APPLICATIONS OF ACCELERATORS TO TUMOUR THERAPY - 2

Ugo Amaldi

University of Milano Bicocca and TERA Foundation
Conventional radiotherapy
Orthovoltage (low energy) X-ray therapy began in January 1896.

Many complications because of the dose to the skin.

Megavoltage (high-energy) radiation in the 50s. Co-60 gamma spared the skin.

**Graph:**
- Build-up
- 6 MV photons are even better
First Cobalt-60 ‘bomb’ in Canada

1951 – first treatment at Victoria Hospital, London, Ontario

Cobalt-60 (1.2 MeV gammas)
has been produced for 50 years in CANDU reactors

Roy Errington
founder of MDS Nordion

Dr. Ivan Smith
After World War II:

old and new ‘cobalt bombs’

10 million patients treated with cobalt gamma rays

Important for developing countries
The electron linac

1939
Klystron invention

1947 - Stanford
The first linac for electrons
4.5 MeV and 3 GHz
‘Conventional’ radiotherapy: linear accelerators dominate

In the world radiation oncologists use 10,000 electron linacs

40% of all the existing accelerators

\[ e^- + \text{target} \rightarrow X \]

Linac for electrons
3 GHz
4-23 MeV

multileaf collimator

tumour
Last 10 years: Intensity Modulated Radiation Therapy = IMRT...

... and now “Image Guided Radio Therapy” for organ motion

9 photon fields

brain stem is the ‘critical organ’

Courtesy T. Lomax (PSI)
Accelerators for protontherapy
The accelerators used today in hadrontherapy are “circular”

**Teletherapy with protons (200-250 MeV)**

CYCLOTRONS (*) (Normal or SC)  
SYNCHROTRONS  

4-5 metres  
6-9 metres

(*) also synchrocyclotrons

**Teletherapy with carbon ions (4800 MeV = 400 MeV/u)**

SYNCHROTRONS  

18-25 metres
The time structures of the beams are very different

CYCLOTRONS (*) (Normal or SC)

SYNCHROTRONS

The pulsed beam of fixed energy is always present

A cycling beam of variable energy has 1 second gaps

(*) A synchrocyclotron cycles at hundreds Hertz
European succes story: ‘spot scanning' with protons

PSI (Villigen- Switzerland)
Gantry 1: 350 patients
The PROSCAN project of PSI: 2007

- ACCEL
- SC cyclotron
- COMET

- Experiment
- OPTIS
- Gantry 1
- Gantry 2
Compact design: 3.5 m radius
Rotation on one side only
Double parallel scanning
Spot scanning technique
Spot scanning at PSI with Gantry 2

In future: fast beam scanning with repainting

1. Lateral scanning with bending magnet upstream at 2 ms/step
2. Depth scanning by changing energy with absorber upstream
3. Lateral scanning with bending magnet and moving the bed

Single ‘spot’
IMPT = Intensity Modulated Particle Therapy with protons

4 NON-UNIFORM FIELDS

Courtesy T. Lomax (PSI)
Protons are quantitatively different from X-rays

9 X-ray fields

4 proton fields

PSI
Protons are quantitatively different from X-rays

9 X-ray fields

4 proton fields

Carbon ions deposit in a cell 24 times more energy than a proton producing not reparable damages.

Carbon ions are qualitatively different from X rays and can control radioresistant tumours.
Five companies offer turn-key centres for 80-100 M€.

If proton accelerators were ‘small’ and ‘cheap’, no radiotherapist would use X rays.
Cyclotrons need a long ESS to reduce the energy.
Protontherapy: a mature market...
Mitsubishi solution for Shizuoka - Japan

4 Bending Magnets
Rinecker Proton Therapy Centre
Munich

250 MeV S.C. Cyclotron
ACCEL
Protontherapy is booming.

- 40,000 patients
- 22 PT centers
- > 50,000 patients
- PT center under operation
Accelerators for carbon therapy
The foundations of hadrontherapy

- **200 MeV Protons** but only 1 nA
- **4800 MeV carbon ions** but only 0.1 nAe

A charged hadron beam that loses energy in matter.

**27 cm**

- **tumour**
- **target**

[Dose Distribution Curve](http://global.mitsubishielectric.com/bu/particlebeam/index_b.html)

- **linac**
- **Cobalt**
- **Proton**
- **Bragg peak**
- **tail**

X rays

protons (carbon ions)
Japan: 4 proton and 2 carbon ion centres

WAKASA BAY PROJECT
by Wakasa-Bay Energy Research Center
Fukui (2002)
protons (≤ 235 MeV)
cyclotron (IBA – SHI)
2 Gantries + 1 hor. beam

TSUKUBA CENTRE
Ibaraki (2001)
protons (≤ 270 MeV)
synchrotron (Hitachi)
2 gantries
2 beam for research

KASHIWA CENTER
Chiba (1998)
protons (≤ 235 MeV)
cyclotron (IBA – SHI)
1 h beam + 1 v beam + 1 gantry

HYOGO MED CENTRE
Hyogo (2001)
protons (≤ 230 MeV) - He and C ions (≤ 320 MeV/u)
Mitsubishi synchrotron
2 p gantries + 2 fixed p beam + 2 ion rooms
200 patients with carbon ions

SHIZUOKA FACILITY
Shizuoka (2002)
Proton synchrotron
2 gantries + 1 h beam

HEAVY ION MEDICAL ACCELERATOR
HIMAC of NIRS (1995)
He and C (≤ 430 MeV/u) 2 synchrotrons
2 h beams + 2 v beams
4000 patients with carbon ions

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HIMAC (Japan) pioneers carbon therapy

4000 patients
No repair mechanism: 6-9 sessions only
The Hyogo ‘dual’ Centre

Mitsubishi: turn-key system
The ‘dual’ centre of the Gunma University is in construction.

G. Kraft

400 patients treated with carbon ions
J. Debus (Heidelberg Univ.)

in-beam PET
The GSI model (G. Kraft, M. Scholz et al) allows the calculation of RBE point by point from the flux of the various ions.

'flat' effective dose

'sloping' physical dose
Physics and results of in-beam-PET

Wolfgang Enghart et al.
Dresden
Potential patients in Europe
The site treated with hadrons

In the world protontherapy:
55'000 patients

carbon ion therapy
4400 patients

BUT
less than 1% with ‘active’ dose distribution systems at PSI and GSI with spot/raster scanning
<table>
<thead>
<tr>
<th>Indication</th>
<th>End point</th>
<th>Results photons</th>
<th>Results carbon HIMAC-NIRS</th>
<th>Results carbon GSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chordoma</td>
<td>local control rate</td>
<td>30 – 50 %</td>
<td>65 %</td>
<td>70 %</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>local control rate</td>
<td>33 %</td>
<td>88 %</td>
<td>89 %</td>
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<tr>
<td>Nasopharynx carcinoma</td>
<td>5 year survival</td>
<td>40 -50 %</td>
<td>63 %</td>
<td></td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>av. survival time</td>
<td>12 months</td>
<td>16 months</td>
<td></td>
</tr>
<tr>
<td>Choroid melanoma</td>
<td>local control rate</td>
<td>95 %</td>
<td>96 % (*)</td>
<td></td>
</tr>
<tr>
<td>Paranasal sinuses tumours</td>
<td>local control rate</td>
<td>21 %</td>
<td>63 %</td>
<td></td>
</tr>
<tr>
<td>Pancreatic carcinoma</td>
<td>av. survival time</td>
<td>6.5 months</td>
<td>7.8 months</td>
<td></td>
</tr>
<tr>
<td>Liver tumours</td>
<td>5 year survival</td>
<td>23 %</td>
<td>100 %</td>
<td></td>
</tr>
<tr>
<td>Salivary gland tumours</td>
<td>local control rate</td>
<td>24-28 %</td>
<td>61 %</td>
<td>77 %</td>
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<tr>
<td>Soft-tissue carcinoma</td>
<td>5 year survival</td>
<td>31 – 75 %</td>
<td>52 -83 %</td>
<td></td>
</tr>
</tbody>
</table>

(*) Preservation of eyesight

Table by G. Kraft - 2007
Elective indications for carbon ion therapy from HIMAC and GSI

Hirohito H. Tsujii (May 2007):
for all these tumours we can obtain a 90% local control with no severe complications

- Chordoma / low grade chondrosarcoma
- Malignant salivary gland tumors
- Malignant melanoma of the paranasal sinus
- Soft tissue sarcomas and bone tumors
- **Lung cancer (85 patients treated in 1 fraction: NO REPAIR!)**
- Liver tumors
- Prostate carcinoma
**Numbers of potential patients**

**X-ray therapy** (40-50 electron linacs)

- every 10 million inhabitants: 20,000 pts/year

**Protontherapy**

- 12% of X-ray patients 2,400 pts/year

**Therapy with Carbon ions for radio-resistant tumour**

- 3% of X-ray patients 600 pts/year

**TOTAL every 10 M**

- about 3,000 pts/year

(*) Combining studies made in Austria, Germany, France, Italy and Sweden - ENLIGHT
European ‘dual’ centres for carbon ions and protons
HIT at Heidelberg: first beams in May 2007

First beam extracted
First patient: beginning 2008

- Ion Sources
- Synchrotron
- LINAC
- High Energy Beam Transport Line
- Gantry
- Treatment halls by Siemens Medical
Heidelberg ion gantry: 600 tons and 400 kW
Siemens Medical is building for 2010 a ‘dual’ centre in Marburg

In 2003 GSI has passed to Siemens Medical its patents and know-how
TERA programmes since 1992

TERA has proposed and designed the ‘dual’ National Centre for carbon ions and protons

1. CNAO is being built in Pavia

TERA has introduced and developed a novel accelerator:

2. Fast cycling “cyclinacs” for protons and carbon ions
CERN–TERA–MedAustron Collaboration for optimized medical synchrotron

Project leader: P. Bryant

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3 extraction systems:
- betatron core
- 1/3 resonance
- RF knock-out

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400 MeV/u synchrotron

RF cavity

Resonance sextupole

Sextupole vert. chromaticity

Circumference: $C = 76.84$ m
- Tune horizontal: $Q_x = 1.67$
- Tune vertical: $Q_z = 1.72$

Betatron core

Sextupole horiz. chromaticity

Injection septum

Extraction septum

Electrostatic septum
CNAO = Centro Nazionale di Adroterapia

CNAO Foundation created by the Italian Government in 2001:
4 Hospitals in Milan, 1 Hospital in Pavia and TERA
Since 2004 INFN is Institutional Participant with important construction responsibilities

In October 2003 TERA passed to CNAO
the design of CNAO (3000 pages) and 25 people

- One linac à la GSI inside the ring
- Multiturn injection
- Short beams
The CNAO Foundation builds the Centre in Pavia

President: Erminio Borloni
Medical Director: Roberto Orecchia  Technical director: Sandro Rossi

Hospital building

High-tech building

MedAustron will build in Wiener-Neustadt a centre based on the CNAO construction drawings
Synchrotron ‘dual’ solution for carbon ions and protons by TERA

- Phase 2
- Area for experiments
- Calvi/Tekne
- PIMMS/TERA

Legend:
- Accelerator
- Treatment
- Simulation
- Waiting area
- Personnel
- Lifts
- Technical area
- Technical plants
CNAO in November 2007
The synchroton vault

Two sources are working

First beam in summer 2008

Girders and supports are in place
In 2007 MedAustron has been approved for Wiener Neustadt

2007: CNAO - MedAustron agreement on the acquisition of the construction drawings

PIMMS/CNAO synchrotron

- 4 medical treatment rooms
- 2 fixed beams
- 1 proton gantry
- 1 ion gantry
- 1.200 patients per year

2 irradiation labs, one for biology and one for physics
In 2007 approved for construction in Lyon
Tendering in 2008

www.projet-etoile.fr
Pr Jacques BALOSSO
Medical director
ENLIGHT = European Network for Light Ion Therapy

- Initiated with a CERN meeting in Feb.2002: Austria, France, Germany, Italy, Sweden, CERN, GSI, ESTRO
- Financed by the Commission for 2002-2005
- Transformed into the ‘ENLIGHT++ Platform’ in 2006 – see www.cern.ch/enlight
- Coordinator of ENLIGHT++ : Manjit Dosanjh (CERN)

- 2007: approval of the Marie Curie Training Network PARTNER
- 2008: submission of ULICE = Union of Light Ion Centres in Europe around Heidelberg and Pavia