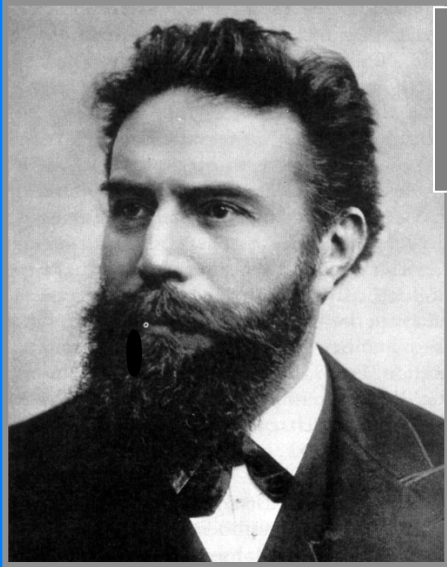


THE IMPACT OF FUNDAMENTAL PHYSICS ON MEDICINE

Ugo Amaldi

The beginnings of fundamental Physics and medical Physics



9 November 1895
Discovery of X rays

Wilhelm C. Röntgen

1898

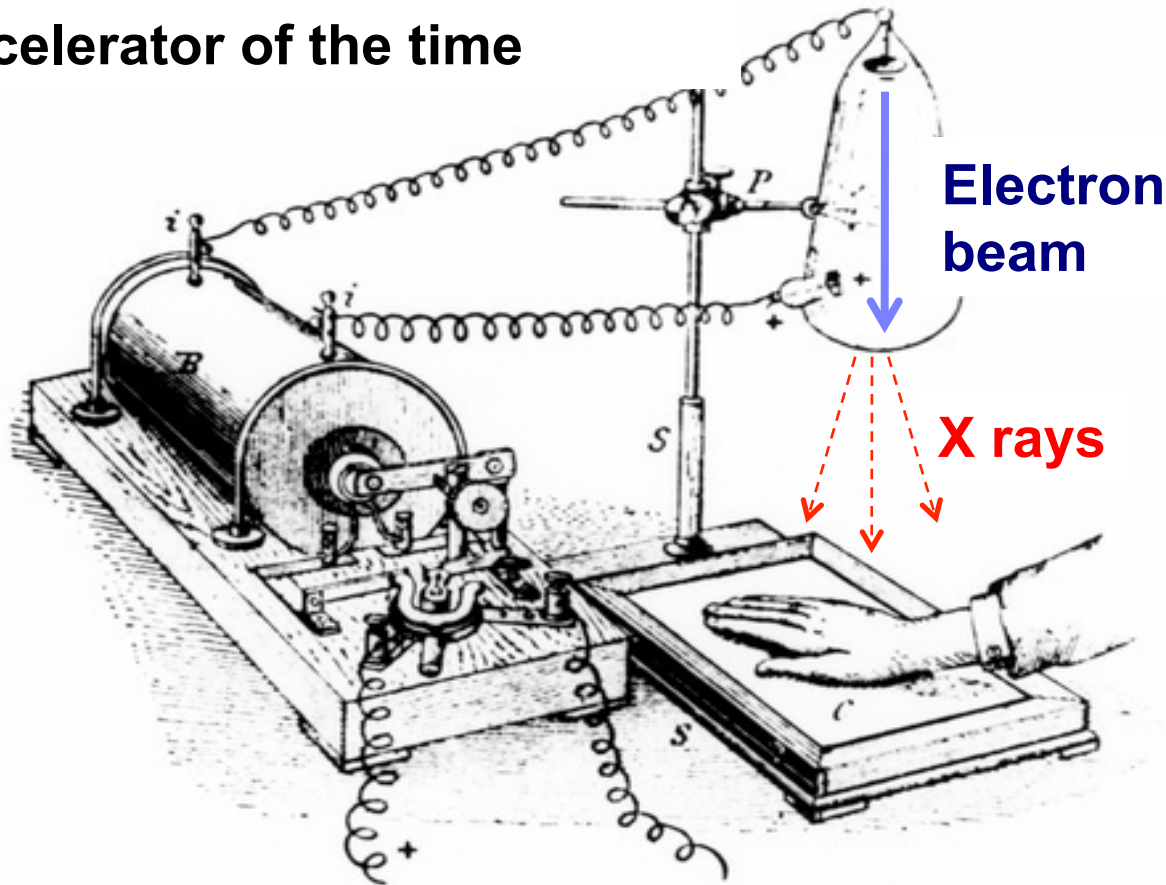
Discovery of radium



Marie Slodowska - Pierre Curie

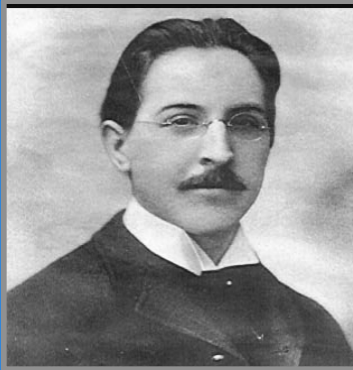
First medical use of an accelerator

Crookes tube : the best accelerator of the time



Announcement: December 28, 1895

First uses of X rays and radium in diagnostics and therapy



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

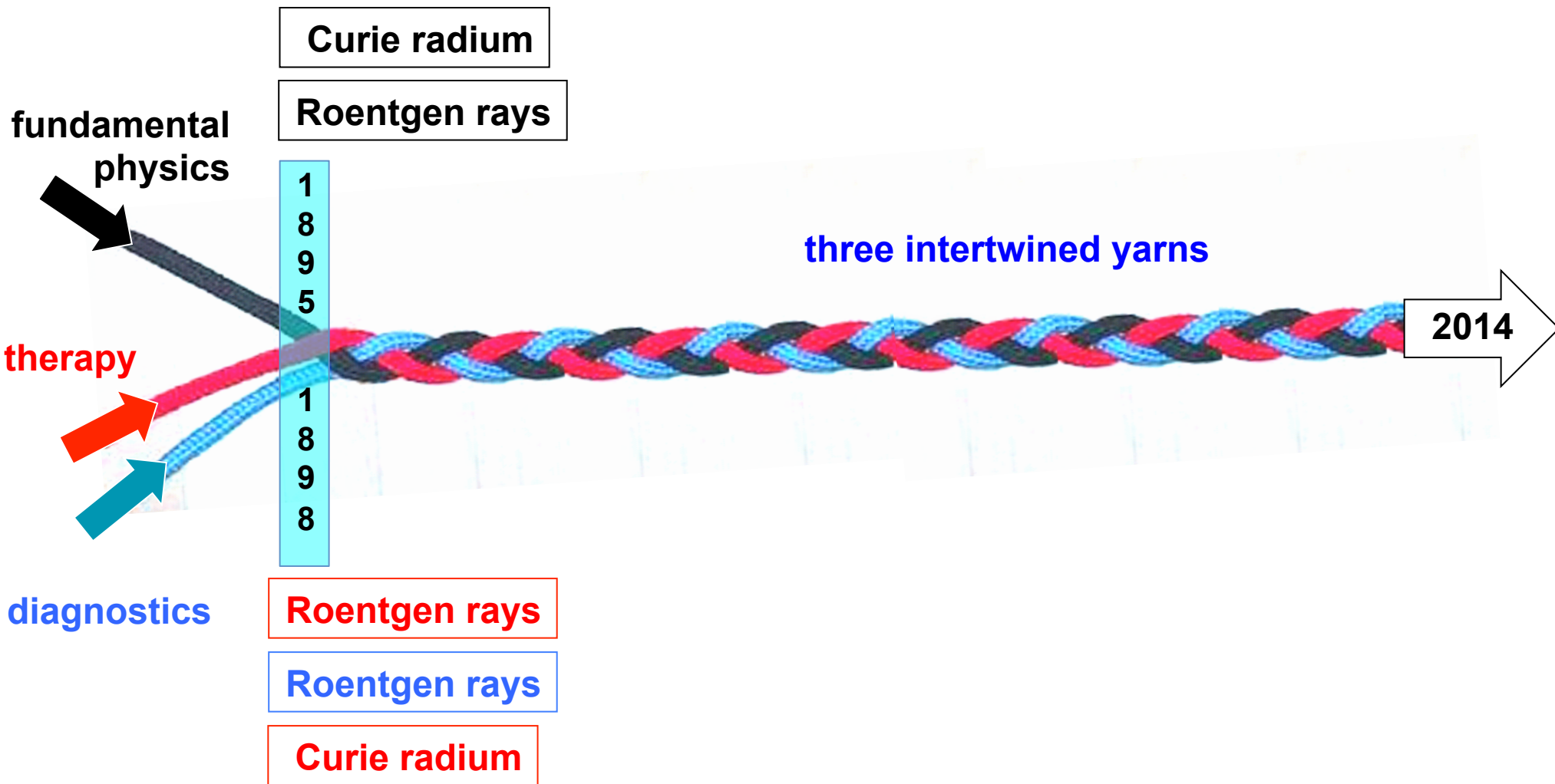


Robert Jones and Oliver Lodge
(Liverpool)
Radiography of a bullet in a hand
February 7, 1896

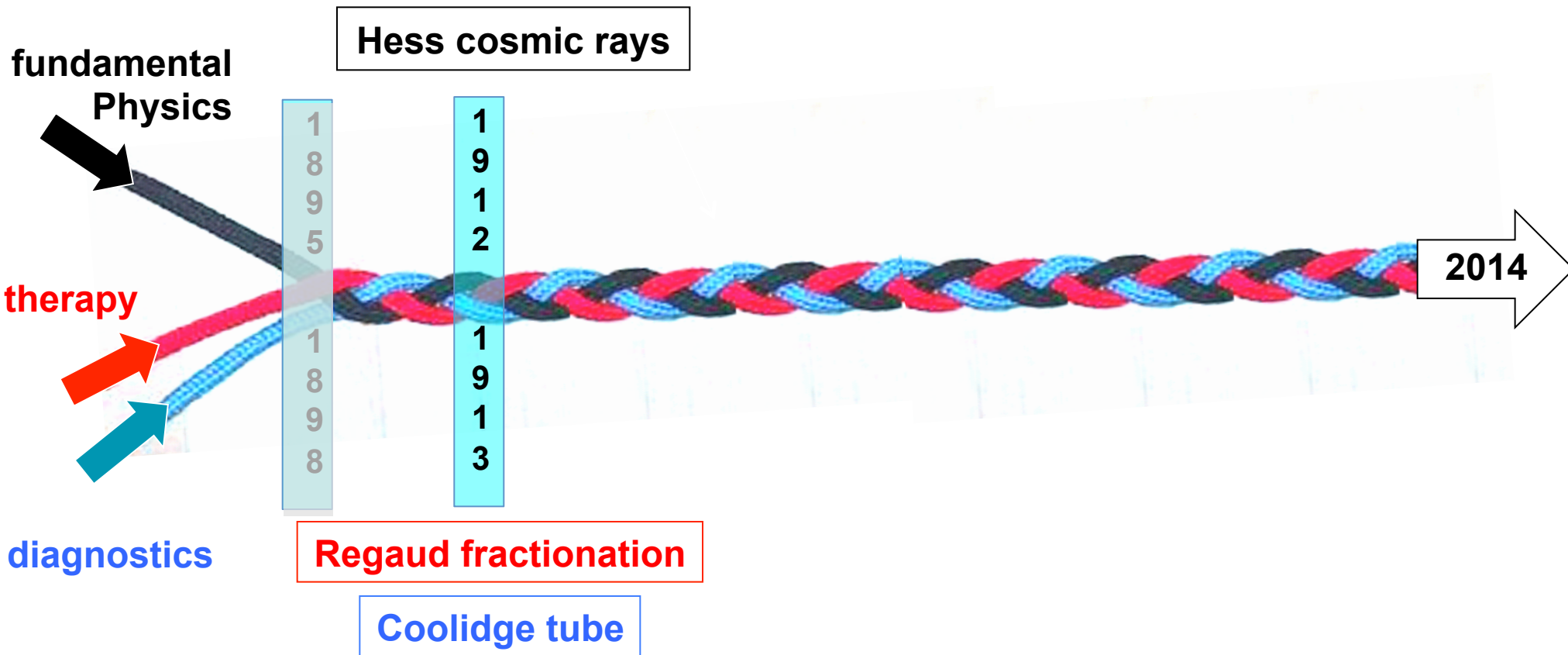


Henri Danlos
(Paris)
Lupus treatment with radium
1901

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



120 years of fundamental (beautiful) and medical (useful) Physics



1912: Victor Hess discovers 'cosmic rays'

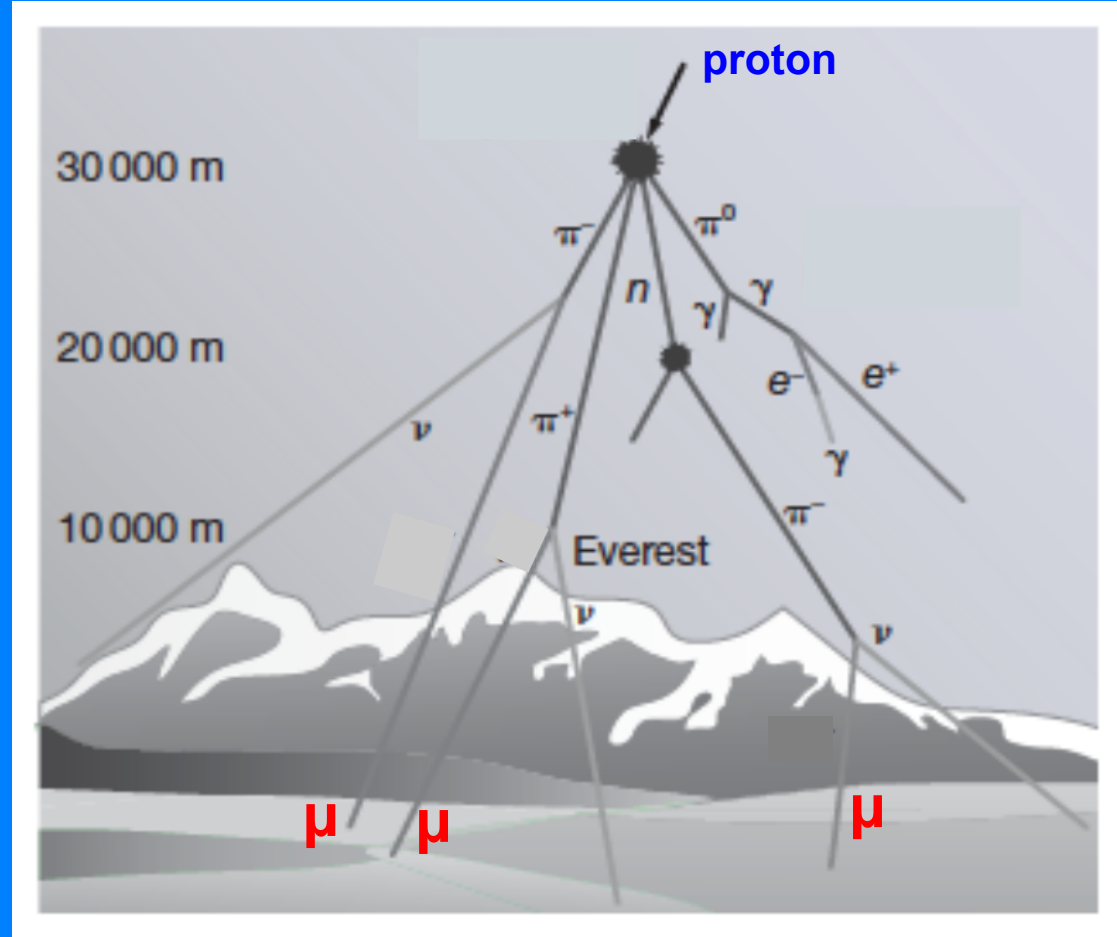


V. Hess

100 YEARS AGO

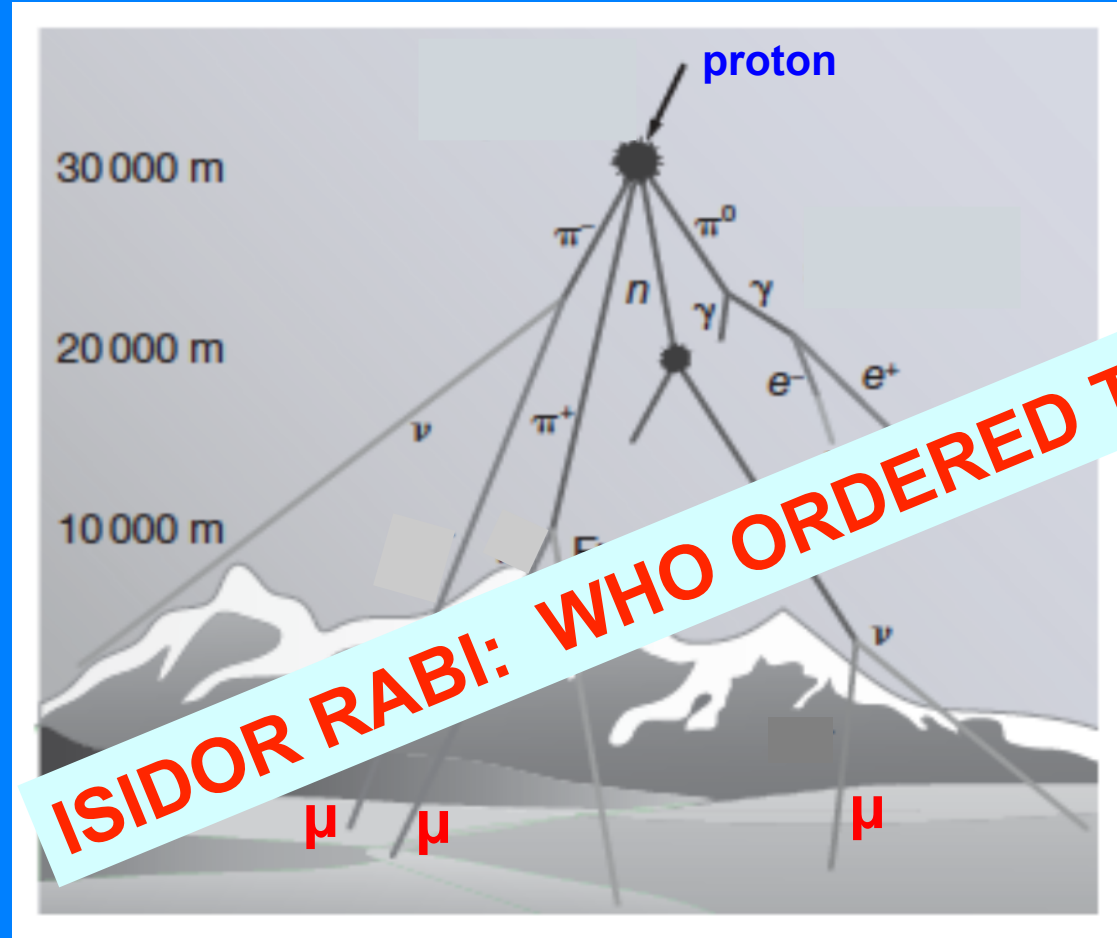
Hess brought precision equipment in ten balloon ascents and discovered that radiation at 5 km altitude is twice larger than at sea level.

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

Fractionation in Radiotherapy

1912 - Paris

Claudius Regaud:

The same dose is more effective if subdivided

Institut du Radium

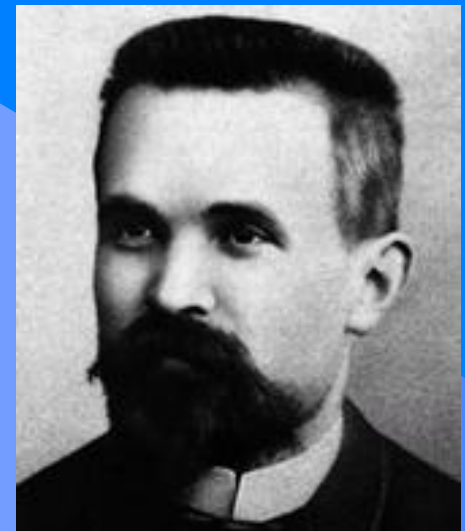
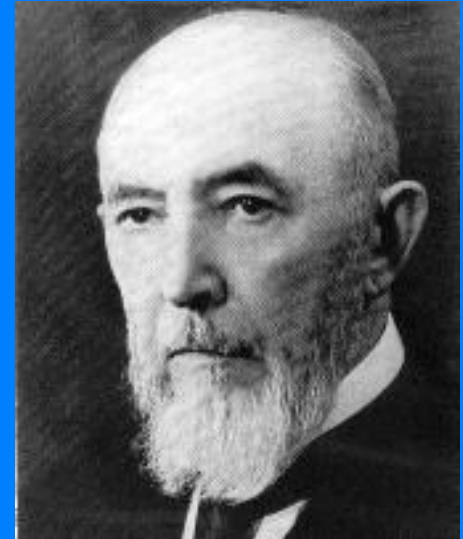
1930 - Claudius Regaud and Henri Coutard:

Standard at 200 keV = 0,2 MeV:

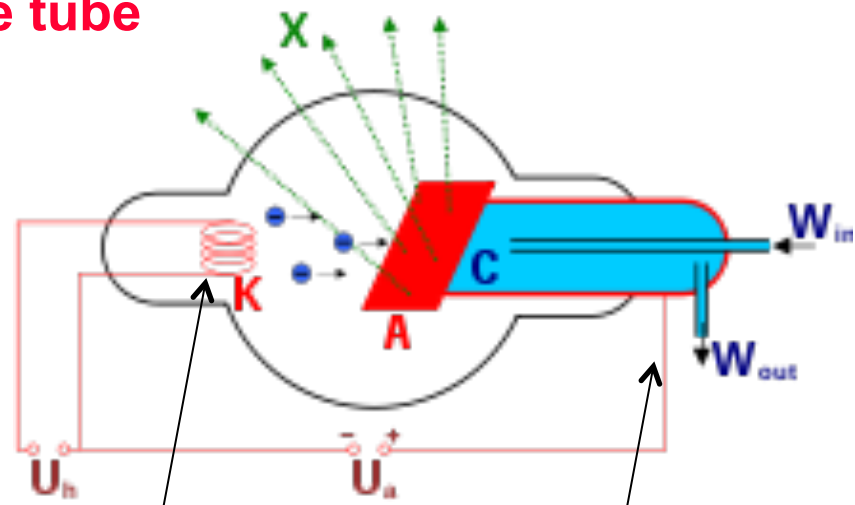
2 grays per session

5 sessions per week

treatment in 5-6 weeks



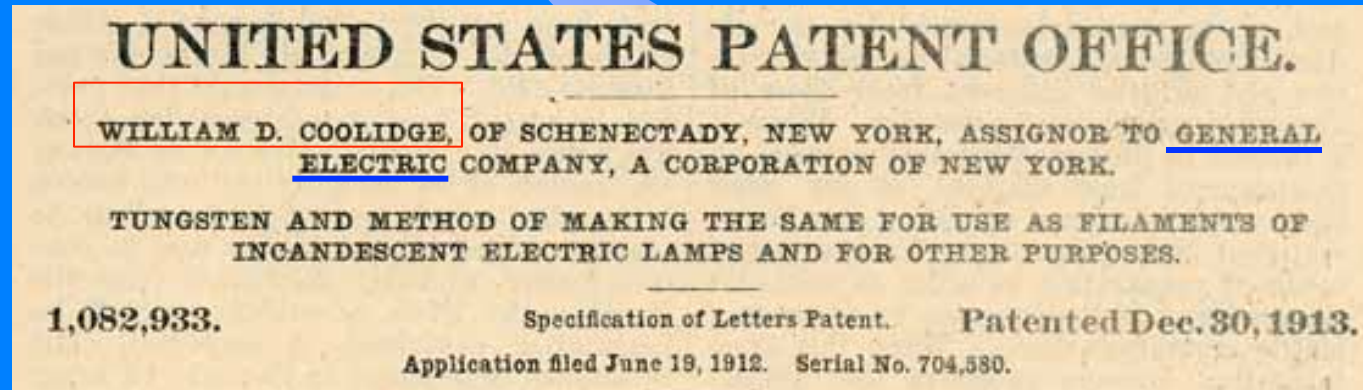
Coolidge tube 1912



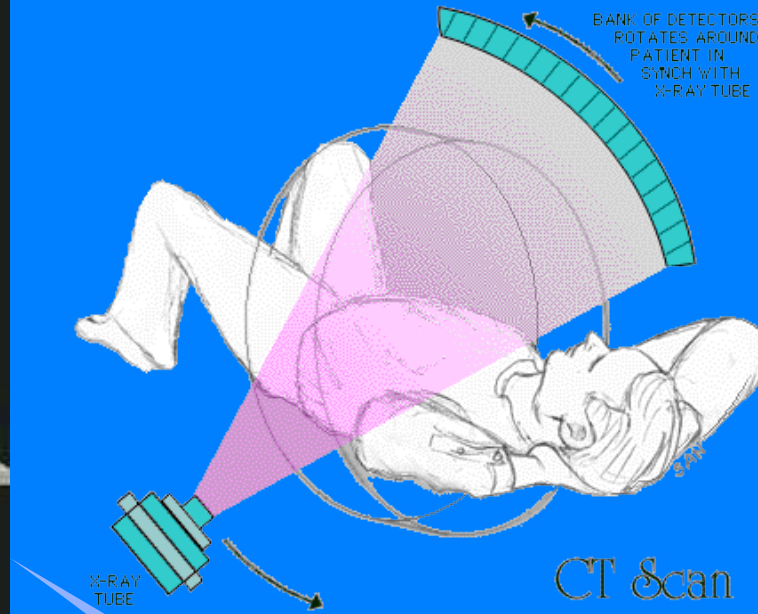
Heated tungsten filament

Cooling water

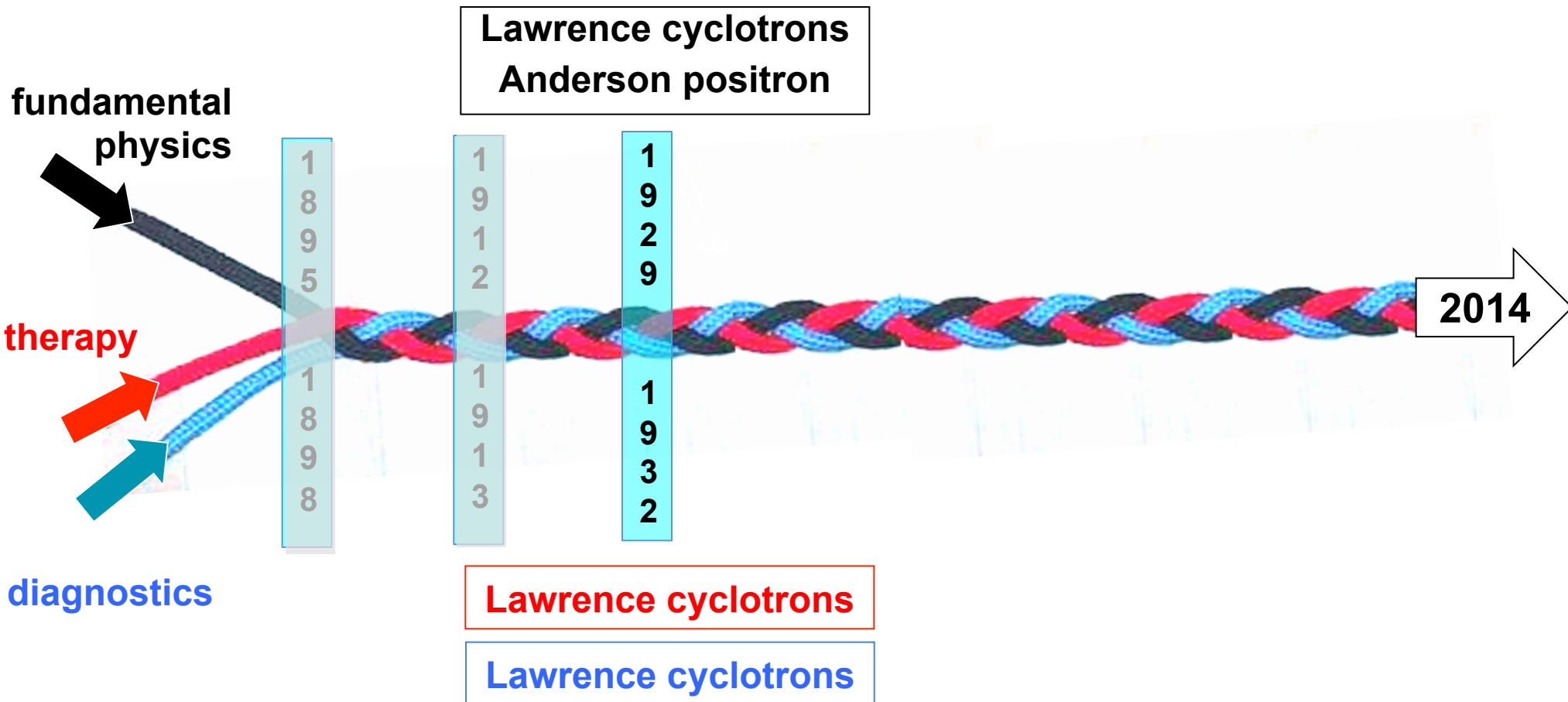
A breakthrough



Today every CT Scan uses a Coolidge tube



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

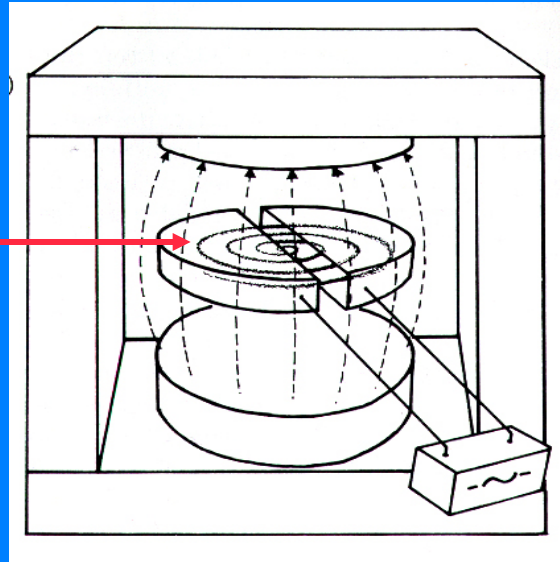


1929: invention of the "cyclotron"

Ernest Lawrence -



**Spiral trajectory of
an accelerated
particle**



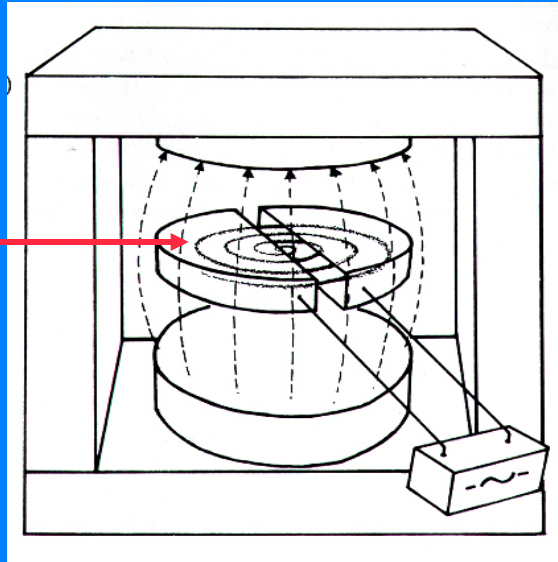
**1 MeV = 1 million electronvolts
= 0.001 GeV**

1929: invention of the "cyclotron"

Ernest Lawrence -



Spiral trajectory of an accelerated particle

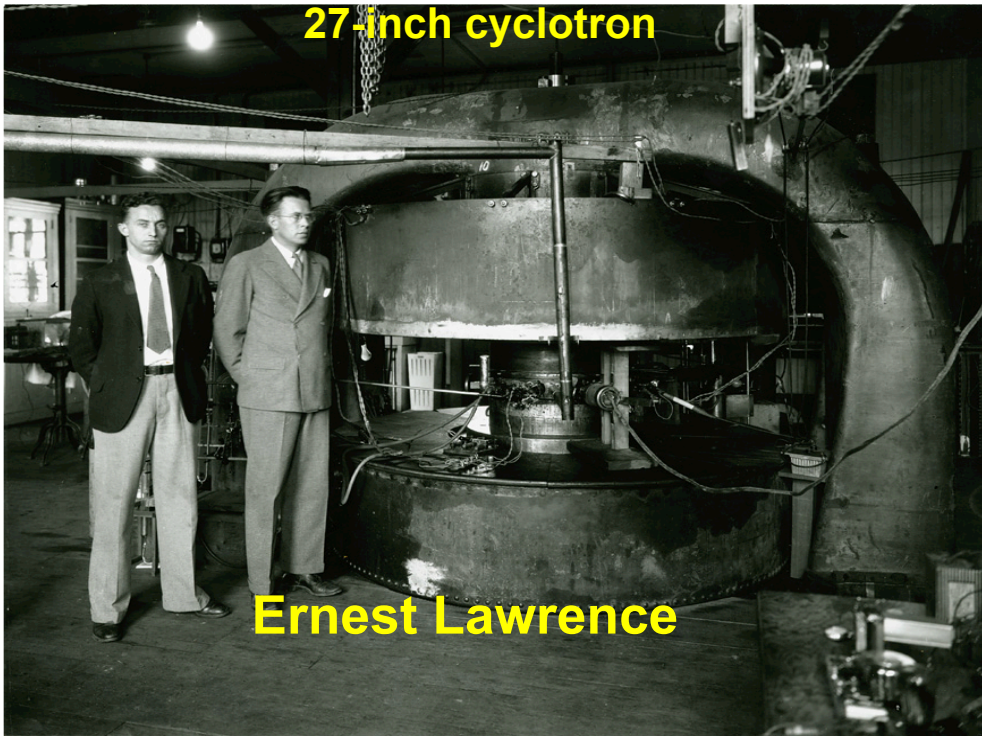


Modern 30 MeV cyclotron for radioisotope production

**1 MeV = 1 million electronvolts
= 0.001 GeV**

Cyclotrons in diagnostics and therapy

27-inch cyclotron



Ernest Lawrence

John Lawrence, MD

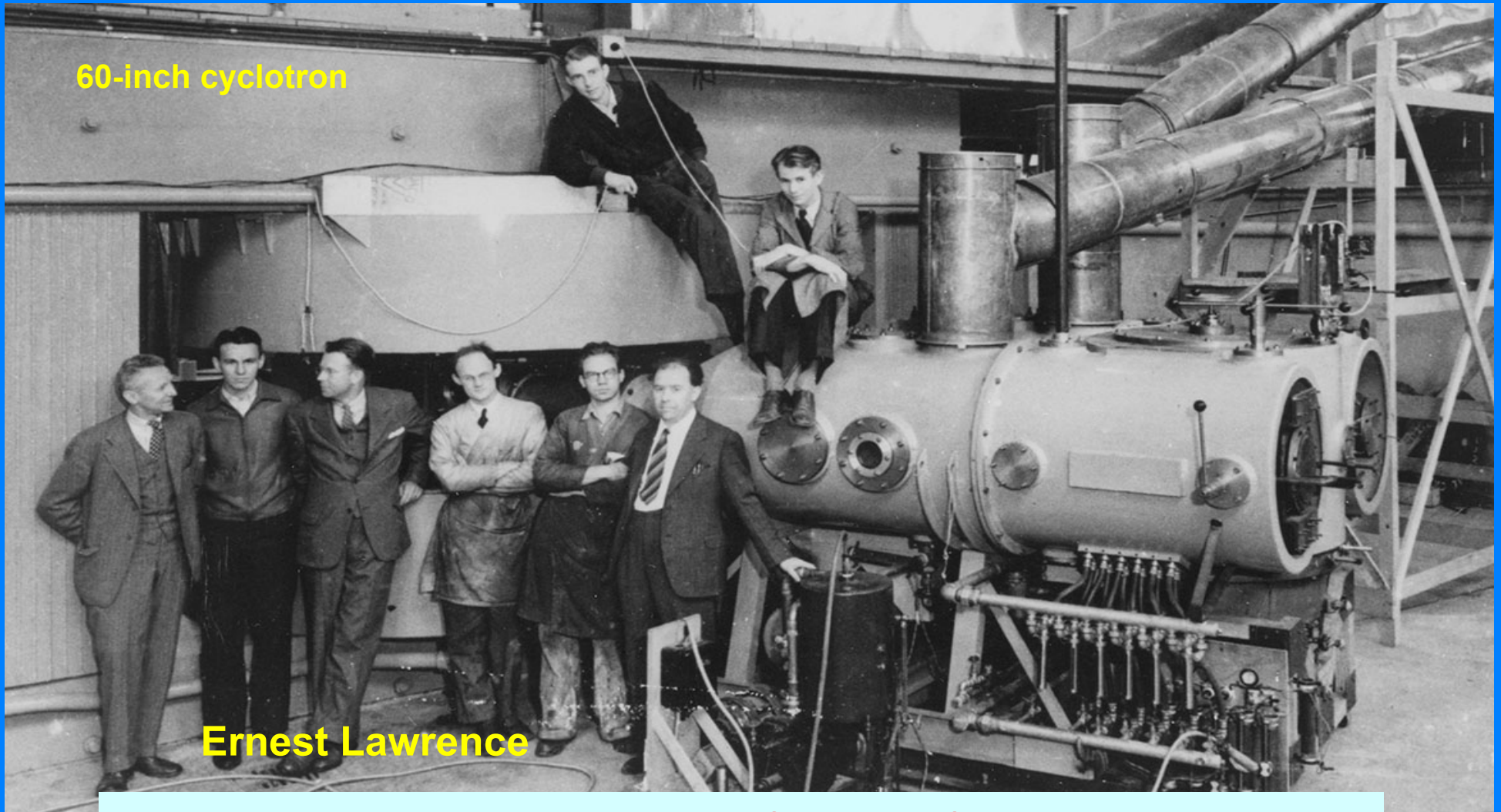


Ernest Lawrence

1936: Radio-sodium to study metabolism

1936: Radio-phosphorus to treat leukaemia

Cyclotrons in diagnostics and therapy



60-inch cyclotron

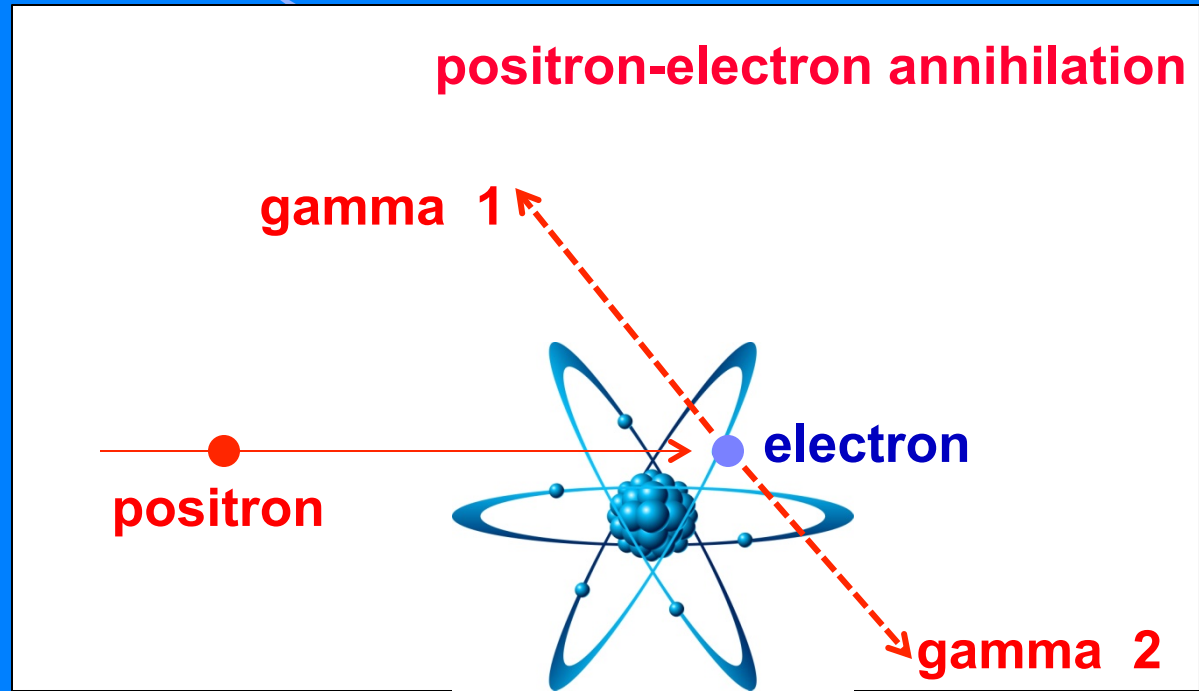
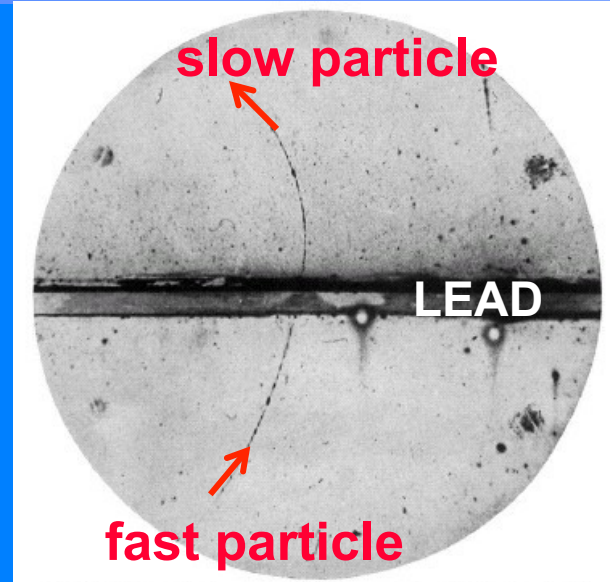
Ernest Lawrence

1939: The 60-inch cyclotron was financed for medical purposes and later used to treat patients with neutron beams

Discovery of the anti-electron

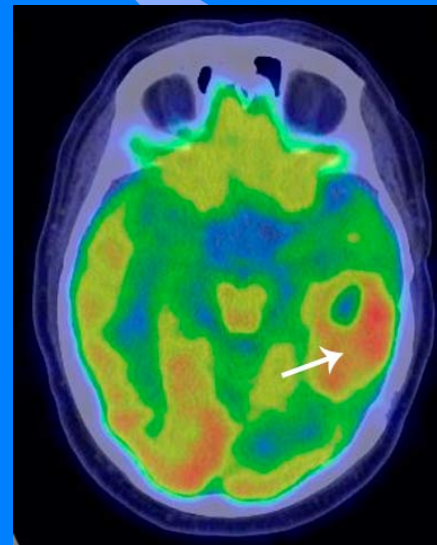
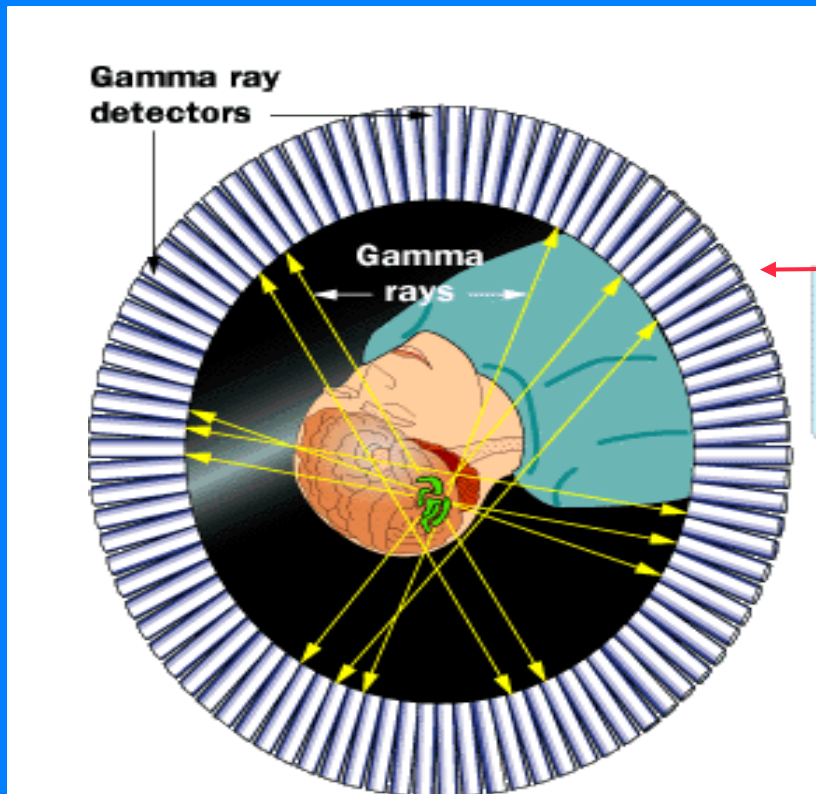
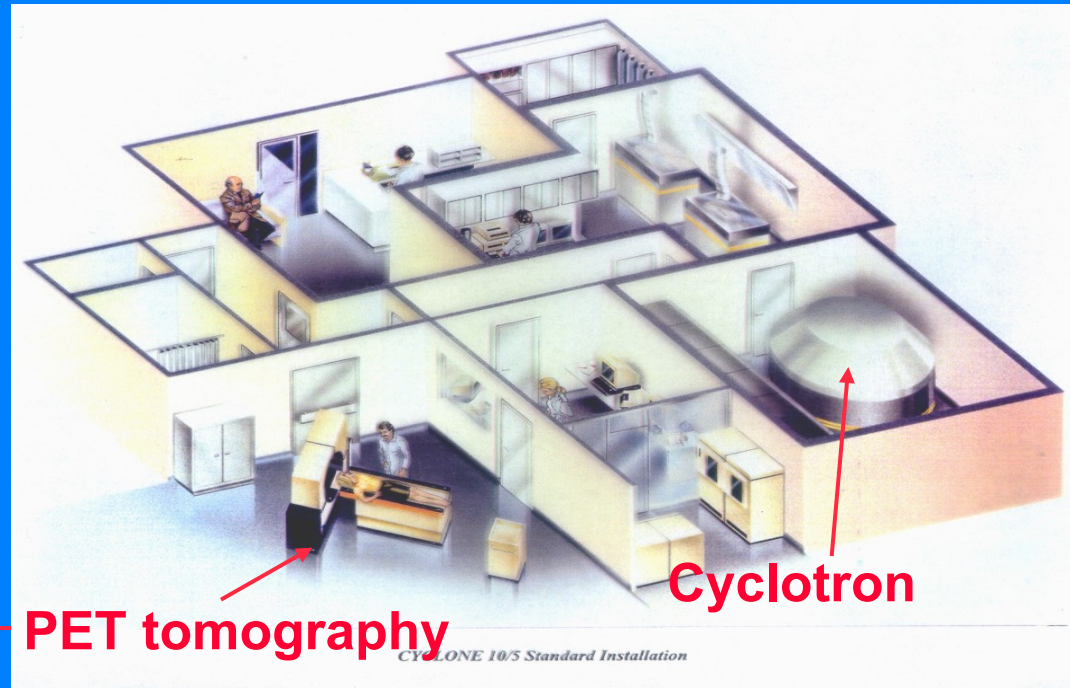


Carl Anderson - CALTECH
1932



PET centre with a 15 MeV cyclotron

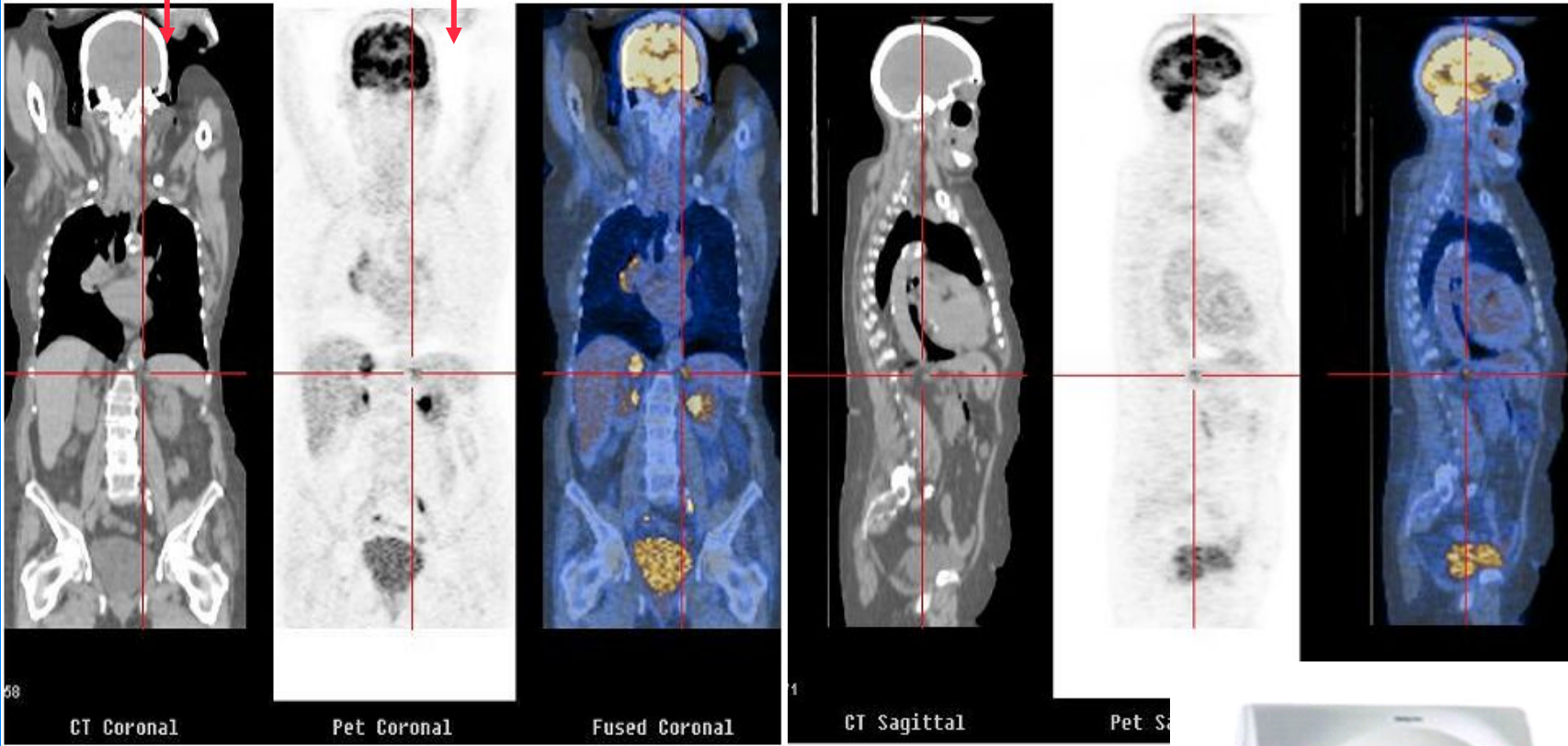
Most used substance
Sugar FDG with Fluorine -18



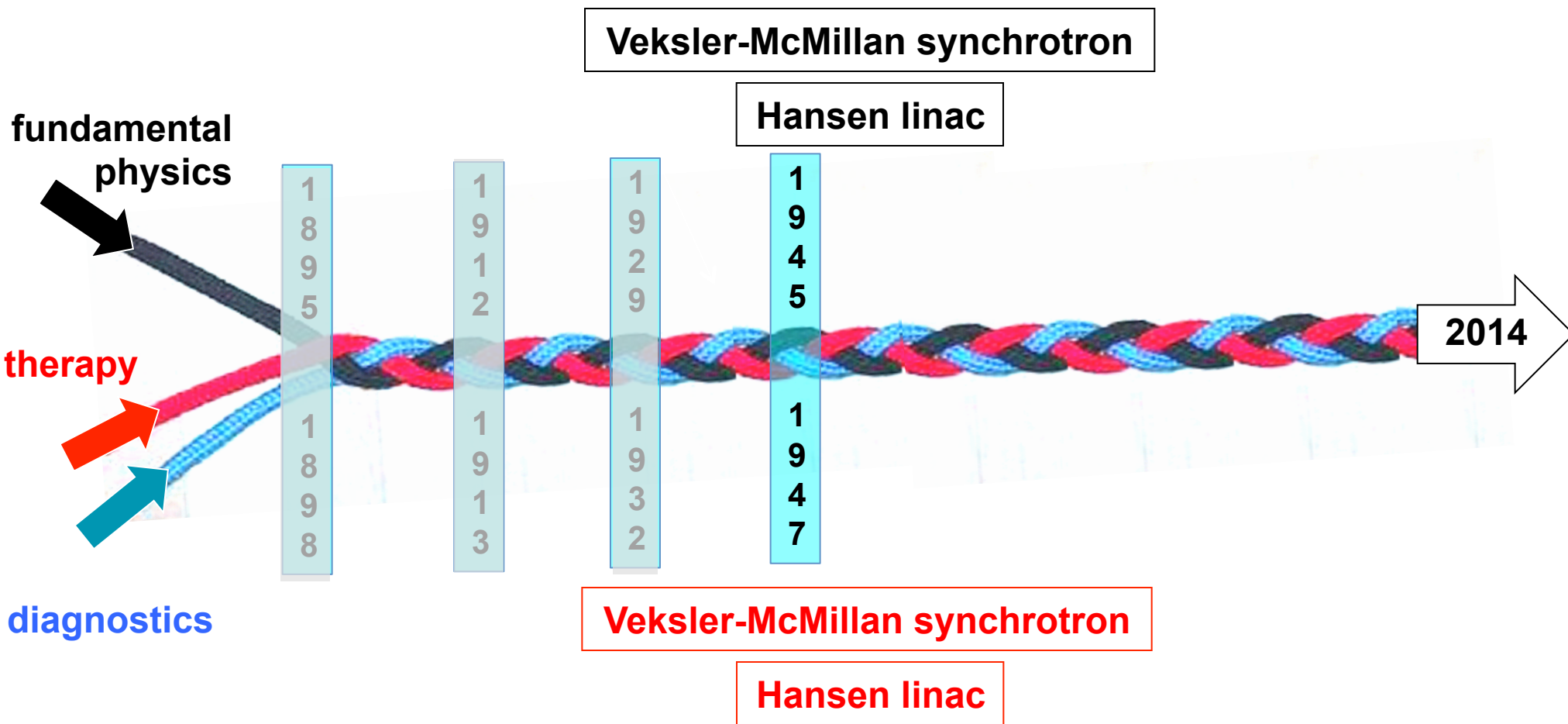
Combination of CT with PET : CT-PET

morphology

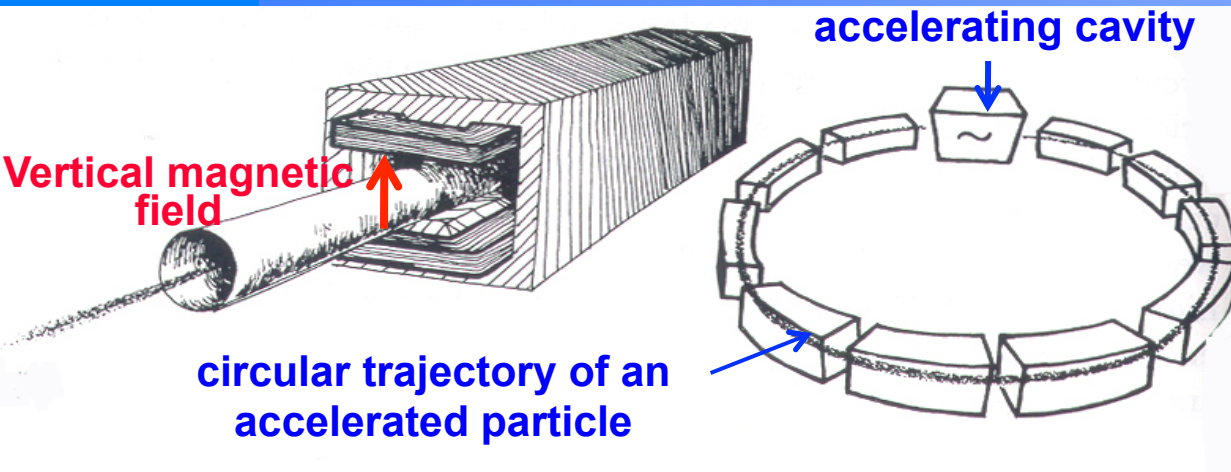
metabolisme



120 years of fundamental (beautiful) and medical (useful) Physics



The invention of the synchrotron came in 1945

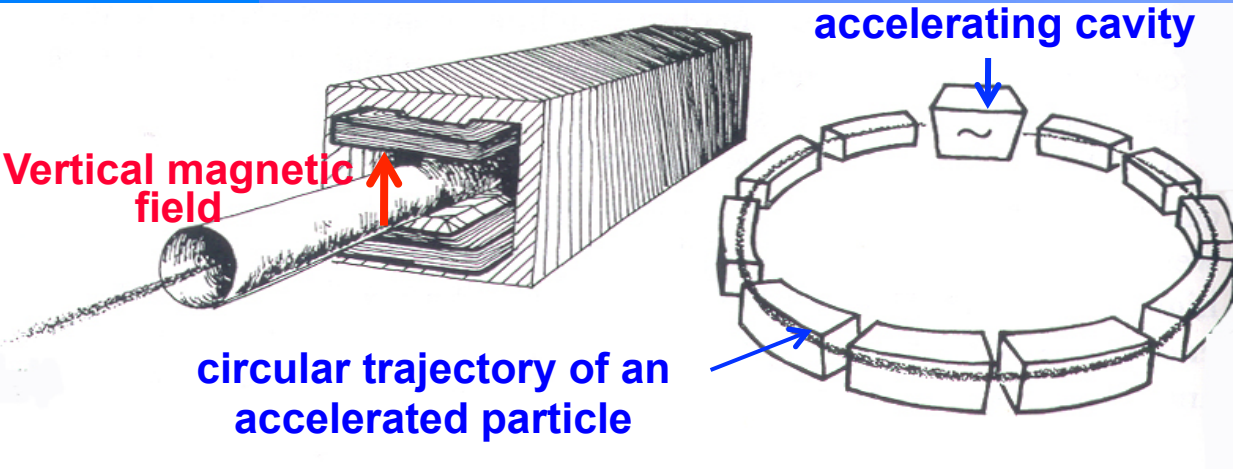


E. McMillan and V.J.Veksler
"Phase stability principle"



1959: Veksler visits McMillan
at Berkeley

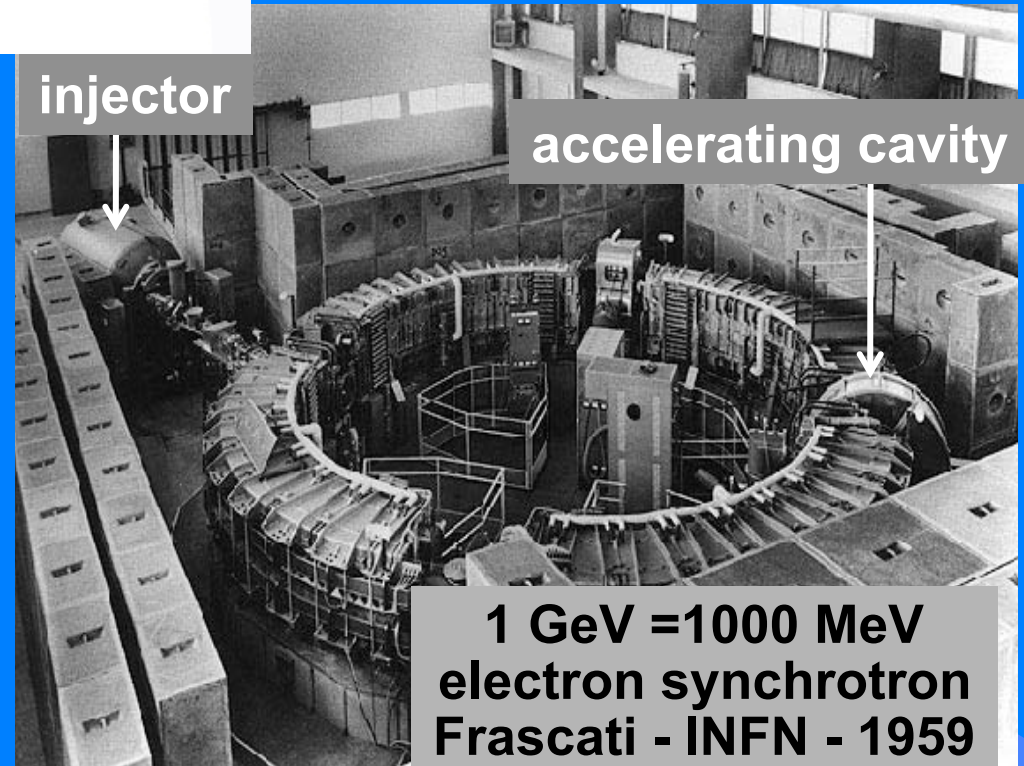
The invention of the synchrotron came in 1945



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



1959: Veksler visits McMillan at Berkeley



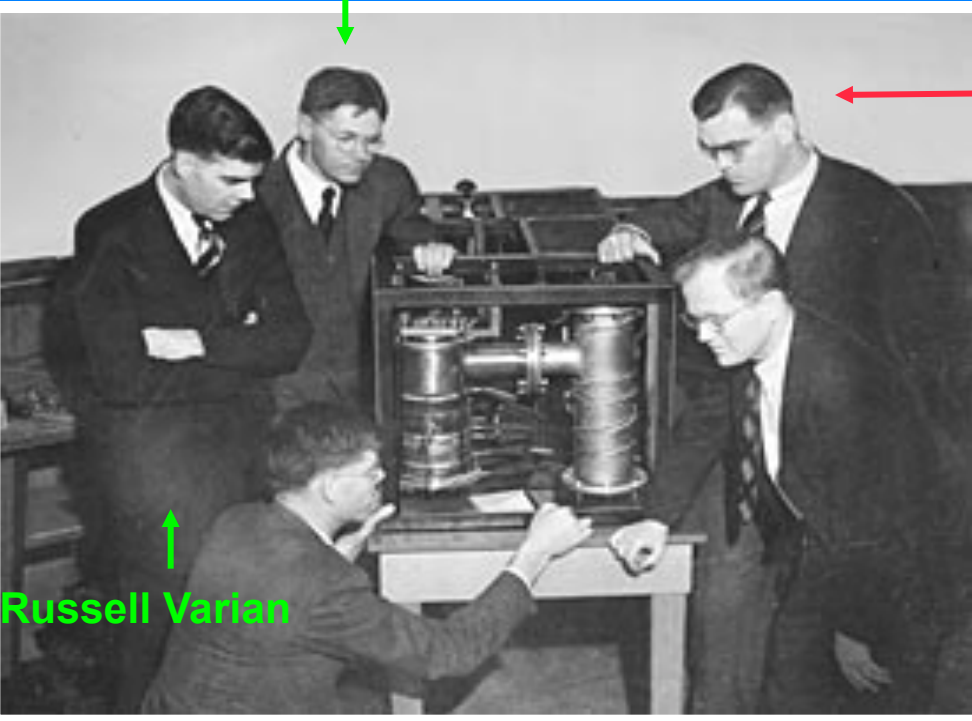
1 GeV = 1000 MeV
electron synchrotron
Frascati - INFN - 1959

The first electron linac above 1 MeV

Sigmur Varian



William W. Hansen



Russell Varian

1939

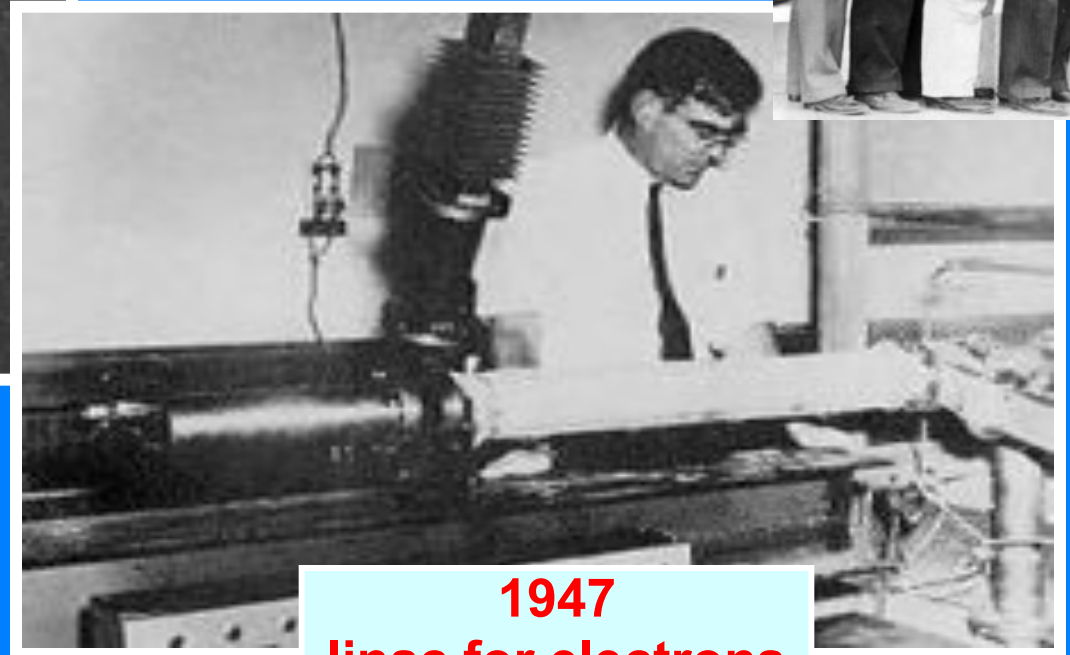
Invention of the klystron

The first electron linac above 1 MeV

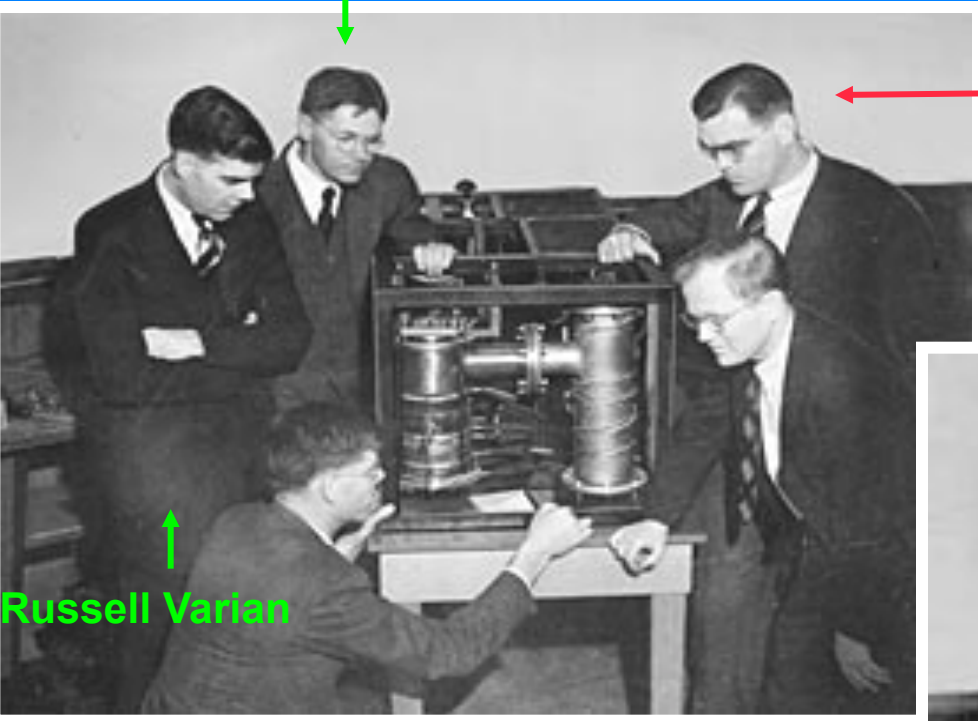
Sigmur Varian



William W. Hansen



1947
linac for electrons
1.5 MeV at 3 GHz



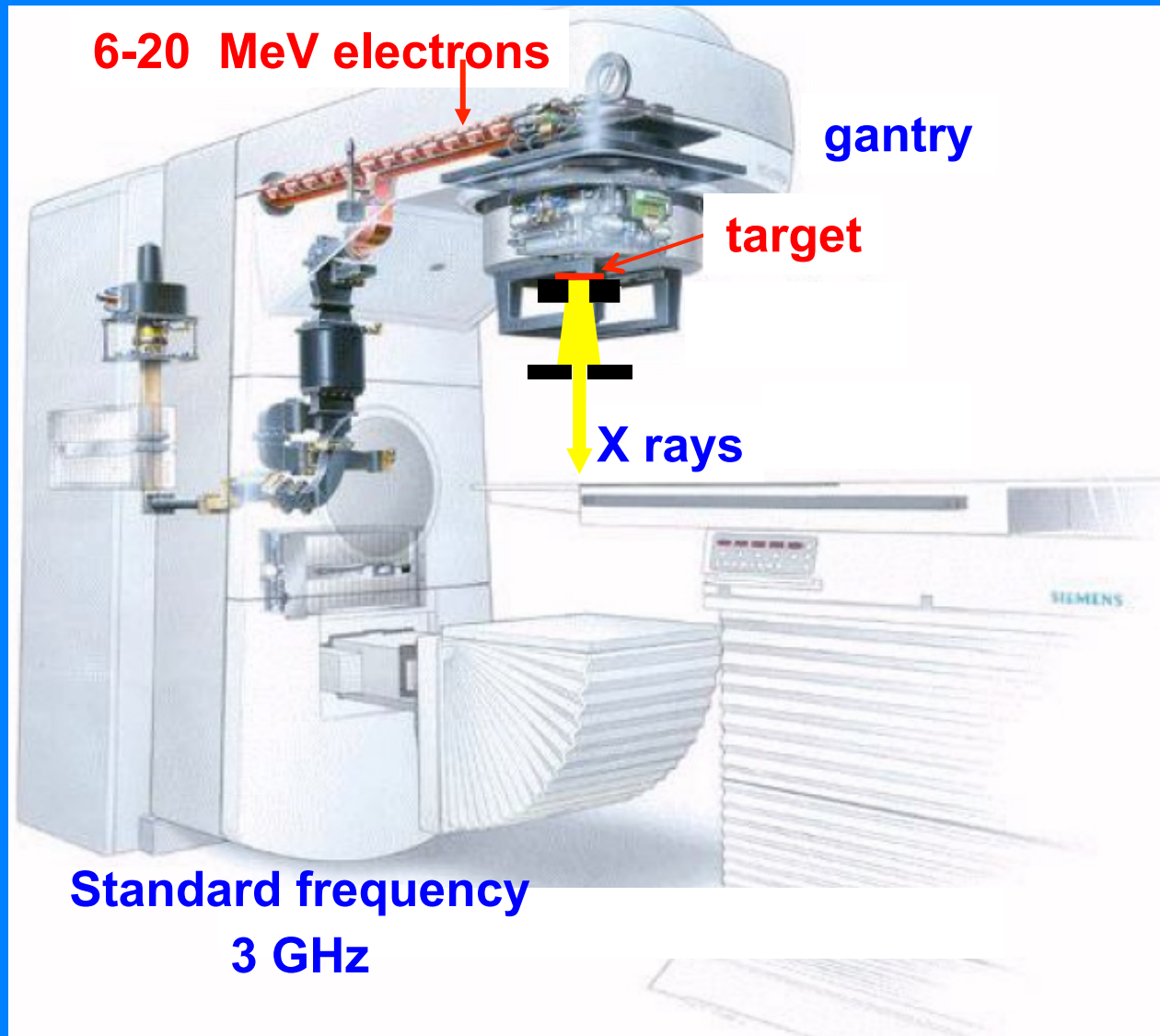
Russell Varian



1939

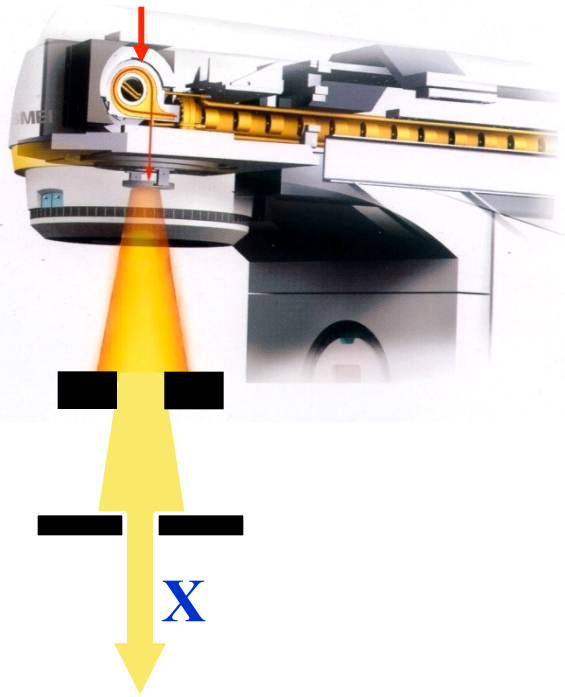
Invention of the klystron

'Conventional' radiotherapy: linear accelerators dominate



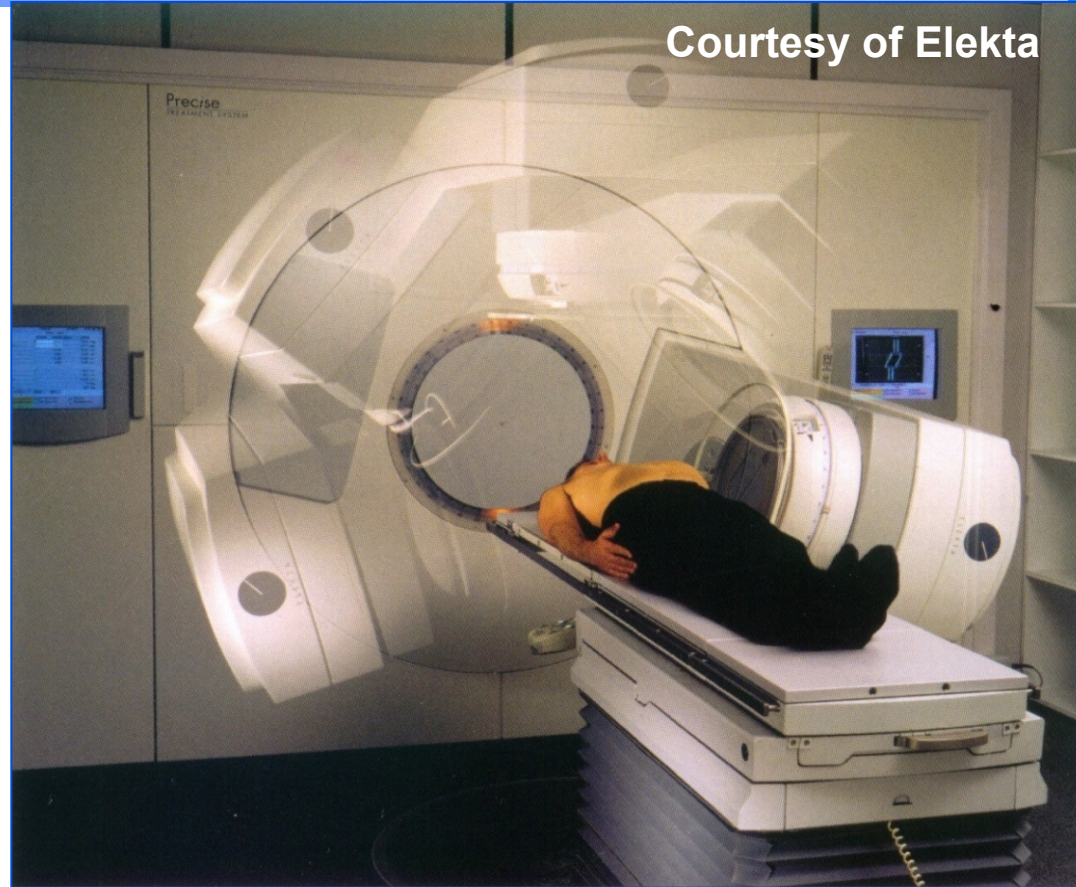
'Conventional' radiotherapy: linear accelerators dominate

electrons



**2000 patients/year every
in 1 million inhabitants**

1 treatment in 30 sessions



Courtesy of Elekta

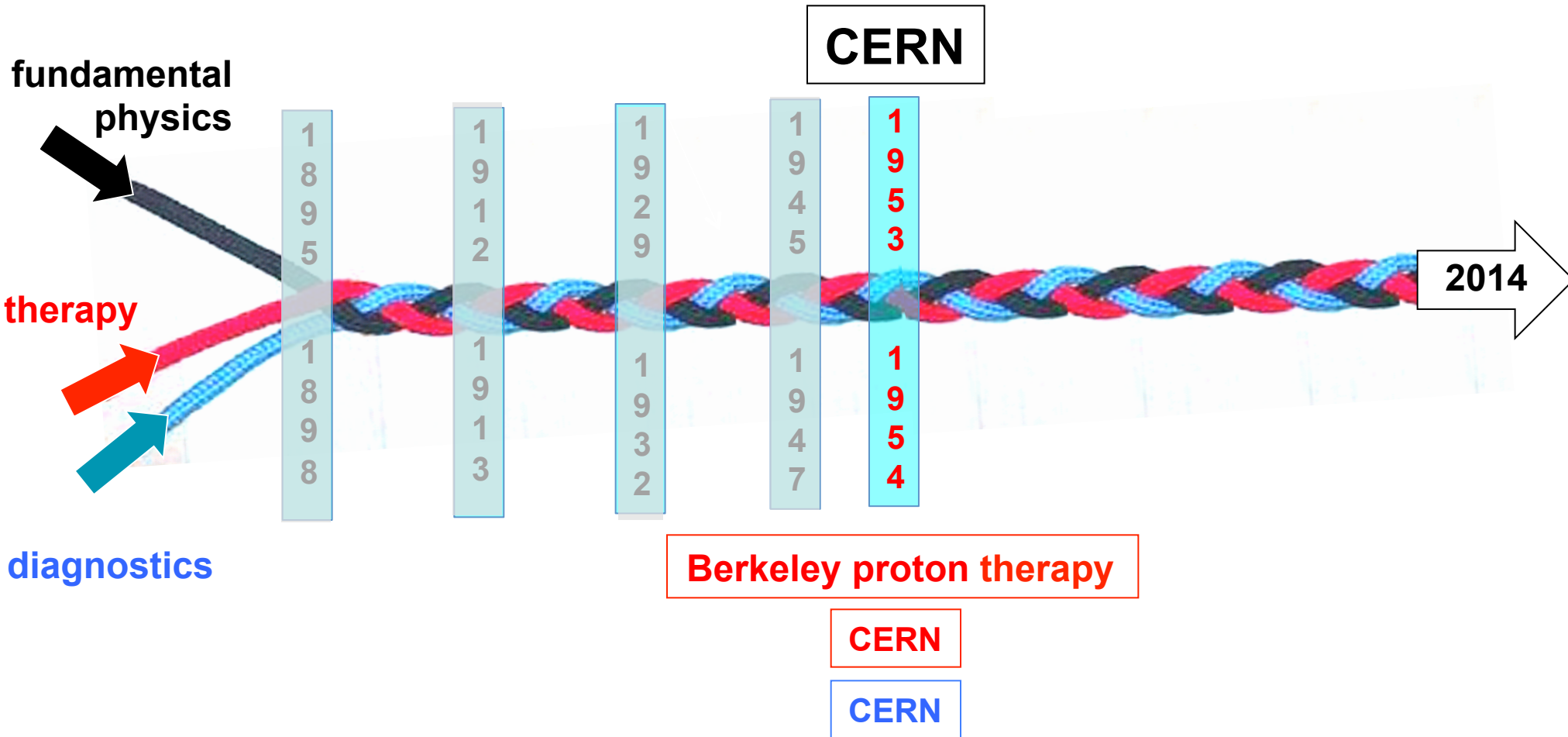
**In the world radiation oncologists
use 20 000 electron linacs**

50% of all the existing accelerators

70 years later VARIAN is still the market leader



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



Following the black yarn: particle physics at CERN

60 years ago: creation of CERN



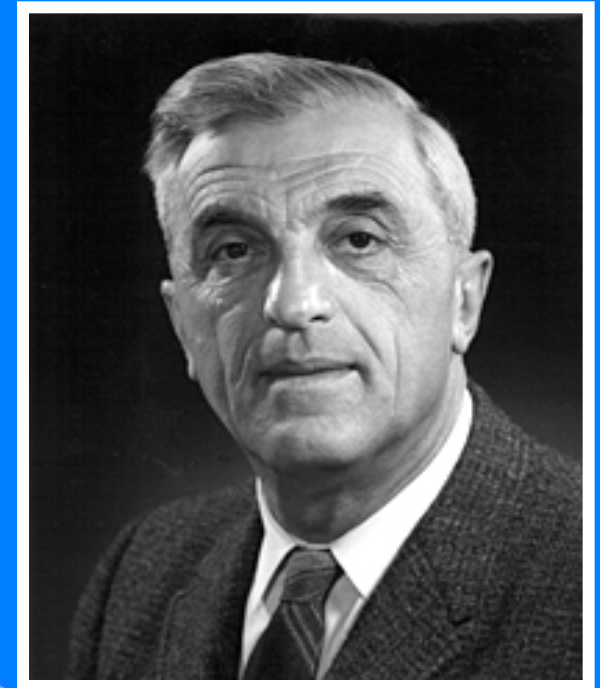
1953 CERN Council

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**



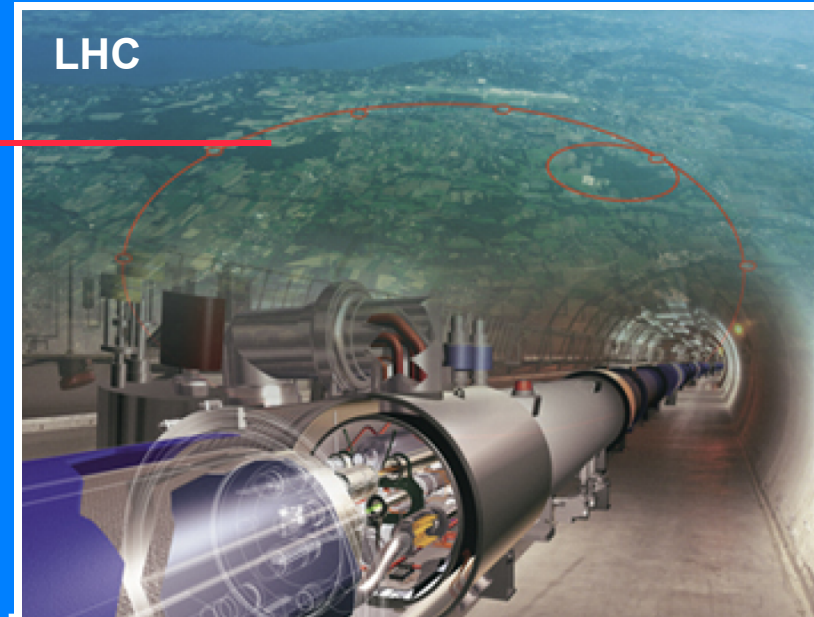
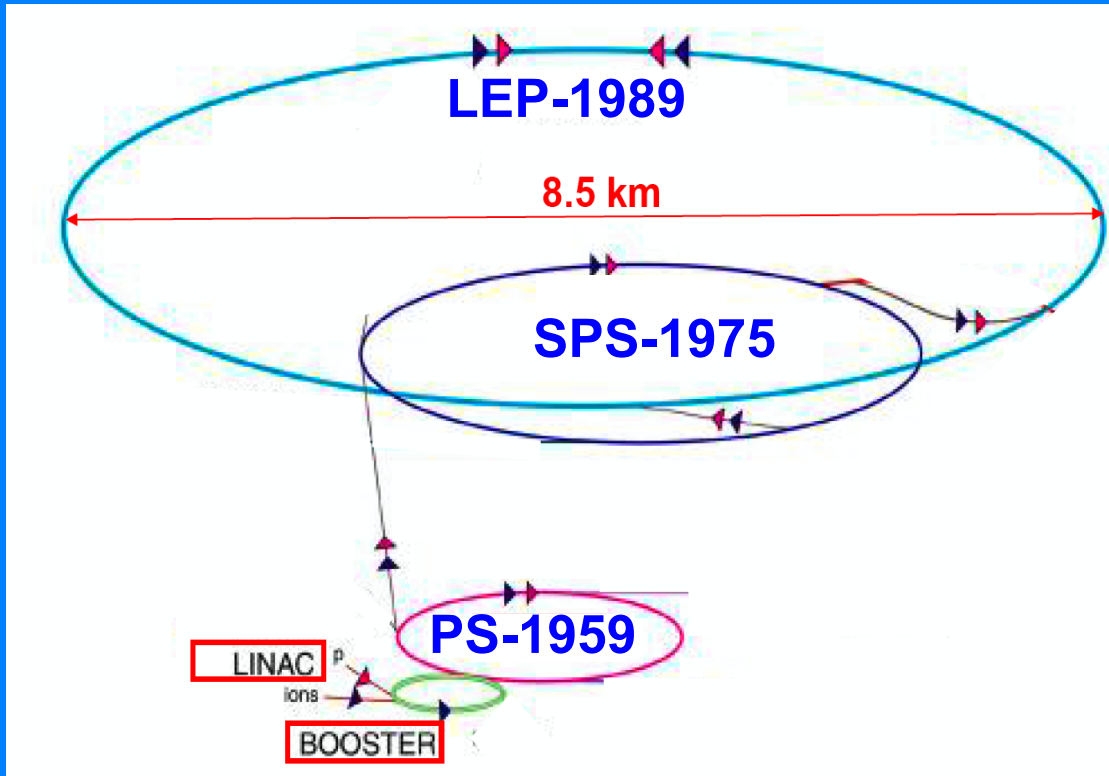
PS 1959

SPS 1975

Large Hadron Collider
27 km

CERN aerial view with the Geneva Airport

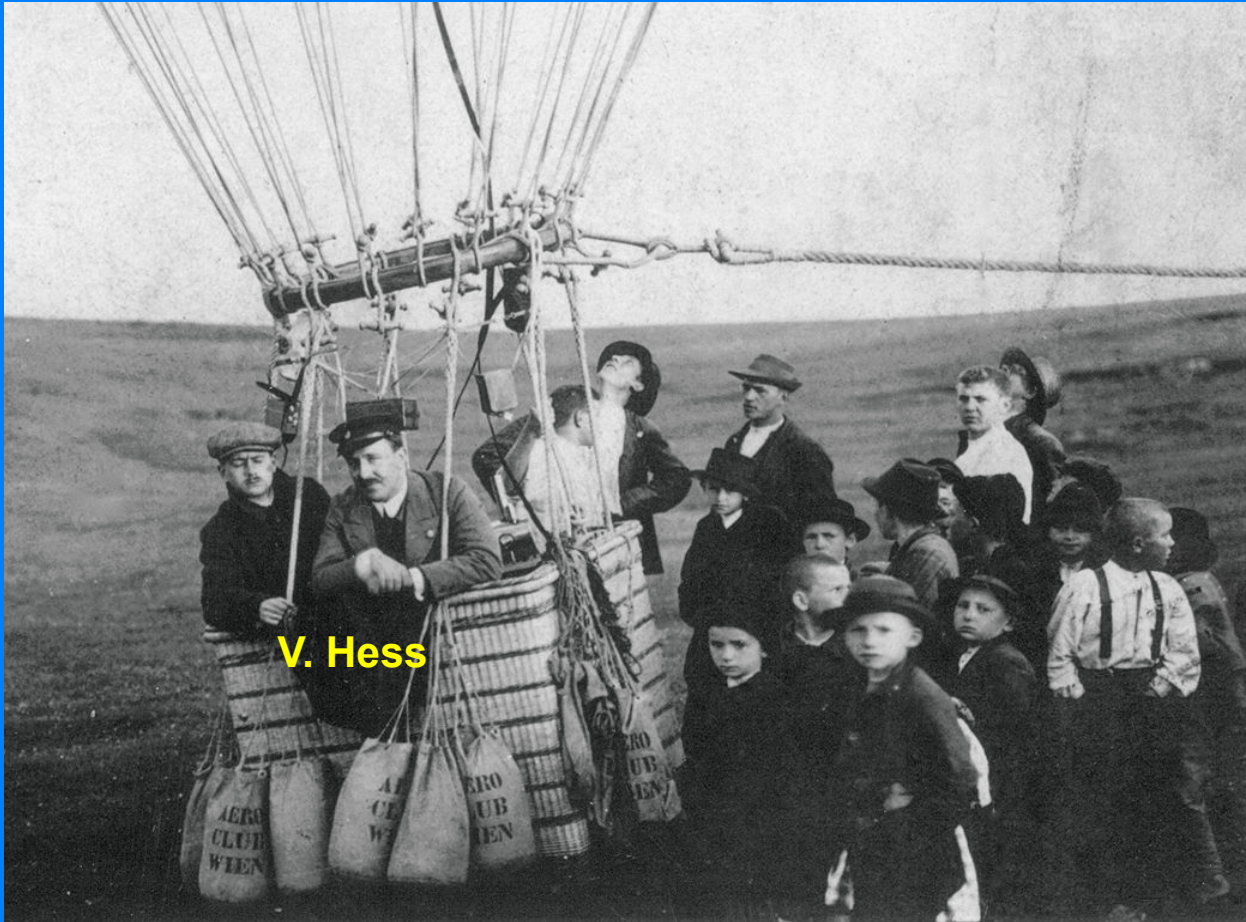
CERN accelerators are synchrotrons used as “colliders”



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



To focus only on the most important discovery made with CERN accelerators we most go back to 'cosmic rays'

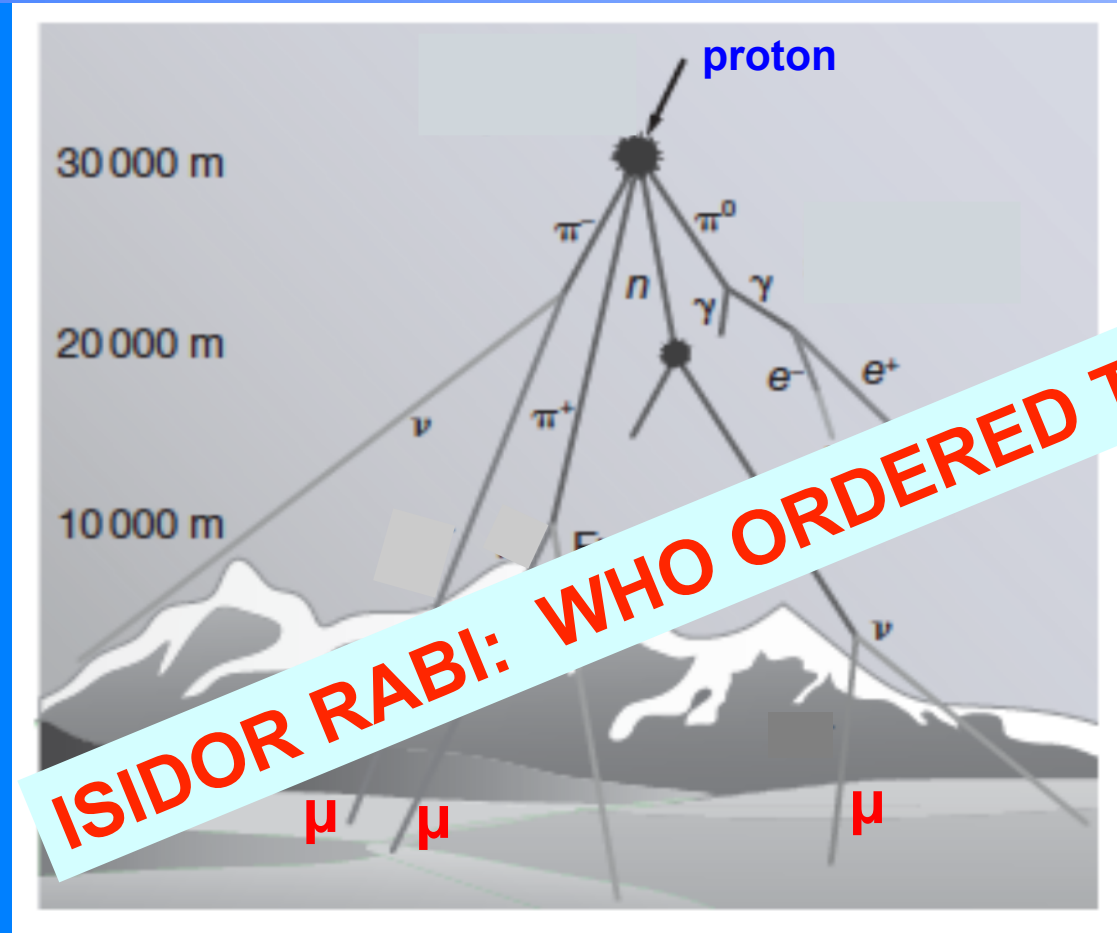


V. Hess

100 YEARS AGO

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

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

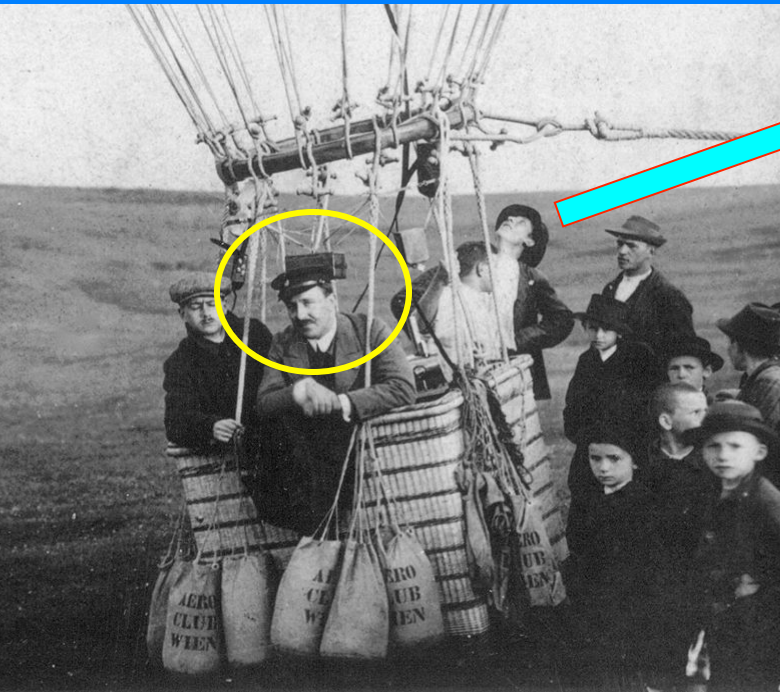
From cosmic rays to the 'Higgs particle'

CERN – 2012

Fabiola Gianotti Peter Higgs



1912
Victor Hess



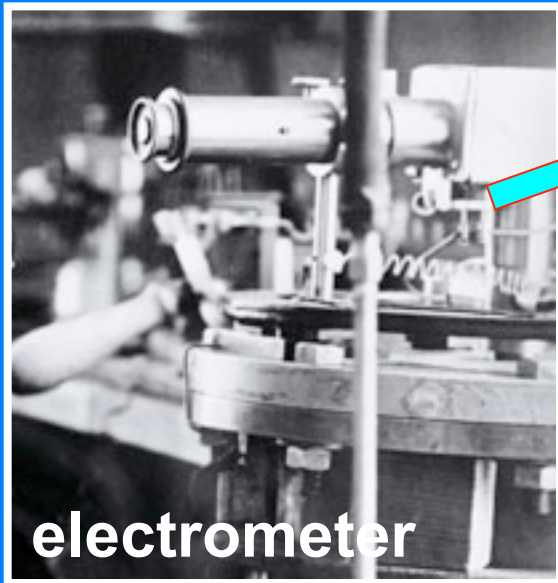
100 years

From cosmic rays to the 'Higgs particle'

CERN – 2012

Fabiola Gianotti Peter Higgs

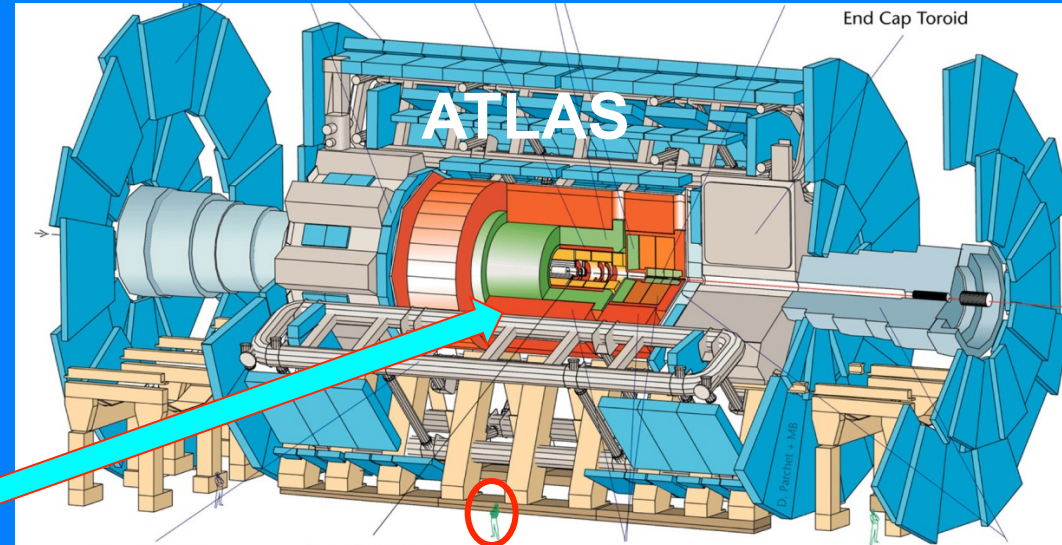
1912
Victor Hess



electrometer

Impact of Physics - UA - Globe - 10.4.14

100 years



2013: the Nobel prize winners



François Englert

Peter Higgs

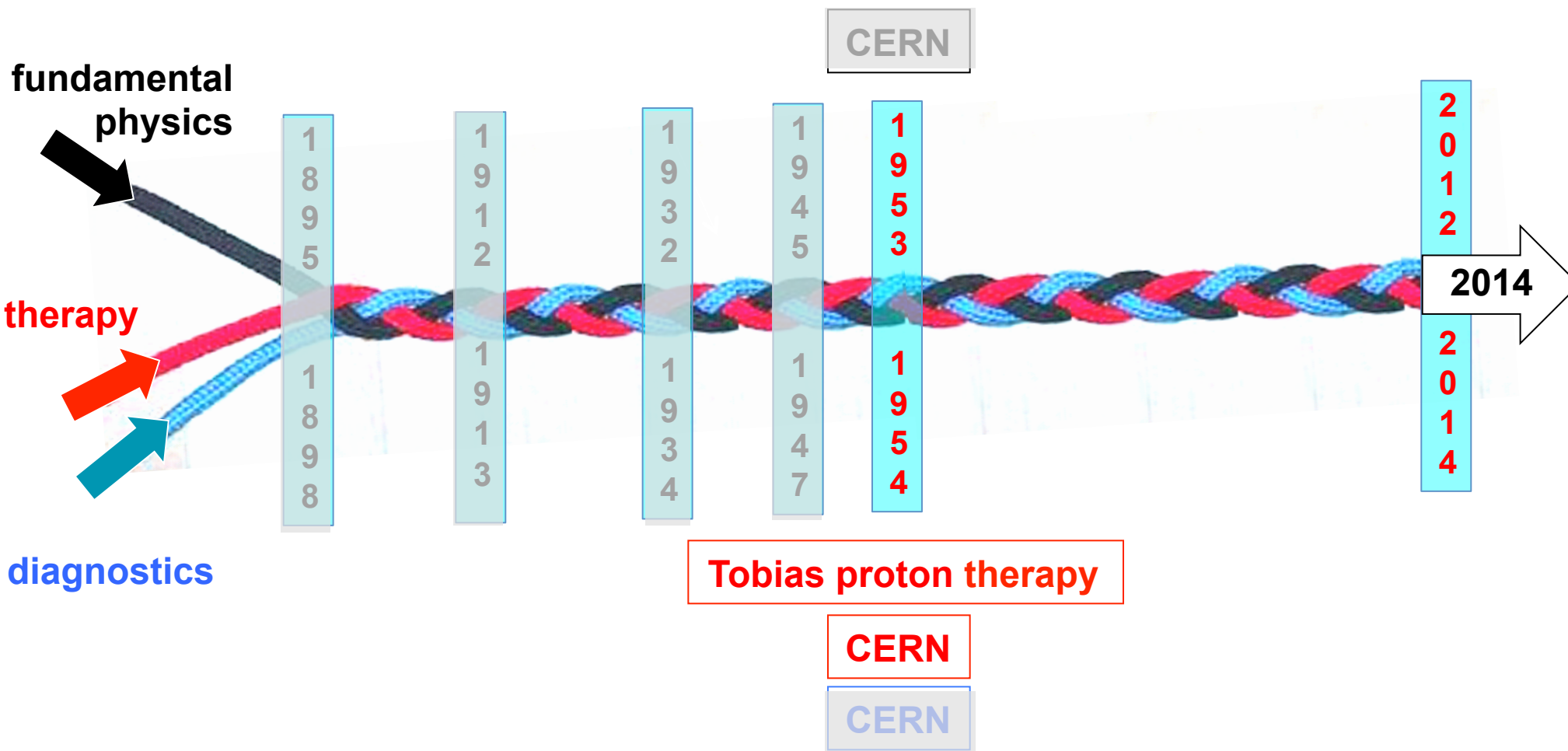


Fabiola Gianotti

Peter Higgs

Following the red yarn

120 years of fundamental (beautiful) and medical (useful) Physics

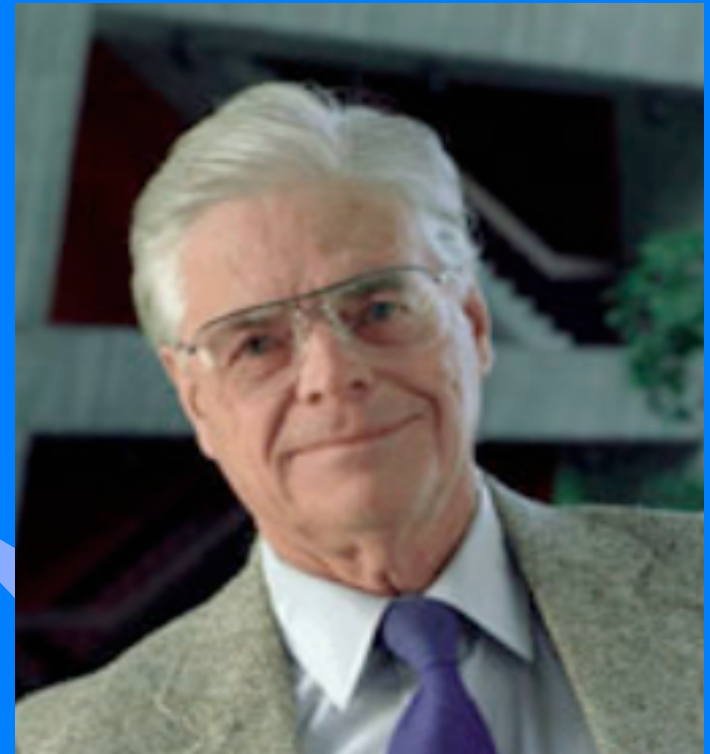


Hadrontherapy (particle therapy)

**1946 : « Bob » Wilson proposes to use protons, helium
and carbon ions**



Lawrence PhD student

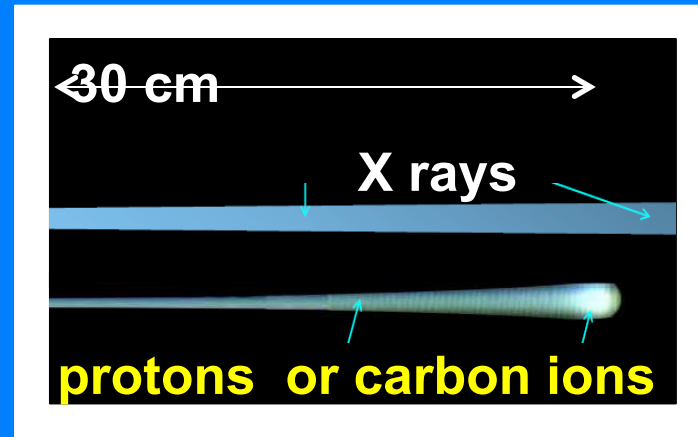


**Founder and first Director
of FERMILAB (Chicago)**

1967-1978

Advantages of protons and carbon ions

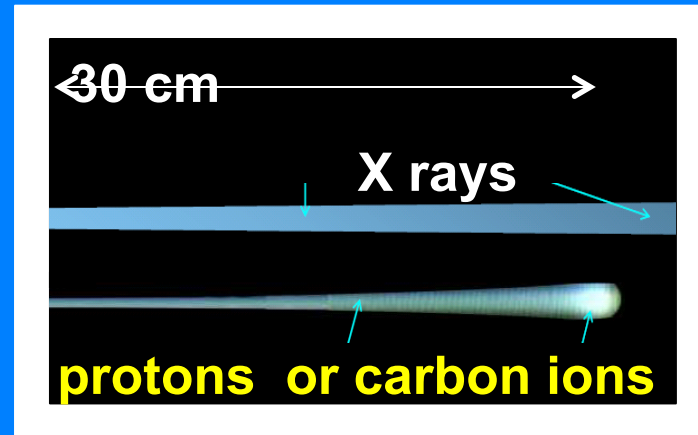
protons: 230 MeV
C ions : 5000 MeV



1. Healthy tissues are spared by protons and carbon ions

Advantages of protons and carbon ions

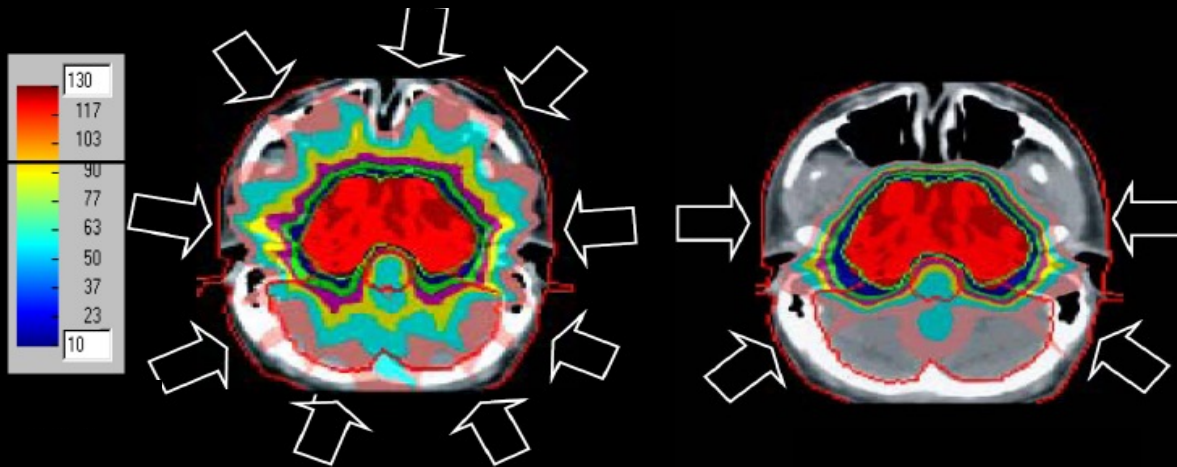
protons: 230 MeV
C ions : 5000 MeV



1. Healthy tissues are spared by protons and carbon ions

9 X ray beams

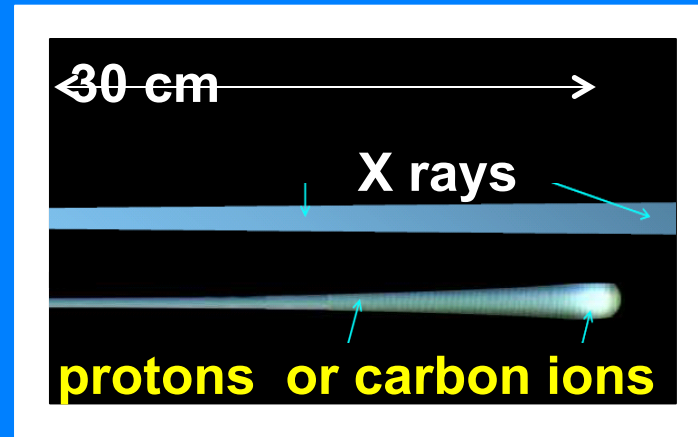
4 hadron beams



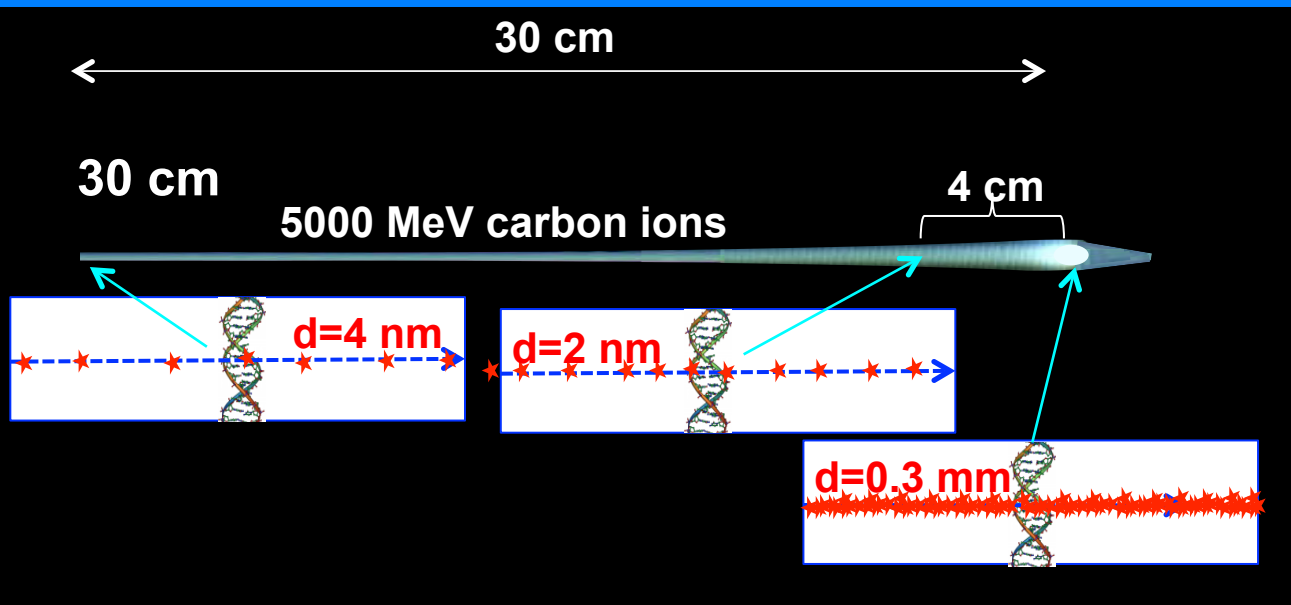
PSI - Villigen

Advantages of protons and carbon ions

protons: 230 MeV
C ions : 5000 MeV

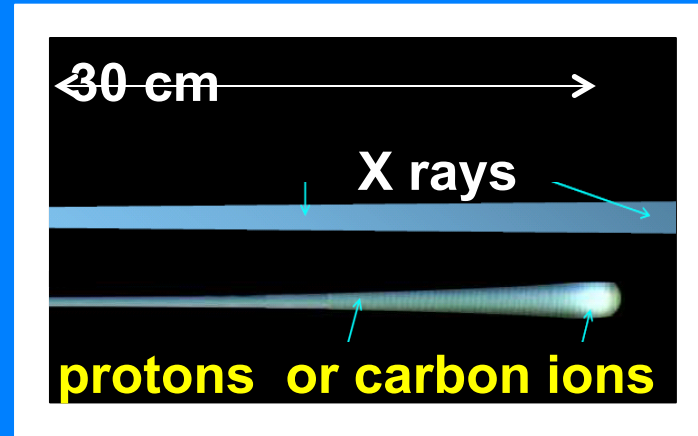


1. Healthy tissues are spared by protons and carbon ions

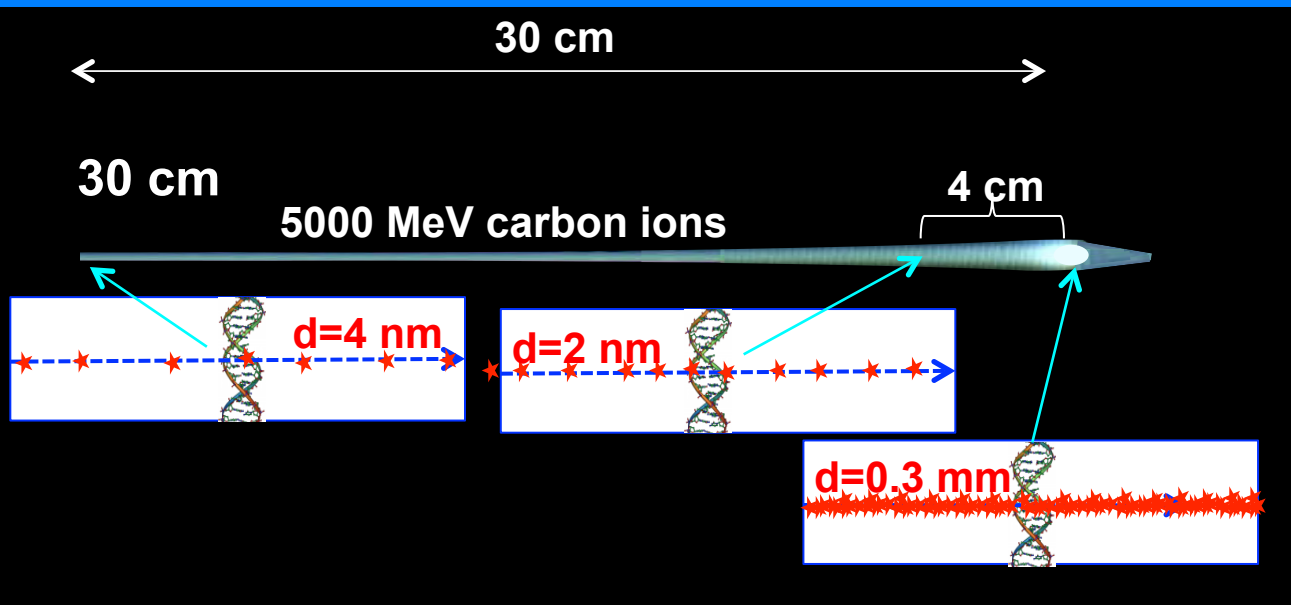


Advantages of protons and carbon ions

protons: 230 MeV
C ions : 5000 MeV



1. Healthy tissues are spared by protons and carbon ions



2. Carbon ions have charge = 6 and produce in the DNA **clustered unreparable damages**

thus killing at the end of the range the cells which are **radioresistant** to both X rays and protons.

60 years ago: first proton treatment at Berkeley

184-inch cyclotron



Cornelius Tobias
"Toby"

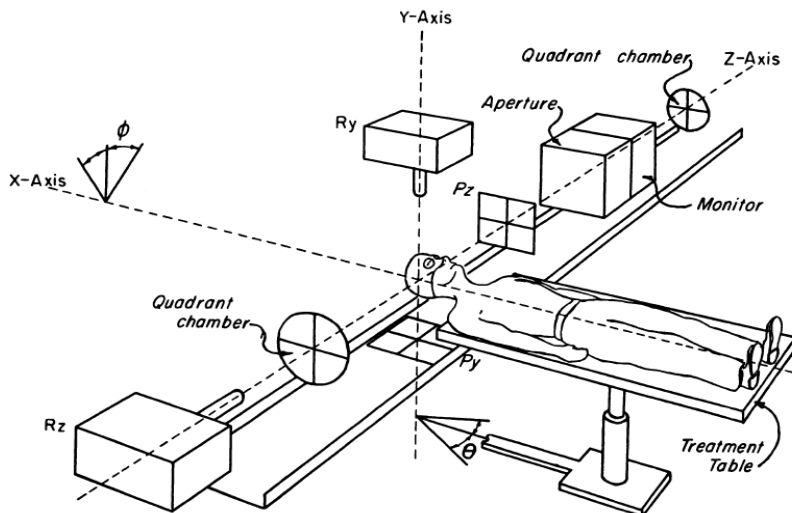


CHART 8.—A schematic drawing of the apparatus for proton irradiation of the human hypophysis

CANCER RESEARCH

VOLUME 18

FEBRUARY 1958

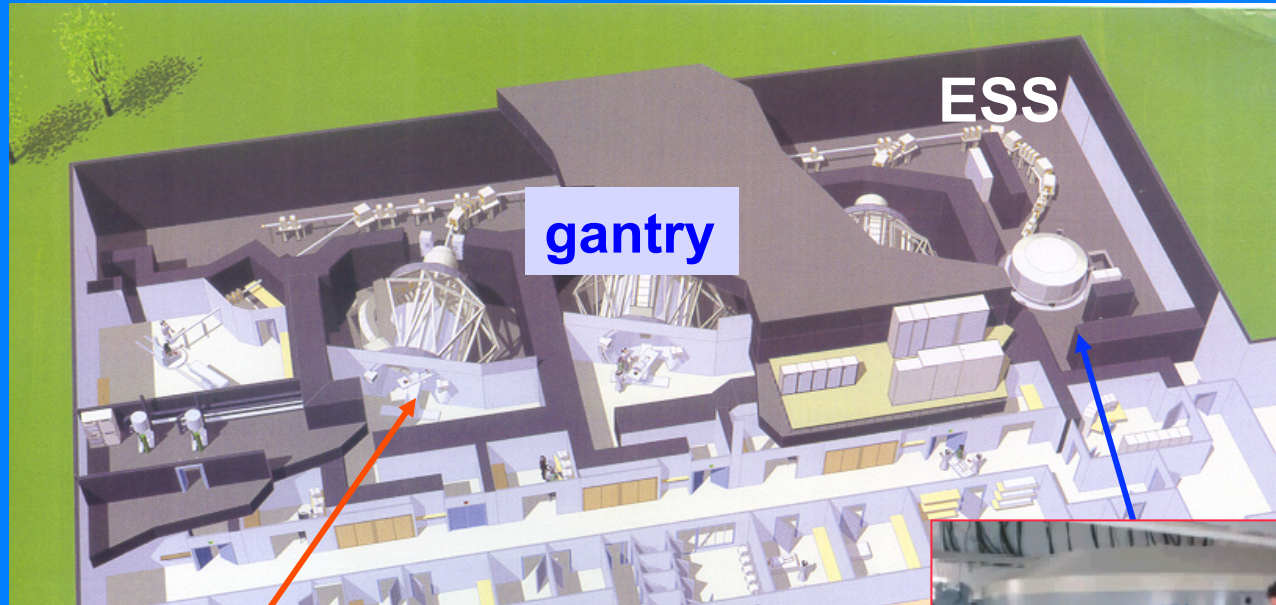
NUMBER 2

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

C. A. TOBIAS, J. H. LAWRENCE, J. L. BORN, R. K. MCCOMBS, J. E. ROBERTS,
H. O. ANGER, B. V. A. LOW-BEER,† AND C. B. HUGGINS‡

(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

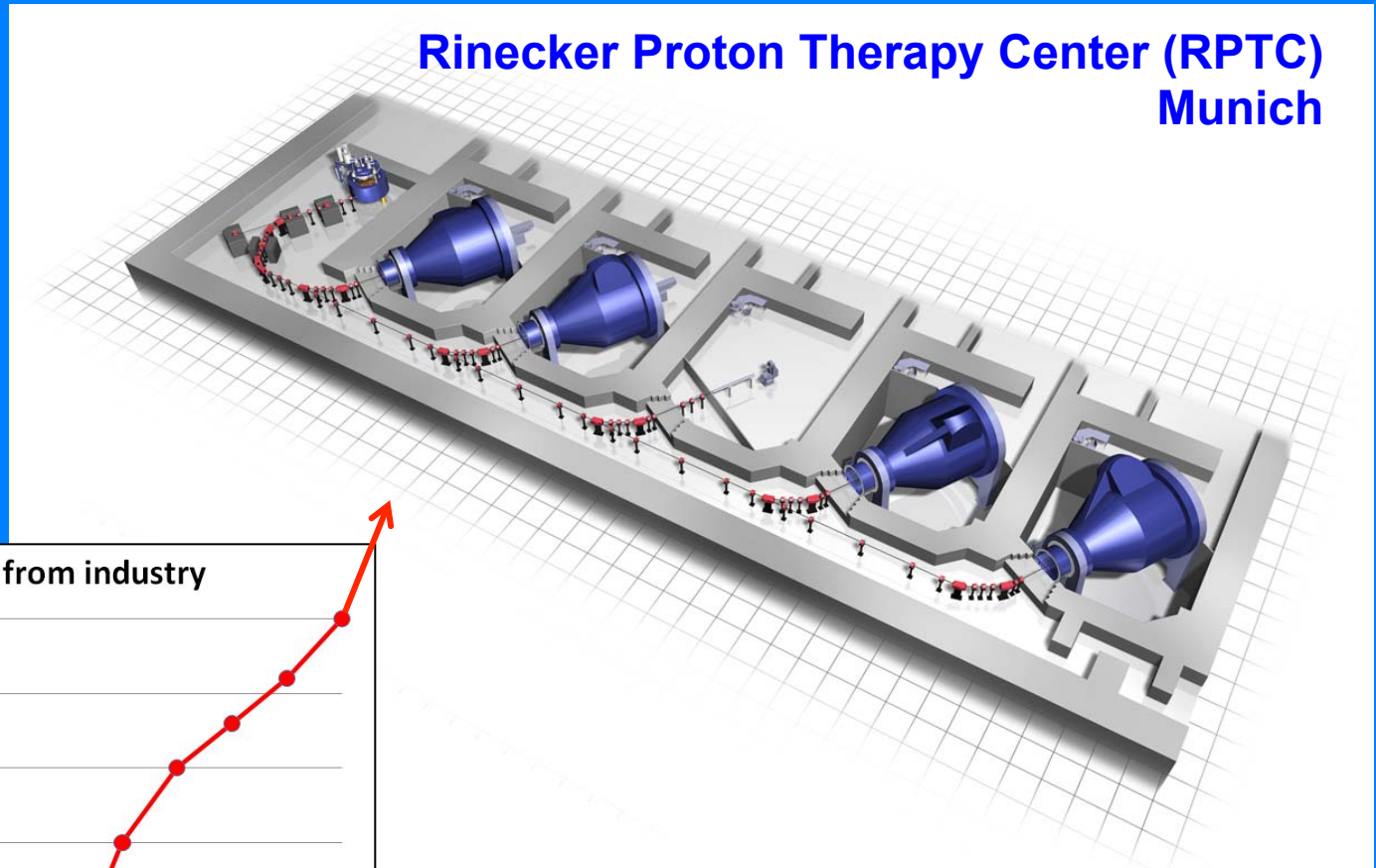


Seven companies offer turn-key centres with 2-3 gantires for 120-150 M€.

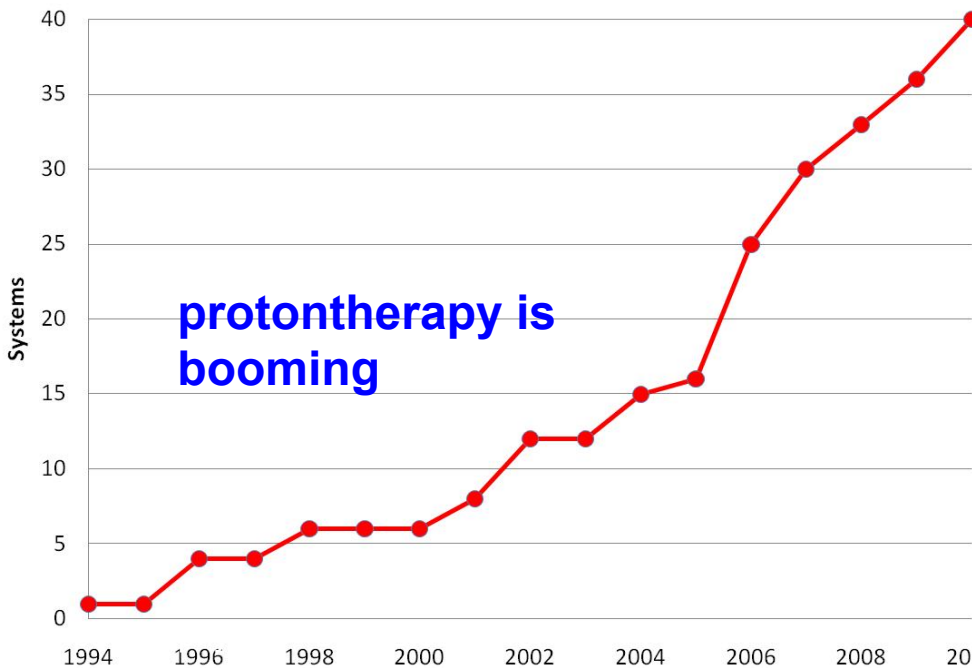
If proton accelerators were 'small' and 'cheap', no radiation oncologist would use X rays.

Superconducting cyclotron solution by Varian

Rinecker Proton Therapy Center (RPTC)
Munich



Number of PT systems ordered from industry

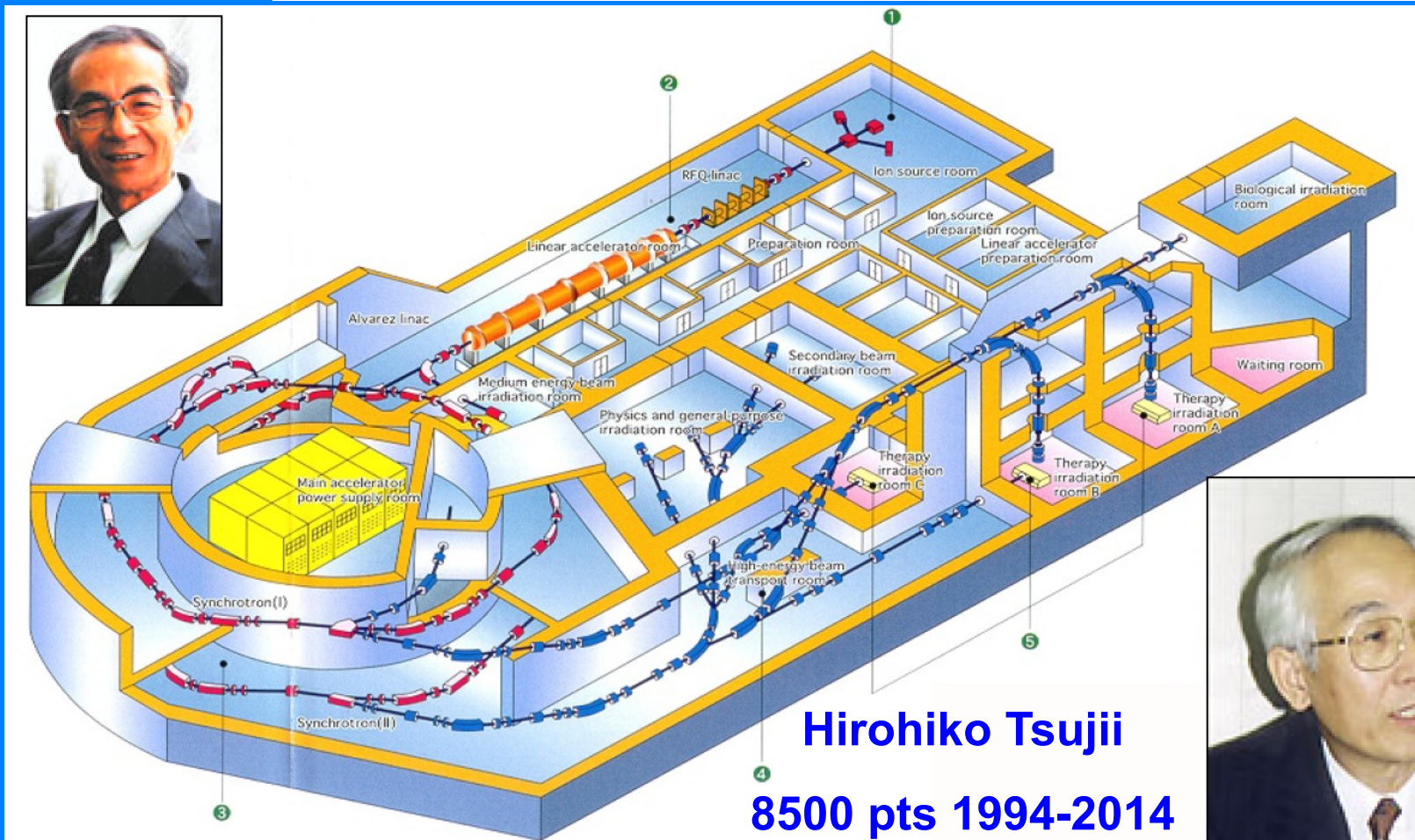


20-25 sessions per patient
European cost of a full treatment:
IMRT: 8-10 k€
Protontherapy: 20-25 k€

HIMAC in Chiba is the pioner of carbon therapy

¹⁵ Hirao, Y. et al, "Heavy Ion Synchrotron for Medical Use: HIMAC Project at NIRS Japan" Nucl. Phys. A538, 541c (1992)

Yasuo Hirao



Hirohiko Tsujii

8500 pts 1994-2014



The GSI pilot project : 1997-2008



Gerhard Kraft



J. Debus

450 patients treated
with carbon ions



GSI - Darmstadt

The GSI pilot project : 1997-2008



Gerhard Kraft



J. Debus

450 patients treated
with carbon ions



GSI - Darmstadt

**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)

Eye and Orbit

- Choroidal Melanoma
- Retinoblastoma
- Choroidal Metastases
- Orbital Rhabdomyosarcoma
- Lacrimal Gland Carcinoma
- Choroidal Hemangiomas

Head and Neck Tumors

- Locally Advanced Oropharynx
- Locally Advanced Nasopharynx
- Soft Tissue Sarcoma
Recurrent or Unresectable
- Misc. Unresectable or Recurrent Carcinomas

Chest

- Non Small Cell Lung Carcinoma
Early Stage—Medically Inoperable
- Paraspinal Tumors
Soft Tissue Sarcomas, Low Grade Chondrosarcomas, Chordomas

Abdomen

- Paraspinal Tumors
- Soft Tissue
Sarcomas,
Low Grade
Chondrosarcomas,
Chordomas

Pelvis

- Early Stage Prostate Carcinoma
- Locally Advanced Prostate Carcinoma
- Locally Advanced Cervix Carcinoma
- Sacral Chordoma
- Recurrent or Unresectable Rectal Carcinoma
- Recurrent or Unresectable Pelvic Masses

Central Nervous System

- Adult Low Grade Gliomas
- Pediatric Gliomas
- Acoustic Neuroma
Recurrent or Unresectable
- Pituitary Adenoma
Recurrent or Unresectable
- Meningioma
Recurrent or Unresectable
- Craniopharyngioma
- Chordomas and
Low Grade Chondrosarcoma
Clivus and Cervical Spine
- Brain Metastases
- Optic Glioma
- Arteriovenous Malformations

Numbers of potential patients by European Network for Light Ion Therapy

X-ray therapy

for 1 million inhabitants: 2'000 pts/year

Protontherapy

12% of X-ray patients 240 pts/year

Therapy with carbon ions for radio-resistant tumour

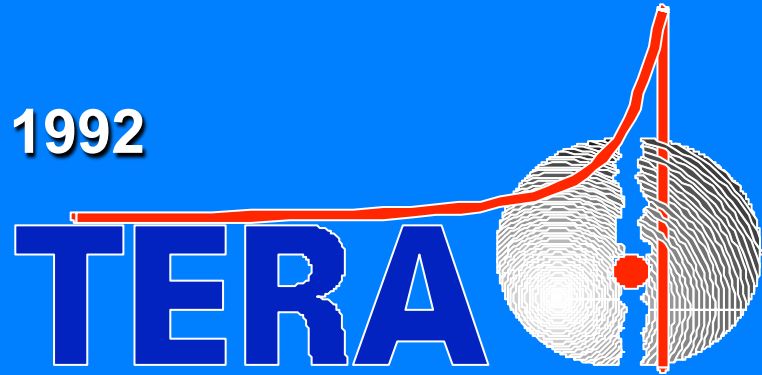
(comparisons with proton therapy are needed to define sites and protocols)

3% of X-ray patients 60 pts/year

TOTAL for 1 M 300 pts/year

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



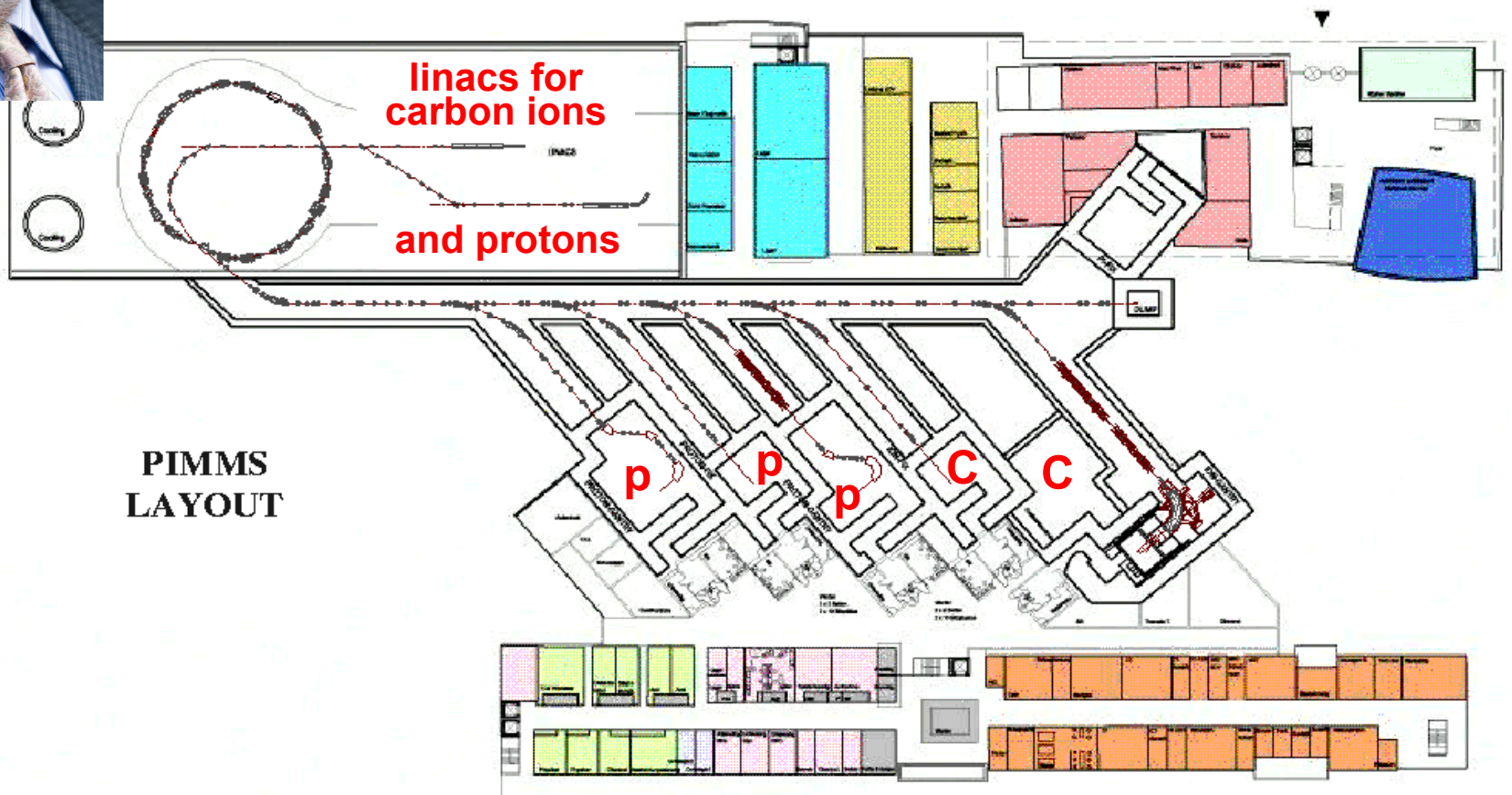
M. Regler

Optimized synchrotron for therapy

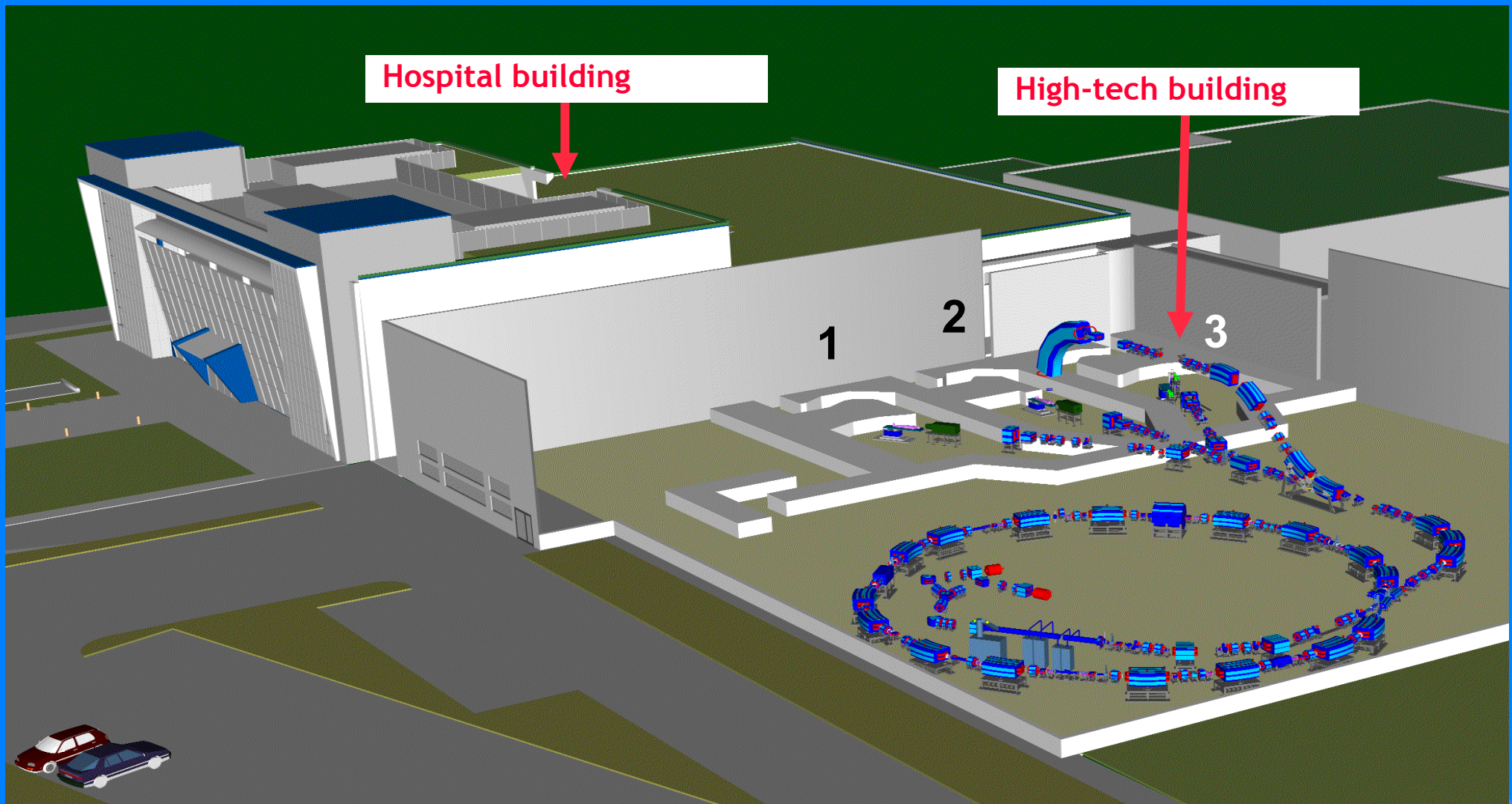
Project Leader: **Phil Bryant**

Chair of PAC: **Giorgio Brianti**

1996-2000



CNAO = Centro Nazionale di Adroterapia Oncologica in Pavia



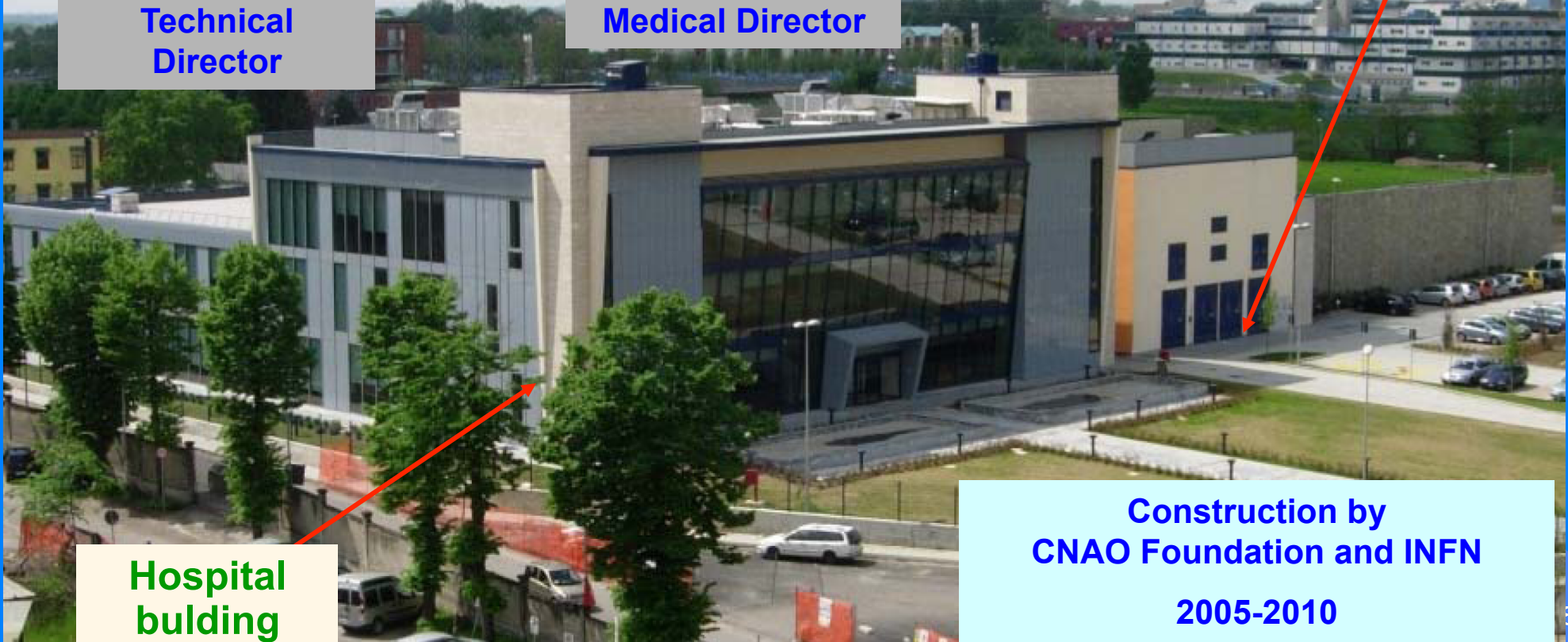
CNAO = Centro Nazionale di Adroterapia Oncologica



Sandro Rossi
Technical
Director



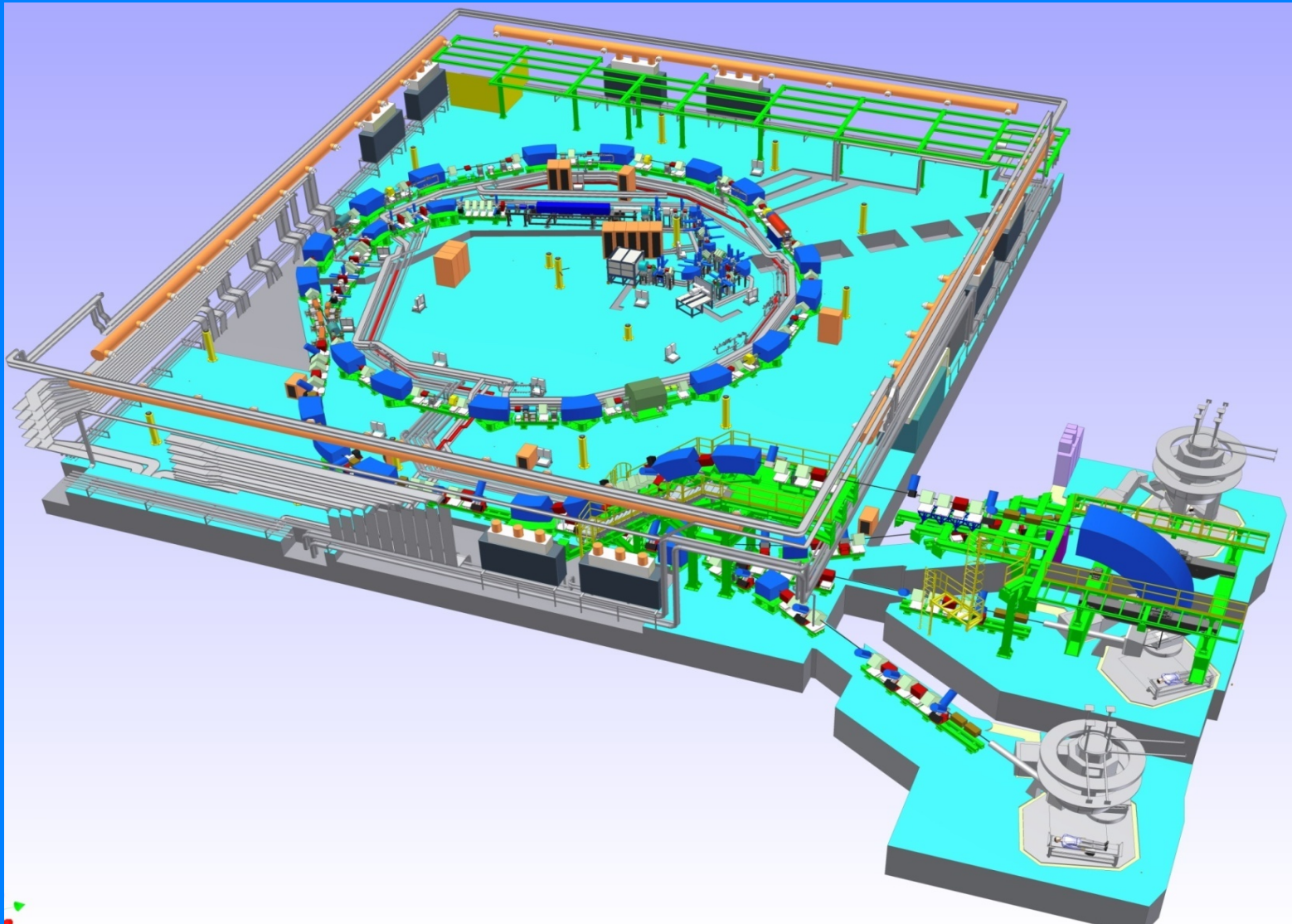
Roberto Orecchia
Medical Director



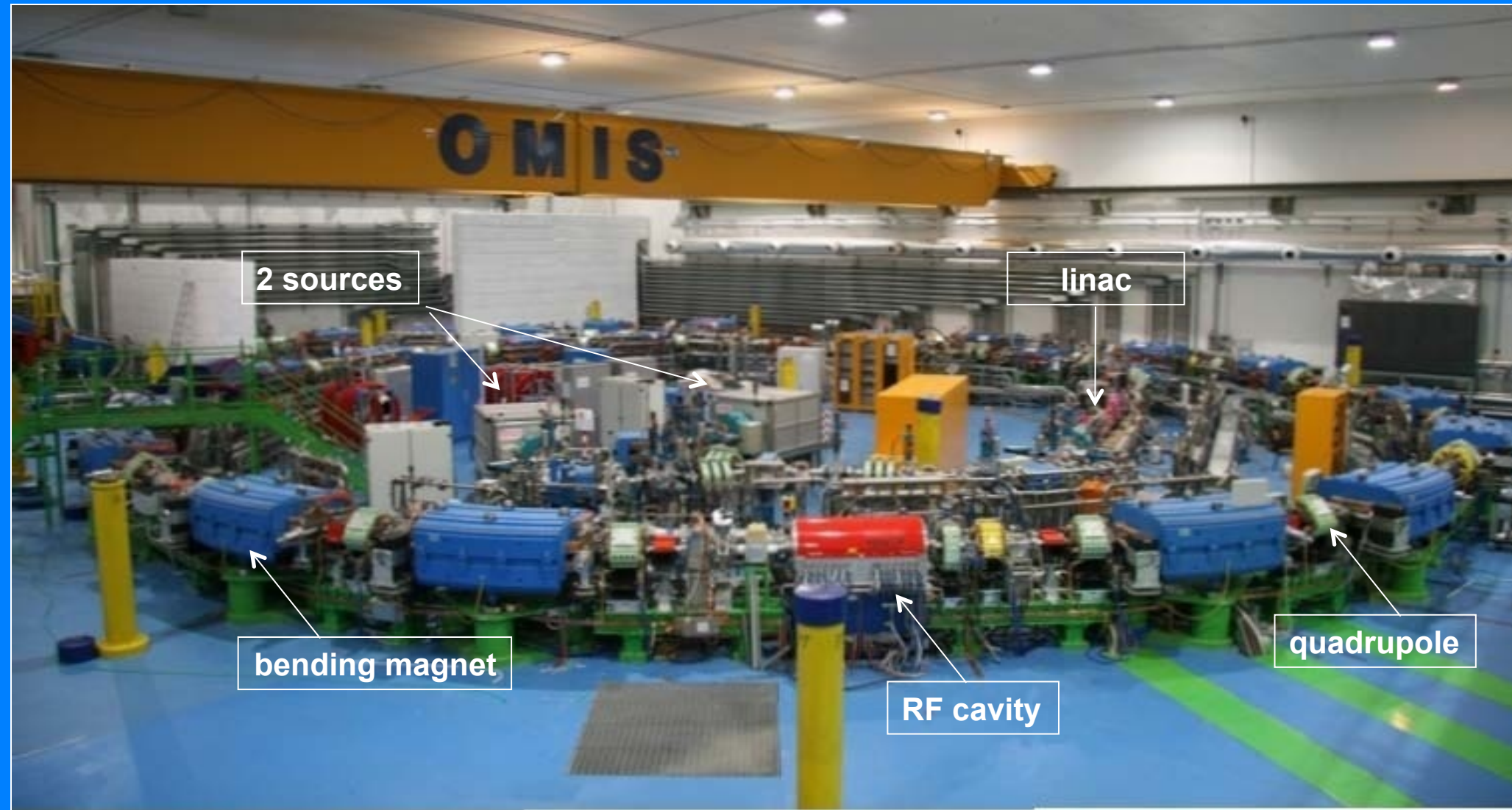
**Synchrotron
building**

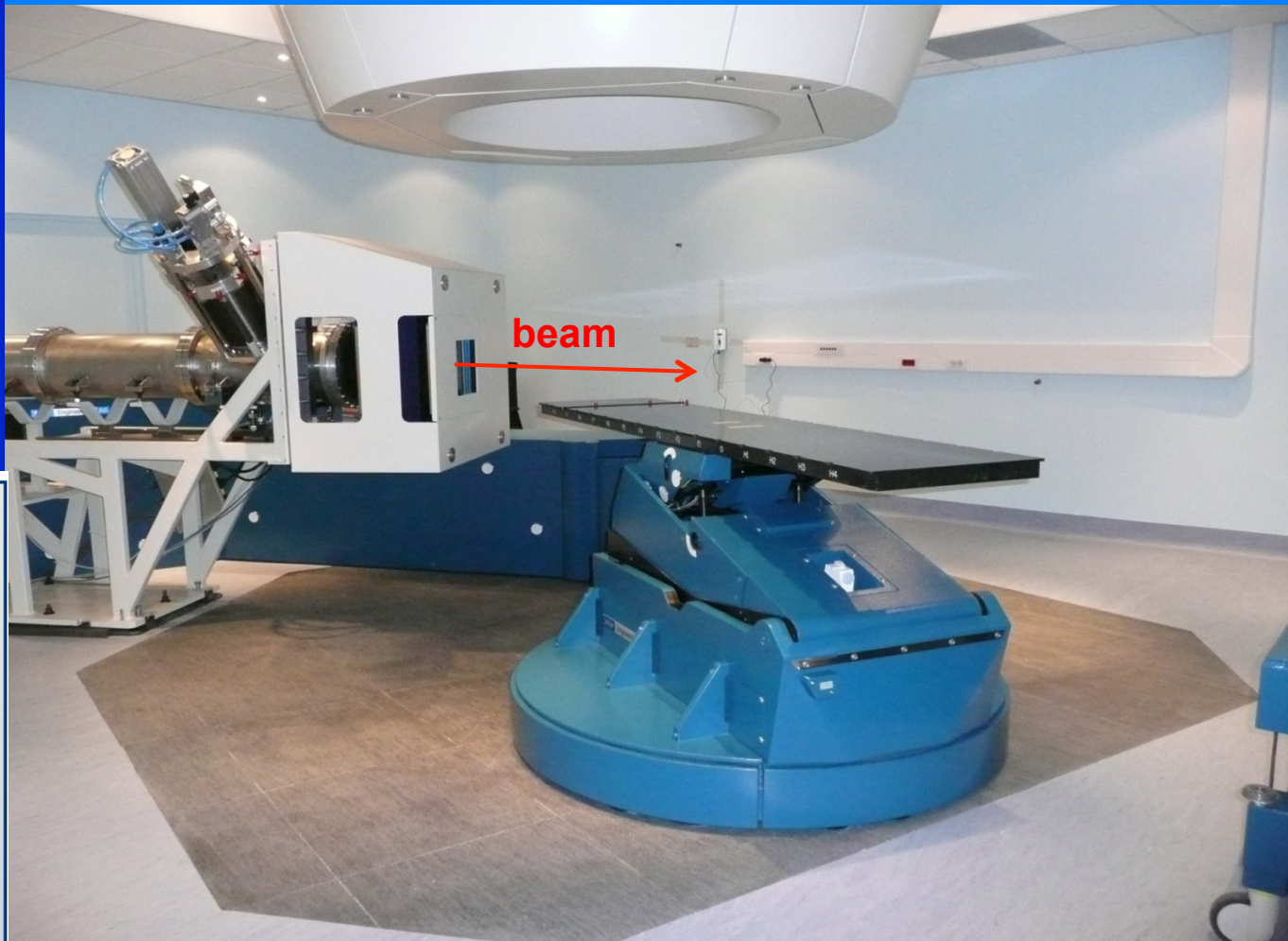
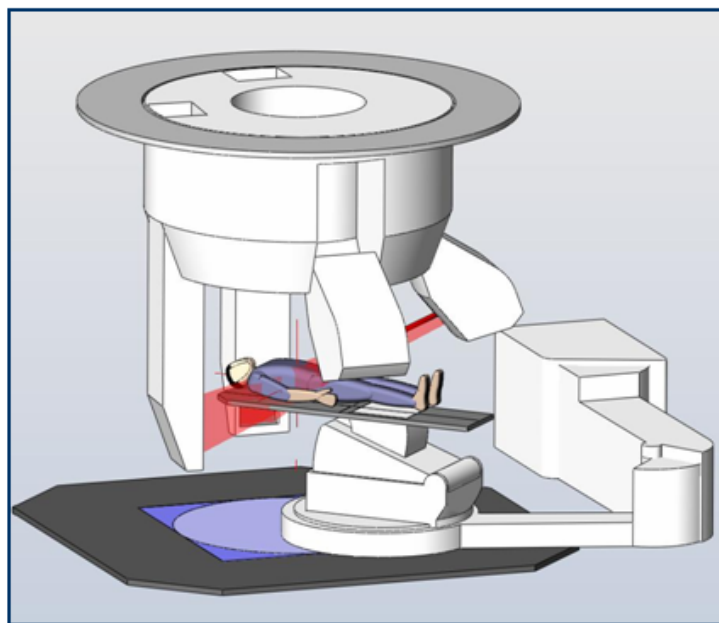
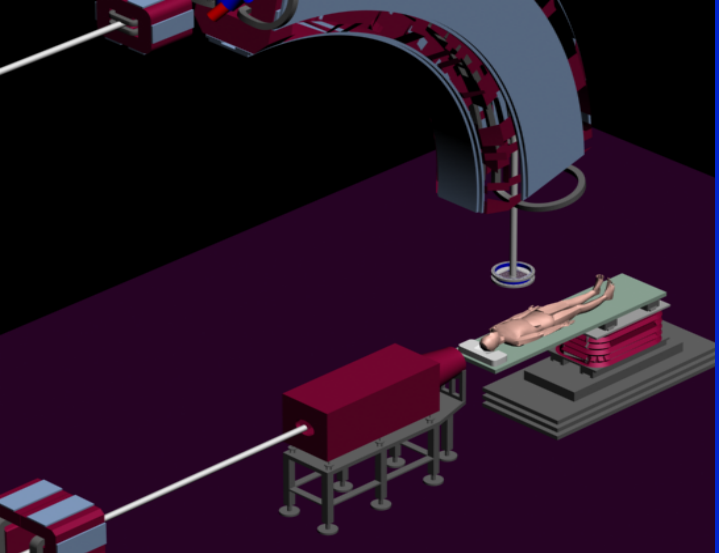
**Hospital
bulding**

**Construction by
CNAO Foundation and INFN
2005-2010**



The synchrotron



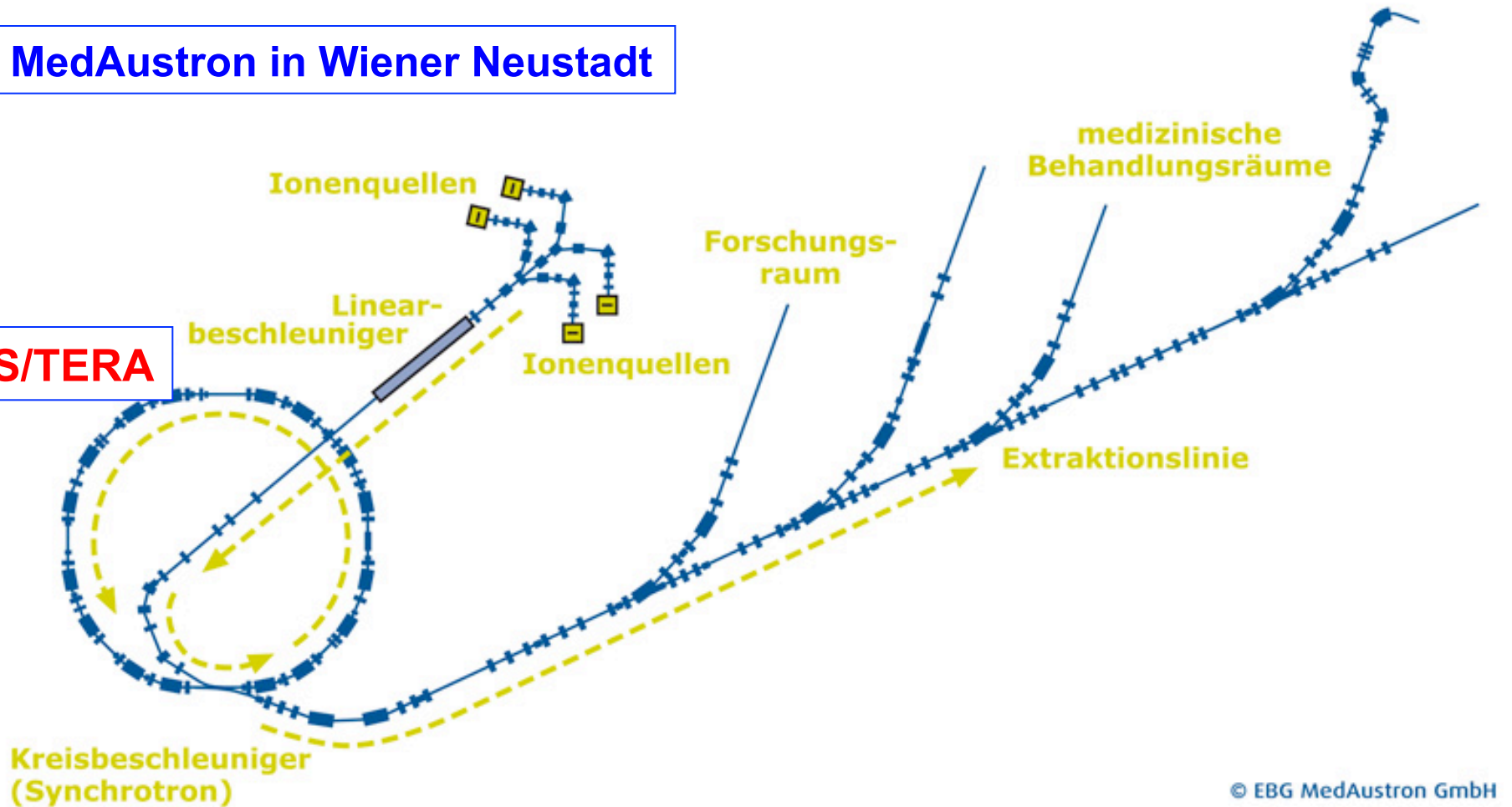


January 2014: 200 patients treated

MedAustron promoted and participated in PIMMS

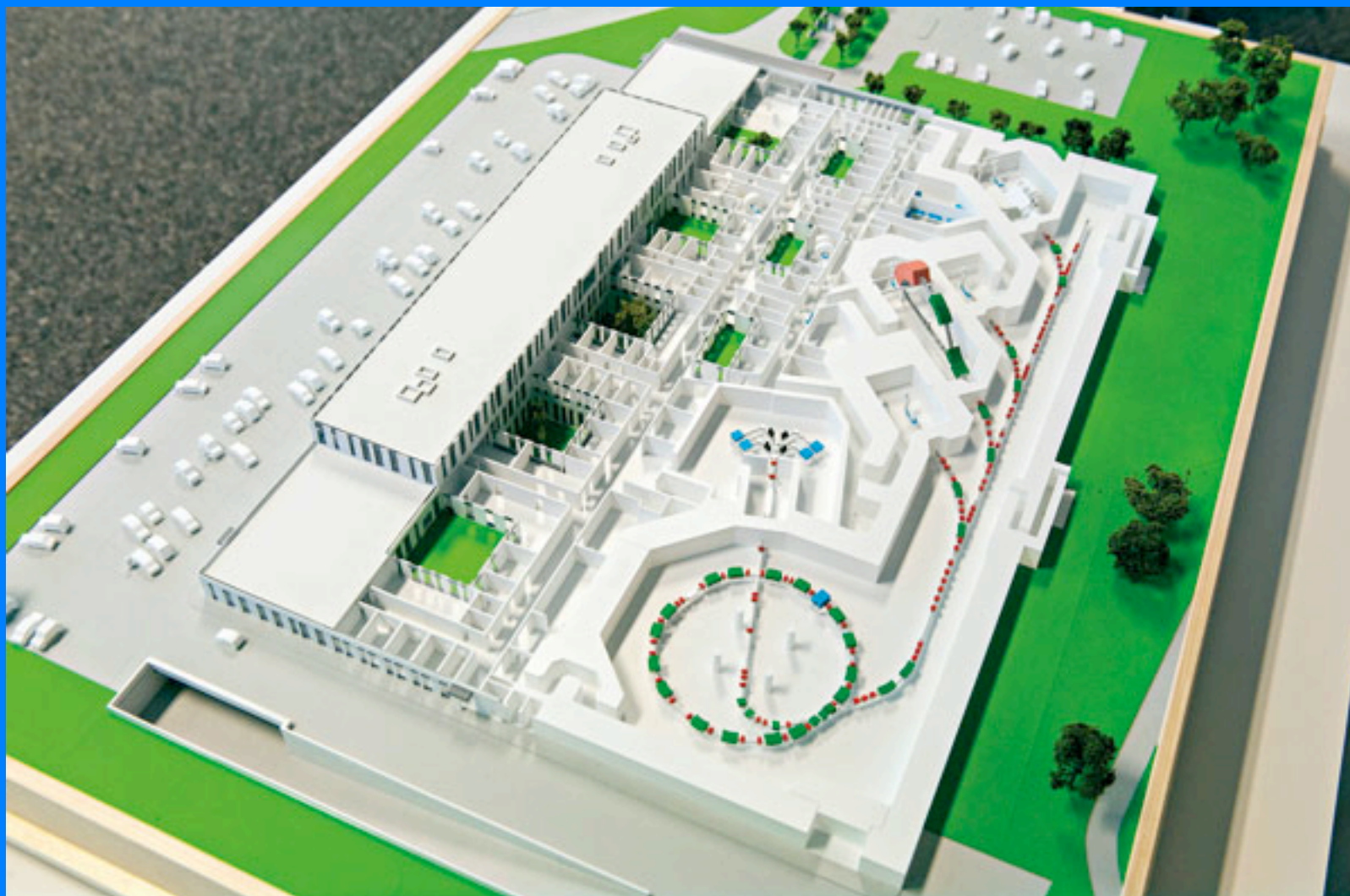
MedAustron in Wiener Neustadt

PIMMS/TERA

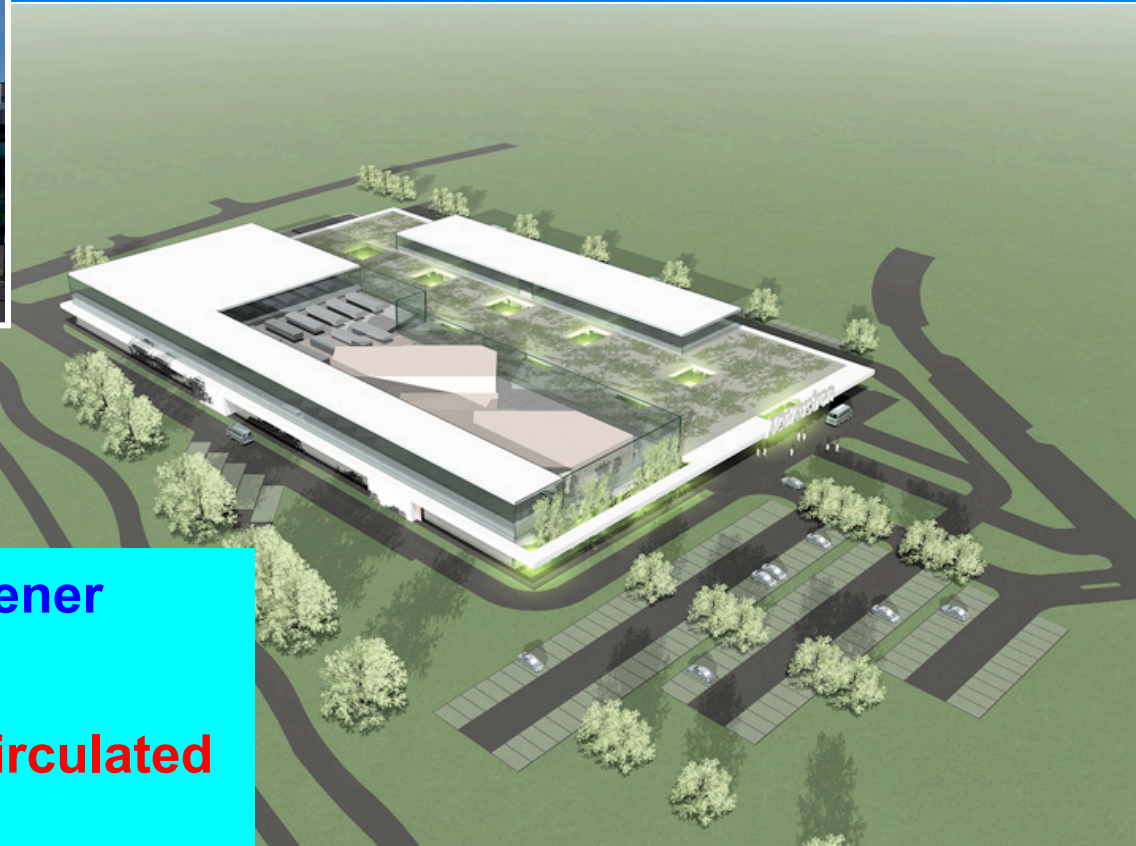


MedAustron has acquired from CNAO Foundation the construction drawings

MedAustron promoted and participated in PIMMS



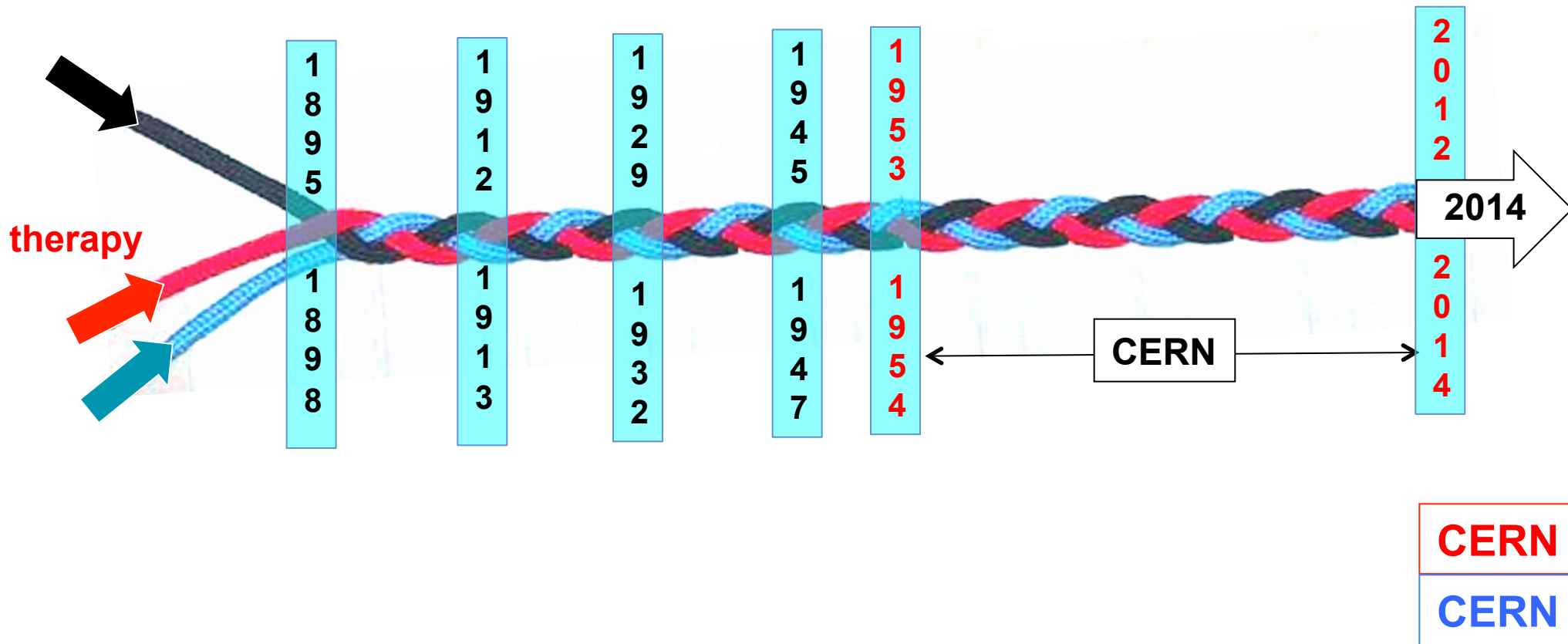
MedAustron promoted and participated in PIMMS



**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

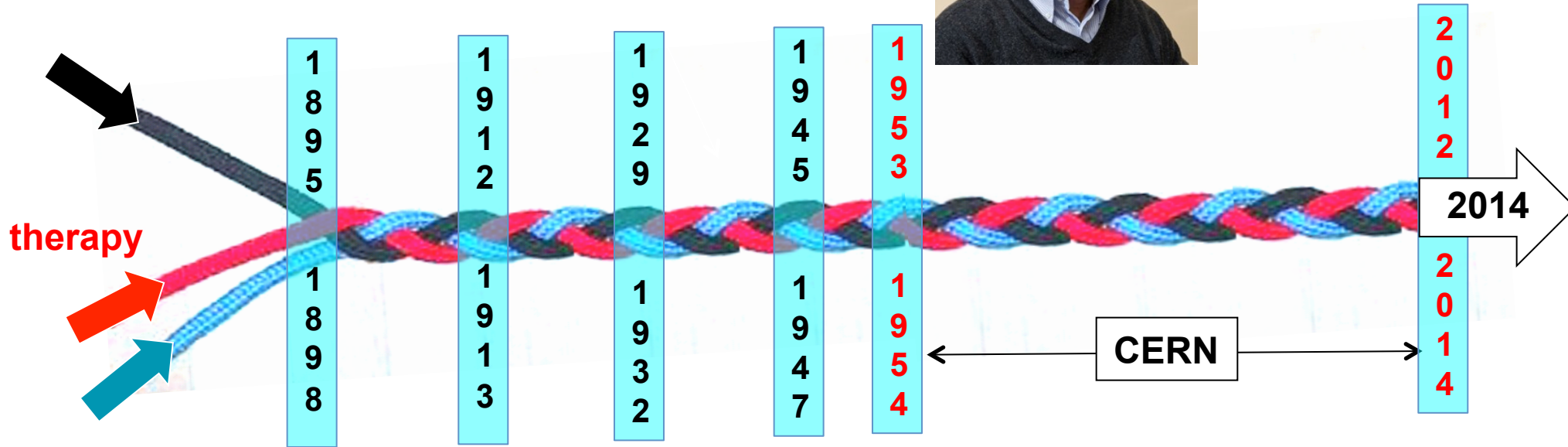


To conclude: in 2014 a further step has been made



Office for CERN
Medical Applications

1st January 2014
Steve Myers



CERN
CERN



CNAO at Pavia

PHYSICS IS BEAUTIFUL AND USEFUL

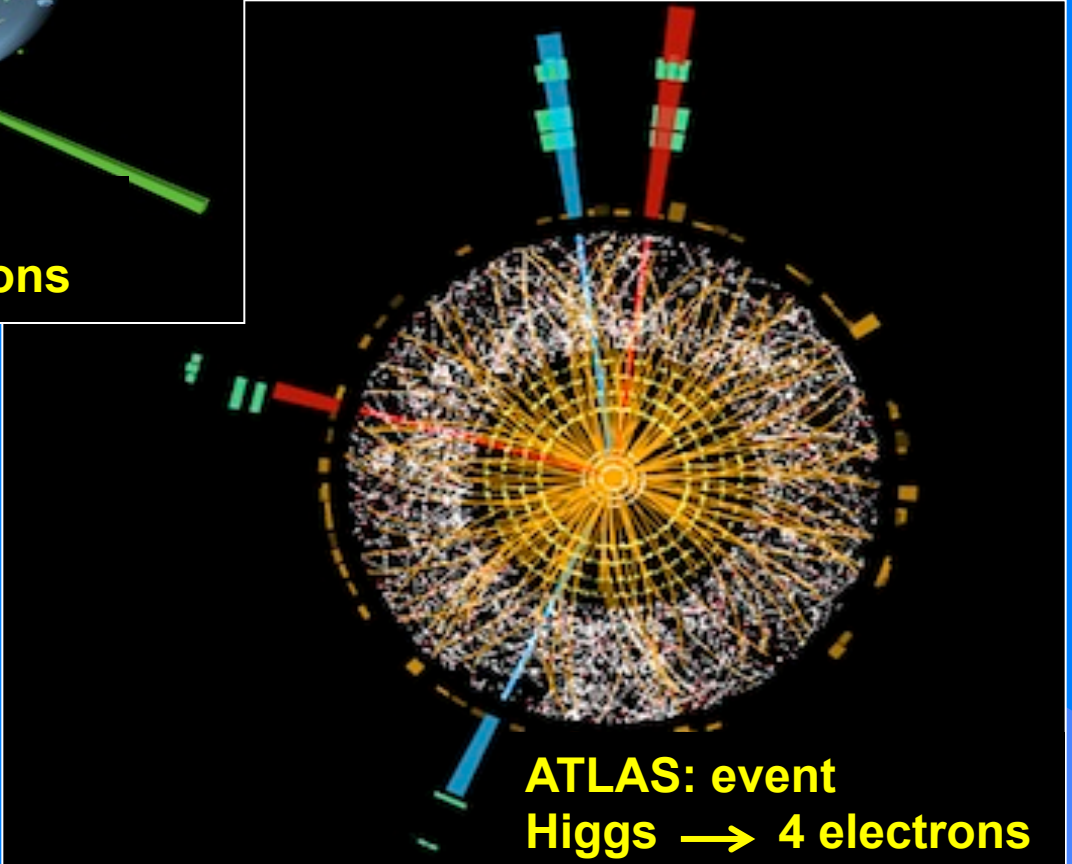
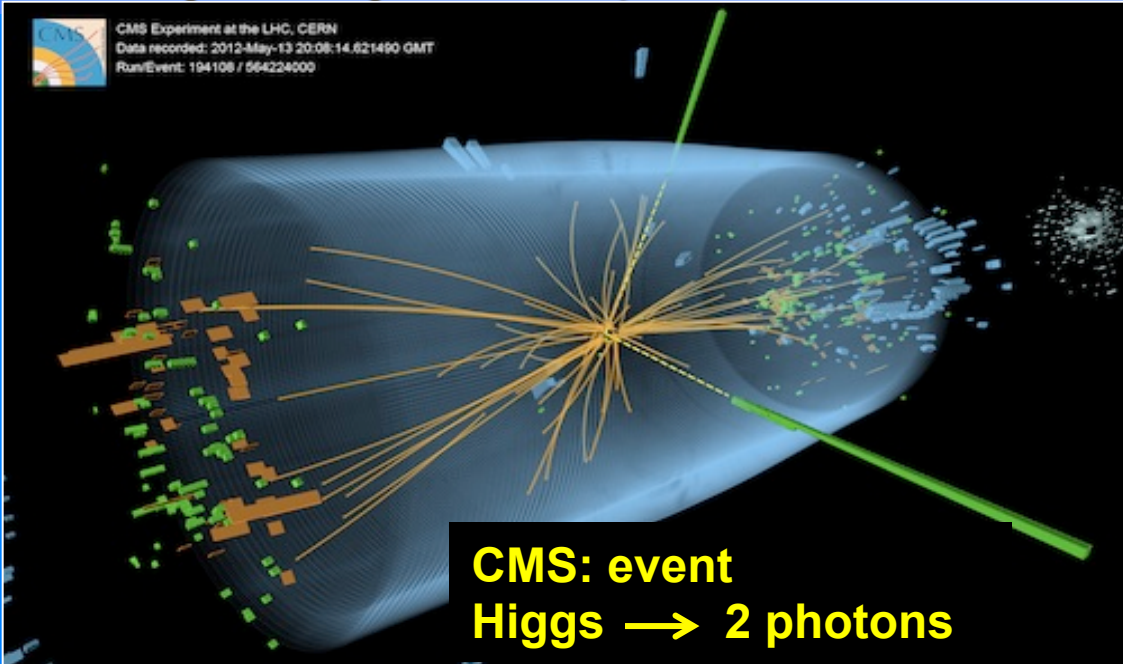
Physik ist schön und nützlich

La Physique est belle et utile

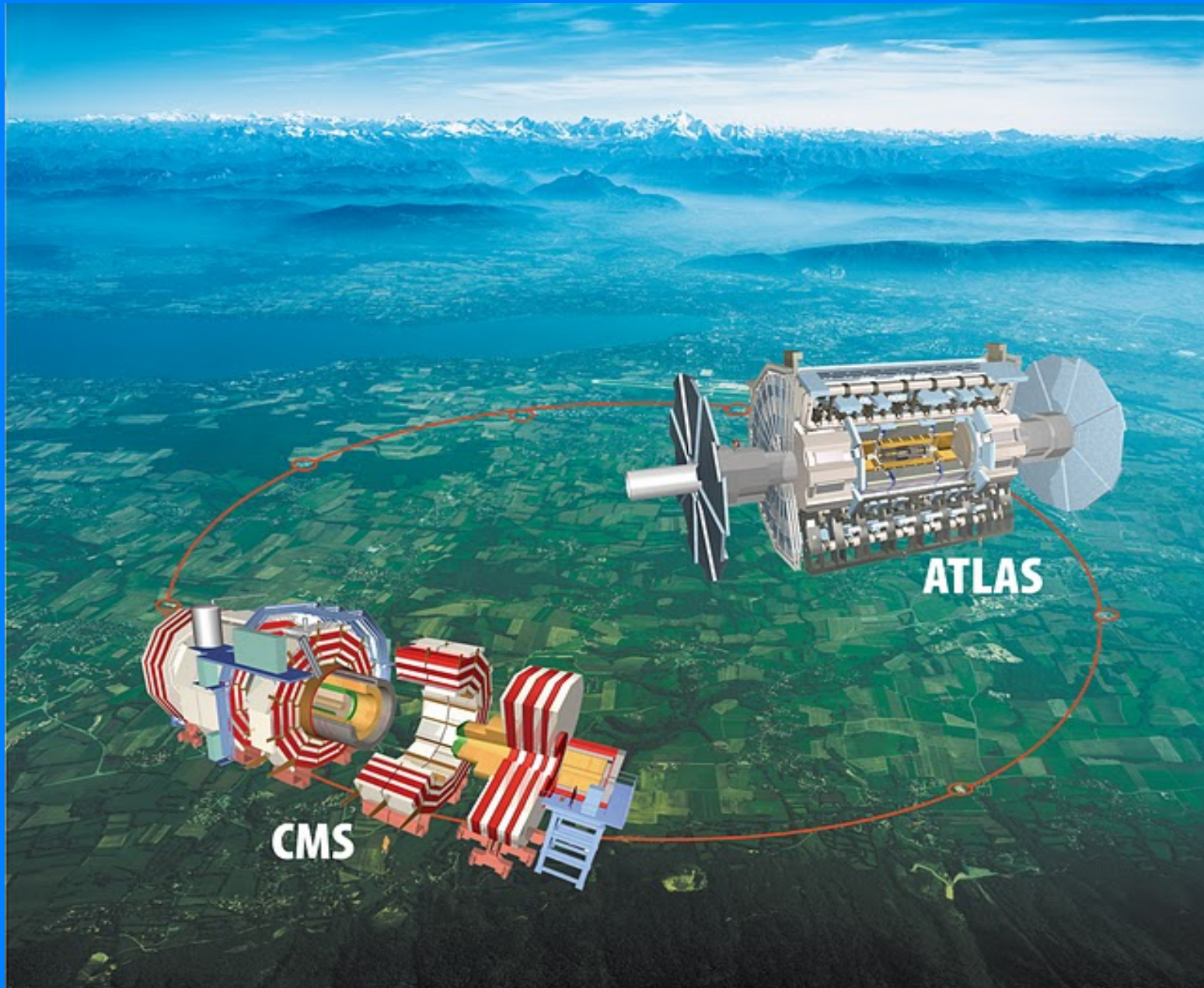
La Fisica è bella e utile

The importance of the Higgs “field”

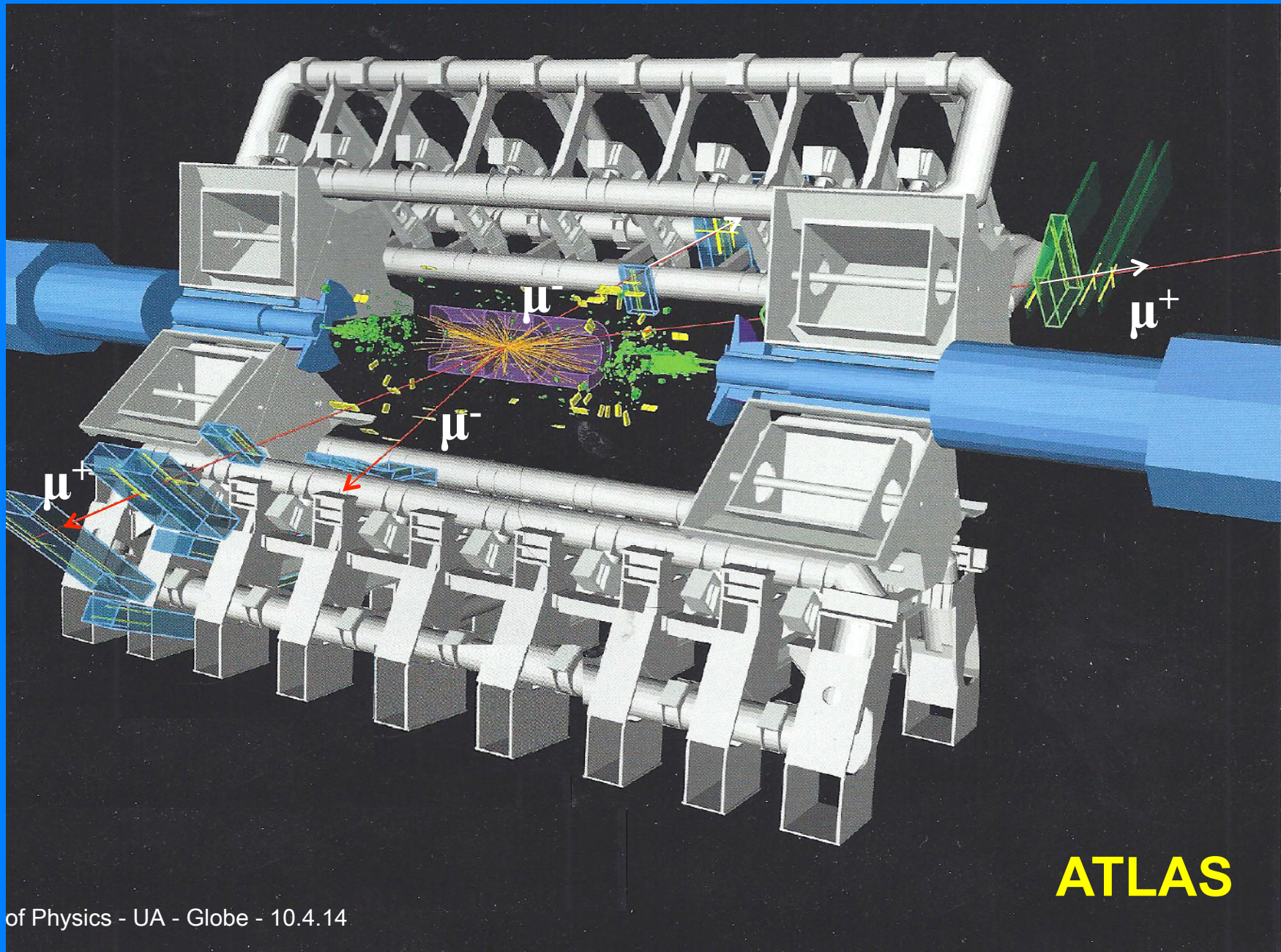
HIGHLIGHTS: 2012 – F.Gianotti and J. Incandela, ATLAS and CMS spokespersons, announce the discovery of the ‘Higgs field’



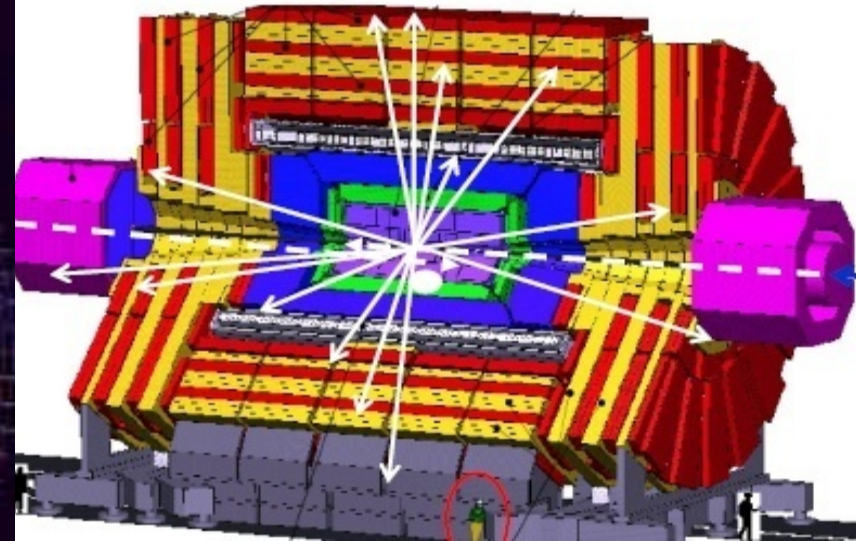
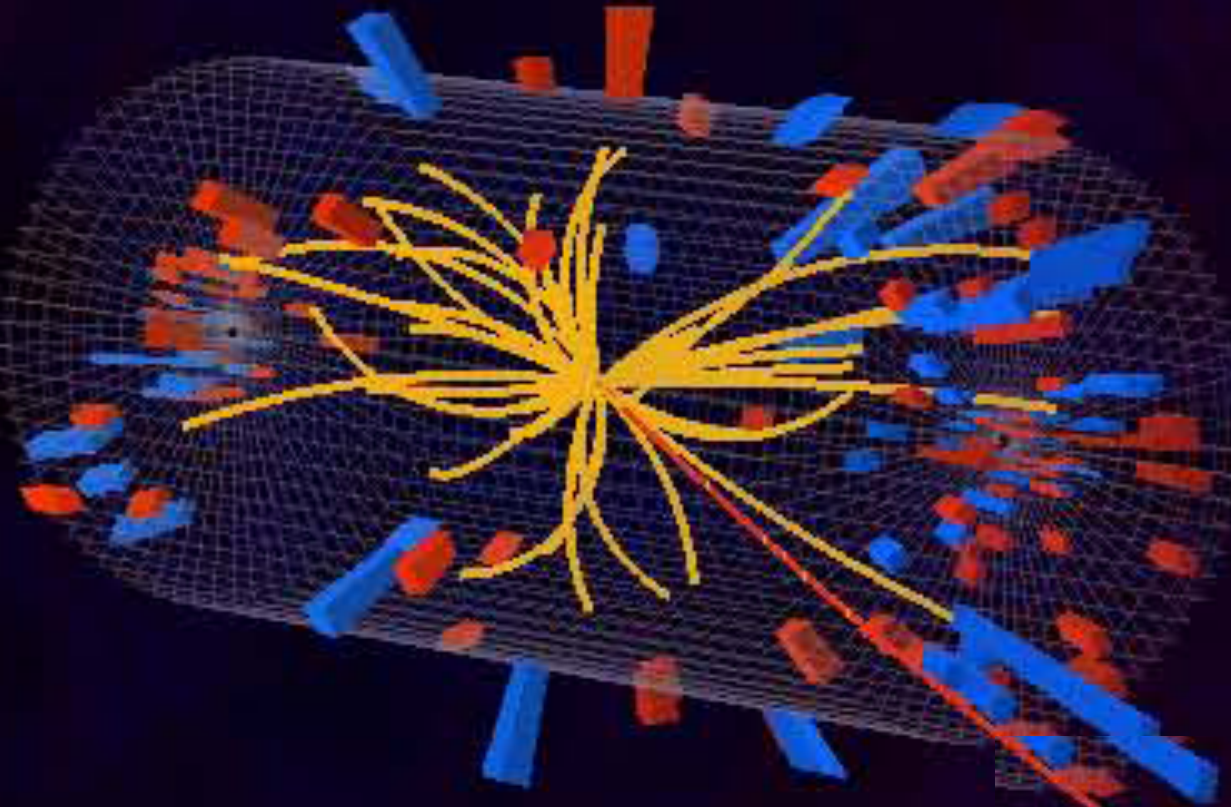
Two large 'detectors' at LHC



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} s) after the Big Bang

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

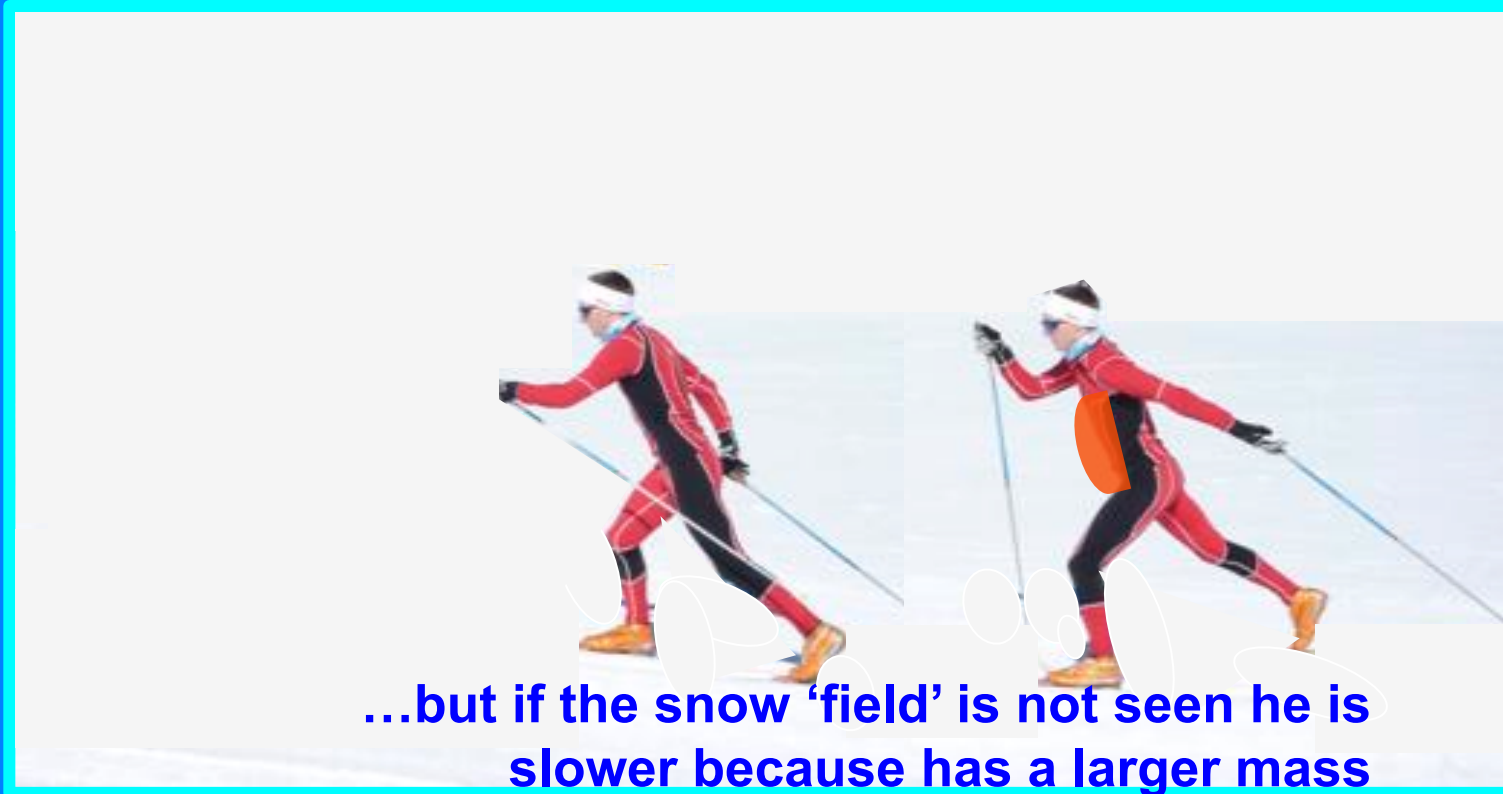
the Higgs 'field' is a continuous medium that fills the space since one hundredth of a billionth of a second (10^{-11} s) after the Big Bang

the particles interact differently with the Higgs field and thus they have different masses

Metaphor of the two twins practicing Nordic sky on a flat snow "field"



Metaphor of the two twins practicing Nordic sky on a flat snow "field"



2013: the Nobel prize winners



François Englert

Peter Higgs



Fabiola Gianotti

Peter Higgs

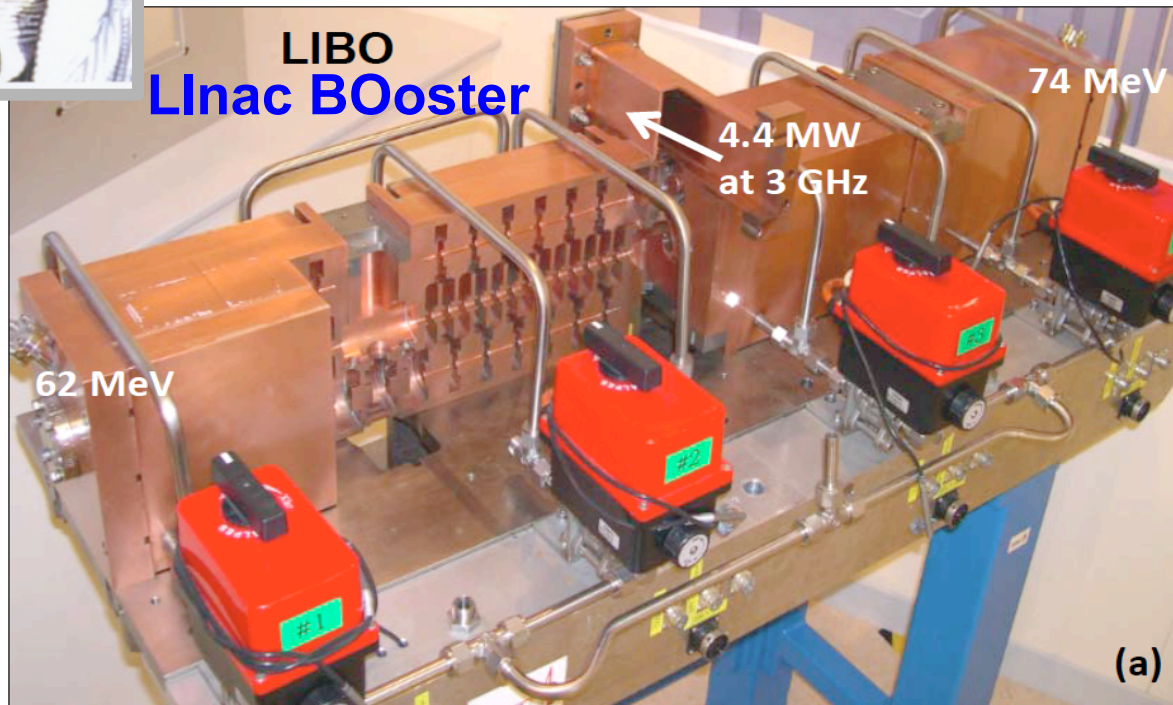
***TERA novel accelerators for cancer therapy:
proton linacs***

Prototype of CCL built and beam tested by TERA-CERN-INFN: 2003



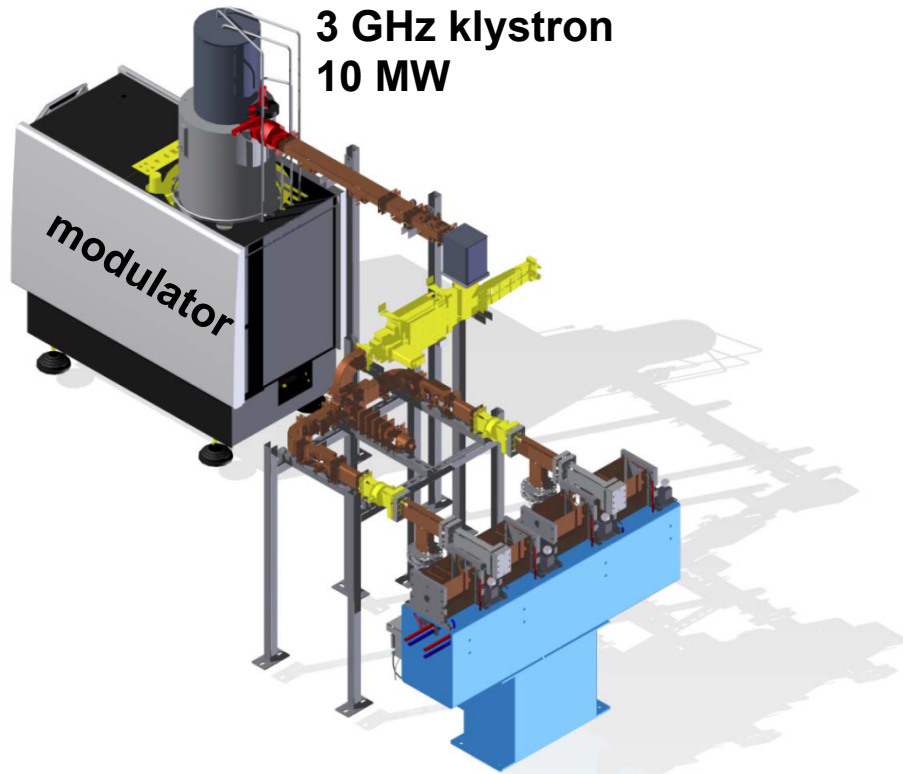
Mario Weiss

LIBO Linac BOoster

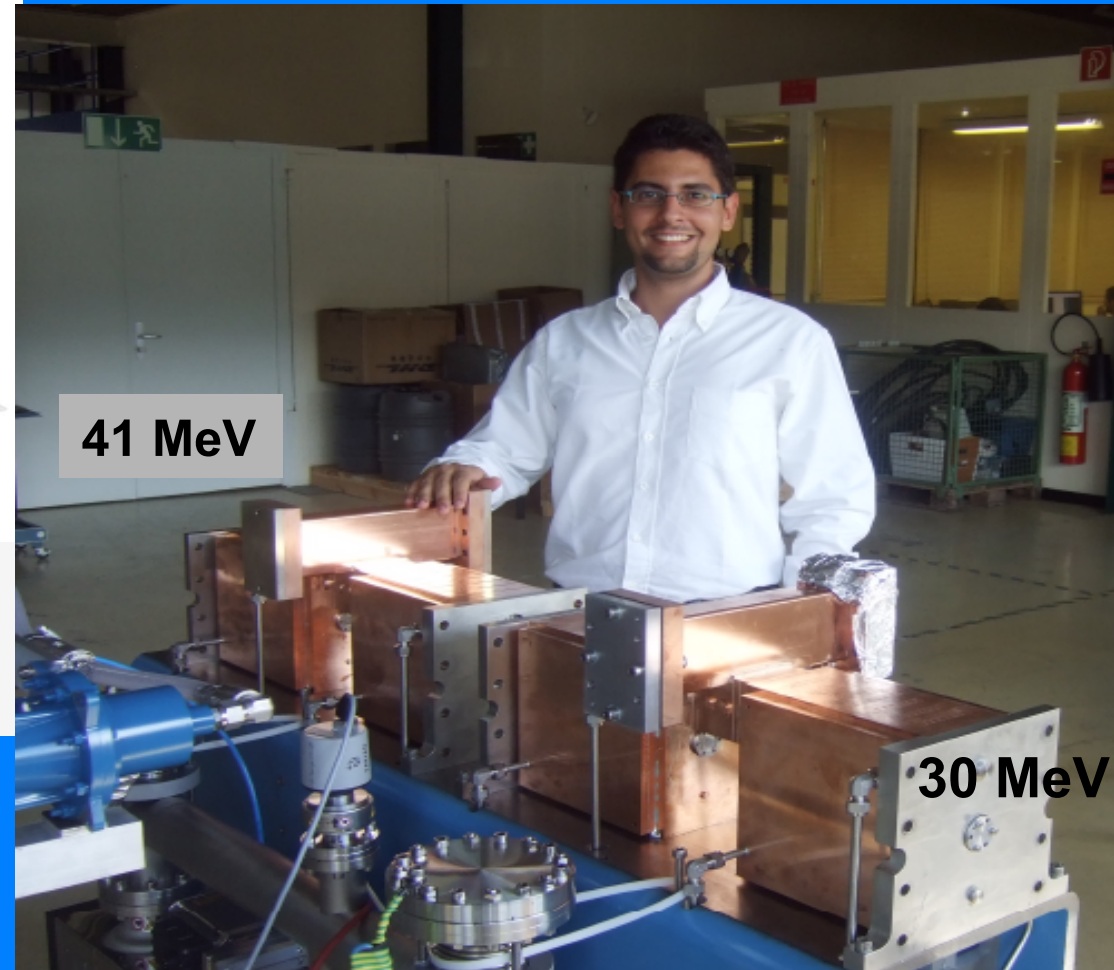


3 GHz proton Linac

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

Inauguration by the CERN DG

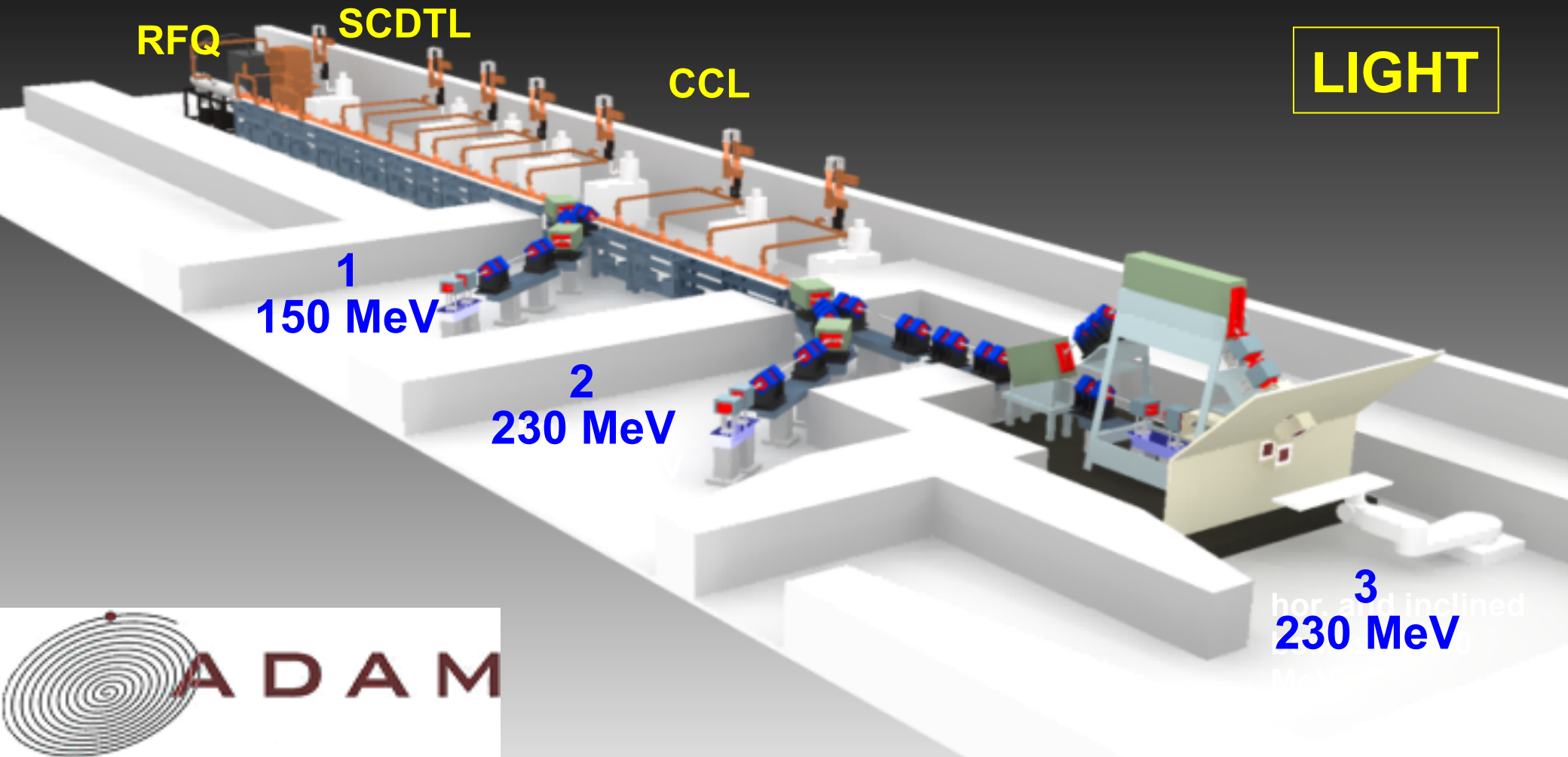


S. Bertolucci

R. Heuer

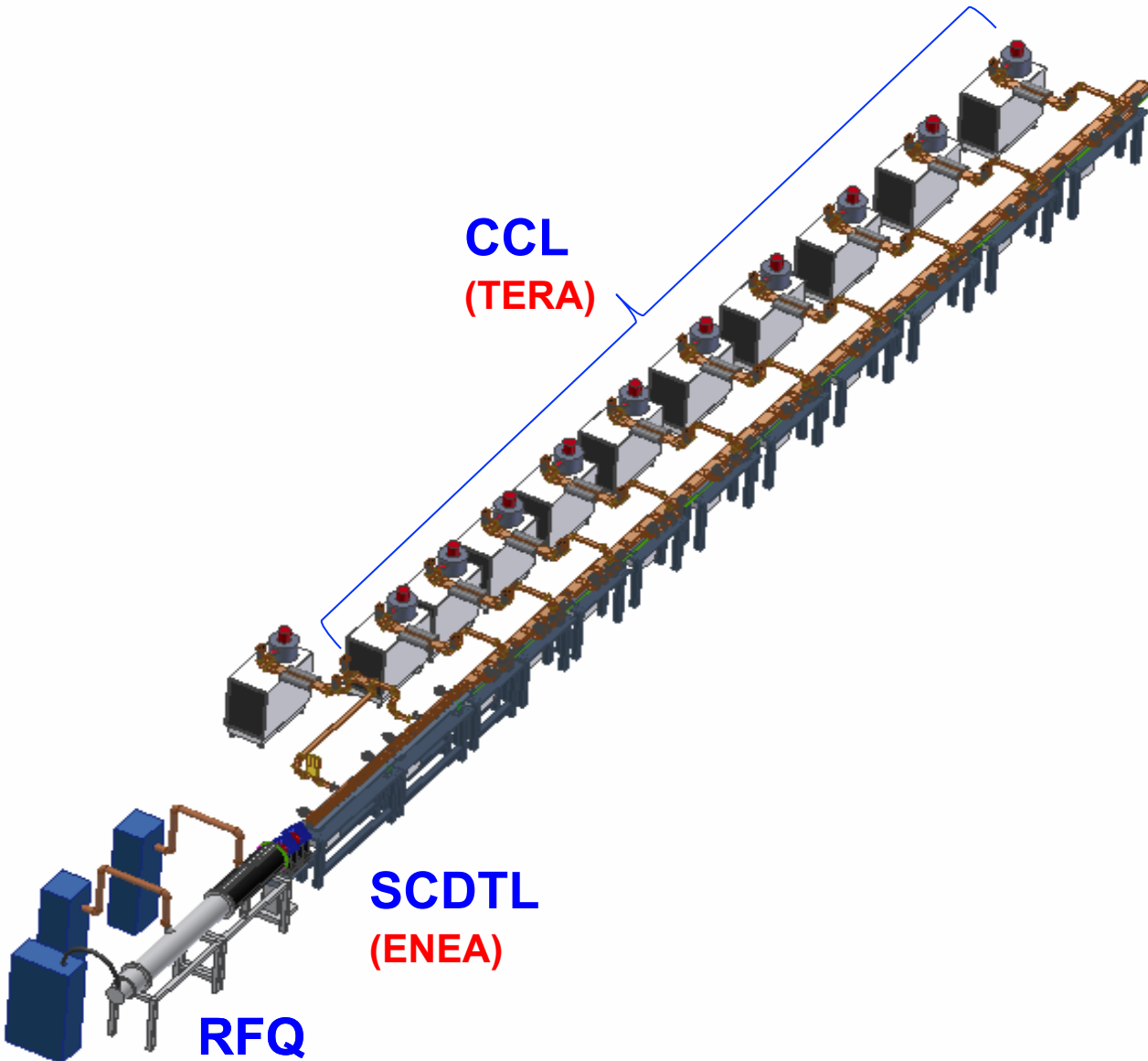
A. Colussi
A.D.A.M.
President

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



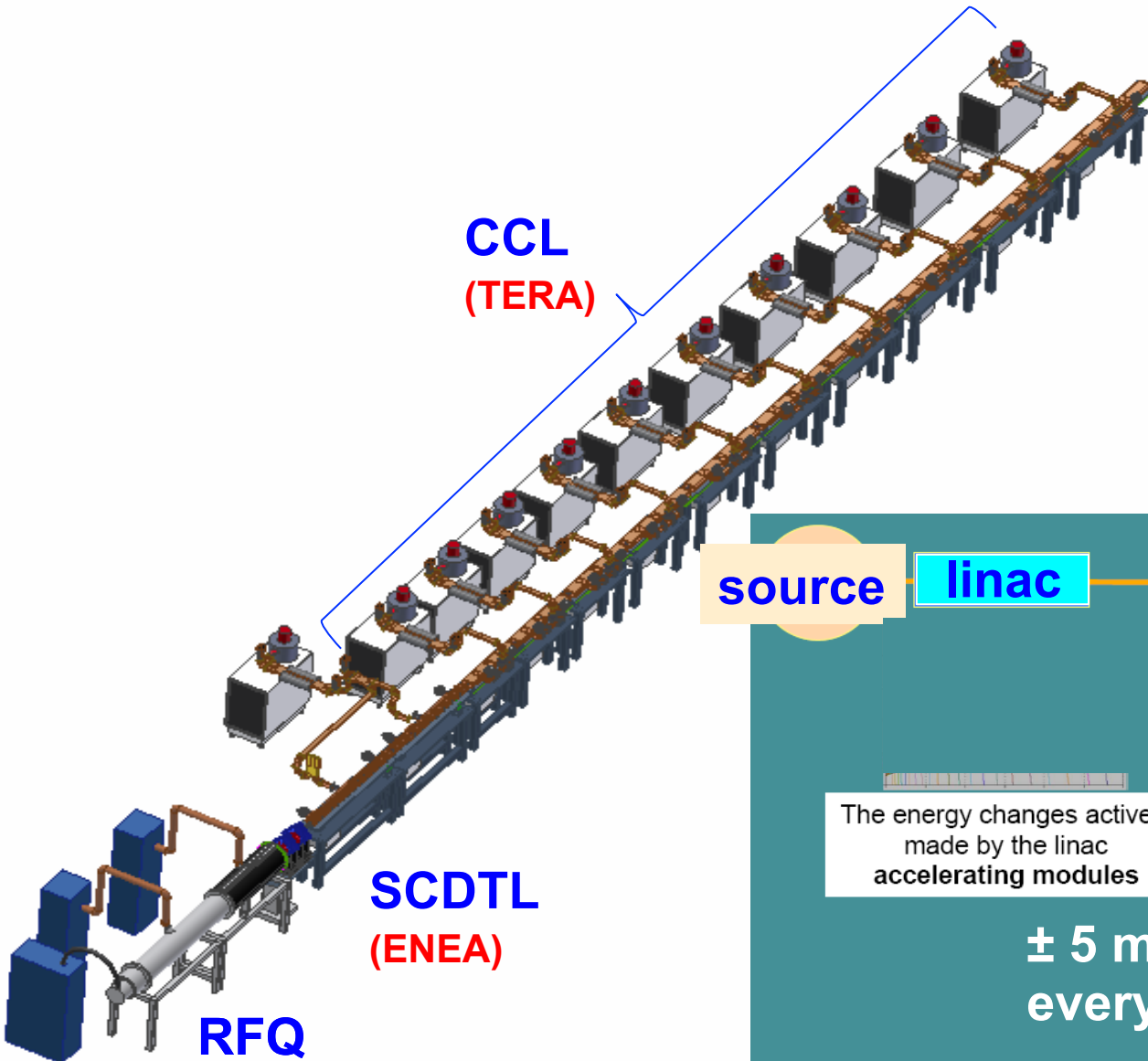
Linac for Image Guided Hadron Therapy

pulses @ 200times
per second



Linac for Image Guided Hadron Therapy

pulses @ 200times per second

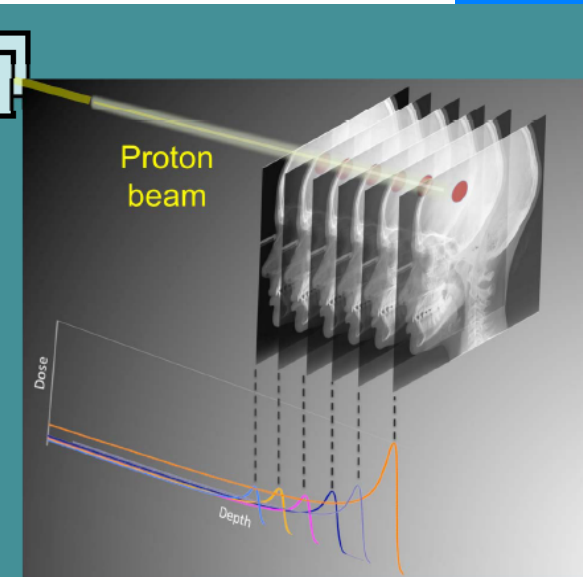


source

linac

The energy changes actively made by the linac accelerating modules

± 5 mm every pulse



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.