Cancer Treatment by Charged Particles
- Carbon Ion Radiotherapy – Part 1

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HIMAC

Site of NIRS

Narita airport

National Institute of Radiological Sciences

Chiba Prefecture
Introduction to National Institute of Radiological Sciences (NIRS)
In these days,

- A series of nuclear weapons tests, above-ground level, in Cold War era,
- Memory of tragedies at Hiroshima and Nagasaki,
- Daigo Fukuryū Maru accident in 1954,
  - A Japanese fishing boat, Daigo Fukuryū Maru ("Lucky Dragon No. 5"), came in direct contact with the fallout from a thermonuclear hydrogen bomb (Castle Bravo) near Bikini atoll.

Creating concerns about radiation for Japanese citizens.
Objectives of NIRS

Studies for Adverse Effects of Radiation on Humans and the Environment - Protection, Diagnosis, and Treatment

Medical Applications of Radiation - Radiation Therapy, Medical Imaging

Countermeasures of Accidental Radiation Emergency

Education and Training of Human Resources

Positive side
NIRS

Organizational Structure:

- Dept. of Planning and Management
- Dept. of General Affairs
- Research, Development and Support Center
- Research Center for Charged Particle Therapy
- Molecular Imaging Center
- Research Center for Radiation Protection
- Research Center for Radiation Emergency Medicine
- International Open Laboratory
- Medical Exposure Research Project
- Audit Office

Staff: 814
  - Full-time: 490
  - Part-time: 324
Research Centers

Research Center for Charged Particle Therapy
- Charged Particle Cancer Therapy -

Molecular Imaging Center
- Molecular Imaging for diagnosing Cancer, etc

Research Center for Radiation Protection
- Low Dose Radiation effects on Humans and Environment -

Research Center for Radiation Emergency Medicine
- Radiation Emergency Medicine and research of high dose radiation effect on humans -

Formation of Radiation Emergency Medicine

Heavy Ion Radiation Therapy

Production of Molecular Markers with Cyclotrons

PET Imaging of a Brain

Dose estimation due to man-made radiation and environmental radiation
Study on biology effect and environmental effect

Research, Development and Support Center
Supporting four research centers in technology, maintaining circumstances safe and suitable for research and training /education of human resources

Supporting and developing technologies

Safety and Security
Training and Education
Cancer is the leading cause of death in developed countries and the second leading cause of death in developing countries.
Treatments of cancer

1. Surgery
2. Chemotherapy
3. Radiotherapy

Advantage: no pain, no infection

Kinds of radiation
- X-rays
  (particle beams)
- Protons
- Carbon beams

Expectation and concern on radiation therapy
- Quality Of Life after the treatment (QOL)
- Malignant, radiation resistant tumor
- Fractionation
Dose distribution

Heavy ions, Protons

- Surface = small LET
- End point = large LET

Dose concentrates at the end point (Bragg peak)

Gamma-ray, Neutrons

- from Surface to End point = constant LET

(LET: Linear Energy Transfer)
Dose distribution of x-rays and C beams

- **X-ray**: 9 directions
- **Carbon beams**: 3 directions

**Bolus**
Heavy Ions and Protons

Scattering effect (transverse)

Heavy ion -> small
(Solid line)

Proton -> large
(Dotted line)
Ionization density and damage of DNA

X-rays

Protons

Carbons

DNA

Truck structure

Lethal damage

RBE

1.0

1.1

2~3
Survival curve

low LET
X-ray, C:13keV/μm

Middle LET
C:30keV/μm

high LET
C:110keV/μm

$$\text{RBE} = \frac{D_L}{D_H}$$

by Y. Furusawa (NIRS)
Biological effectiveness

Heavy Ion Beam = High LET

- Large RBE
  (RBE: Relative Biological Effectiveness)

- Low OER
  (OER: Oxygen Enhancement Ratio)
Oxygen effect

Surviving fraction vs. Dose (Gy)

- γ-ray
- Hypoxic
- Oxic

Result of clinical trials

Head & Neck cancer
(but before / treatment planning / after)

before 36 month after

48.6 GyE/18 f/6 wks
1. **Protocol**
   - A predetermined plan for carrying out treatments
   - Phase I: Adverse effect? $\rightarrow$ Phase II: Dose escalation

2. **How doctors decide success or not for cancer treatment?**
   - What should be observed?
   - Local control
   - 5-year (3-year) survival

3. **Fractionation**
Number of patients enrolled for carbon ion radiotherapy from June 1994 to February 2012

Total 6,512 AM: 3,488

- Blood vessel 11 (0.2%)
- Lacrimal gland 21 (0.3%)
- Abdominal lymph node 38 (0.6%) AM: 31
- Gastrointestinal tract 67 (1.0%)
- Skull base 84 (1.3%) AM: 55
- Central nervous 106 (1.6%) AM: 74
- Eye 116 (1.8%) AM: 74
- Gynecological region 180 (2.8%) AM: 3
- Pancreas 183 (2.8%) AM: 3
- Rectum (PO*) 331 (5.1%) AM: 267
- Bone & soft tissue 829 (12.7%) AM: 622
- Head & neck 794 (12.2%) AM: 471
- Lung 673 (10.3%) AM: 95
- Liver 425 (6.5%) AM: 200

*Postoperative
Number of patients, yearly base

Total number of patients: 6512
(Advanced medicine: 3488)

Fiscal year

Period: 1994.6 - 2012.2.15
Highlight of Carbon Ion Radiotherapy

1) C-ion RT is successful in the not treatable by other means
   - Advanced Head & Neck cancers
   - Large skull base cancers
   - Post-op recurrent rectal cancer
   - Inoperable sarcoma
   - Re-irradiation after photon radiotherapy

2) Promising results are obtained in C-ion hypofractionated RT
   - Lung cancer (Single irradiation)
   - Liver cancer (Two fractions)
   - Pancreatic cancer (8-12 fractions)
   - High risk prostate cancer (16 fractions)
Requirements for the therapy at HIMAC

- Ion species: high LET (100keV/μm) charged particles
  \[ \Rightarrow \text{He, C, Ne, Si} \]
- Range: 30cm in soft tissue
  \[ \Rightarrow 430\text{MeV/u (C)} \]
  \[ \Rightarrow 800\text{MeV/u(Si)} \]
- Maximum irradiation area: 22cm in diameter
- Dose rate: 5GyE/min
  \[ \Rightarrow 2 \times 10^9\text{pps} \]
- Beam direction: horizontal, vertical, etc...

-> “large accelerator” used for physics experiments
History of constructing HIMAC

Heavy Ion Medical Accelerator in Chiba (HIMAC)

- 1984: 10 years strategy for confronting the cancer
- 1986: International Workshop on Heavy Ion Treatment Facility
- 1989: Start of the construction
- 1993: Commissioning ended, beams were successfully accelerated.
- 1994: Clinical Trials began.
- 2003: Advanced Medicine (Advanced Medical Therapy).
- June 2012: 6,512 patients were treated. (AM 3,488)
Bird’s eye view of HIMAC and hospital
Devices of HIMAC

(HI\textsuperscript{2}M\textsubscript{3}A\textsubscript{C}) (Heavy Ion Medical Accelerator in Chiba)

130m
HIMAC
(Heavy Ion Medical Accelerator in Chiba)

Devices of HIMAC

130m
Devices of HIMAC

HIMAC
(Heavy Ion Medical Accelerator in Chiba)

130m
Irradiation method

Beams from the accelerator ≠ beams for treatment

- Large area
  - Uniform field
- Large thickness
  - Making of SOBP (Spread Out Bragg Peak)
    - Physical dose distribution consists of many Bragg peaks with various range
    - Biological equivalent dose
Beam Delivery System

Making of Spread Out Bragg Peak

Ridge Filter

Ridge Filter

Range Shifter

Range Shifter

Cancer Tumor

Irradiation area

Scattering material

Dose monitor

Controller

Wobbling Magnet

Multi Leaf Collimator

Bolus Collimator
Irradiation system of coincident with a patient’s respiratory motion

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

**Positioning area**
- X-ray TV
- Respiration waveform
- PSD

**Irradiation room**
- Reference Image
- Positioning Image
- Planning simulation

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

**Gate**
- Ion beam

**Gate**
- Treatment control

**Positioning system using x-ray TV images**
Respiration gating for irradiation

No gating

Gating

Reduction of volume

Minohara et al. IJROBP 47:1097-1103, 2000
Key Tech in C-ion RT at HIMAC

**Respiration gating:** 3089 patients
- lung, liver, pancreas, kidney, sarcoma etc

**Patch field:** 294 patients
- Head & Neck, para-spinal etc.

**Spacer insertion:** 108 patients
- pelvis and abdomen

More than 3000 patients were treated with these techniques at NIRS.
Classification of shielding and activation

- **Radiation shielding**
  - Fast neutrons
  - Gamma rays -> negligible small

- **Devices irradiated by beams**
  -> Accelerator and irradiation system
  - Beam stoppers, beam monitors, deflector, septum magnets, targets used in basic research
  - Dose monitor, ridge filter, range shifter, multi-leaf collimator, bolus collimator, patient collimator
  - Air
Induced activity

- Not irradiated by beams: neutron captures?
  -> Devices and buildings
  - Vacuum ducts, magnets
  - Neutron shutters
  - Building material, concrete etc.
  - Cooling water for devices
  - Underground water
  - Air

- No radioisotopes for treatment
  - PET -> Diagnosis only (not in the HIMAC building)
Regulation in Japan

(Japanese laws: based on ICRP standards.)

Irradiation rooms, accelerator rooms: no entry while beam is on.

Regulations related to accelerators.
Area 1: 1 mSv/week
   Controlled area. Registered workers can enter all the time.
Area 2: 1.3 mSv/3 months
   Border of a controlled area.
Area 3: 250 μSv/3 months
   Border of an institute’s site.
Thickness of the shielding wall

-> Equations of Hirayama & Ban

-> Numerical simulation
Design of treatment rooms

- **Multi-legged chicane**
- **Door**: 10cm Polyethylene
- **Effe. 317cm** (250cm concrete + 30cm iron)
- **Neutron monitor**
- **Effe. 395cm** (concrete + iron)

**Periodic measurements:**
- 2/year

**Display**
- 11hs/w
- 18hs/w
- 11hs/w
Devices irradiated by beams

495μSv/h
14μSv/h at 1m
Devices irradiated by beams

<10μSv/h at 1m

Mostly <1μSv/h
Measured: Exhaust (FY2006)

- Air
- Detection limit
- Machines not working

Bq/cc

- Average
- Max.
Measured: water (FY2003)
Summary of the safety issue

- Medical accelerator for cancer treatment
  - fast neutrons -> needs careful design!
  - activation by beams -> very small, safe, but needs careful handling
    - Use plastic, not metal, if possible
      - (small activation, short life)
  - induced activity : no problem!
    - High energy but low intensity, short irradiation time
      - Beam intensity : HIMAC -> $\sim 10^9$ pps $< nA$
      - RI production -> $\sim 10 \mu A$
      - 70 patients x 5 min = 350 min + cond. + meas. /day 3 rooms