Cancer Therapy Using Ion Accelerators

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Cern Accelerator School 2009
Rationale / Physics

- inverted depth-dose distribution
- mild lateral scattering
Increased Relative Biological Effectiveness
radiation induced myelopathy in rats after 2 carbon fractions

RBEs:
Plateau: ~1.4
Peak: ~ 2.3

Debus, Karger, Peschke, Scholz, …
Rad. Res. 2003

Th. Haberer, Heidelberg Ion Therapy Center
Goal

The key element to improve the clinical outcome is **local control!**

- **Entrance channel:**
  - low physical dose
  - low rel. biol. effiency

- **Tumour:**
  - high physical dose
  - high rel. biol. effiency

*275 MeV/u $^{12}$C in Water, 3mm FWHM*
Standard Approach

- Facilities being built at existing research accelerators
- Fixed energy machines with moderate flexibility (if at all)
- Dose delivery not exactly tumor-conform
Ernest Orlando Lawrence
Nobel Prize 1939

Th. Haberer, Heidelberg Ion Therapy Center
184 inch Cyclotron @ LBL 1947 / 1986

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Passive Dose Delivery

pristine beam profile
transversal direction

scattering system

spread out beam profile
transversal direction

pristine bragg peak
depth

range modulator

spread out bragg peaks
depth
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**Standard / System + Dose Distr.**

**typical set-up (Tsukuba)**

- Scatterer
- Fine degrader
- Ridge Filter
- First collimator
- Bolus
- Final collimator

**Figure 3-2 Ridge Filter**

**Figure 3-3 Bolus**

**Figure 3-4 Final collimator**

Distal edge shaping using a bolus pulls dose back into healthy tissue.
• In 1994 the first dedicated clinic-based facilities, LLMUC (protons) and HIMAC (carbon), started
• Nowadays more than 50 proton treatment protocols are approved and reimbursed in the US
• LLUMC treats up to 180 patients per day
Requirement engineering

Application
• treatment of tumors with ion beams (conform, precise)

1st level requirements
• dose deposition in patient → dose delivery at isocenter

2nd level requirements
• beam application system

3rd level requirements
• accelerator specifications ↔ beam application system

→ accelerator requirements: interface to scanning system
Idea:
Dose distributions of utmost tumor conformity can be produced by superimposing many thousands Bragg-peaks in 3D. Sophisticated requirements concerning the beam delivery system, the accelerator, the treatment planning, QA, ... result from this approach.

Realization:
Dissect the treatment volume into thousands of voxels. Use small pencil beams with a spatial resolution of a few mm to fill each voxel with a pre-calculated amount of stopping particles taking into account the underlying physical and biological interactions.

⇒ Extreme intensity modulation via rasterscanning
Beam Scanning

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Ions (Haberer et al., GSI): raster scanning, 3D active, 2D magnetic pencil beam scanning plus active range stacking (spot size, intensity) in the accelerator

Protons (Pedroni et al., PSI): spot scanning gantry 1D magnetic pencil beam scanning plus passive range stacking (digital range shifter)

+ scanning in depth = 3d conformed dose
Active / Fluence Distribution

Fluence distribution of a single slice through the target volume
Accelerator requirements

• **scanning ready pencil beam library:**
  - energy: up to 30 cm WE, ~1 mm steps, ΔE/E ~1%
  - spot sizes: 4 – 10 mm (3-4 steps), 2D Gaussian
  - intensity: ~10^{10} (p), ~10^{8} (C) per spill
  - ~ 100,000 combinations

• beam purity
• several quasi parallel particle types
  – change of particle type < 60 s
• availability ~95%
• low operational & maintenance cost
The Proton Data Base for HIT

K. Parodi and A. Mairani, (HIT and FLUKA Collaboration)
Rasterscan Method

scanning of focussed ion beams in fast dipole magnets

active variation of the energy, focus and intensity in the accelerator and beam lines

Haberer et al., NIM A, 1993
Proton-Synchrotron, Shizuoka, Japan
Cyclotron-based

Accelerator 230 MeV

Energy Slits

Degrader + collimator

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Cyclotron-based
Economic requirements

- change of particle type $<$ 60 s (dead time)
- change of treatment room $<$ 30 s (dead time)
- number of treatment rooms $\leftarrow$ utilization of accelerator
- 300 days per year, 16 hours per day
- $\sim$1-2 min per treatment field ($\sim$1l, $\sim$1-2 Gy)
  (target fraction duration: 15 min incl. 4 min beam)

- initial cost
- operational & maintenance cost
Scanned Carbon vs. Intensity Modulated Photons

- **scanned carbon 3 fields**
  - reduced integral dose
  - steeper dose gradients
  - less fields
  - increased biological effectiveness

- **IMRT 9 fields**

*courtesy O. Jäkel, HIT*
Therapy @ GSI

Fig. 4-4a The GSI Accelerator Facility
Process

- patient immobilization
- 3D-imaging (CT, MRI, PET, ...)
- definition of target volume + organs at risk
- definition of treatment modality
- dose calculation + treatment plan evaluation
- patient positioning
- treatment
- follow-up
Stereotactic Immobilization

- couple a coord.-system to the body
- localizer with fiducials
- calculate stereotactic coordinates for the target
Treatment Planning

- 1960: contours in 1 plane only
- today: 3D data set, density correction, ...

Gross Tumor Volume (GTV):
klinisches manifestes Tumorvolumen

Clinical Target Volume (CTV) =
GTV + subklinisches Tumorvolumen

Planning Target Volume (PTV) =
CTV + Sicherheitsraum (z.B. Bewegungen)

Treated Volume:
Behandlungsvolumen, z.B. D > 90%

Irradiated Volume:
Bestrahltes Volumen, z.B. D > D_{significant}
Treatment Planning
Pencil Beam Position

- position of the pencil beam depends on the beam energy and the beam spot size
- check the position and width at the iso-center using a tungsten sphere in front of a X-ray film
QA / Rasterscansystem

homogeneity of 2d dose distributions
QA / Rasterscansystem

verification of depth-dose distributions
Patient Positioning

• alignment with the room laser system
• setting of the stereotactic coordinates
Position Verification

- comparison of X-ray image with a digitally reconstructed X-ray image (source: planning CT)
- accuracy at the base of the scull 1-2 mm (Karger 2001, IJROBP)
Combined photon and carbon ion RT for adenoid cystic carcinomas clinical phase I/II trial

**Treatment parameters**

- Photon IMRT 54 Gy to the CTV
- Carbon ion boost 18 GyE (6x3.0 GyE) to the GTV
FSRT / IMRT vs FSRT / IMRT+C12: locally advanced adenoidcystic carzinoma

- early toxicity acceptable
- late toxicity > CTC grade 2 < 5%

Schulz-Ertner, Cancer 2005
Heidelberg University Hospital
Th. Haberer, Heidelberg Ion Therapy Center

- compact design
- full clinical integration
- rasterscanning only
- low-LET modality: Protons (later He)
- high-LET modality: Carbon (Oxygen)
- ion selection within minutes
- world-wide first scanning ion gantry
- > 1000 patients/year
  > 15,000 fractions/year
- integrated R+D-infrastructure
### Some Facts

- **Effective area**: 5.027 m²
- **Concrete**: 30.000 tons
- **Constructional steel**: 7.500 tons
- **Capital Investment**: 106 M€

**Start of construction**: November 2003
**Completion of building and acc.**: June 2006
**Accelerator settings established**: April 2008
**First patient planned**: 2nd half of 2009

### Project Partners:

- **University** pays, owns and operates the facility
- **GSI** built the accelerator
- **Siemens** supplies all components related to patient environment
  - **GSI, DKFZ, Siemens** … are research partners
HIT / Linac

- compact design
- proven technology
- fast change of the ion species
- fast intensity variation (1000-times)
- constant beam parameter

Cooperation: GSI + IAP@ Univ. Frankfurt/M.

ECRIS 2
H⁺

ECRIS 1
12C⁴⁺

SOL

Switching Magnet

RFQ

IH - Drift Tube Linac

5 m

8 keV/u

400 keV/u

7 MeV/u

SOL

QT

QT

QT

QT

Stripper

Foil

Ion source

RFQ

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HIT / Synchrotron

- compact design
- proven technology
- multiturn-injection => high intensities
- rasterscanning optimized, extremely flexible beam extraction
- fast variation of energy (range)

Multiple extraction
0,5 bis 10 sec

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RF-KO-Extraction

• **Principle**
  – resonant HF-excitation (betatron frequency)
  – constant separatrix

• **Characteristics**
  – slow extraction
  – constant ion-optical settings during extraction
  – Multiple extractions available
  – Spillshaping via amplitude modulation
Synchroton/HEBT Commissioning

1. Turn in Synchrotron: Febr. 2007
2. Beam in Cave: March 2007

Beam Intensity in 10 second spill (20.04.07)

1. Turn Synchrotron
1. Beam in Isocenter
Accelerator Status

- **Sources, injector and synchrotron** fully commissioned for protons, carbon and oxygen (256 energies each)
- **H1 / H2**: pencil beam libraries (E F I ) for protons and carbon in therapeutical quality reached in April, 2008
  - **Outstanding beam quality**: very high position and focus stability, small intensity fluctuations
- **R+D-cave**: protons, carbon and oxygen energy libs established
- **Gantry**: proof of principle for protons and carbon
  (representative settings in the full phase space (E F I α ))
- **To do**: intensity upgrade (x3) under way (sources, LEBT, RFQ)
- **Operation scheme**:
  2007: 24 h / 5 days
  2008ff: 24 h / 7 days, 330 days, 2 shutdowns 14 days each
- **Availability** of the pencil beams @ H1/2: ≈ 98%
Advantages of a synchrotron

- It works and fulfills all requirements.
- Proven technology
- Stable & reliable operation
- Built-in flexibility
  (particle types, energy, timing)
- Active energy variation
  - Maximum beam purity
  - Minimum radiation protection effort
Disadvantages of a synchrotron

Particle therapy facility
• size of footprint
• initial cost
• (several treatment rooms required)

Objections (no real disadvantages)
• current uniformity
• repetition rate

440 patients
• each field verified

HIT

GSI
ACC Conclusion

• gold standard in ion therapy: SYNCHROTRON
  – all C-patients: NIRS, GSI
  – new facilities: HIT, CNAO, Marburg, NROCK, Gunma

• future
  – improved accelerators wellcome
    • lower initial, operational, maintenance cost
  – HOWEVER
    • decrease in treatment quality unacceptable
    • loss of flexibility questionable (25 years)
Dose Delivery and Medical Equipment

Identical patient positioning systems
- fixed beam
- Gantry

Workflow optimization
- automated QA procedures
- automated patient hand over from shuttle

Inroom position verification
- 2D
- 3D Cone beam CT

Open for future applications and workflows

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commissioning result, Protons @ H1: 3d dose delivery vs. treatment planning 24 thimble-type ICs in a water phantom, standard deviation 2.2 %
Motivation

Gantry

Advantage of a rotating beamline

Pancreas, supine position via gantry advantageous
Scanning Ion Gantry

- optimum dose application
- world-wide first ion gantry
- world-wide first integration of beam scanning
- 13m diameter
  25m length
  600to overall weight
  0,5mm max. deformation
- prototype segment tested at GSI

MT Mechatronics
The HIT Gantry Rotates
Gantry: first beam at the isocenter

January 4th, 2008
Thank you for your attention!

(Intensity modulated raster scan, \( ^{12}\text{C} \) at 430 Mev/u, October 15\textsuperscript{th} 2007)