International Carbon Ion Therapy Treatment Modalities: How to Use an Accelerator to Treat Cancer

Dr Dale Prokopovich
Accelerator Technology Forum
8 May 2014
What Is Particle Therapy?

• High energy protons (225 MeV) or carbon ions (up to 430 MeV/u), for a range of ~30 cm in tissue used to irradiate a tumour volume
• Current carbon ion therapy uses a synchrotron for acceleration while proton therapy uses cyclotron or synchrotron
• Very high localisation of radiation to treatment volume compared to conventional gamma or x-ray therapy

Advantages
• Highly accurate dose delivery
• Low entry dose
• Higher biological effect on tumour
• Faster treatment and less fractions

Disadvantages
• Possible location uncertainty of treatment from motion
• Carbon ion fragmentation?
• Not suitable for multiple metastases
United States

- United States has 15 proton therapy centres in operation and another 7 currently under construction.

- A particle beam therapy R&D centre, was launched in August of 2012, at the Walter Reed National Military Medical Center (WRNMMC) in Bethesda, Maryland.

- Mayo Clinic has expressed interest in delivering carbon ion therapy to the United States with a “Permission to Plan” granted in 2012.

http://www.proton-therapy.org/map.htm
Particle Therapy Centres in Japan

- Osaka Carbon Ion Therapy Facility
- Osaka Proton Therapy Facility
- Tsuyama Proton Therapy Centre
- Hyogo Ion Beam Medical Centre
- Fukuoka Prefectural Hospital Proton Therapy Centre
- Medipolis Proton Therapy and Research Center
- University of Tsukuba Proton Medical Research Center
- National Cancer Center Hospital East
- Gunma University Heavy Ion Medical Center
- National Institute of Radiological Sciences
- Kanagawa Cancer Center
- Southern Tohoku Proton Therapy Center
- SAGA HIMAT
- Kochi
- Kumamoto
- Miyazaki
- Kagoshima
# European Carbon Ion Therapy Facilities

<table>
<thead>
<tr>
<th>Name</th>
<th>Year</th>
<th>Total €x10^6</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIT</td>
<td>2009</td>
<td>119</td>
<td>First dedicated carbon ion therapy facility in Europe, based on GSI experiments and treatments. Substantially subsidised by GSI &amp; German government. 2 treatment rooms + gantry</td>
</tr>
<tr>
<td>CNAO</td>
<td>2012</td>
<td>150</td>
<td>Purchased PIMMS design from CERN. Significant support for commissioning from CERN for equipment testing and construction. 3 treatment rooms</td>
</tr>
<tr>
<td>Shanghai</td>
<td>2013</td>
<td>140</td>
<td>Constructed by Siemens/Danfysik. Based on same design as Kiel and Marburg. Constructed to be a dedicated treatment facility unlike Lanzhou. 4 treatment rooms</td>
</tr>
<tr>
<td>Shanghai</td>
<td>2013</td>
<td>240 (240 total)</td>
<td></td>
</tr>
<tr>
<td>MedAustron</td>
<td>2014</td>
<td>193</td>
<td>Started as the Austron spallation source but evolved into MedAustron. Based on CNAO PIMMS design. No medical community support. 3 treatment rooms + proton gantry</td>
</tr>
<tr>
<td>Marburg</td>
<td>2015-2016</td>
<td>140</td>
<td>Constructed by Siemens/Danfysik. Delay in start due to both financial troubles as well as the failure of Kiel. HIT is likely to take over management to ensure success. 4 treatment rooms</td>
</tr>
<tr>
<td>Name</td>
<td>Year</td>
<td>Total ¥x10^8</td>
<td>Notes</td>
</tr>
<tr>
<td>---------</td>
<td>------</td>
<td>--------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>HIMAC</td>
<td>1994</td>
<td>326</td>
<td>3 passive &amp; 2 active treatment rooms. Superconducting scanning gantry. Development, testing and therapeutic trials of new modalities</td>
</tr>
<tr>
<td>Hyogo^+</td>
<td>2001</td>
<td>280</td>
<td>Proton and carbon passive beam. 6 treatment rooms: 2 proton gantries, 1 Horizontal &amp; Vertical, 1 45°, 1 seated, 1 experimental.</td>
</tr>
<tr>
<td>Gunma</td>
<td>2010</td>
<td>126</td>
<td>3 therapy rooms, passive dose stacking, 1 research room with scanning beam. Plans to expand and upgrade some rooms to scanning beam</td>
</tr>
<tr>
<td>Saga#</td>
<td>2013</td>
<td>140</td>
<td>Two passive dose stacking rooms, 1 Horizontal &amp; Vertical, 1 Horizontal &amp; 45° (being commissioned) and a spare room for future fast scanning</td>
</tr>
<tr>
<td>Kanagawa</td>
<td>2014</td>
<td>106</td>
<td>Currently being commissioned, two scanning beam treatment rooms. Space for later implementing a superconducting rotating</td>
</tr>
</tbody>
</table>

^ Originally designed as an experimental facility to compare proton and carbon therapies however an earthquake repurposed funding and it had to become a commercially viable treatment facility.

# Privately owned facility, required full expenditure for hospital facility including diagnostics and imaging.
Example pencil beam in muscle

Carbon Ions
- Range 286 ± 1.33 mm
- Lateral Spread 1.21 ± 1.77 mm

Protons
- Range 286 ± 8.42 mm
- Lateral Spread 4.16 ± 7.15 mm
Protons vs Carbon Ions

Target Ionization
Total Ionization = 217859.1 keV / Ion
Total Phonons = 39.4 keV / Ion
Total Target Damage = 1.56 keV / Ion

Target Ionization
Total Ionization = 4999234.9 keV / Ion
Total Phonons = 733.1 keV / Ion
Total Target Damage = 31.97 keV / Ion

Ion = H (218. MeV)

Ion = C (5000. MeV)
Enhancement of Dose to Tumour
Creation of a Spread Out Bragg Peak

- Passive, hybrid and active methods for SOBP available
Creation of a Spread Out Bragg Peak
Treatment Rooms and Beamline Equipment
Superconducting Rotating Gantry

Conventional method

IMIT (Intensity Modulated Ion Therapy)
Superconducting Rotating Gantry

Conventional method

IMIT (Intensity Modulated Ion Therapy)
During planning for a facility we have identified several key areas required for the successful implementation of carbon ion therapy in Australia

Not a static list! More fact sheets added as technology evolves
CDI - Selection of Dose Delivery Method

Critical Decisions to be made:
- Selection of dose delivery method between
  - a) passive broad beam,
  - b) passive dose stacking
  - c) hybrid scanning
  - d) modulating scanning
- Staged upgrade between a), b), c) and d).

Key Factors Likely to Influence Decisions:
- Dose delivery Accuracy
- Treatment cost per patient (active scanning more expensive up front but lower cost per treatment)
- System compatibility
- Facility infrastructure e.g. available space and budget
- Associated issues of low level active waste production in passive systems (activated brass collimators and polyethylene bolus); facility workshop

Systems Affected by Decisions:
- Treatment planning software
- Accelerator control systems, ion source, beam monitoring and beam extraction
- Treatment room layout and patient imaging during irradiation
- Facility workshop (manufacture of patient specific components) and facility radioactive waste storage arrangements

Information Required:
- Types of tumours to be treated during early stage operations
- Knowledge on interface between active scanning technology and treatment planning software
- Identification of obsolete components following system upgrades in dose delivery method (e.g. ridge filters and wobbler magnets)

Diagram:
- Broad Beam
- Dose Stacking
- Scanning Beam
Dose verification
- Current methods of treatment delivery do not directly measure dose deposition. Accurate real-time dose verification will allow for smaller treatment margins and increased confidence in treating cancers close to critical organs.
- PET systems can be used to directly image hadron induced positron emitters either during treatment or immediately after treatment.

Ion species
- Protons have an advantageous dose profile while carbon ions have an enhanced RBE and decreased OER.
- Treatment is not limited to these two ion species and other ion species could have an important role in hadron therapy.

Shielding of both treatment rooms and accelerator
- Trade off between shielding wall thickness, material composition/costs and requirements
- Simulation of shielding materials and optimal thickness and design can significantly reduce expense as well as improve functionality

Emergency Stop
- Critical for stopping treatment and is tied in to interlocks, dose monitoring systems and accelerator feedback systems
- Recovery of treatment plan after emergency stop is critical and a current topic of research. Over/under dosing within a tumour volume is a significant complication following a stop
CDI - Room Design

- In-room imaging and/or simulation room for patient alignment
- Scanning or passive treatment modalities significantly impact room design
- Rooms with horizontal, vertical and both beam nozzles are required
- Wall thickness and entrance are critical design issues which can limit future use and expansion possibilities

![Diagram of CDI Room Design with annotations]

1. Ion Beam
2. 360° Table
3. Ion Beam Range Monitor
4. X-ray Generator (bottom) and X-ray Digitizer (top)
5. Large Bore CT
6. Patient Lounge
7. Suspended X-ray Imaging Plate
8. Ion Beam Monitor
FDO – Patient Positioning

- Millimetre precision in patient positioning is a requirement of hadron therapy, increasingly so with hyper-fractionation of dose.

- Time taken to correctly position a patient is a major factor in the overall treatment time equating to patient throughput and return on investment.

- Patient positioning can either occur in the treatment room or in an external room necessitating consideration of facility layout.

- Patient positioning is an area of potential development especially if patient rotation is incorporated in dose delivery processes.
Patient Immobilisation
Organ motion compensation is required so as to not limit the tumor types which can be treated and ensure that the advantageous dose distribution of hadrons is achievable.

Current techniques track external markers and gate irradiation according to this motion.

Organ motion tracking is further complicated if active scanning is utilised since individual spots are treated rather than the whole tumour.

CDI - Organ Motion Tracking

- Organ motion compensation is required so as to not limit the tumor types which can be treated and ensure that the advantageous dose distribution of hadrons is achievable.
- Current techniques track external markers and gate irradiation according to this motion.
- Organ motion tracking is further complicated if active scanning is utilised since individual spots are treated rather than the whole tumour.

Diagram showing the effect of gating and non-gating on the irradiation pattern.
Collaboration Strategy

Key Considerations:

• Engage with international leaders in Particle Therapy

• Engage with multiple partners so as to not ‘lock in’ on singular technology approach at this stage

• Engage and work together with the Australian oncology community to maximise patient benefit from proposed particle therapy options

• Ensure partners present diversity of benefit (Research/Technical exchange/Project management etc)
ANSTO Particle Therapy Collaborations

UniversitätsKlinikum Heidelberg

Active Research

MOU

Possible MOU

Active Research

fondazione CNAO

INFN

Australian Particle Therapy Collaboration
ANSTO signed an MOU with CNAO as part of visit by Sandro Rossi and Roberto Orecchia to ANSTO and the Particle Therapy collaboration in Canberra, September 2013

Visit by John Boldeman and Dale Prokopovich in October 2013

Information on costs and expenses involved in running and maintaining a particle therapy facility

Collaborative investigation into patient treatments and hypofractionation (less fractions = more patients)
Other European Facilities Collaboration

• MedAustron
  – Purchased Modified PIMMS plan from CNAO
  – Improvements to patient positioning and treatment room design

• Heidelberg Ion Therapy
  – Supported by GSI
  – Will be administering the Marburg facility

• Danfysik
  – Took over design, implementation and maintenance responsibilities for future particle therapy facilities from Siemens
The NIRS HIMAC Collaboration has had three experimental beam time allocations since 2011 in collaboration with CMRP at UOW. The results from these experiments have been very successful and include:

- 1st, 2nd & 3rd Generation SOI Microdosimetry
- ΔE-E Monolithic particle telescope (with Politecnico di Milano)
- Thin 3D Detectors
- MOSSkin MOSFET dosimetry
- Ionisation chamber measurements
- TLD nanodosimetry

There is strong interest in the application of solid state detectors for in-vivo dosimetry and patient plan verification. An invitation to re-apply for more beam time later this year is available. Additionally, sponsored attendance for the NIRS Particle Therapy Workshop is also offered.
• Hypofractionation (financial and therapeutic benefits)
• Rapid rescanning for organ motion
• PET based treatment position verification
• Angular irradiation and patient rotation
• Helium ion for proton therapy replacement
• In-vivo dose monitoring
• Cellular survival modelling (RBE verification)
• Advanced treatment planning tools and treatment optimisation

OUR CURRENT AREAS of ENGAGEMENT
Particle Therapy Research

• Particular research activities in particle therapy research:
  – Silicon microdosimetry (ARC Discovery grant application)
  – Patient positioning (NHMRC application)
  – ΔE-E particle telescope fragment identification
  – MOSFET dosimetry
  – Out of field dose characterisation
  – Monte Carlo Simulation (GEANT4 & TOPAS-beta testing)

• List of collaborators:
  – ANSTO
  – CMRP at University of Wollongong
  – Sydney University
  – NIRS HIMAC
  – DKFZ at Heidelberg Ion Therapy
  – Politecnico di Milano
  – Loma Linda University Medical Center

Not an exclusive and complete list of activities by Australians
• Establish a comprehensive picture and plan
Experiments Performed at Particle Facilities

- HIMAC
  - Passive Monoenergetic and SOBP
  - $^4$He and $^{12}$C ions

- HIT
  - Active Scanning Monoenergetic and SOBP

- CNAO
  - Future experimentation planned
HIT (Germany)

- Scanning energy modulated Spread Out Bragg peak in a PMMA phantom (1.17 g/cm³)
- Actual treatment plan for a deep seeded brain tumour
- Limited measurements due to time constraints but future work planned with larger array of SOI microdosimeters

Left: (top to bottom) The Transverse, Coronal and Sagittal slices of the dose treatment plan for a patient brain tumor treatment along the beam isocentre. The red marks indicate measurement positions.

Right: The response along the isocentre of the SOI Microdosimeter.
Collaboration and future work

• An Australian particle therapy facility would facilitate not only clinical research but have advantages for future of high energy physics and electronics research
• Advantage in patient positioning and rotation research will allow delay in acquisition of a rotating gantry or angled beam lines
• Research into QA of the RBE for carbon ions (variable RBE along ion range) is opportunity for Australian improvement of global carbon ion therapy. ARC grant application with UOW
• Experience from particle therapy facilities on patient rotation and organ motion

Kosaki et al. Radiation Oncology 2012, 7:44 http://www.ro-journal.com/content/7/1/44