Review of Ion Therapy Machine and Future Perspective

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1. Introduction

2. Development for Ion RT

3. Future Plan

4. Summary
1946- RR Wilson (USA) proposed applying accelerated ion beams to cancer therapy.
1975- Clinical research started using an accelerator for physics research (Lawrence Berkeley Laboratory).
1984- R&D of heavy ion cancer radiotherapy started.
1993- We (QST-NIRS) succeeded in completing a Carbon-Ion cancer radiotherapy (HIMAC) machine for the first time in the world.
1994- Clinical study of Carbon-Ion Radiotherapy began. Yasuo Hirao
2019- More than 12,000 patients were treated.

Carbon-Ion Radiotherapy Facilities in Japan
○NIRS (1994)
○Hyogo HIRT Center (2002)
○Gunma University (2010)
○Kyushu International HIRT Center (2013)
○Kanagawa Cancer Center (2015)
○Osaka Cancer Center (2018)
Physical Characteristics of Ion RT

High longitudinal dose localization owing to the Bragg peak.

High transverse dose localization owing to the low multiple scattering.
Biological Characteristics of Ion RT

Introduction

Biological dose should be higher in tumor than that in normal tissue.

Carbon-ion has the highest bio-dose contrast.

LET dependence of RBE & OER
First Facility Dedicated to HI RT

- Ion species: High LET (100keV/μm) charged particles
  → He, C, Ne, Si, Ar
- Range: 30cm in soft tissue
  → 800MeV/u (Si)
- Maximum irradiation area: 22cmΦ
- Dose rate: 5Gy/min
- Beam direction: horizontal, vertical

More than 12,000 pts treated since ‘94.

HIMAC (Heavy Ion Medical Accelerator in Chiba)
A single fraction treatment against Stage I NSCLC has been carried out since 2003. The treatment result shows 3-y OS rate of 94% with 50 GyE irradiation, which is almost comparable to surgery while keeping high QOL.
Clinical Results

Treatment against Radio-Resistive tumor

Before treatment

(52.8 GyE)

After 8 Year
Clinical Results

Treatment against Radio-Resistive tumor

Before treatment

( 52.8 GyE )

After 8 Year
The HIMAC clinical trial with carbon-ion has proven:

- a short course treatment, such as one fractional treatment of lung cancer, is possible.
- very effective against radio-resistive cancer.

**National Insurance** covers the followings since 2016:
Prostate and Bone&Soft tissue for Carbon-ion RT
Prostate and Pediatrics for Proton RT
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Passive Beam-Delivery Method

Wobbling Method with RF, since 1994

◎ Easy dose management
◎ Relatively low beam-position accuracy
× Low beam-utilization efficiency
× Require bolus and patient collimator
Passive Beam-Delivery Method

Wobbling Method

Innovations in HIMAC passive method are
- Layer stacking method
- Respiratory-gated irradiation

◎ Easy dose management
◎ Relatively low beam-position accuracy
× Low beam-utilization efficiency
× Require bolus and patient collimator
Respiratory gated irradiation

- Irradiation system of coincident with a patient’s respiratory motion -

**Accelerator**
- Interlock system
- Gated beam extraction system (RF knockout method)

**Irradiation room**
- PSD
- Respiration waveform
- X-ray TV

**Treatment control**
- Gate signal generator
- Watch & record system
- Beam monitor

**Positioning area**
- Reference Image
- Compare
- Positioning Image
- Positioning system using x-ray TV images

**Planning simulation**

**Ion beam**
- Irradiation system of coincident with a patient’s respiratory motion -

**Interlock system**
There are three kinds of slow-extraction methods from synchrotron: Q-Driven, Acc-Driven, and RF-KO-Driven. The RF-KO extraction has been employed at HIMAC, because of quick response to beam “ON/OFF”.
There are three kinds of slow-extraction methods from synchrotrons: Q-Driven, Acc-Driven, and RF-KO Driven. The RF-KO extraction has been employed at HIMAC, because of quick response to beam "ON/Off".

RF-KO Extraction

- RF-KO Driven
- Q-Driven
- Acc-Driven

Passive
Pencil-Beam 3D Scanning

We should modify a treatment planning corresponding to change of target during treatment, ⇒ Adaptive Cancer Treatment

- 3D Scanning (Active method)
Pencil-Beam 3D Scanning

We should modify a treatment plan corresponding to change of target during treatment.

⇒ Adaptive Cancer Treatment

- 3D Scanning (Active method)
We should modify a treatment planning corresponding to change of target during treatment, which leads to Adaptive Cancer Treatment.

Pencil-Beam 3D Scanning

- Beam utilization efficiency \(~100\%\)
- Irradiation on irregular shape target
- No compensator & patient collimator
- Sensitive beam error
- Longer irradiation time

- Especially sensitive to organ motion
Fast Scanning for Moving Target

Key Technology ⇒ Fast 3D Scanning within Torelable Time for Moving Tumor Treatment

A) TPS for Fast Scanning ⇒ × 5
B) Extended Flattop Operation ⇒ × 2
C) Fast Scanning Magnet ⇒ × 10

Simulation

100-times speed up !!
• External and tumor positions were good correlation.
• But external gating could cause < 3mm gating error.
• Setup: 6.0 min
• Treatment: 3.5 min/field
• Beam on rate: 38.4%
Variable-Energy Operation

Beam-size growth due to Multiple scattering
⇒ *Penumbra growth*
Variable-Energy Operation

- High speed slice change
- Suppressing beam-size growth
- Reduction of 2\textsuperscript{nd} neutron
Variable-Energy Operation

- High speed slice change
- Suppressing beam-size growth
- Reduction of 2nd neutron

NIRS ⇒ Variable-E operation in one cycle!
Full Energy Depth Scan

- Beam direction
- Lower energy
- Higher energy

Current pattern of BM
- Scanning magnet (X)
- Scanning magnet (Y)
- Extracted beam
- Beam current in ring
- Irradiation gate

Energy ID

3mm step in water range
Rotating Gantry

3D Scanning + R-Gantry
- Reduction of Patient’s Load
- High accurate treatment

Shorter Course Treatment
HIMAC and New Treatment Facility

Treatment in a day (Oct. 10, 2018)

<table>
<thead>
<tr>
<th>Treatment site</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>23 pat.</td>
</tr>
<tr>
<td>Head &amp; neck</td>
<td>14 pat.</td>
</tr>
<tr>
<td>Bones &amp; soft tissues</td>
<td>10 pat.</td>
</tr>
<tr>
<td>Uterus</td>
<td>6 pat.</td>
</tr>
<tr>
<td>Lung</td>
<td>4 pat.</td>
</tr>
<tr>
<td>Recurrent rectal cancer</td>
<td>9 pat.</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6 pat.</td>
</tr>
<tr>
<td>etc. (lymph node...)</td>
<td>3 pat.</td>
</tr>
<tr>
<td></td>
<td>75 patients</td>
</tr>
</tbody>
</table>

Repainting & Respiration Gating: ~1/3 of pts.

All patients are treated in the new treatment facility in the present.
Contents

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Current C-ion Radiotherapy

1) Facility is still huge and expensive.
   →Cost and size now 1/3rd the HIMAC, but still high!

2) Currently, not always satisfactory in tumor control.
   →Higher performance is required.

“Quantum Scalpel” Project

1st Generation

1994-NIRS
120x65m, 300M USD

2nd/3rd generation

2010 – Gunma Univ.
60x45m, 100M USD
Superconducting Technology

Number of the quench of superconducting magnets for rotational gantry is only one time in this year.

- Differences between rotational gantry and synchrotron.
  - Maximum field: 2.9 T (G) -> 4.0 T (S)
  - Excitation time: 60 sec (G) -> <10 sec (S)
  - Fine NbTi cable with low AC loss
Design of SC Synchrotron

- Superconducting magnet
  - Number: 8
  - Bending angle: 45 degree
  - Magnetic field: 4 T
  - Excitation rate: \( \sim 0.5 \text{ T/s} \)
  - Cooling: GM cryocooler w/o Liq.He

- Synchrotron
  - Circumference: \( \sim 28 \text{ m} \)
  - Energy: 4 \( \sim 430 \text{ MeV/u} \)

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  - Energy: 4
Compact 3D-scanner

1. XY combined type new scanner
2. High magnetic field
3. Changing gap in beam direction
Compact 3D-scanner

1. X
2. H
3. C

Compact Gantry

9 m
3.5 m
Compact 3D-scanner

- XY combined type new scanner
- High magnetic field
- Changing gap in beam direction

Compact Gantry

9 m

3.5 m
Compact 3D-scanner

HIMAC

NIRS

Compact Gantry

3.5 m
Compact 3D-scanner

1st SC gantry in NIRS

2nd SC-gantry
Design Considerations

- Beam matching to keep beam-size independent
- Set the compact 3D-scanner in the downstream of the SC magnets to reduce bore radius
- SC magnet of 5 T will be employed
**Laser Acceleration Technology**

**Conventional linac : RF field**

- High electric field is required for compact linac.
- There is a limitation due to discharge.
- There is no discharge problem in plasma.

**Electric Field : $10^7$V/m**

**Plasma : Mixture of ions and electrons**

**Light pressure creates the charge separated plasma**

**Electric Field : $>10^{12}$V/m**
Development of Laser injector

- Determination of laser driven ion acceleration scheme

  With J-KAREN-P etc., the acceleration scheme for generating $10^9$ carbons/m$^2$/sec @ 4 MeV/u in 10 % b.w. will be determined.

- Demonstration of high repetition rate laser driven ion acceleration over 10 Hz

  Front end of over 10 Hz ion generation platform laser system has been developed.  
  100 Hz, 1 mJ, 2~3 % stability achieved.

  Over 10 Hz repeatable target systems are under preparation.

  Tape type target
  Merit:
  Long time supply
  Demerit:
  Too thick target

  Thin foil type target
  Merit:
  Submicron foil
  Demerit:
  Limited supply

  Carbon: $1.6 \times 10^6$ counts/mSr/shot
Development of Laser injector

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Multi-Ions Irradiation

C-ion RT with chemo-therapy has brought 2-y OS of 60% for pancreatic cancer treatment. On the other hand, 5-y OS is not improved due to insufficient dose, because it is difficult to increase the dose due to a tumor surrounded by radiosensitive organs.

Multi-Ions Irradiation

- Multi-Ions Irrad. : Optimization of ion specifies for high performance
  - Malignant part $\rightarrow$ higher bio-effect than C-ion for Suppressing Recurrence
  - Boundary between tumor and normal tissue $\rightarrow$ Lower Bio-Effect for Reducing Toxicity
  - Other Part $\rightarrow$ C-ion owing to C-ion RT result

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In the electron beam cooler, electrons are constrained by a solenoid field for efficient cooling.

What happens when solenoid field is applied on tumor to constrain the secondary electrons induced by ions?

**External Magnetic Field on Tumor**

- DNA damaged by 2nd electrons
- Cluster in core region
- Track in core region
- After image analysis

2nd electrons along ion orbit

DSB-marker after 30 min by EOB of HI
RBE Controlled by Mag. Field

Transverse field

Solenoid field

Inaniwa et al. JRB (2020)
SR by $B_{\parallel}$ and SR by Ion Species

Reference Data

Survival rates of cancer cells (HSGc-C5), irradiated by He, C, O and Ne-ions with the range of 15 cm WEL.

Decrease of $D_{30}$ by Ion-Species

- $^4\text{He}$ : 3.43 Gy
- $^{12}\text{C}$ : 2.80 Gy (-18%)
- $^{16}\text{O}$ : 2.46 Gy (-28%)
- $^{20}\text{Ne}$ : 2.13 Gy (-38%)

Decrease of $D_{30}$ by $B_{\parallel}$

2.11 Gy $\rightarrow$ 1.42 Gy (-33%)
SR by $B_{//}$ and SR by Ion Species

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Technology Development

HIMAC

- He~Ar
- Max. 800 MeV/n
- Beam-Wobbling Method
- Respiratory-Gated Irrad.
- Layer Stacking Irrad.

Summary

- Standard-version@Gunma
- Max. 400 MeV/n
- Spiral Wobbling Method
- Respiratory-Gated Irrad.
- Layer Stacking Irrad.

- New Treatment System
- C, O
- Max. 430 MeV/n
- Fast 3D-Scanning
- Respiratory-Gated Irrad.
- Rotating Gantry

1994~

Advanced Standard Version
Summary

Advanced Standard Version

Saga HIMAT: 2013~
P: (H&V), H&45°, Scan: (H&V)

Osaka_HIMAK: 2017~
S: 2*(H&V), (H&45°)

KCC_iROCK: 2015~
S: 2*(H&V), 2*H

Yamagata: 2020
S: Gantry, H
Advanced Standard Version

HiRT+ Compact Machine + RBE Control = Quantum Scalpel

Roadmap

Quantum Technology

- Laser Ion Acceleration ~MeV/u
- Superconductor NbTi
- Multiple-ion Radiotherapy

Quantum Scalpel

2018  2023  2028  2033

Quantum scalpel 1.0  Quantum scalpel 2.0

Superconductor High-temperature

- Laser Ion Acceleration ~GeV/u
- Superconductor High-temperature

- ????
A Healthy, Long-living Society with Zero-Cancer-Death

Quantum Scalpel

- Molecular target therapy
  Pinpoint micrometastasis treatment
- Targeted isotope radiotherapy
  High therapeutic effect, even with multiple metastases

Solid Cancer (Primary Tumor)

- Few side effects
- High quality of life
- Any tumor is eligible
- Preservation of Immunity

Immunotherapy

Alpha beam

Immune system Activation

Brake stop or accel. enhancement

Aim for zero cancer death

Summary

A Healthy, Long-living Society with Zero-Cancer-Death
A Healthy, Long-living Society with Zero-Cancer-Death

NIRS HIMAC

Quantum Scalpel

Molecular target therapy
• Targeted isotope radiotherapy
  High therapeutic effect, even with multiple metastases
• Immunotherapy
  • Molecular target therapy
    Pinpoint micrometastasis treatment

Aim for zero cancer death

α beam
Targeted isotope treatment

Activation
Immune system
Brake stop or accel. enhancement

Metastasis
Solid Cancer (Primary Tumor)

Quantum Scalpel enables 1-day treatment
→ Treatment while working
→ Reduction of cost for treatment

Contribution to a healthy, long-living society

• Few side effects
• High quality of life
• Any tumor is eligible
• Preservation of Immunity

Thank you for your attention