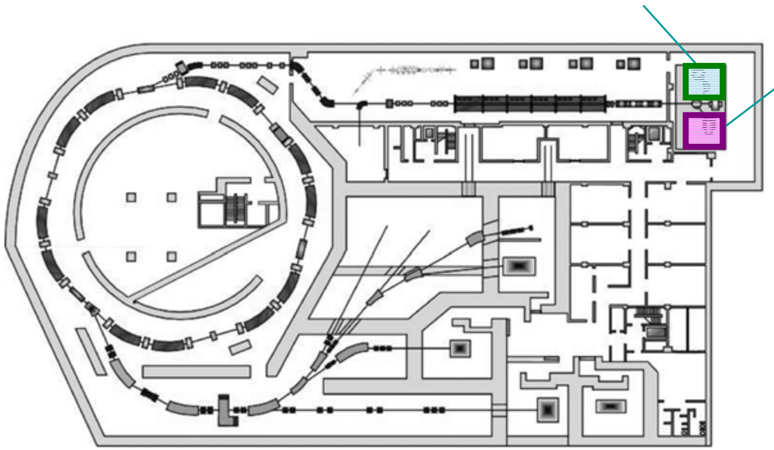
ECRISs at facilities

NIRS-ECR

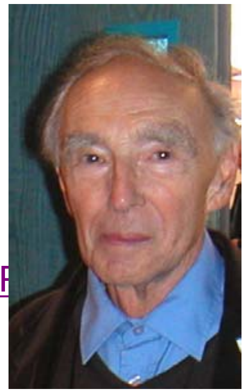


Requirements:
- Long life time
- Long-term stability
- Reproducibility
- Easy operation
- Easy maintenance

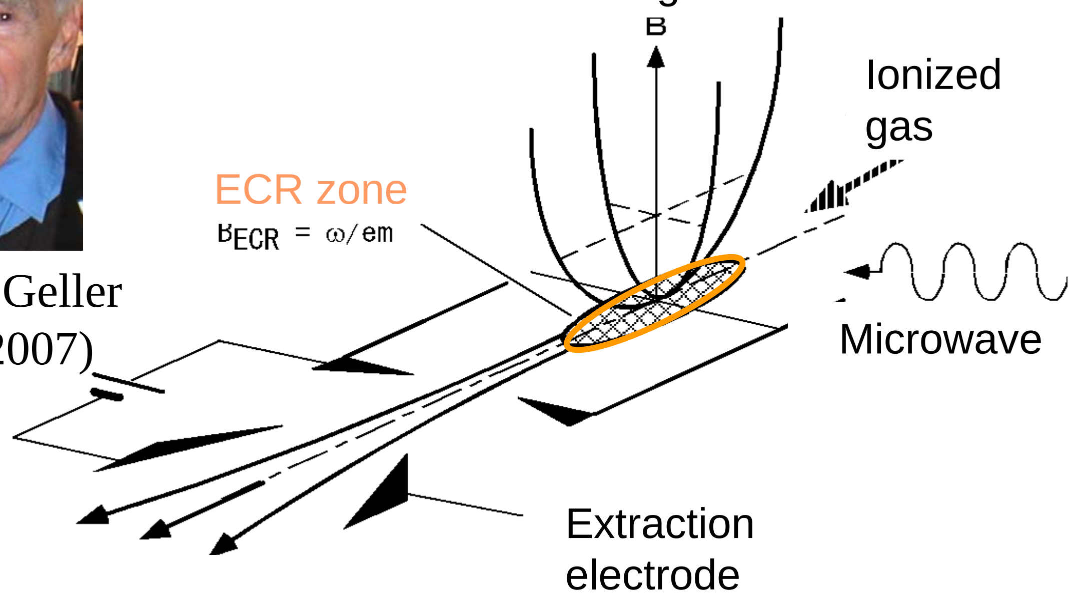
The carbon ions are produced from a gaseous compound like CH_4 or CO_2.
Since the ECR ion source has no consumptive or deteriorate parts, it is expected from view points of long lifetime, easy operation and maintenance.



HIMAC



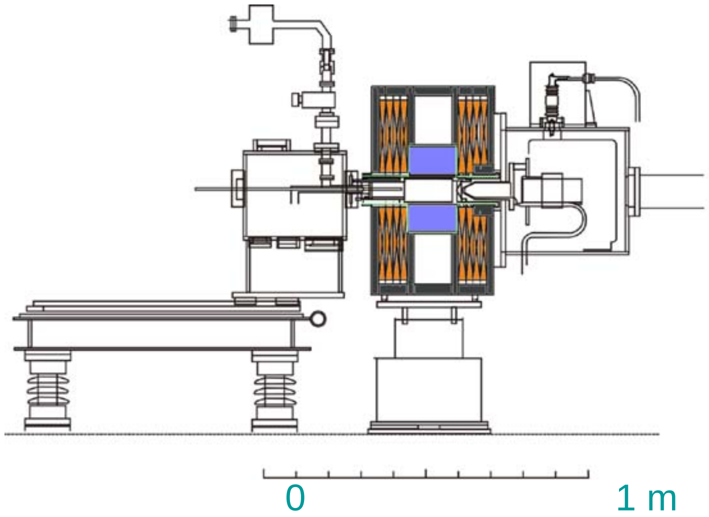
Richard Geller
(1927-2007)



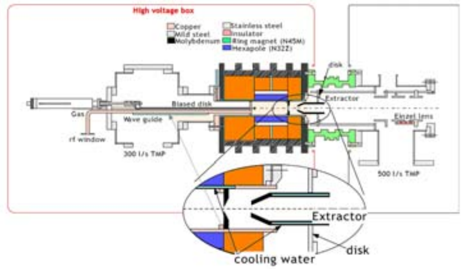
QST NIRS HIMAC

ECRISs at facilities

NIRS-ECR

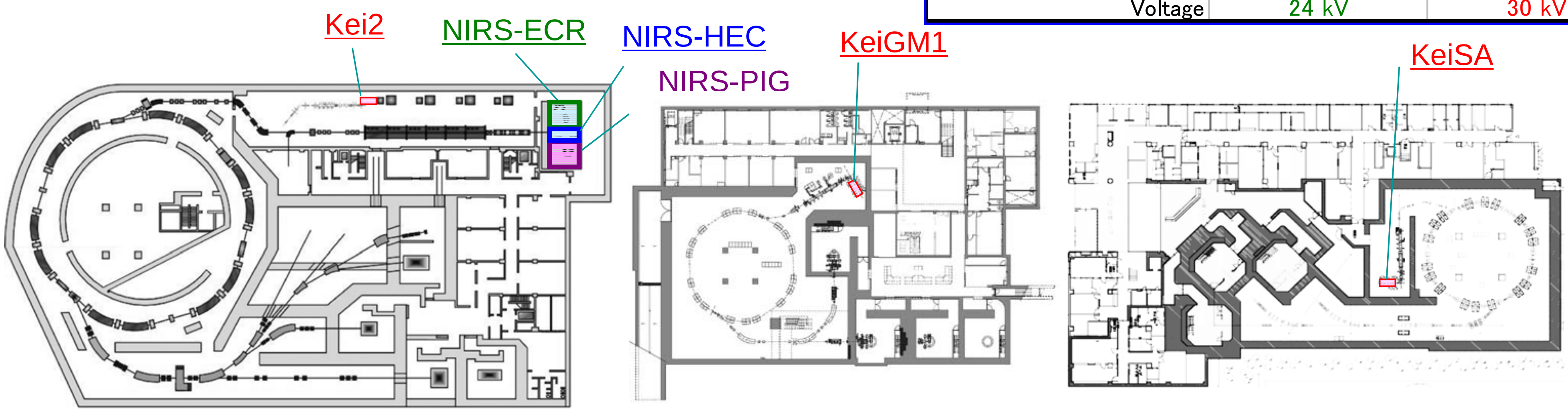


Kei2



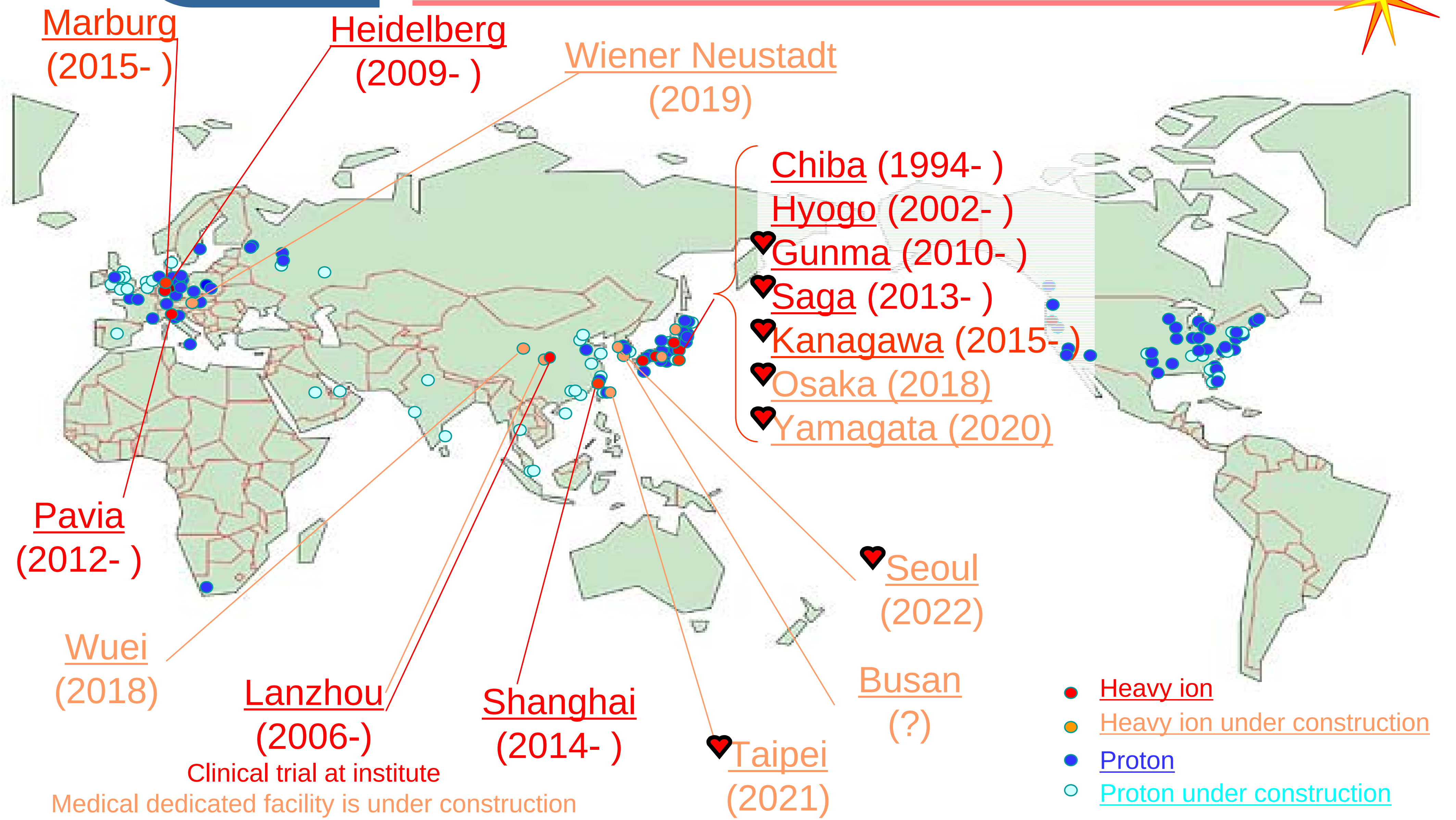
M. Muramatsu *et al.*, Rev. Sci. Instrum. 76, 113304 (2005).

	NIRS-ECR	Kei2
Mirror magnetic field		
material	Electric coil	Permanet (NdFeB)
Injection field	0.87 T (max. 9.3)	0.87 T (fixed)
Minimum B field	0.25 T (max. 4)	0.25 T (fixed)
Extraction field	0.59 T (max. 7.6)	0.59 T (fixed)
Axial magnetic field		
material	Permanent (NdFeB)	Permanent (NdFeB)
Surface field	0.8	0.75
Effective chamber size		
Length	150	105
Diameter	70	55
Microwave		
Frequency	10 GHz (fixed)	8 – 11 GHz
Power	300 W (max. 1500)	300 W
Extraction		
Voltage	24 kV	30 kV



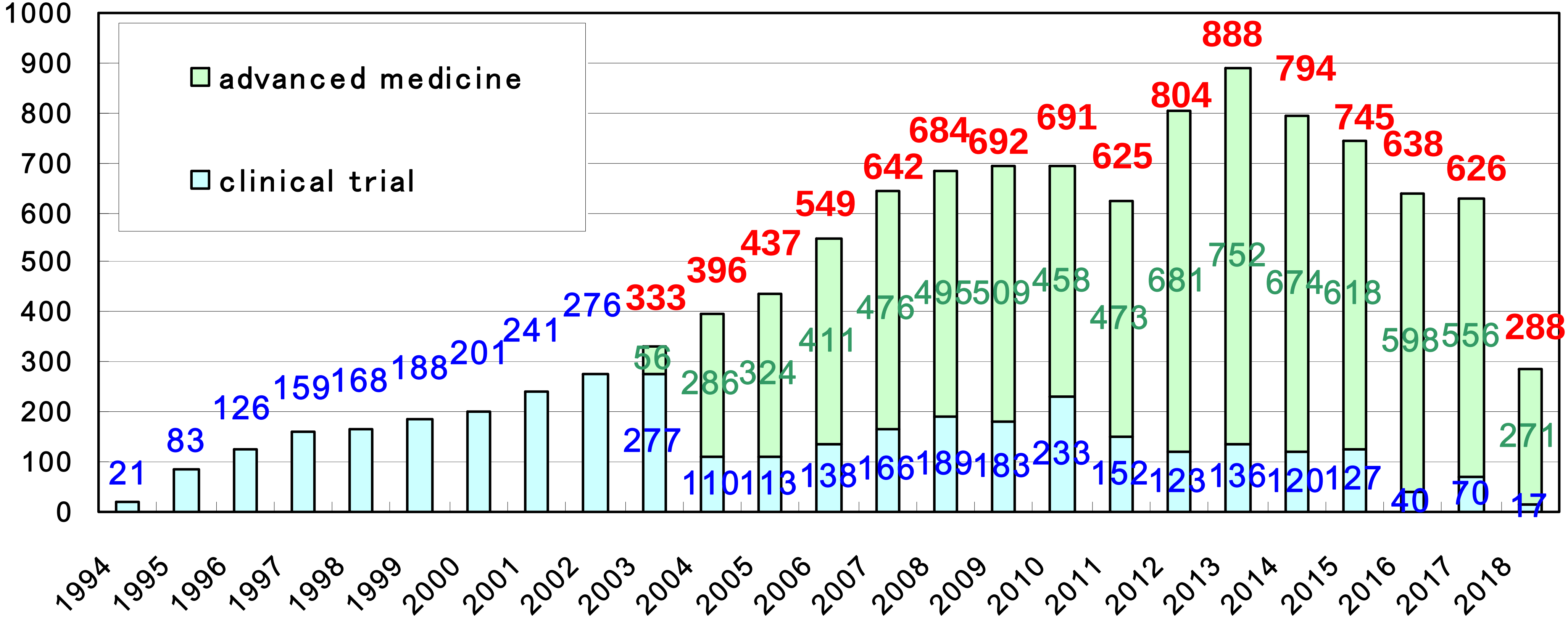
HIMAC **GHMC** **Saga-HIMAT**

Heavy ion radiotherapy facilities worldwide



3. Clinical result

Registered patient number at HIMAC



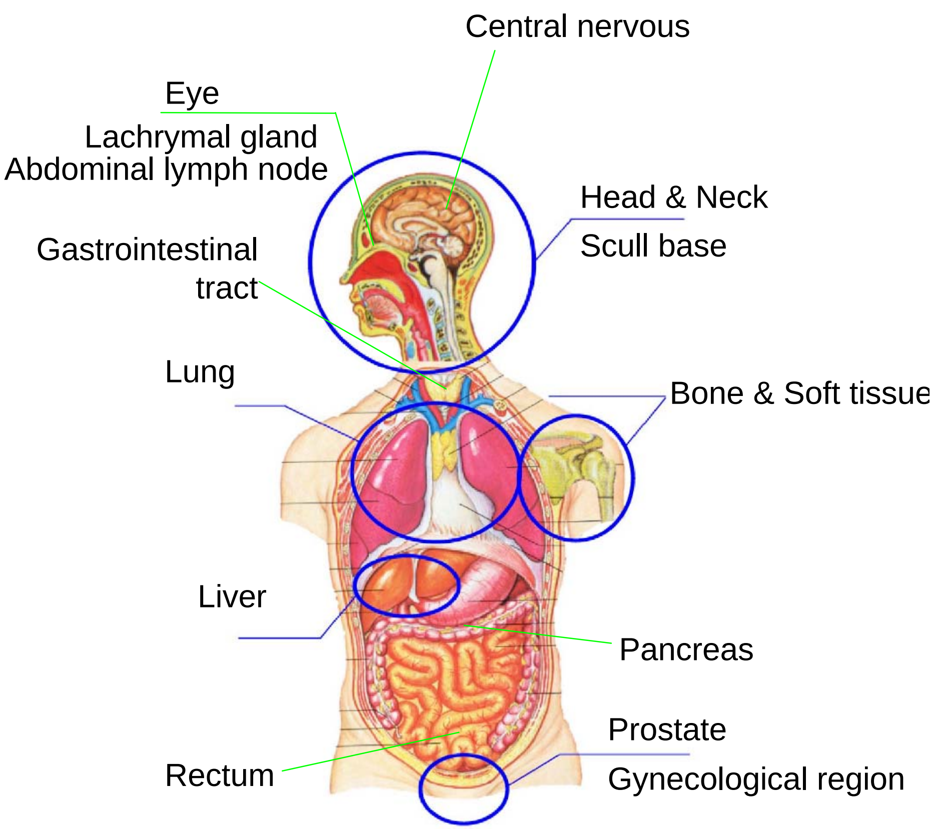
Total = 11,318 patients (from June 1994 to August 2018)
Fiscal year in Japan is from April to March
About 180 days per year are utilized for the treatment.

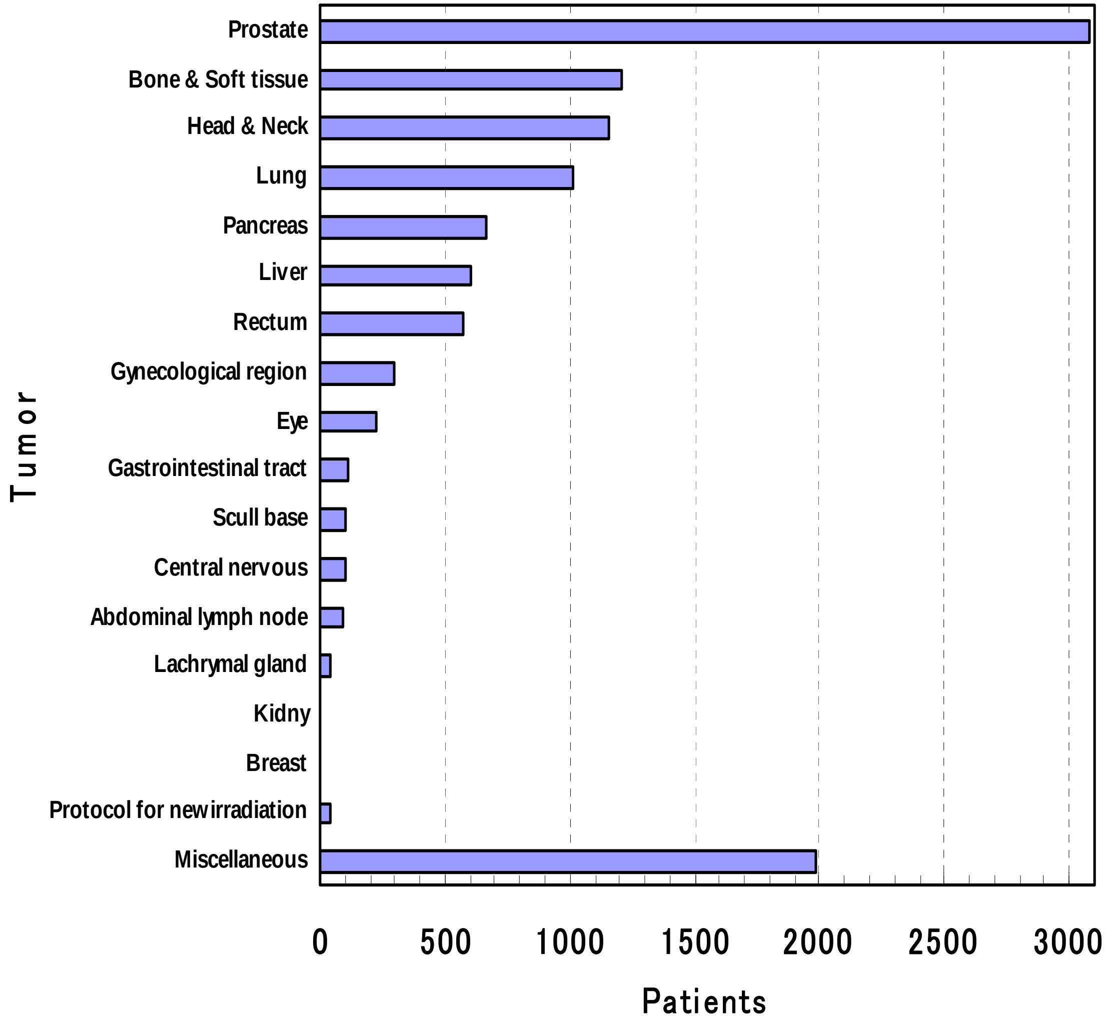
QST NIRS HIMAC

3. Clinical result

Types of tumors

Statistics of deceases (Jun. 1994 – Aug. 2018)



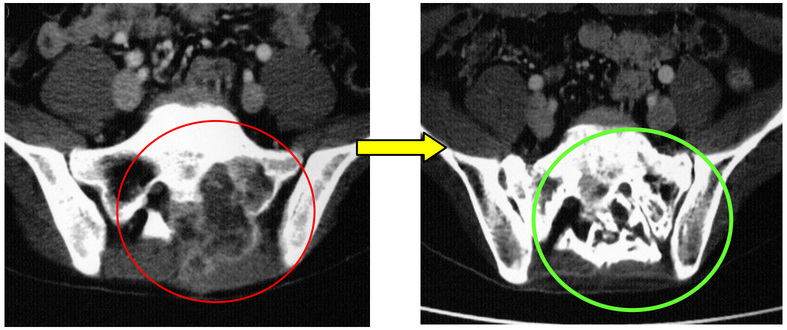


QST NIRS HIMAC

Clinical results

Carbon ion radiotherapy has 3 large advantage:

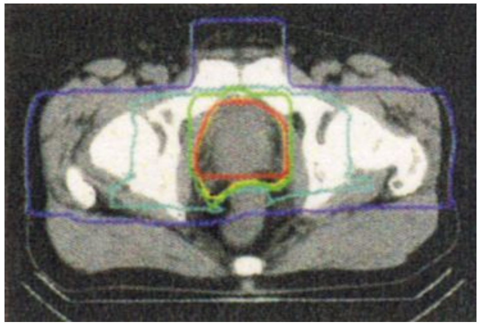
Better local control / survival ratios



before **5 years after**

5 years overall survival ratio 33% (46% for <500cc)
Local control ratio 62% (87% for <500cc)
with 70.4 Gy(RBE) / 16 fractions

Lower toxicities



Delayed adverse reaction rate (>=G2)
- 0.8% (Rectum)
- 1.6% (Genitourinary system)

with 51.6 Gy(RBE) / 12 fractions

Hypo-fractionation:The treatment period can be shorten

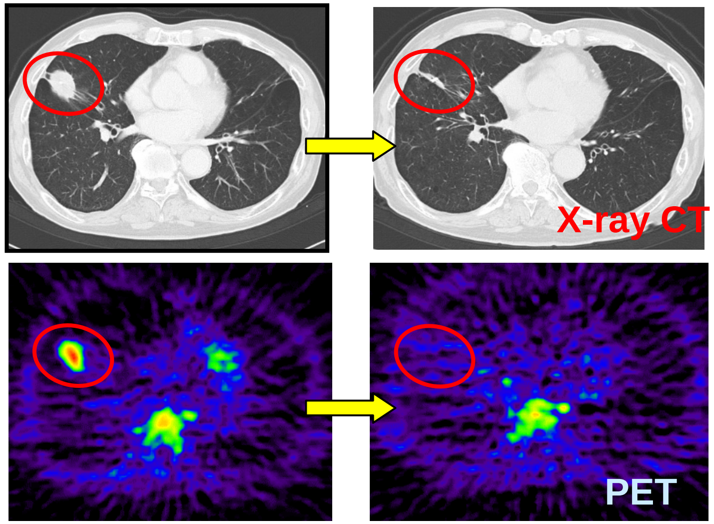
1 day treatment

50.0Gy(RBE) /1fraction in 1 day

5 year Local control 95.0%

5 years overall survival 69.2%

Median follow up 58.6 month



before **1 year after**

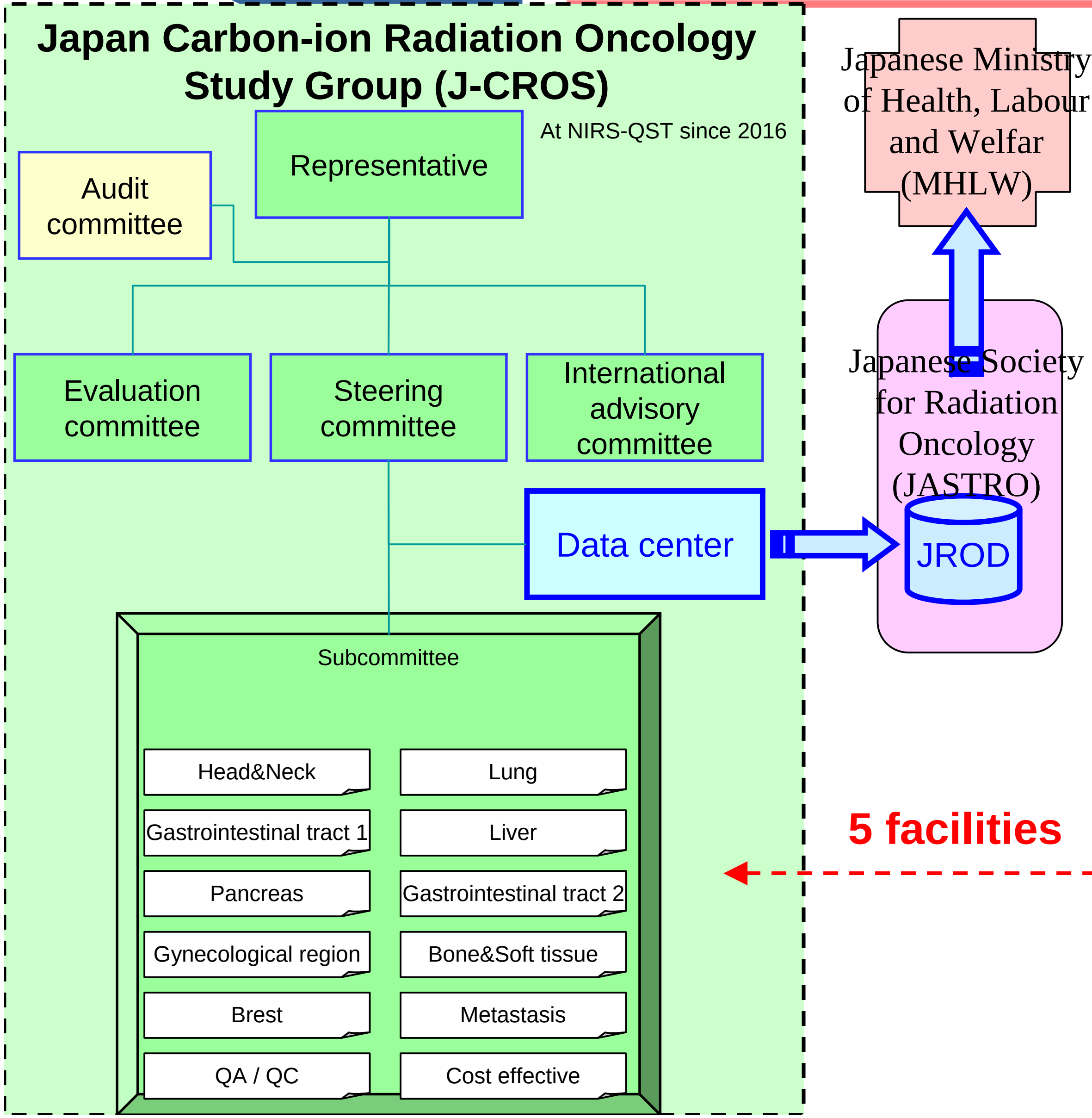
Recent Publications
- D. K. Ebner and T. Kamada, Front. Oncol. 6, 140, 2016.
- R. Imai et al., Int. J. of Rad. Onco. Bio. Phys. 95, 322, 2016.
- T. Nomiya et al., Rad. Onco. 121. 288, 2016.
- M. Koto et al., Int. J. of Rad. Onco. Bio. Phys. 100, 639, 2018.
- N. Yamamoto et al., J. Thorac Oncol. 12(4), 673, 2017.
- S. Kawashiro et al., J. of Rad. Onco. Bio. Phys. 101, 1212, 2018.

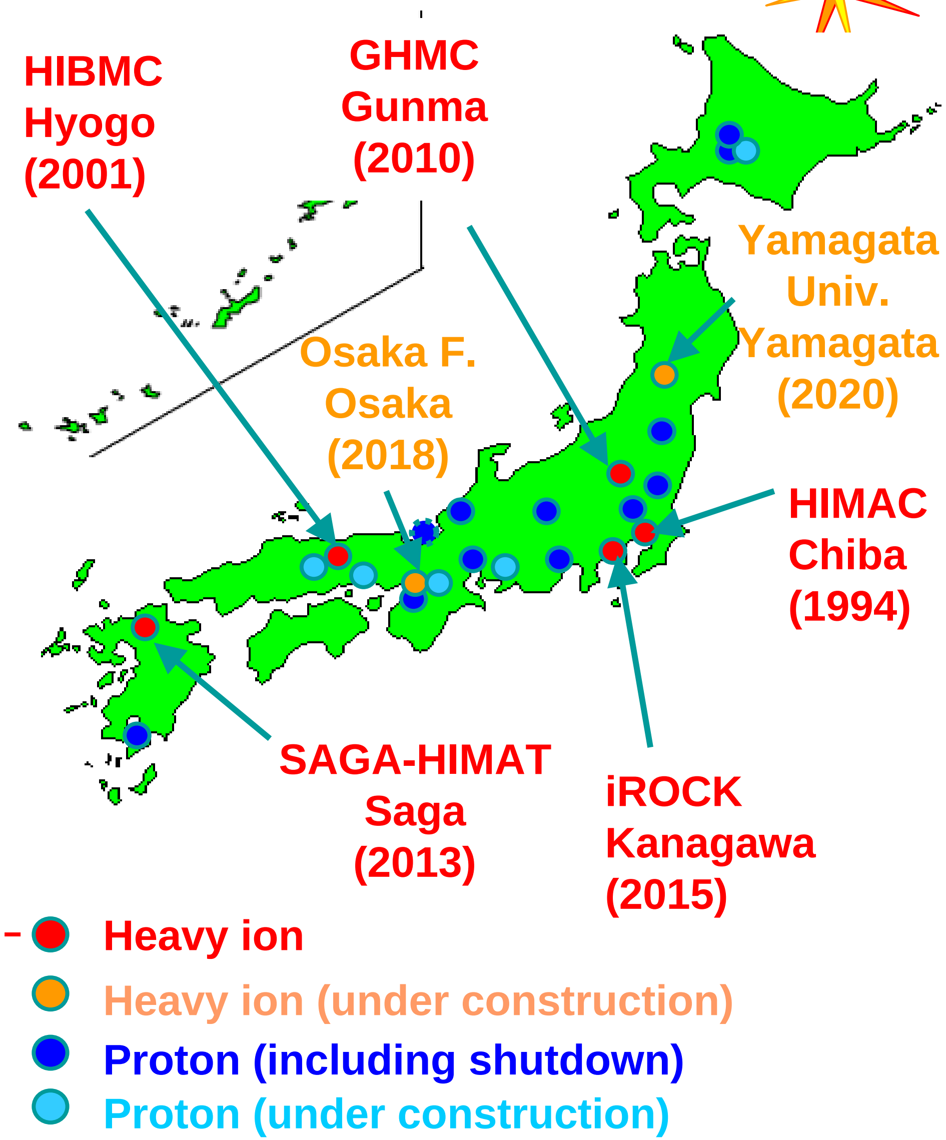
4. Present status under the Japanese national health insurance

QST NIRS HIMAC

4. Present status under the Japanese national health insurance

Network of clinical data





NIRS HIMAC QST

4. Present status under the Japanese national health insurance

Japanese Health Insurance system

Development of new medical devices → **Permission for "advanced medicine" (Pharmaceutical Affairs Law)** → **Covered by National Health Insurance system**

- Uterus
- Brest ….

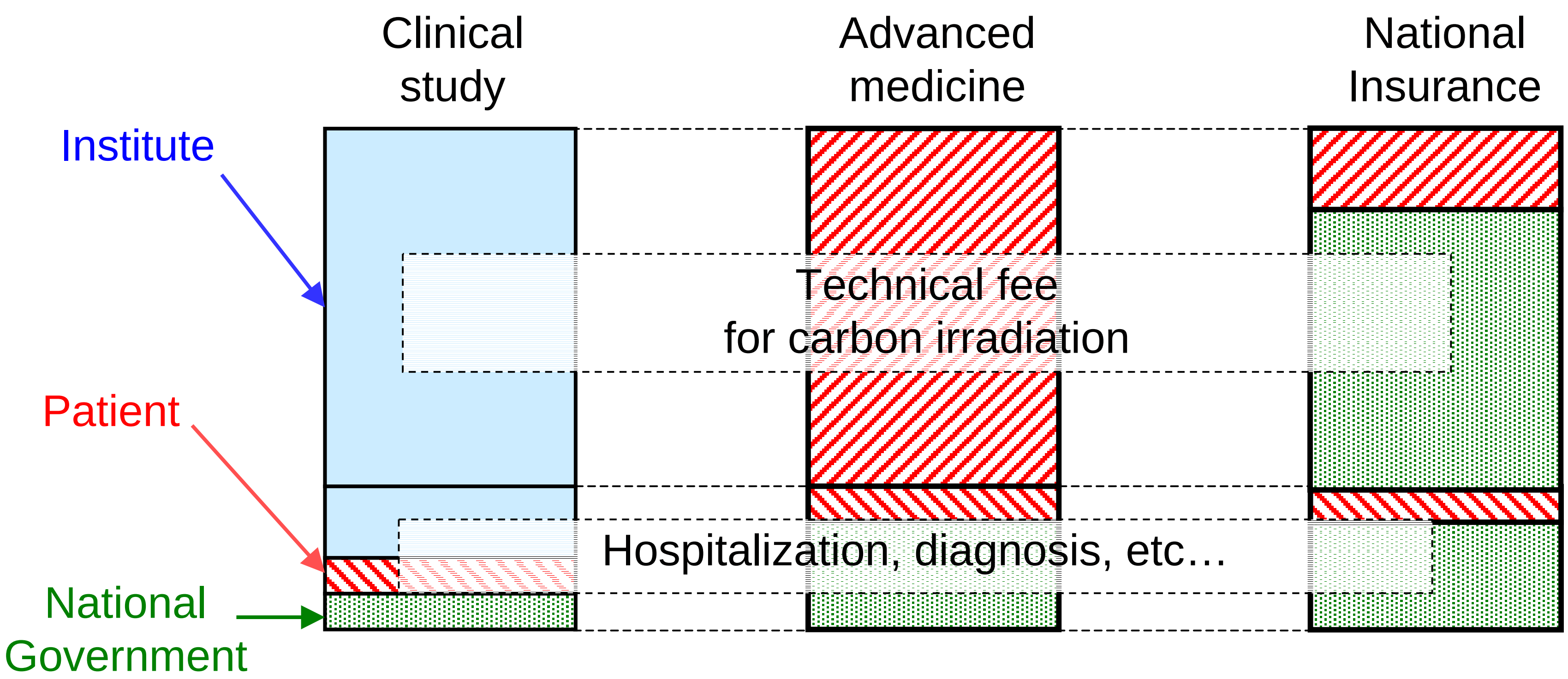
- Lung
- Pancreas
- Liver ….

- Bone & Soft Tissue
- Head & Neck
- Prostate

Bone & Soft Tissue, Head & Neck: 2.37 MJPY

Prostate: 1.6 MJPY

in 2018



5. Future prospect of heavy ion radiotherapy

5. Future prospect of heavy ion radiotherapy

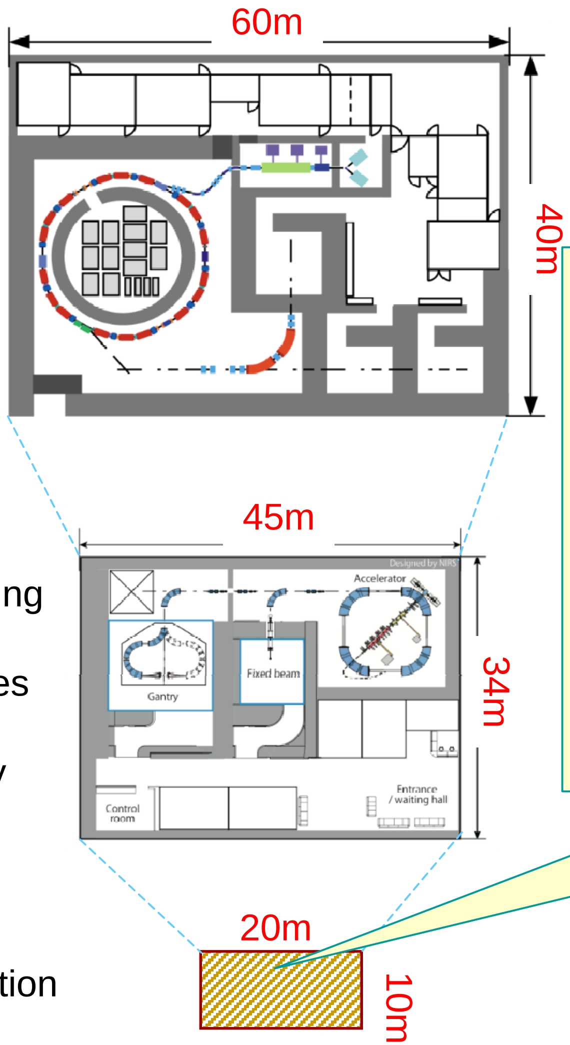
Quantum Scalpel Project

1st Gen. HIMAC → 120m x 60m

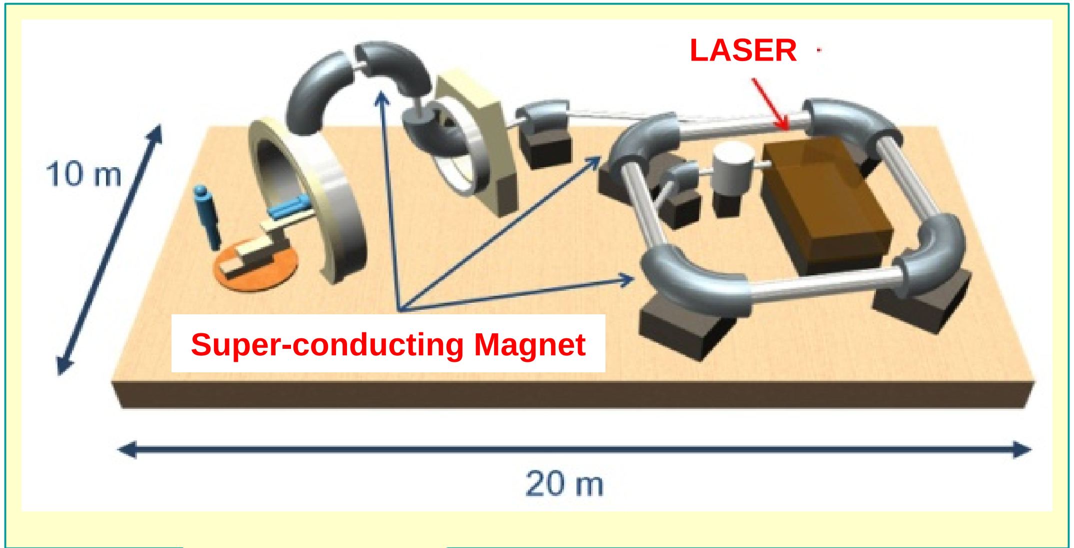
2nd Gen. Heidelberg
Gunma
:
3rd Gen. Saga
Kanagawa
Yamagata
:
:

4th Gen.
- Super conducting technology
- Multi ion species painting
- Rotating gantry
:
:

5th Gen.
- Laser acceleration technology



5th Generation Quantum Beam Cancer Treatment
(**Quantum Scalpel**)



The project has started since 2016.

T. Shirai *et al.*, Proc. of 14th Annual Meeting of PASJ, Sapporo, 2017, p. 155 (in Japanese).

NIRS

HIMAC

5. Ion sources for heavy ion radiotherapy

New developments

Name of institute	Type of ion souce	Name of ion source	Target deseases	Irradiation method for treatment	Ion species	Max. Energy applied for treatment	Expected beam intensity from accelerator	Type of main accelerator	Type of injector	Charge state	Extraction voltage	Requirement of intensity from ion source
						MeV/u						
IBA, JINR, Sigmaphi	ECR		whole body	Raster scanning / Wobbler	C, p, 4He, 6Li, 10B	400	300enA	Cyclotron	none	6+	25kV	3emicroA
T. Univ. Dresden, DREE	EBIS	Dresden	whole		C, p, H2	400		Synchrotron	RFQ +	4+ / 6+	8keV/u	4-8E9ppp
T. Uni DREE												0E8ppp
BNL												7E7ppp (60Hz)
GSI	Laser IS							Synchrotron	none	6+		
Kyoto Univ., JAEA	Laser IS							Synchrotron	cooler ring	6+		
JAEA	Laser accelerator							none	none	6+	>100MeV/u	1E9pps
LANL	Laser accelerator							none	none	6+		

ECRIS will be taken over its place by another technology in the future?

A. Kitagawa, Review talk at ICIS '09

NIRS HIMAC

5. Future prospect of heavy ion radiotherapy

Multiple ion-species irradiation

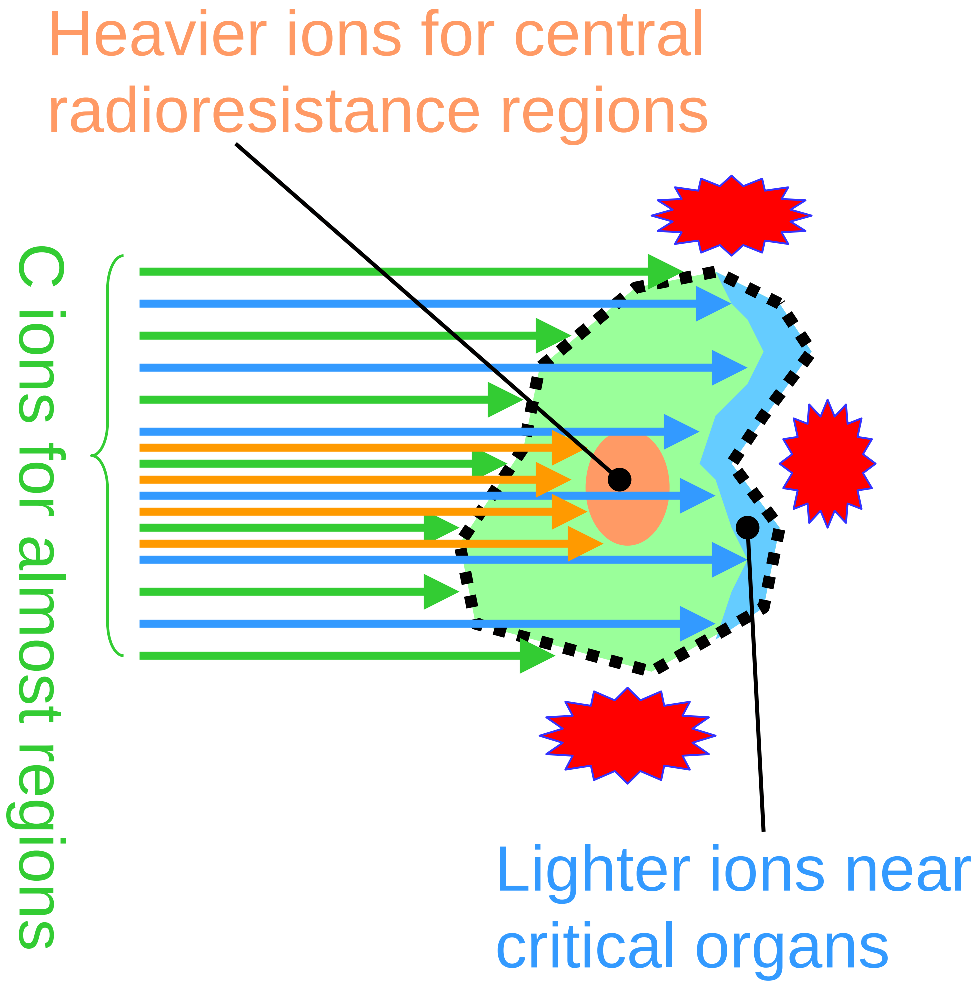
He ⟵ C ⟶ Ne

<Physical>

Logitudinal Distribution
- **Bragg peak**
- **Projectile fragmentation**

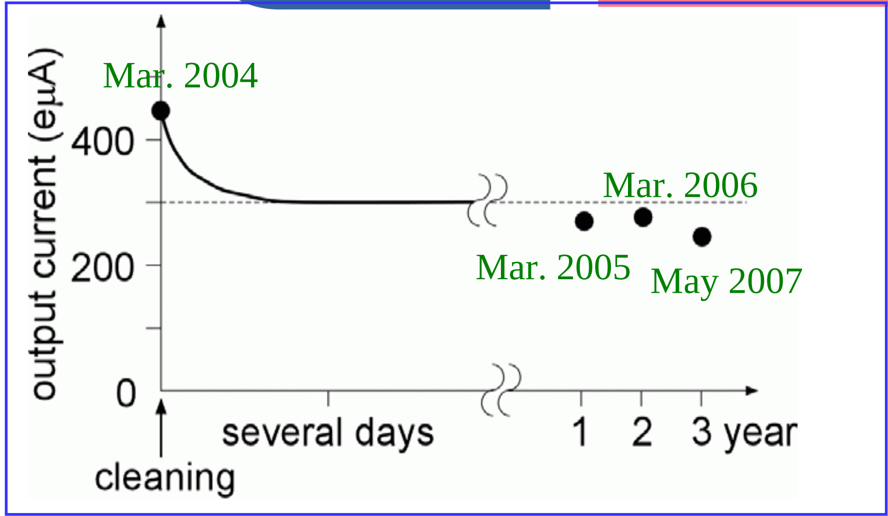
Lateral Distribution
- **Multiple scattering**

<Biological>
- **Relative Biological Effectiveness**
- **Oxygen Enhancement Ratio**
- **Cold spot problem**



5. Future prospect of heavy ion radiotherapy

Life time and stability



Results:

- Long life time > OK
- Long-term stability > OK
- Reproducibility --- Weak from changing gas
- Easy operation > OK
- Easy maintenance > OK

M. Muramatsu, poster in Tue. PM

Daily carbon operation

(Vacuum evacuation during one night)

Operation of other ion species, O, Ne…

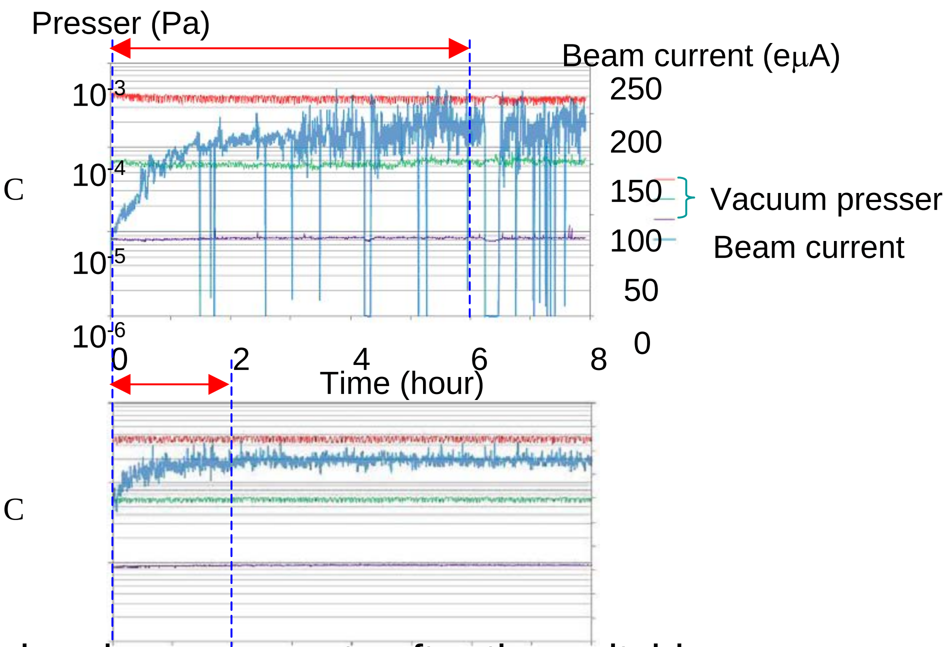
(Vacuum evacuation during one night)

Carbon operation
- Set the previous parameter
- Measure the transient time to the stable operation

Procedure of the switching of ion species

Case 1: C → O → C

Case 2: C → Ne → C



Carbon beam currents after the switching from oxygen and neon beam

Summary

1. **Status of heavy ion radiotherapy**
   - Heavy ion radiotherapy has verified its effectiveness and safety and has reached to the National Health Insurance phase.
   - The treatment fee has decreased to affordable price.
   - The ECRISs have effectively contributed to the stable operation of facilities.

2. **Future prospect of heavy ion radiotherapy and developments of ECRIS**
   - ECRIS will be taken over its place by another technology in the future.
   - However, ECRIS still has a scope of the present research and development to produce various ion species in order to improve clinical dose distribution for intractable radioresistance tumors.