IBT with Ions Heavier than Protons: Performance and Prospects

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Forschungszentrum Jülich

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IBT with Ions Heavier than Protons: Performance and Prospects

- patients treated with IBT -

<table>
<thead>
<tr>
<th>Year</th>
<th>Total No. of Treatments</th>
<th>Treatments with Ions A&gt;1</th>
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</thead>
<tbody>
<tr>
<td>1987</td>
<td></td>
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<tr>
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<td>2013</td>
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</table>
IBT with Ions Heavier than Protons: Performance and Prospects

• pros and cons of heavier ions •

- narrower dose peak
- increased biological effectiveness
- less lateral scattering
- nuclear fragmentation
- more expensive
IBT with Ions Heavier than Protons: Performance and Prospects

• general requirements for IBT accelerators •

• High reliability
• Easy to operate
• Easy to maintain
• Easy to upgrade
• Low maintenance costs
• Low follow-up costs
IBT with Ions Heavier than Protons: Performance and Prospects

- synchrotron: slow cycling -

<table>
<thead>
<tr>
<th>Facility</th>
<th>Ions</th>
<th>Collaborators</th>
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<tbody>
<tr>
<td>HIMAC, Chiba, JP</td>
<td>He-Xe</td>
<td>NIRS/Hitachi, Toshiba</td>
</tr>
<tr>
<td>HIBMC, Harima SGC, JP</td>
<td>H, C</td>
<td>Hitachi, Toshiba</td>
</tr>
<tr>
<td>HIT, Heidelberg, D</td>
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<td>CERN</td>
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<td>Saga HIMAT, Tosu, JP</td>
<td>H-C</td>
<td>Mitsubishi</td>
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<td>SPHIC, Shanghai, CN</td>
<td>H, C</td>
<td>Siemens</td>
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<td>HIRFL, Lanzhou, CN</td>
<td>H, C</td>
<td>IMP</td>
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<td>MedAustron, WN, A</td>
<td>H, C</td>
<td>CERN</td>
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<td>i-ROCK, Kanagawa, JP</td>
<td>C</td>
<td>Toshiba</td>
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**IBT with Ions Heavier than Protons: Performance and Prospects**

* synchrotron: slow cycling *

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<thead>
<tr>
<th>Synchrotron Center</th>
<th>Species</th>
<th>Institution</th>
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**established extraction method**

**high beam stability in time, position, and size**
IBT with Ions Heavier than Protons: Performance and Prospects

- slow-cycling synchrotron: HIT -

C$^{6+}$
430 MeV/u
1 x $10^9$ pps

Data: HIT
IBT with Ions Heavier than Protons: Performance and Prospects

- slow-cycling synchrotron: new design study -

NIRS

$^6\text{C}^+$

60-430 MeV/u

$\varnothing \approx 6.4 \text{ m}$

$\varnothing \approx 10.1 \text{ m}$

superconducting

Data: K. Noda
IBT with Ions Heavier than Protons: Performance and Prospects

- cyclotron: new design study -

**IBA C400**

<table>
<thead>
<tr>
<th>Ion</th>
<th>H, He, C</th>
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<tr>
<td>Energy (MeV/u)</td>
<td>400 (H:250)</td>
</tr>
<tr>
<td>Outer diameter (m)</td>
<td>6.6</td>
</tr>
<tr>
<td>Height (m)</td>
<td>3.4</td>
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<tr>
<td>Weight (t)</td>
<td>700</td>
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<tr>
<td>Extracted current (nA)</td>
<td>8</td>
</tr>
<tr>
<td>RF power (kW)</td>
<td>2x100</td>
</tr>
<tr>
<td>Magnetic field</td>
<td>4.5 T</td>
</tr>
<tr>
<td>RF Frequency</td>
<td>75 MHz</td>
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</table>

Data: D. Bertrand, IBA & A. Olshevskiy, JINR
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- clinical relevance of a gantry

- Irradiation should occur from the optimum angle to reduce unnecessary radiation exposure

- The beam should be directed to the target not the target to the beam
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- gantry: HIT -

Rotation
range: ± 185°
accuracy: ± 0.3°
step size: 0.3°
time: 1 min/circle
braking distance: 1°

Spot
size: $\sigma_x$, $\sigma_y < 3$ mm
divergence: $\sigma_x', \sigma_y' < 1/200$ rad
position accur.: $\Delta \sigma_x, \Delta \sigma_y < 1$ mm

HIT
length: 25 m
diameter: 13 m
weight: 600 t
range: 30 cm
aperture: 24x22 cm$^2$
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- new gantry concepts -

HIMAC II (2015)
length: 13 m
Ø: 11 m
weight: 300 t
range: 30 cm
aperture: 20x20 cm²

HIT
length: 25 m
diameter: 13 m
weight: 600 t
range: 30 cm
aperture: 24x22 cm²

HIMAC II (2010)
length: 17 m
Ø: 14 m
weight: 300 t
range: 25 cm
aperture: 15x15 cm²
IBT with Ions Heavier than Protons: Performance and Prospects

**new gantry concepts II**

**HIMAC II (2015)**
- length: 13 m
- Ø: 11 m
- weight: 300 t
- range: 30 cm
- aperture: 20x20 cm²

**HIT**
- length: 25 m
- diameter: 13 m
- weight: 600 t
- range: 30 cm
- aperture: 24x22 cm²

**NS-FFAG**
- length: 30 m
- Ø: 20 m
- weight: ≈ 7 t
- range: 25-27 cm
- aperture: ? cm²
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- the optimum ion -

- high RBE in the tumor
- sparing of normal tissue
- low risk for late toxicity
- high benefit-cost ratio
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- the optimum ion: RBE vs. LET -

Data: LBL
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- the optimum ion: RBE vs. LET -

![Graph showing RBE vs. LET for different cell lines and tissue types.]

- Human kidney T-1
- Chinese hamster V-79
- Rat rhabdomyosarcoma
- Mouse BALB/C 3T3
- Mouse C3H/10T1/2
- Mouse mammary EMT6
- Chinese hamster ovary
- Rat gliosarcoma 9-L

**LET (keV/µm)**

**RBE**

- Photons
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- the optimum ion: RBE vs. LET -

- Ideal for entrance and exit zone
IBT with Ions Heavier than Protons: Performance and Prospects

- the optimum ion: RBE vs. LET -

The diagram shows the relationship between RBE (relative biological effectiveness) and LET (linear energy transfer). The optimum ion is ideal for different zones:

- **Entrance and exit zone**: low LET (1-20 keV/µm)
- **Target zone**: high LET (200-1000 keV/µm)
- **Photons**: ideal for both low and high LET

The graph includes data points for various biological targets, such as human kidney, Chinese hamster, and mouse organs, illustrating the effectiveness of different LET values for different tissues.
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- the optimum ion: RBE vs. LET -

![Graph showing RBE vs. LET for different ions]

- ideal for entrance and exit zone: H, He
- ideal for target zone: Li, C, Ne

- photons

LET (keV/µm):

- 1
- 10
- 100
- 1000

20 200
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- the optimum ion: LET vs. depth dose -

Data: Kantemiris, 2011
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- the optimum ion: properties as function of nucleons -
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- the optimum ion: properties as function of nucleons -

- Penumbra
- high-LET (pre-BP)

Relative lateral penumbra vs. Number of nucleons for ions with different atomic numbers (H to Ne). The graph shows a trend of decreasing penumbra with increasing number of nucleons, approximated by the formula $\sim 1/\sqrt{N}$. The pre-BP high-LET values are also plotted for comparison.
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• the optimum ion: properties as function of nucleons •

- Relative lateral penumbra

- Number of nucleons

- Neutrons/Projectile (a.u.)

- pre-BP high-LET (cm)

The optimum ion properties as a function of nucleons.
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- the optimum ion: cost and properties as function of nucleons -

**Graph**
- Y-axis: Relative lateral penumbra
- X-axis: Number of nucleons
- Data points for different elements (H, He, Li, Be, BC, N, O, Ne)
- Line indicating cost proportional to $1/\sqrt{N}$
- Points for high-LET (pre-BP) and neutrons

**Equation**
- Cost: $\sim 1/\sqrt{N}$
IBT with Ions Heavier than Protons: Performance and Prospects

• clinical issues •
IBT with Ions Heavier than Protons: Performance and Prospects

• clinical trials I •

- ion passive vs ion active
- ion w/ vs w/o gantry
- Center A vs Center B
- phase I/II
- phase III
- tumor stage
- tumor type
- ion dose A vs B
  HIT: recurrent GB
  NIRS: NSCLC I
- ion (H) vs ion (C)
  HIT: CS/CD and prostate ca
- ion fraction #A vs #B
  HIT: GB; 5 vs 6 fx C
IBT with Ions Heavier than Protons: Performance and Prospects

- clinical trials II -

therapy alternatives

- Intensity-modulated RT
- Image-guided RT
- Stereotactic RT
- Stereotactic radiosurgery
- Gamma knife
- Brachytherapy
- Surgery
- Thermotherapy
- Cryotherapy
- Photodynamic therapy

endpoints

- local control
- disease-free survival
- progression-free survival
- disease-specific survival
- overall survival
- acute toxicity
- late toxicity
- biochemical endpoint
- quality of life
- second malignancy

Randomized Trials

ion dose A vs B
HIT: recurrent GB
NIRS: NSCLC I
ion (H) vs ion (C)
HIT: CS/CD and prostate ca
ion fraction #A vs #B
HIT: GB; 5 vs 6 fx C
IBT with Ions Heavier than Protons: Performance and Prospects

- clinical trials III -

therapy alternatives
Intensity-modulated RT
Image-guided RT
Stereotactic RT
Stereotactic radiosurgery
Gamma knife
ion w/ vs w/o gantry
Brachytherapy
Surgery
Thermotherapy
Cryotherapy
Center A vs Center B
Photodynamic therapy

new ion (Li, Be, B) vs
standard ion (H, C)
or
therapy alternatives

disease-free survival
progression-free survival
disease-specific survival
overall survival
acute toxicity
late toxicity
biochemical endpoint
quality of life
second malignancy
HIT: CS/CD and prostate ca
HIT: GB; 3 vs 6 tx C

endpoints
ion dose A vs B
HIT: recurrent GB
death rate
NIRS: NSCLC I
ion (H) vs ion (C)
ion fraction #A vs #B

phases I/II/III
C/D tumor stage
tumor type
IBT with Ions Heavier than Protons: Performance and Prospects

- clinical trials: challenges -

- duration
- financing
- continuity
- balancing of patient cohorts
- diagnostic accuracy
- diagnostic effort
- uniformity of treatment
- protocol compliance
- drop-outs
- lost to follow-up
IBT with Ions Heavier than Protons: Performance and Prospects

- clinical trials: example -

Question: Does IBT reduce the number of second malignancies?

Incidence with standard RT: 0.5% in 15 years
Assumption: 60% reduction

<table>
<thead>
<tr>
<th>Arm 1</th>
<th>Arm 2</th>
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<tbody>
<tr>
<td>X</td>
<td>ion</td>
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<tr>
<td>5000</td>
<td>5000</td>
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<td>25</td>
<td>10</td>
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<tr>
<td></td>
<td>patient numbers</td>
</tr>
<tr>
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<td>modality</td>
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- clinical trials: example -

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<tbody>
<tr>
<td>X ion</td>
<td>X ion</td>
</tr>
<tr>
<td>5000 modality</td>
<td>5000 ion</td>
</tr>
<tr>
<td>25 patient numbers</td>
<td>10 expected cases</td>
</tr>
</tbody>
</table>

duration of study ≈ 20 years
IBT with Ions Heavier than Protons: Performance and Prospects

• tasks to improve performance and prospects •

• Reduce weight
• Reduce power consumption
• Reduce neutron activation
• Minimize system downtime
• Save resources

• Optimize patient flow
• Standardize patient reporting
• Optimize fractionation schedules
• Establish standard treatment protocols
IBT with Ions Heavier than Protons: Performance and Prospects

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• Acknowledgments •

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