Tumor Therapy with Heavy Ions at GSI Darmstadt

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The GSI Pilot Project

Interdisciplinary project
Univ. Clinics and Cancer Research Center Heidelberg
GSI Darmstadt, FZ Rossendorf (Dresden)

260 patients treated since Dec.1997
Local head/neck and spinal/sacral tumors

New clinical-based project HIT in Heidelberg
Operational in 2007

Treatment room at GSI

Patient immobilization

Treatment plan
Ion Beams in Radiotherapy

1946  R.R. Wilson, Radiology 47,487
„potential benefits of heavy charged particles in radiotherapy“

1957 - 92  $^4$He  184-inch SC  Berkeley  patients 2054
1975 - 92  $^{20}$Ne  BEVALAC  Berkeley  433

Current ion-beam facilities:

1994  $^{12}$C  HIMAC  Chiba  1800
1997  $^{12}$C  SIS-18  Darmstadt  260
2003  $^{12}$C  HIBMC  Hyogo  30

Projects for clinical facilities in Austria, China, Germany, Italy…
Ion Beam Therapy Pilot Project at GSI

Fig. 4-4a  The GSI Accelerator Facility
**Ion Therapy Pilot Project at GSI**

GSI Darmstadt - Radiol. Clinics Heidelberg - DKFZ Heidelberg - FZ Rossendorf

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**Time Table**

<table>
<thead>
<tr>
<th>Year Range</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993 – 1997</td>
<td>Construction phase</td>
</tr>
<tr>
<td>Dec. 1997</td>
<td>First patient treatment</td>
</tr>
<tr>
<td>1998 – 2007</td>
<td>Treatment of ~ 40 patients per year</td>
</tr>
<tr>
<td></td>
<td>Tumors in head/neck and pelvic region</td>
</tr>
<tr>
<td>2007</td>
<td>End of pilot project</td>
</tr>
</tbody>
</table>

**Future:** HIT Heidelberg Ion Beam Therapy

Clinical Operation 2007

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**Technical Data**

**Beam:** $^{12}$C ions 80 - 430 MeV/u

Intensity-controlled rasterscan system

**Operation:** 3 Treatment blocks of 20 d per year

→ Time sharing with physics experiments

**Cost:** 6 Million EUR (Investment)
1. Advantages of ion beam therapy

2. Clinical results

3. Status of the HIT-project
Clinical advantages of heavy-ion beams

- Excellent depth-dose profile (Bragg curve)  \( p, \text{ions} \)
- Increased biological efficiency  \( \text{only ions} \)
- Tumor-conform treatment  \( p, \text{ions} \)
  - beam scanning + energy variation
- In-vivo range localisation  \( (p), \text{ions} \)
  - Positron-emitting beam fragments (PET)
Clinically relevant properties of heavy-ion beams

- Inverted depth-dose profile (Bragg curve)

Unmodified Bragg peak

Extended target volume

Typically 30 energy steps needed for a ripple < 5%
Lateral beam spread

Film dosimetry, LBL Berkeley

Protons

$^{12}\text{C}$ ions
Clinically relevant properties of heavy-ion beams

- Increased biological efficiency

Survival curves
CHO cells

\[
\text{RBE} = \left[ \frac{D_Y}{D_p} \right]_{\text{Isoeffect}}
\]

\[
\text{Biol. Effect} \propto \int f(Z,E) \cdot \text{LET}(Z,E) \cdot \text{RBE}(Z,E) \, dV
\]
Track structure

Monte Carlo Simulation (TRAX)

Increased biological efficiency
Beam delivery systems

passive system

much better: **Intensity-controlled beam scanning**
Intensity-controlled raster scan

Fast scanning magnets

Beam Monitor

Target volume

Power supplies

Operator

Therapy Control System

Intensity + position feedback

Synchrotron Control System

Treatment plan

Patient data

Safety Interlocks
- Iso-Energy slices
- typ. 20,000 beam positions in a treatment plan
- Beam position checked every 150 µs
Rasterscan irradiation
Treatment plan for a Chondrosarcoma, Carbon beam 3 fields
Tumor-conform irradiation

- Photons 4 fields
- Carbon ions 2 fields
**Extension to moving targets**

Precision of stereotactic fixation:
- 1mm in the head to
- 3mm in the pelvic region

Not feasible for regions with internal motion, e.g., respiration in thorax and abdomen.

For ions: variations in radiological path length extremely important.
3D online motion compensation (3D-OMC)

- Magnetic scanner system
- PMMA wedge system
- Suitable motion tracking system
- Dynamic treatment plan

- Static
- Moving, non-compensated
- Moving, compensated

➤ Real-time, highest precision
Verification of beam delivery

- In-beam PET monitoring
Formation of positron-emitters by projectile fragmentation
In-beam PET-Monitoring

**carbon ions**

**protons**

**Activity density:**

\(~ 200 \text{ Bq cm}^{-3} \text{ Gy}^{-1}\)

Compare with tracer imaging:

\(10^4 \sim 10^5 \text{ Bq cm}^{-3}\),

even \(10^6 \text{ Bq cm}^{-3}\) (mice PET)
In-beam PET monitoring of carbon ion therapy at GSI


- Control of the carbon ion range
- Verification of field position
- Detection of deviations between real and planned treatment (misalignments or local anatomical changes) => Effect on dose?
Clinical results:
The detection of tissue density modifications

Local density modifications:
- filling of cavities with mucus
- tissue reduction after surgery
- slight mispositioning
Clinical results

- Tumor regression
- Local tumor control
- Side effects
Patient treatments

12/2003  n=205
chordoma / chondrosarcoma SB  81/42  123*
sacral / spinal chordoma / CS  22
Adenoid cystic carcinoma  30
Other skull base tumors  15
Reirradiations skull base  15

*67 treated within phase I/II study
## Chordomas / Chondrosarcomas

### Results of Radiation Therapy

<table>
<thead>
<tr>
<th>Author, year</th>
<th>n</th>
<th>RT</th>
<th>local control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Romero, 1993</td>
<td>18</td>
<td>conv.RT</td>
<td>17% (CH)</td>
</tr>
<tr>
<td>Debus, 2000</td>
<td>45</td>
<td>FSRT</td>
<td>50%/5y (CH) 100%/5y (CS)</td>
</tr>
<tr>
<td>Munzenrider, 1999</td>
<td>519</td>
<td>Prot. (+ Phot)</td>
<td>73%/5y (CH) 98%/5y (CS)</td>
</tr>
<tr>
<td>Castro, 1994</td>
<td>223</td>
<td>He</td>
<td>63%/5y (CH) 78%/5y (CS)</td>
</tr>
<tr>
<td>Noel, 2001</td>
<td>67</td>
<td>Prot + Phot</td>
<td>71%/3y (CH) 85%/3y (CS)</td>
</tr>
<tr>
<td>Schulz-Ertner, 2003</td>
<td>67</td>
<td>C12</td>
<td>81%/3y (CH) 100%/3y (CS)</td>
</tr>
</tbody>
</table>
Local tumor control

Carbon

photon IMRT

Debus et al., 5/2000
Tumor regression

Prior to therapy

3 months after carbon ion therapy total tumor dose 60 GyE
Tumor regression (Chordoma)

Prior to therapy 6 weeks after treatment
Petroclivale Chondrosarcoma

Prior C12-RT

6 weeks after C12-RT
Recurrent Chordoma
60 GyE
<table>
<thead>
<tr>
<th>Study Type</th>
<th>Frequency</th>
<th>Year(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skull base CH+CS</td>
<td>30 / year routine treatment</td>
<td></td>
</tr>
<tr>
<td>Phase I/II ACC</td>
<td>10 / year</td>
<td>2003, 2004</td>
</tr>
<tr>
<td>Phase I/II spinal/sacral CH + CS</td>
<td>5 / year</td>
<td>2005, 2006</td>
</tr>
<tr>
<td>Phase I/II prostate cancer</td>
<td>10 / year</td>
<td></td>
</tr>
</tbody>
</table>
The Heidelberg project  
HIT

1 Isocentric Gantry (360 deg.) and 2 horizontal treatment stations

Heavy-ion Gantry

Weight: 600 t
25 m long
13 m diameter
Deformation < 0.5 mm

Manufacturer: MAN

Design capacity:
1000 patients/year

Radiological University Clinics Heidelberg
Time table HIT project

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>05/ 2004</td>
<td>Laying the foundation-stone</td>
</tr>
<tr>
<td>05/ 2005</td>
<td>Ion sources and LINAC commiss.</td>
</tr>
<tr>
<td>06/ 2005</td>
<td>Start Gantry installation</td>
</tr>
<tr>
<td>11/ 2005</td>
<td>Synchrotron commiss.</td>
</tr>
<tr>
<td>04/ 2006</td>
<td>Gantry commiss.</td>
</tr>
<tr>
<td>11/ 2006</td>
<td>Clinical operation of 2 horizontal stations</td>
</tr>
<tr>
<td>End 2007</td>
<td>Clinical operation total facility</td>
</tr>
</tbody>
</table>
The Heidelberg project  HIT
The Heidelberg project

Groundwork  May 2004
The Heidelberg project  HIT
Summary

– Heavy-ion beams offer favorable conditions for the treatment of deep-seated local tumors
  → *Depth-dose profile and enhanced RBE in the target volume*  \( \text{ion} \)

– Highly tumor-conform treatment
  → *Beam scanning + active energy variation*  \( \text{p, ion} \)

– In-vivo irradiation monitoring
  → *online PET-system*  \( \text{p, ion, RIB} \)

– Encouraging clinical results

– *Construction of clinical ion-facilities in progress*
  → HIT (Heidelberg), TERA (Milano), MedAustron (Vienna)