THE IMPACT OF FUNDAMENTAL PHYSICS ON MEDICINE

Ugo Amaldi
The beginnings of fundamental Physics and medical Physics

9 November 1895
Discovery of X rays

1898
Discovery of radium

Wilhelm C. Röntgen

Marie Skłodowska - Pierre Curie
First medical use of an accelerator

Crookes tube: the best accelerator of the time

22 December 1895: La radiographie

Electron beam

X rays

Announcement: December 28, 1985
First uses of X rays and radium in diagnostics and therapy

- Robert Jones and Oliver Lodge (Liverpool)
  Radiography of a bullet in a hand
  February 7, 1896

- Emile Grubbe (Chicago)
  4 hour irradiation of a breast cancer
  January 27, 1896

- Henri Danlos (Paris)
  Lupus treatment with radium
  1901
120 years of fundamental (beautiful) and medical (useful) physics

fundamental physics

Roentgen rays

Curie radium

therapy

1895

1898

diagnostics

Roentgen rays

Roentgen rays

Curie radium

three intertwined yarns

2014

Impact of Physics - UA - Globe - 10.4.14
120 years of fundamental (beautiful) and medical (useful) Physics

fundamental Physics

Hess cosmic rays

therapy

diagnostics

Regaud fractionation

Coolidge tube

2014
1912: Victor Hess discovers ‘cosmic rays’

Hess brought precision equipment in ten balloon ascents and discovered that radiation at 5 km altitude is twice larger than at sea level.
Thirty years later the mechanism of cosmic rays was understood and marked the beginning of particle physics.

Muons are ‘heavy electrons’ with a mass that is 200 times larger.
Thirty years later the mechanism of cosmic rays was understood and marked the beginning of particle Physics.

Muons are ‘heavy electrons’ with a mass that is 200 times larger.

Isidor Rabi: Who ordered THAT?
Fractionation in Radiotherapy

1912 - Paris
Claudius Regaud:
The same dose is more effective if subdivided

Institut du Radium

1930 - Claudius Regaud and Henri Coutard:
Standard at 200 keV = 0.2 MeV:
  2 grays per session
  5 sessions per week
  treatment in 5-6 weeks
Coolidge tube
1912

Heated tungsten filament

Cooling water

A breakthrough

United States Patent Office

WILLIAM D. COOLIDGE, OF SCHENECTADY, NEW YORK, ASSIGNEE TO GENERAL ELECTRIC COMPANY, A CORPORATION OF NEW YORK.

TUNGSTEN AND METHOD OF MAKING THE SAME FOR USE AS FILAMENTS OF INCANDESCENT ELECTRIC LAMPS AND FOR OTHER PURPOSES.

1,082,933.


Application filed June 19, 1912. Serial No. 704,580.
Today every CT Scan uses a Coolidge tube
120 years of fundamental (beautiful) and medical (useful) physics

Lawrence cyclotrons
Anderson positron

fundamental physics

therapy

diagnostics

Lawrence cyclotrons
Lawrence cyclotrons
1929: invention of the “cyclotron”

Spiral trajectory of an accelerated particle

Ernest Lawrence

1 MeV = 1 million electronvolts
= 0.001 GeV
1929: invention of the “cyclotron”

Spiral trajectory of an accelerated particle

Ernest Lawrence -

Modern 30 MeV cyclotron for radioisotope production

1 MeV = 1 million electronvolts
= 0.001 GeV
Cyclotrons in diagnostics and therapy

- 1936: Radio-sodium to study metabolism
- 1936: Radio-phosphorus to treat leukaemia
1939: The 60-inch cyclotron was financed for medical purposes and later used to treat patients with neutron beams.
Discovery of the anti-electron

Carl Anderson - CALTECH
1932

Fast particle

Slow particle

LEAD

Positron-electron annihilation

Gamma 1

Gamma 2

Positron

Electron
PET centre with a 15 MeV cyclotron

Most used substance
Sugar FDG with Fluorine -18
Combination of CT with PET: CT-PET

- morphology
- metabolism
120 years of fundamental (beautiful) and medical (useful) Physics

fundamental physics

Veksler-McMillan synchrotron

Hansen linac

therapy

2014

diagnostics

Veksler-McMillan synchrotron

Hansen linac
The invention of the synchrotron came in 1945.

E. McMillan and V.J. Veksler
“Phase stability principle”

Vertical magnetic field

circular trajectory of an accelerated particle

accelerating cavity

1959: Veksler visits McMillan at Berkeley
The invention of the synchrotron came in 1945.

E. McMillan and V.J. Veksler

“Phase stability principle”

1 GeV = 1000 MeV

Electron synchrotron
Frascati - INFN - 1959

1959: Veksler visits McMillan at Berkeley
The first electron linac above 1 MeV

1939
Invention of the klystron

Sigmur Varian
Russell Varian
William W. Hansen
The first electron linac above 1 MeV

1939

Invention of the klystron

1947

Linac for electrons 1.5 MeV at 3 GHz

- Sigmur Varian
- Russell Varian
- William W. Hansen

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‘Conventional’ radiotherapy: linear accelerators dominate

6-20 MeV electrons

Standard frequency
3 GHz

gantry

X rays

target
‘Conventional’ radiotherapy: linear accelerators dominate

- 2000 patients/year every in 1 million inhabitants
- 1 treatment in 30 sessions

In the world radiation oncologists use 20,000 electron linacs
50% of all the existing accelerators

Courtesy of Elekta
120 years of fundamental (beautiful) and medical (useful) physics

fundamental physics

therapy

diagnostics

Berkeley proton therapy

CERN
Following the black yarn: particle physics at CERN
60 years ago: creation of CERN

Pierre Auger
Science Director of UNESCO

Edoardo Amaldi
Secretary General of provisional CERN 1952-1954

Felix Bloch
Physics Nobel Prize in 1952
First CERN Director General 1954-1955
CERN aerial view with the Geneva Airport

PS 1959

SPS 1975

Large Hadron Collider
27 km
CERN accelerators are synchrotrons used as “colliders”

LEP-1989
8.5 km
SPS-1975
PS-1959

LHC in 2012
Large Hadron Collider
4 000 + 4 000 GeV

PS nel 1959 – 25 GeV
To focus only on the most important discovery made with CERN accelerators we must go back to ‘cosmic rays’

Hess brought precision equipment in ten balloon ascents and discovered that radiation at 5 km altitude is twice larger than at sea level.

100 YEARS AGO

V. Hess
To focus only on the most important discovery made with CERN accelerators we most go back to ‘cosmic rays’

muons are ‘heavy electrons’ with a mass that is 200 times larger
From cosmic rays to the Higgs particle

CERN – 2012
Fabiola Gianotti  Peter Higgs

1912
Victor Hess

100 years
From cosmic rays to the Higgs particle

CERN – 2012
Fabiola Gianotti  Peter Higgs

1912
Victor Hess

100 years

electrometer
2013: the Nobel prize winners

François Englert  Peter Higgs

Fabiola Gianotti  Peter Higgs
Following the red yarn
120 years of fundamental (beautiful) and medical (useful) Physics

fundamental physics

therapy

diagnostics

Tobias proton therapy

CERN
Hadrontherapy (particle therapy)
1946: "Bob" Wilson proposes to use protons, helium and carbon ions.

Lawrence PhD student

Founder and first Director of FERMILAB (Chicago) 1967-1978
Advantages of protons and carbon ions

1. Healthy tissues are spared by protons and carbon ions

protons: 230 MeV
C ions: 5000 MeV
Advantages of protons and carbon ions

1. Healthy tissues are spared by protons and carbon ions.

protons: 230 MeV
C ions: 5000 MeV

9 X ray beams
4 hadron beams

PSI - Villigen
Advantages of protons and carbon ions

1. Healthy tissues are spared by protons and carbon ions

protons: 230 MeV
C ions: 5000 MeV

5000 MeV carbon ions

X rays

protons or carbon ions

Impact of Physics - UA - Globe - 10.4.14
Advantages of protons and carbon ions

1. Healthy tissues are spared by protons and carbon ions

2. Carbon ions have charge = 6 and produce in the DNA clustered unrepairable damages thus killing at the end of the range the cells which are radioresistant to both X rays and protons.

protons: 230 MeV
C ions : 5000 MeV
60 years ago: first proton treatment at Berkeley

CANCER RESEARCH

Volume 18          FEBRUARY 1958          Number 2

Pituitary Irradiation with High-Energy Proton Beams
A Preliminary Report*


(Donner Laboratory of Biophysics and Medical Physics, Donner Pavilion, and the Radiation Laboratory, University of California, Berkeley, Calif.)
Cyclotron solution for protons by IBA - Belgium

Seven companies offer turn-key centres with 2-3 gantries for 120-150 M€.

If proton accelerators were ‘small’ and ‘cheap’, no radiation oncologist would use X rays.
Superconducting cyclotron solution by Varian

Rinecker Proton Therapy Center (RPTC) Munich

Number of systems ordered from industry

protontherapy is booming

20-25 sessions per patient
European cost of a full treatment:
IMRT: 8-10 k€
Protontherapy: 20-25 k€
HIMAC in Chiba is the pioneer of carbon therapy

Yasuo Hirao

Hirohiko Tsujii
8500 pts 1994-2014

The GSI pilot project: 1997-2008

450 patients treated with carbon ions

Gerhard Kraft

J. Debus

GSI - Darmstadt
The GSI pilot project: 1997-2008

450 patients treated with carbon ions

GSI designed HIT (Heidelberg Ion Therapy centre) where 1800 patients have been treated since 2009
The site treated with hadrons

In the world protons:
100'000 patients (8% per year)

carbon ions
10'000 patients (most at HIMAC)
### Numbers of potential patients by European Network for Light Ion Therapy

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Potential Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>X-ray therapy</strong></td>
<td></td>
</tr>
<tr>
<td>for 1 million inhabitants:</td>
<td>2,000 pts/year</td>
</tr>
<tr>
<td><strong>Protontherapy</strong></td>
<td></td>
</tr>
<tr>
<td>12% of X-ray patients</td>
<td>240 pts/year</td>
</tr>
<tr>
<td><strong>Therapy with carbon ions for radio-resistant tumour</strong></td>
<td></td>
</tr>
<tr>
<td>(comparisons with proton therapy are needed to define sites and protocols)</td>
<td></td>
</tr>
<tr>
<td>3% of X-ray patients</td>
<td>60 pts/year</td>
</tr>
<tr>
<td><strong>TOTAL for 1 M</strong></td>
<td>300 pts/year</td>
</tr>
</tbody>
</table>

ENLIGHT coordinator: Manjit Dosanjh
Non-profit Foundation created in 1992

Two programmes:

- Synchrotron for C ions (and protons): CNAO in Pavia
- Linacs for protons and carbon ions: A.D.A.M.
In 1995 U.A. and M. Regler convinced CERN to start Proton Ion Medical Machine Study, PIMMS

Optimized synchrotron for therapy

Project Leader: Phil Bryant
Chair of PAC: Giorgio Brianti
1996-2000

M. Regler
CNAO = Centro Nazionale di Adroterapia Oncologica in Pavia

Hospital building

High-tech building
CNAO = Centro Nazionale di Adroterapia Oncologica

Sandro Rossi
Technical Director

Roberto Orecchia
Medical Director

Synchrotron building

Hospital building

Construction by
CNAO Foundation and INFN
2005-2010
The synchrotron

- 2 sources
- linac
- bending magnet
- quadrupole
- RF cavity
January 2014: 200 patients treated
MedAustron promoted and participated in PIMMS

MedAustron has acquired from CNAO Foundation the construction drawings
MedAustron promoted and participated in PIMMS
MedAustron promoted and participated in PIMMS

Construction completed in Wiener Neustadt:

three days ago the protons have circulated in the synchrotron
To conclude: in 2014 a further step has been made
To conclude: in 2014 a further step has been made.
PHYSICS IS BEAUTIFUL AND USEFUL

Physik ist schön und nützlich

La Physique est belle et utile

La Fisica è bella e utile
The importance of the Higgs “field”
HIGHLIGHTS: 2012 – F.Gianotti and J. Incandela, ATLAS and CMS spokespersons, announce the discovery of the ‘Higgs field’

ATLAS: event
Higgs → 4 electrons

CMS: event
Higgs → 2 photons

ATLAS: event
Higgs → 4 electrons
Two large ‘detectors’ at LHC
Event in ATLAS: production of 4 muons = heavy electrons
Event in CMS

muon
The Higgs particle is the 37th field but it is the most important one because...

the Higgs ‘field’ is a continuous medium that fills the space since one hundredth of a billionth of a second \((10^{-11} \text{s})\) after the Big Bang
The Higgs particle is the 37th particle but it is the most important one because…

the Higgs ‘field’ is a continuous medium that fills the space since one hundredth of a billionth of a second \((10^{-11}\text{ s})\) after the Big Bang.

the particles interact differently with the Higgs field and thus they have different masses.
Metaphor of the two twins practicing Nordic ski on a flat snow “field”

The second twin has applied a wrong glide wax...
Metaphor of the two twins practicing Nordic ski on a flat snow “field”

…but if the snow ‘field’ is not seen he is slower because has a larger mass.
2013: the Nobel prize winners

François Englert  Peter Higgs
Fabiola Gianotti  Peter Higgs
TERA novel accelerators for cancer therapy: proton linacs
Prototype of CCL built and beam tested by TERA-CERN-INFN: 2003

Mario Weiss

Linac BOoster

LIBO

4.4 MW at 3 GHz

74 MeV

62 MeV

3 GHz proton Linac

Proton trajectory

$E_0 = 16 \text{ MV/m}$
Commercial prototype built and power tested by A.D.A.M.: 2011

A.D.A.M. = Applications of Detectors and Accelerators to Medicine

First Unit of LIGHT Linac for Image Guided Hadron Therapy

- 3 GHz klystron
- 10 MW

41 MeV

30 MeV

30 MeV
Centre offered by A.D.A.M. - CERN spin-off Company acquired by Advanced Oncotherapy in 2013

1. 150 MeV
2. 230 MeV
3. 230 MeV
Linac for Image Guided Hadron Therapy

CCL (TERA)

SCD TL (ENEA)

RFQ

pulses @ 200times per second
Linac for Image Guided Hadron Therapy

- Pulses at 200 times per second

- Source

- Linac

- ± 5 mm every pulse

- The energy changes actively made by the linac accelerating modules.

- CCL (TERA)

- SCDTL (ENEA)

- RFQ
It is clear to anybody who visits a hospital that Physics applications are everywhere. Medical doctors use Physics when they measure a blood pressure, when they perform an ultrasound scan to determine the sex of an unborn child, when they take radiography or a CT scan. In particular fundamental physics, which aims at understanding how particles and forces act in the subatomic world and are organized to form everything we observe around us, has numerous medical applications.

Everything started in 1895 with the discovery of X-rays by Roentgen, who was using the best particle accelerator of the time. In the lecture the theme of the title will be exposed by following the 120 years long story of particle accelerators used to cure tumours. The time is well chosen because the year 2014 marks the 60th anniversary of CERN, the largest particle physics laboratory in the world, and of the first cancer treatment with protons done at Berkeley.