The status and perspectives of hadrontherapy

The Italian National Centre CNAO

Part II

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CNAO Foundation

ANSTO - Sydney
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Hadrontherapy?

Electrons (X-rays): conventional radiotherapy

Carbon ion is 12×2000 times heavier than electron

Nucleus of Carbon made of 6 protons (p) and 6 neutrons (n)

Simplest nucleus: the proton (p)

Proton is 2000 times heavier than electron
Which advantages with hadrons?

+ PRECISION

Conformal irradiation of tumour volume
(= reduced damages to healthy tissues)

Hadrons: conformal irradiation

Abdomen

X-rays (IMRT) – 9 fields
Protons – 1 field
Increased radiobiological efficacy of carbon ions wrt X-rays (= DNA of tumour cells directly destroyed in multiple hits)

Which advantages with hadrons?

+ EFFICACY

Reduced effect dependence from Oxygen content (M. Belli et al.)
Not-for-profit Foundation
created and financed by the Italian Ministry of Health
with Law n. 388/2000

to build a Centre with two main goals:

To treat patients using hadrontherapy

To perform clinical and radiobiological research

The Board of CNAO

Fondatori:
Fondazione Policlinico Ospedale Maggiore - Milano
Fondazione Istituto Neurologico C. Besta - Milano
Fondazione Istituto Nazionale dei Tumori - Milano
Istituto Europeo di Oncologia - Milano
Fondazione Policlinico San Matteo - Pavia
Fondazione TERA - Novara

Partecipanti Istituzionali:
Istituto Nazionale di Fisica Nucleare
Università di Milano
Politecnico di Milano
Università di Pavia
Comune di Pavia

Partecipanti:
Fondazione Cariplo
**CNAO Model: core group of 100 persons**

*Integrated by Technical-Scientific Collaborations*

**NATIONAL**
- **TERA Foundation**: final design and high tech specifications
- **INFN**: co-direction HT, technical issues, radiobiology, research, formation
- **University of Milan**: medical coordination and formation
- **University of Pavia**: technical issues, radiobiology, formation
- **University of Catania**: medical physics
- **University of Florence**: medical physics
- **University of Turin**: interface beam-patient, TPS
- **Polytechnic of Milan**: patient positioning, radioprotection, authorisations
- **European Institute of Oncology**: medical activities, authorisations
- **San Matteo Foundation**: medical activities, logistics
- **Town of Pavia**: land and authorisations
- **Province of Pavia**: logistics and authorisation

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**CNAO Model: the Technical-Scientific Collaborations**

**INTERNATIONAL**
- **CERN (Geneva)**: technical issues, PIMMS heritage
- **GSI (Darmstadt)**: linac and special components
- **LPSC (Grenoble)**: optics, betatron, low-level RF, control system
- **Med-Austron (Vienna)**: technical collaboration for MA centre
- **Roffo Institute (Buenos Aires)**: medical and research activities
- **NIRS (Chiba)**: medical activities, radiobiology, formation
- **HIT (Heidelberg)**: research activities
CNAO in Pavia: 30 km SW of Milan

5 MARCH 2005
Lay of the foundation stone
The CNAO is operational in Pavia since 2010

View of the site
patient access

personnel area

simulation and verification area

patient preparation area

waiting area

treatment rooms

treatment rooms

treatment rooms

treatment rooms

extra spaces for CNAO Phase 2

personnel area

main control room

synchrotron maze

L. -1 H
1 (+1) CT Medical Imaging rooms

1 MR (3T) room

1 (+1) CT-PET rooms

Advanced 3D molecular imaging modalities
- tumour molecular profiling
- dose painting with different LET ions
  (sources and accelerators choices)

(O. Jäkel, in IBT, Springer 2011)
**From 1996 to 1999 at CERN**

**PIMMS (Proton-Ions Medical Machine Study)**

CERN-GSI-MedAUSTRON-Oncology2000-TERA

PL: P. Bryant (CERN+experts)
PAC: G. Brianti chairman
TERA: 25 man×yrs
MedA.: 10 man×yrs
O2000: 3 man×yrs
GSI: experts advices

**Objective:** define the optimal hadrontherapy centre without constraints

**Hospital based: safety, efficiency, reliability, maintainability**

**Very Compact Design!**
### Starting point... THE PATIENT

**Hospital based: safety, efficiency, reliability, maintainability**

<table>
<thead>
<tr>
<th>No.</th>
<th>Specification</th>
<th>Details/Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Beam particle species</td>
<td>( \text{p, He}^+, \text{Li}^+, \text{Be}^+, \text{B}^+, \text{C}^+, \text{O}^+ )</td>
</tr>
<tr>
<td>2</td>
<td>Beam particle switching time</td>
<td>( \leq 10 \text{ min} )</td>
</tr>
</tbody>
</table>
| 3   | Beam range                                        | 1.0 g/cm\(^2\) to 27 g/cm\(^2\) in one treatment room  
\( 3.1 \text{ g/cm}^2 \) to 27 g/cm\(^2\) in two treatment rooms  
Up to 20 g/cm\(^2\) for O\(^{16+}\) ions |
| 4   | Bragg peak modulation steps                        | 0.1 g/cm\(^2\)                                      |
| 5   | Range adjustment                                  | 0.1 g/cm\(^2\)                                      |
| 6   | Adjustment/modulation accuracy                     | \( \leq 0.025 \text{ g/cm}^2 \)                   |
| 7   | Average dose rate                                 | 2 Gy/min (for treatment volumes of 1000 cm\(^3\)) |
| 8   | Delivery dose precision                            | \( \leq 2.5\% \)                                 |
| 9   | Beam axis height (above floor)                    | 150 cm (head and neck beam line)  
120 cm (elsewhere) |
| 10  | Beam size\(^1\)                                   | 4 to 10 mm FWHM for each direction independently |
| 11  | Beam size step\(^2\)                              | 1 mm                                              |
| 12  | Beam size accuracy\(^2\)                          | \( \leq 0.25 \text{ mm} \)                        |
| 13  | Beam position step\(^3\)                          | 0.8 mm                                            |
| 14  | Beam position accuracy\(^3\)                      | \( \leq 0.2 \text{ mm} \)                        |
| 15  | Field size\(^1\)                                  | 5 mm to 34 mm (diameter for ocular treatments)  
2x2 cm\(^2\) to 20x20 cm\(^2\) (for H and V fixed beams) |
| 16  | Field position accuracy\(^2\)                     | \( \leq 0.5 \text{ mm} \)                        |
| 17  | Field dimensions step\(^3\)                       | 1 mm                                              |
| 18  | Field size accuracy\(^3\)                         | \( \leq 0.5 \text{ mm} \)                        |

(Basic specifications of CNAO facility)
LEBT

0.008 MeV/u H\(^{3+}\)
0.008 MeV/u C\(^{4+}\)

I \sim 0.5\ mA\ (H^{3+})
I \sim 0.2\ mA\ (C^{4+})

Two ECR sources
Continuous beam
LEBT Chopper

ECR SUPERNANOGAN

Ion sources produced by Pantechnik
in collaboration with: INFN-LNS

O1 and O2 sources inside the Synchrotron ring

Significant improvements have been provided by INFN-LNS: frequency tuning effect, gas control, extractor reliability, etc.
Linac=RFQ+IH

217 MHz

RFQ
0.008-0.4 MeV/u H³⁺
0.008-0.4 MeV/u C⁴⁺

IH
0.4-7 MeV/u H³⁺
0.4-7 MeV/u C⁴⁺

Internal structure

Ions input

Four-rods like type
Energy range = 8 - 400 keV/u
Electrode length = 1.35 m,
Electrode voltage = 70 kV
RF power loss (pulse): about 100 kW
Low duty cycle: around 0.1%

(In collaboration with GSI and INFN)
IH tank

- Integrated magnetic triplet lenses
- 56 Accelerating gaps
- Energy range: 0.4 – 7 MeV/u
- Tank length: 3.77 m
- Inner tank height: 0.54 m
- Inner tank width: 0.28 m
- Drift tube aperture diam.: 12 – 18 mm
- RF power loss (pulse): = 1 MW
- Averaged eff. volt. gain: 5.3 MV/m

Linac commissioning

Request at LINAC exit

<table>
<thead>
<tr>
<th></th>
<th>measured</th>
<th>nominal</th>
</tr>
</thead>
<tbody>
<tr>
<td>current for C6+ (7 MeV/u)</td>
<td>135 microA</td>
<td>120 microA</td>
</tr>
<tr>
<td>current for H+ (7 MeV)</td>
<td>1.2 mA</td>
<td>0.75 mA</td>
</tr>
</tbody>
</table>

Successfully commissioned in July 2009

In about 6 meters the beam increases the energy by a factor 1000 - to reach 1/10th of light speed... 30’000 km/sec
MEBT

- 7 MeV \( p \)
- 7 MeV/u \( \text{C}^{6+} \)

- \( I \sim 0.75 \text{ mA (p)} \)
- \( I \sim 0.12 \text{ mA (C)'} \)

- Stripping foil
- Current selection
- Debuncher
- Emittance dilution
- Match betas
- \( (x,x')_{\text{eq}} \)

**Carbon foils**

<table>
<thead>
<tr>
<th>Positions:</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foil material:</td>
<td>Carbon</td>
</tr>
<tr>
<td>Foil thickness:</td>
<td>100-200 ( \mu g/cm^2 )</td>
</tr>
<tr>
<td>Foil diameter:</td>
<td>15 mm</td>
</tr>
<tr>
<td>Beam diameter:</td>
<td>5 mm</td>
</tr>
<tr>
<td>Position accuracy:</td>
<td>( \pm 0.5 \text{ mm} )</td>
</tr>
</tbody>
</table>
Intensity degrader

4 transmission levels: 100%, 50%, 20%, 10%
Keep overall emittance unchanged

Multiturn injection

Create an orbit “bump”

Incoming beam
Septum
Bumper
Bumper

Generally there are 2, 3 or 4 bumpers.
The bump collapses in tens of turns
D = D' = 0
D = D' ≠ 0

P inj  P – 60 MeV  P – 250 MeV  C6 inj  C6+ – 120 MeV  C6+ – 400 MeV
Bp (T m)  0.4  1.1  2.4  0.8  3.3  6.4

Demanding requirements on magnet power supplies

Diameter ~ 25 m

Betatron core

RF cavity

Resonance sextupole

Synchrotron

7-250 MeV p
7-400 MeV/u C

I ~ 0.1-5 mA (p)
I ~ 0.03-1.5 mA (C)

Slow extraction
MAGNETIC SYSTEM
The higher the speed the bigger the force
(SYNCHRO-TRON)

- 16 Dipoles to bend (1 fam.)
- 24 Quadrupoles to focus (3 fam.)
- 20 Correctors to steer

Smooth spill to allow tumour painting

Intensity ripple ($\Delta I/I$) \(\leq\) 20\% at 2 kHz
(extraction with a betatron core - PIMMS)
Hardt condition

Only betatron varies

Smoothes ripples

The betatron core

Amplitude-momentum selection

HEBT

60-250 MeV p
120-400 MeV/u C

$10^{10}$ p/spill (~2nA)
$4 \times 10^8$ C/spill (~0.4nA)

different settings for

• Treatment Line
• Horizontal beam size
• Vertical beam size
• Extraction energy
Safety is an issue
(like: efficiency, reliability and maintainability)

Irradiation technique
active scanning

(Courtesy of Siemens Medical)
Monitoring system (CNAO)

Double system of ICs:
(integral, stripX,Y) - (integral, pixel)

Two measures: Intensity, Position, Profile

Redout frequency: 1 MHz (integral), 10 kHz (strip, pixel)
Resolution: 0.1 mm strip, 0.2 mm pixel
Area: 20 x 20 cm²
Non uniformity < 1%
Short term stability < 0.3%

(NIMA 698 (2013) 202-207)

In construction copy for EBG-MedAustron

Collaboration CNAO-PoliMi
The numbers of CNAO

**N. 14** European tenders completed

**More than 1000** Orders and contracts

**N.600 (500 Italian)** Firms worked for CNAO

**About 80** Authorisation procedures completed

**Cost 125 MEuro** About 50% less than market cost

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The Phases of CNAO

**Phase 0: specs+organisation**

- **Years:** 2002 - 2004

**Phase 1: construction**

- **Years:** 2005 - 2009

**Phase 2: experimentation**

- **Years:** 2010 - 2013

**Phase 3: running**

- **Years:** 2014 ...
October 2010 approved by:
- Ministry of Health
- Region Lombardy

Main Tasks:
- Dosimetry characterisation
- Radiobiology characterisation
- Patient treatments

CE label of 1st protocol !!!

9 July 2013
Chordomas and chondrosarcomas of skull base with protons

October 2013
Sarcoma of skull base and spine with carbon ions

Goal: close the experimental phase by end 2013 and start recognised treatments in 2014
The running phase

The treatments will be performed in the frame of the National Health System.

During routine operation at CNAO, in three treatment rooms, will be treated about 2000 patients per year.

A network will connect CNAO to the national and international health system to guarantee efficient recruitment of the patients on a national basis.

Future and R&D
Research is a must

Project by Spring 2014

Beam line devoted to clinical, radiobiology and physics research, without interfering with daily treatments
Setting up user survey for best use of this future facility

Improvements: On-line imaging

“Minimal” choice: breathing synchronisation (already applied in Chiba and HIT)

Interesting also for IMRT: lots of efforts and devices

External surrogates with correlation models
X-rays
Ultrasound, MRI
Particle radiography

(Review in Riboldi et al, Lancet Oncology 2012)
(Courtesy of Medical Intelligence)
**Improvements: tumour tracking with active scanning**

**GSI approach**

$^p\text{C}^4$ or $^C\text{C}^6$

- **Tranverse variation**
- **Energy variation**

**Dose visualisation: “in beam PET”**

**ISSUES:** low statistics; blood flow dilution; off-line PET → logistics

**Dose**

- **Activity $\beta^+$**

**Counts [10^3]**

- **Dose [kGy]**

**Pre-collision**

- Projectile
- Atomic nucleus of tissue

**Post-collision**

- Projectile fragment
- Neutron
- Target fragment

**Courtesy of GSI**
Secondaries emission and reconstruction

Proton Range Radiography (PRR)
Electronic telescope for the measure of position and residual range of protons; it gives the density map of the traversed volumes; it permits to check in real time the treatment planning assumptions on position and dimensions of the traversed tissues and organs.

Nuclear Scattering Tomography (NST)
Three-dimensional map of the tissues densities obtained by vertex reconstruction of high energy protons interactions (> 600 MeV).

Interaction Vertex Imaging (IVI)
Density of interaction vertex reconstruction gives information on the Bragg peak position.

PROMPT radiation (Gamma) - Enlight

Gantry for beam direction selection
Comparison of dimensions

Conventional RT
Proton Gantry
PSI proton gantry
Carbon Ion Gantry
GSI carbon ion gantry

(Courtesy M. Pullia)
Novel gantry for carbon ions

The ULICE WP6 collaboration realized a conceptual design of a mobile isocenter gantry.

### Rationale for the choice

- Innovative layout
- Cheaper and simplified mechanical structure
- Less magnets in the gantry line
- Total weight reduced as well as deformations
- Well known magnet technology
- Layout scalable to SC magnets
Conclusions

The collaboration with many Institutions have been fundamental for CNAO and this model can be fruitful for all the hadrontherapy community in the World.

CNAO is willing to contribute to the growth of physics applications to medicine and to collaborate to the creation of hadrontherapy centres in the World (e.g. EBG-MedAustron).

CNAO is open to team in research projects and in programmes of technology transfer to industry.

Hadrontherapy: medical application of accelerators  
... with feeling ...

Thank you!