INTRODUCTION TO MEDICAL PHYSICS
WITH ACCELERATORS

Ugo Amaldi

University of Milano Bicocca and TERA Foundation
Three types of accelerators
1930: invention of the cyclotron

Spiral trajectory of an accelerated nucleus

Ernest Lawrence
with a 1 MeV cyclotron
(1901 – 1958)

Modern cyclotron
1945 the principle of phase stability and the synchrotron

Vertical magnetic field
Circular trajectory of the particles accelerated in a “synchrotron”

1 GeV electron synchrotron
Frascati - INFN - 1959
The first electron linac

In 1939, the invention of the klystron was made by Sigmund Varian and Russell Varian.

In 1947, William W. Hansen developed the first electron linac for electrons, reaching 4.5 MeV and 3 GHz.
Accelerators for isotope production in diagnostics and endotherapy
At BNL the « cow » was made productive

In reactors slow neutrons produce

\[ ^{98}\text{Mo} + n = ^{99}\text{Mo} + \gamma \]

\[ ^{99}\text{Mo} \ (66 \text{ h}) = ^{99m}\text{Tc} \ (6 \text{ h}) + e^- + \nu \]

BNL
“generator”

Walter Tucker and Powell Richards

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85% of all nuclear medicine examinations use molibdenum/technetium.

Generators for diagnostics of

... liver

... lungs

... bones ...

SPECT scanner

Lead collimators to channel the gammas of 0.14 MeV.

Rotating head
With detectors

0.14 MeV gammas
A. Fission chain in nuclear reactors

B. Reprocessing of the special fuel bars

Worldwide production of 100 000 curies per year at aging nuclear reactors for 30 million examinations/year:
- BR2 Belgium
- NRU Canada (50%)
- OSIRIS France
- HFR Netherlands (40%)
- SAFARI-1 South Africa
Production of $^{99}\text{Mo}$: possible solutions of a serious problem

**Photofission of Uranium**

- 50 MeV electrons
- 100 mA
- Neutron capture on $^{98}\text{Mo}$
- $^{238}\text{U}$
- Superconducting linac

**Triumph and NDS Nordion (Canada): could cover 10% of the market**

- 1 mA of 1000 MeV protons
- Pb moderator with $^{98}\text{Mo}$ targets
- Superconducting linac

**Advanced Accelerator Applications (CERN spin-off): could cover 100% of the market**

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High-current cyclotrons used in medicine

Baby Cyclotrons (below 18 MeV)

*In-house facility*

Mainly used for production of short-lived positron emitters like $^{18}\text{F}$, $^{11}\text{C}$, $^{13}\text{N}$, $^{15}\text{O}$.

Medium Energy Cyclotrons (below 40 MeV)

*Centralised facility*

Majority of the cyclotron produced isotopes are produced using such machine viz, $^{123}\text{I}$, $^{201}\text{Tl}$, $^{67}\text{Ga}$, $^{68}\text{Ga}$, $^{103}\text{Pd}$ etc.

High Energy Cyclotrons (above 40 MeV)

*Centralised facilities and research institutions*

Used for production of few radioisotope requiring high energy for production viz, $^{67}\text{Cu}$, $^{82}\text{Sr}$, $^{211}\text{At}$....
Baby cyclotrons

General Electric
16.5 MeV

Ion Beam Applications
18 MeV

Accelerated particles: H⁻
2-[^18F]fluoro-2-deoxy-D-glucose = FDG for PET exams in oncology, cardiology, neuro-receptor imaging
Medium energy cyclotrons

30 MeV protons, 500-1000 μA

IBA
Belgium

ACS
Canada

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High-energy cyclotrons

IBA’s ARRONAX in Nantes

4 Particles: H⁻ / D⁻ / He²⁺/ HH⁺

Variable energy: 15 MeV → 70 MeV

Performances:
- 750 µA H⁻
- 35 µA He²⁺

70 MeV  350 µA
Examples of endotherapy with radioisotopes

- **131I**
  - Beta-decay: electron
  - Image showing 1000 µm

- **213Bi, 211At**
  - Alfa-decay: Helium nucleus
  - Image showing 70 µm
  - It can be called: “Systemic hadrontherapy”

From ARRONAX – Nantes - France
Cancer therapy with X ray and hadron beams
‘Conventional’ radiotherapy: linear accelerators dominate

In the world, radiation oncologists

use 15,000 electron linacs

40% of all the existing accelerators

Conventional radiation oncology: linear accelerators dominate

1 linac every <250,000 inhabitants

Linac for electrons
3 GHz
5-20 MeV

In the world, radiation oncologists use 15,000 electron linacs
40% of all the existing accelerators
Protons and ions spare healthy tissues

200 MeV - 1 nA protons

4800 MeV – 0.1 nA carbon ions which can control radioresistant tumours

charged hadron beam that loses energy in matter

30 cm
tumour target

X rays protons or carbon ions
Charged hadrons can deliver the dose in three dimensions

Longitudinal movement by varying the energy of the beam
Charged hadrons can deliver the dose in three dimensions

Lateral movement with a transverse magnetic field
Protons are quantitatively different from X-rays

9 X ray beams

4 proton beams

Courtesy of PSI - Villigen
Protons are qualitatively different from X-rays

Carbon ions deposit in a cell 24 times more energy than a proton producing not reparable multiple close-by double strand breaks.

Carbon ions can control radio-resistant tumours.
Accelerators for hadrontherapy (*)

(*) The accelerator is only a ‘small’ part of a therapy centre
The accelerators used today in hadrotherapy 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
Loma Linda Medical University Centre: first patient 1992

- First hospital-based proton-therapy centre

Built at Fermilab
Protontherapy: cyclotrons and synchrotrons...
Five companies offer turn-key centres
If proton accelerators were ‘small’ and ‘cheap’, no radiotherapist would use X rays.
Protontherapy is booming

> 60 000 patients

PT centers

40,000 patients

22 PT centers
Therapy with carbon ions
HIMAC in Chiba is the pioneer of carbon therapy (Prof H. Tsujii)

Hirohiko Tsujii
5000 pts 1994-2009

End of 2008
protons: 2000 patients
carbon ions: 500 patients

Mitsubishi: turn-key system
Germany: the GSI pilot project

1998-2009
500 patients treated with carbon ions

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Patients of hadrontherapy
The site treated with hadrons

In the world protontherapy:
60,000 patients

carbon ion therapy
5,000 patients mainly at HIMAC
First important results obtained with proton therapy

- Cordomas, protons
  - 100% at 5 years
  - 98% at 10 years
  - <35% at 15 years

- Condrosarcomas, protons
  - 70% at 5 years

- Conventional RT
  - Control rate: 5 years: 100%, 10 years: <35%, 15 years: <35%

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<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>
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<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>
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<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>
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</tbody>
</table>

Table by G. Kraft 2007
Results of C ions
**Numbers of potential patients (*)**

**X-ray therapy**

every 10 million inhabitants: 20'000 pts/year

**Proton therapy**

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
New centres for carbon ion therapy
HIMAC new facility

Completion: end 2010

- Treatment room
- Simulation room
- Preparation room
- Control room
- Gantry room

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Medical Director: J. Debus
Technical Director: T. Haberer
HIT at Heidelberg

First beam extracted in 2007
First patient: summer 2009

Ion-Sources
Synchrotron
LINAC
High Energy Beam Transport Line
Quality Assurance
Gantry
Treatment halls by Siemens Medical
Heidelberg ion gantry: patient room

Patient Gantry Room November 2007

Tilt floor, pending on Gantry position

Nozzle
Bumber mats
Patienttable, Roboter
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 type of accelerator:
the “cyclinac”

2. “cyclinacs for protons and carbon ions

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PIMMS at CERN from 1996 to 2000

CERN–TERA–MedAustron Collaboration for optimized medical synchrotron

Project leader: P. Bryant          Chairman of the PAC: G. Brianti

CERN−Summer Students - 3.8.09 - UA
CNAO = Centro Nazionale di Adroterapia

CNAO Foundation created by the Italian Government in 2002: 4 Hospitals in Milan, 1 Hospital in Pavia and TERA

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

Since 2004 INFN is “Istitutional Participant” with people and important construction responsibilities (Caudio Sanelli)

INFN runs CATANA for eye protontherapy in Catania

PIMMS/TERA
CNAO = Centro Nazionale di Adroterapia at Pavia

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

Hospital building
High-tech building
CNAO = Centro Nazionale di Adroterapia at Pavia

May 2009

Hospital building

Synchrotron building
Perspective view of CNAO
The synchrotron
Chair for head and neck

Robotic bed (installed)

First patient foreseen by the end of 2010 - 2800 patients per year in 2014

Courtesy of Schaer Engineering AG, Switzerland
Siemens Medical is building for 2010 a ‘dual’ centre in Marburg based on the GSI know-how.
Siemens Medical is building for 2012 a ‘dual’ centre in Kiel
**In 2007 MedAustron has been approved for Wiener Neustadt**

MedAustron will build a centre based on the CNAO construction drawings (by agreement with CERN-CNAO-INFN)

- 2 (3) Sources, (p, C, redundancy)
- RFQ
- IH (7 MeV/n)
- Synchrotron 400 MeV/n, 800 MeV
- 3 (4) Treatment rooms
- 2 Experimental beam lines
End of 2009: Choice of the constructor
“Archade” (At Ganil in Caen, Fr) is based on the new IBA400 MeV/u superconducting cyclotron

As soon as the agreement with Archade is finalized, IBA will start the construction of the prototype
ENLIGHT and the European projects
European Network for LIGht-ion Hadron Therapy – 2002 - 2005

- GSI project for the University of Heidelberg Clinics (ready to treat)
- TERA project for CNAO in Pavia (completing construction)
- Marburg and Kiel centres (in construction by Siemens Medical)
- Med-Austron for Wiener Neustadt (approved)
- ETOILE in Lyon (approved)
  Competitive tendering

SINCE 2002 THESE GROUPS + CERN + GSI AND MANY OTHERS ARE PART OF THE
ENLIGHT PLATFORM co-ordinated by Dr. Manjit Dosanjh
Programs approved in FP7: PARTNER, ULICE, ENVISION for a total of 20 MEuro
The next fast cycling accelerators for carbon ion therapy
GSI approach to treat moving organs: depth with fast absorbers

**BETTER SOLUTION:**
fast energy variation by electronics and not mechanics

Fast cycling allows ‘repainting’ and error correction
The energy is adjusted in 2 ms in the full range by changing the power pulses sent to the 16-22 accelerating modules.

The charge in the next spot is adjusted every 2 ms with the computer controlled source.
A.D.A.M. SA, Application of Detectors and Accelerators to Medicine, a CERN spin-off company will build LIGHT, and has an agreement with IBA for the delivery of the rest and the overall control.
The two phases of the dual centre for Catania

Superconducting cyclotron by LNS/IBA (250 MeV protons and 3600 MeV carbon ions) is commercialized by IBA

1st phase:
32 cm protons
17 cm carbon ions

2nd Phase
32 cm protons
32 cm carbon ions
Another solution still in design: Fixed Field Alternating Gradient

Cyclotron isochronous

Synchrotron
*const. closed orbit (varying magnetic field)

FFAG
*varying closed orbit (const. magnetic field)

Scaling and non scaling FFAG
Scaling FFAGs have been built

KURRY 150 MeV proton scaling FFAG

booster (20MeV)

injector (spiral FFAG)

main ring (150MeV)
Design of a non-scaling FFAG accelerator for proton therapy

D. Trbojevic A.G. Ruggiero E. Keil
N. Neskovic Vinca Belgrade A. Sessler

Non-scaling FFAG proposal

Scaling and non-scaling FFAG

35 basic cells

Figure 3. Orbits of particles during acceleration.
### Properties of fast-cycling accelerators

<table>
<thead>
<tr>
<th>Accelerator</th>
<th>Beam always present during treatments</th>
<th>Energy variation by electronic means</th>
<th>Time needed for varying the energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclotron</td>
<td>Yes</td>
<td>No</td>
<td>50 ms (*)</td>
</tr>
<tr>
<td>Synchrotron</td>
<td>No</td>
<td>Yes</td>
<td>1 second</td>
</tr>
<tr>
<td>FCA</td>
<td>Yes</td>
<td>Yes</td>
<td>1 millisecond</td>
</tr>
</tbody>
</table>

(*) With movable absorbers

The energy is changed by adjusting the RF pulses to the modules.

The beam is ideal to paint many times moving tumours in 3D without variable absorbers.
Many 15-70 MeV high-current cyclotrons are commercially available for isotope production. Accelerators may solve the technetium crysis.

For proton therapy five companies offer cyclotron/synchrotron based turn-key centres.

For carbon ion therapy, Europe is well advanced and four companies offer synchrotron based centres, but the difficulty still is in the dimensions of the ion gantry (1st challenge: new superconducting gantries).

For the 2nd challenge, i.e. the following of moving tumor targets, a fast cycling accelerator with variable energy would allow electronically driven multipainting: cyclinacs and FFAG.
CNAO in Pavia

THE END