Medical Applications of Particle Physics

Saverio Braccini

TERA
Foundation for Oncological Hadrontherapy

Outline

- Introduction: a short historical review
- Applications in medical diagnostics
- Applications in cancer radiation therapy
  - Conventional radiation therapy
  - Hadrontherapy, the new frontier of cancer radiation therapy
- Conclusions and outlook

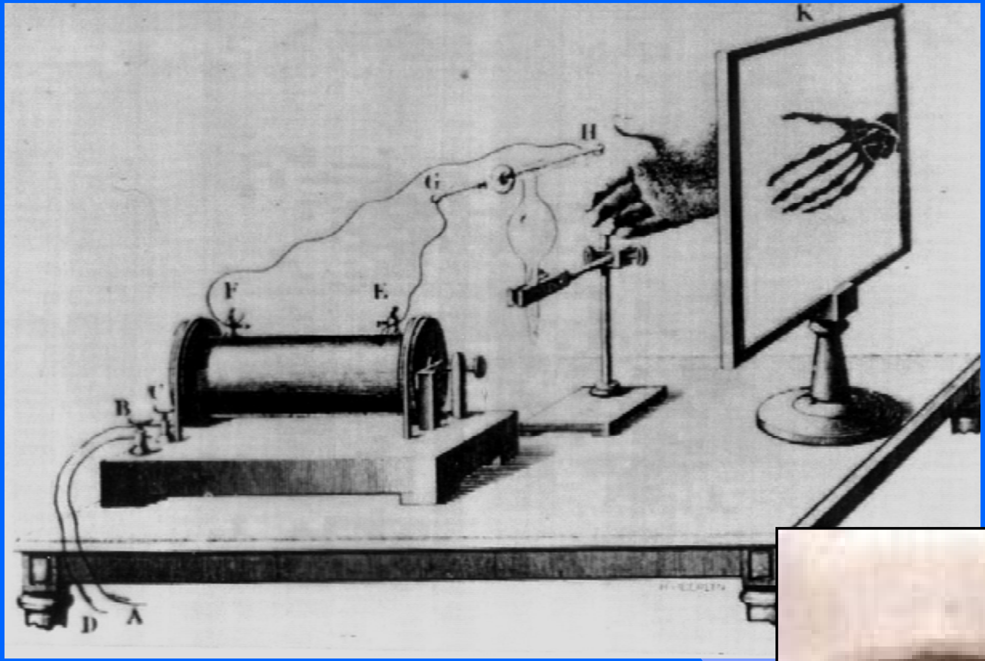
Introduction

Fundamental research in particle physics and medical applications

The starting point

• **November 1895 : discovery of X rays**

Wilhelm Conrad Röntgen



• **December 1895 : first radiography**

The beginning of modern physics and medical physics

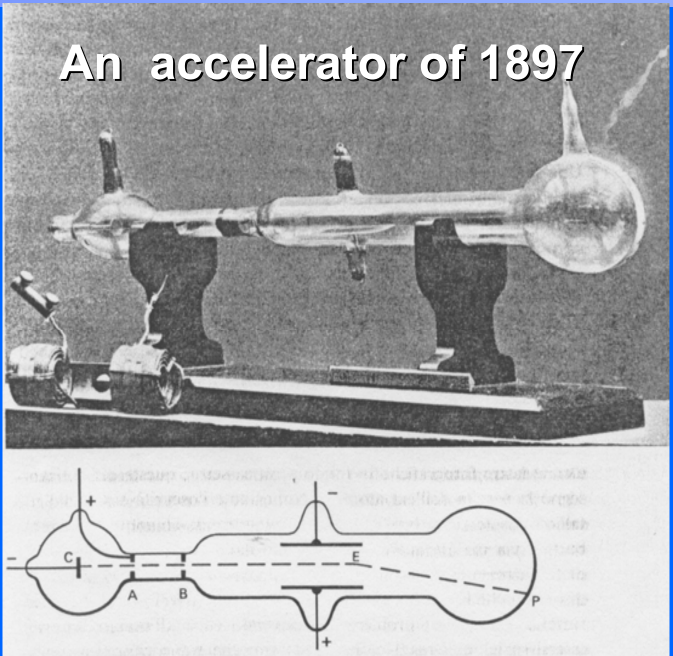
Wilhelm Conrad Röntgen

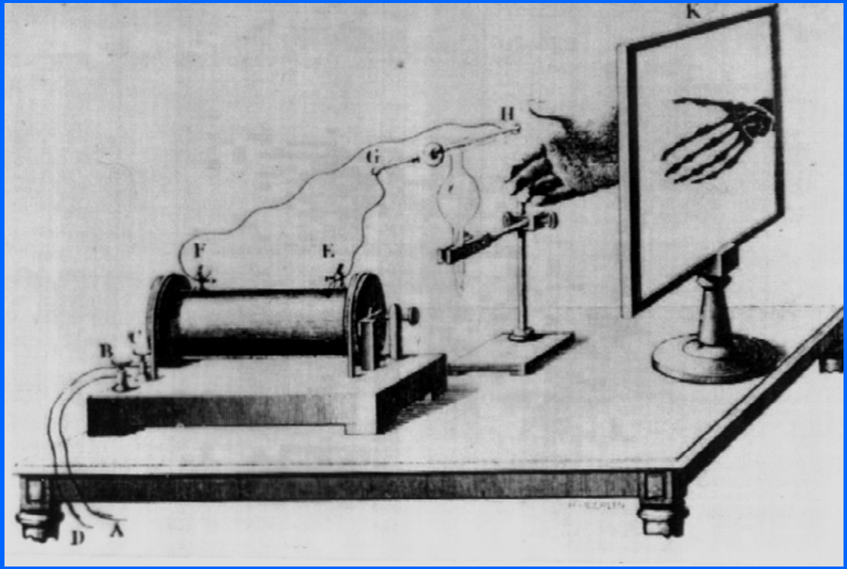
1895

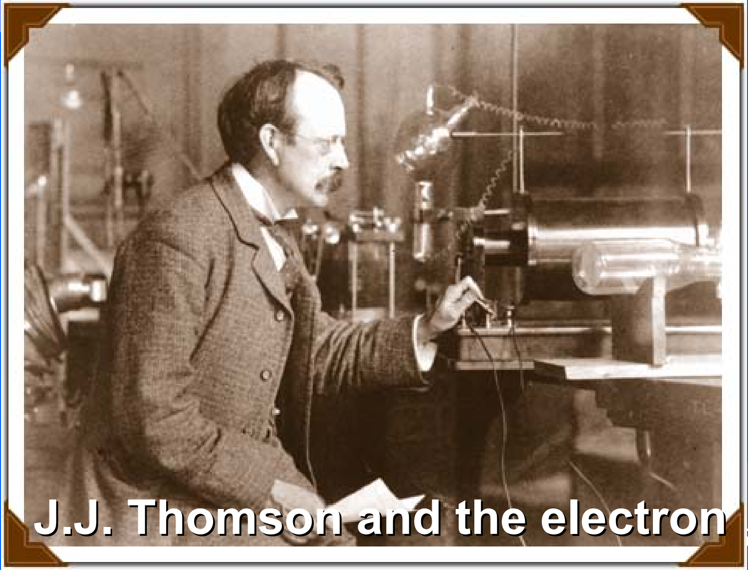
discovery of X rays

1895 – starting date of four magnificent years in experimental physics

An accelerator of 1897

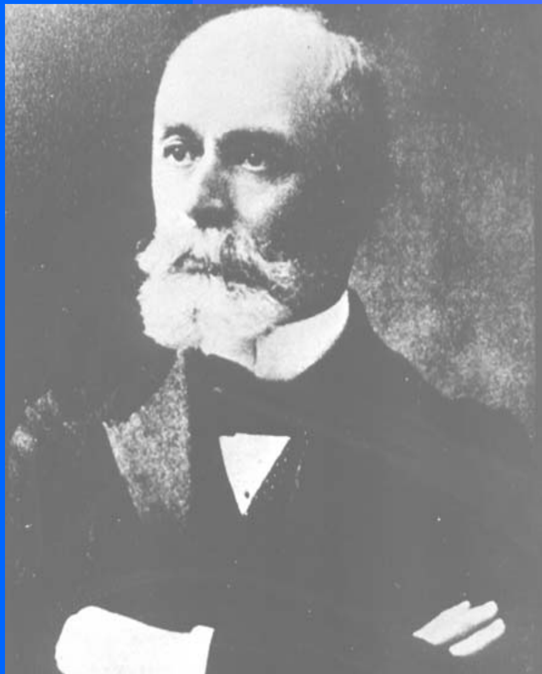






J.J. Thomson and the electron

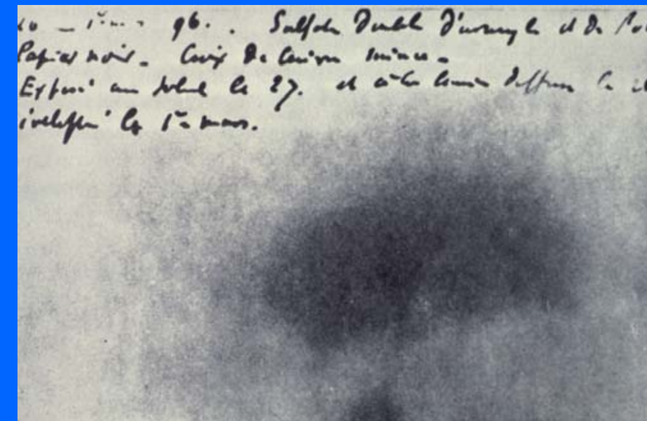
The beginning of modern physics and medical physics



Henri Becquerel
(1852-1908)

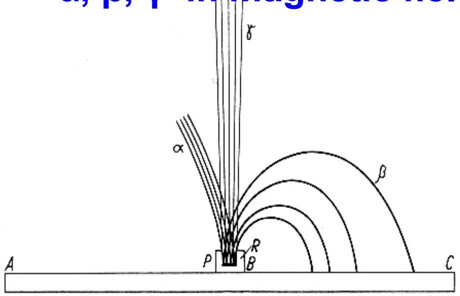
1896:

Discovery of natural radioactivity



Thesis of Mme. Curie – 1904

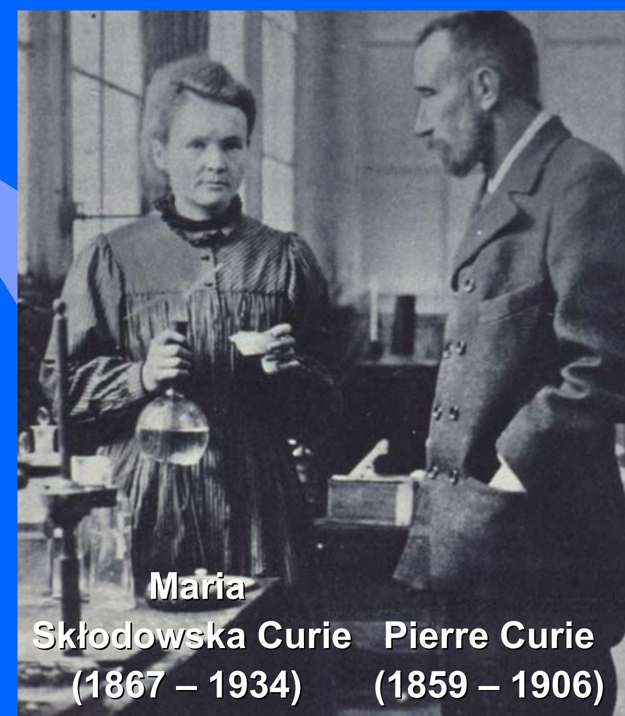
α, β, γ in magnetic field



About one hundred years ago

1898

Discovery of radium



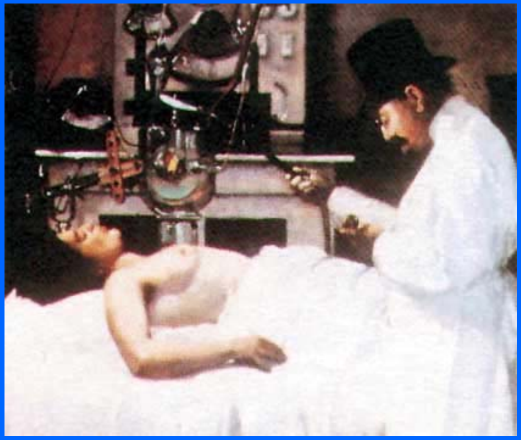
Maria Skłodowska Curie (1867 – 1934)

Pierre Curie (1859 – 1906)

First applications in cancer therapy

Basic concept

Local control of the tumour



1908 : first attempts of skin cancer radiation therapy in France ("*Curiethérapie*")

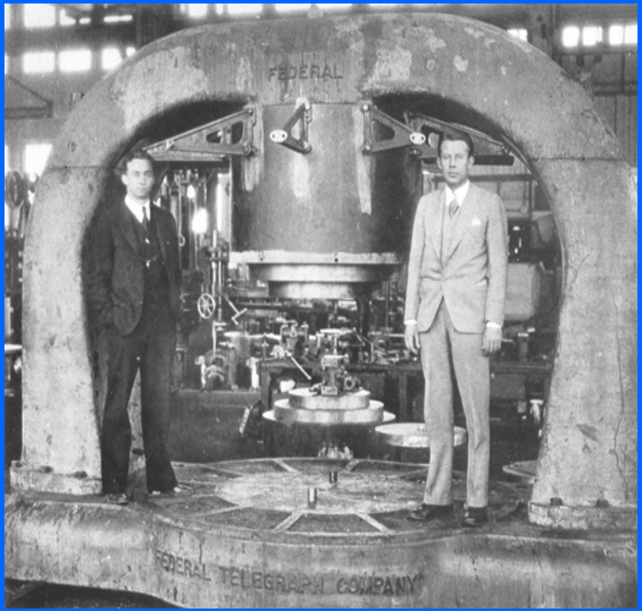
A big step forward…

…in physics and in

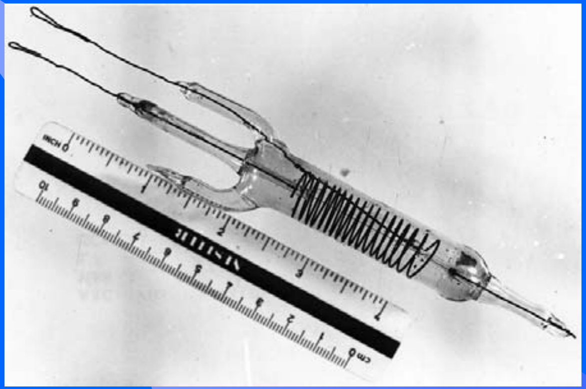
- Medical diagnostics
- Cancer radiation therapy

due to the development of three fundamental tools

- Particle accelerators
- Particle detectors
- Computers



M. S. Livingston and E. Lawrence with the 25 inches cyclotron

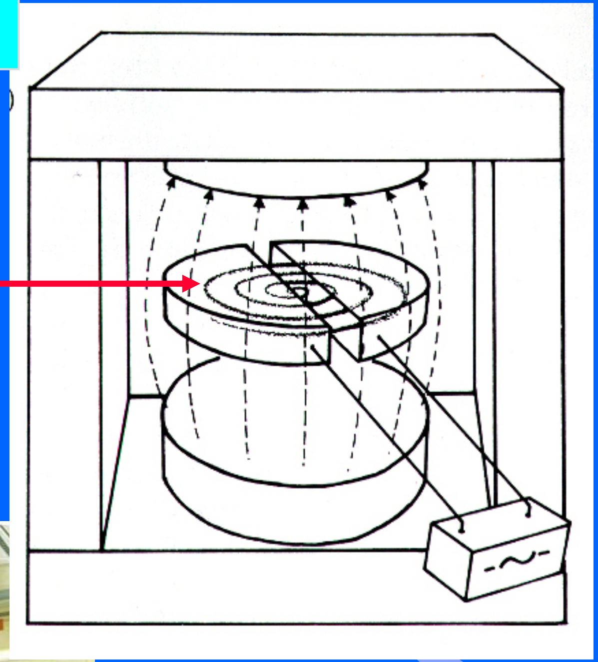


Geiger-Müller counter built by E. Fermi and his group in Rome

1930: invention of the cyclotron

1930: the beginning of four other magnificent years

Spiral trajectory of an accelerated nucleus



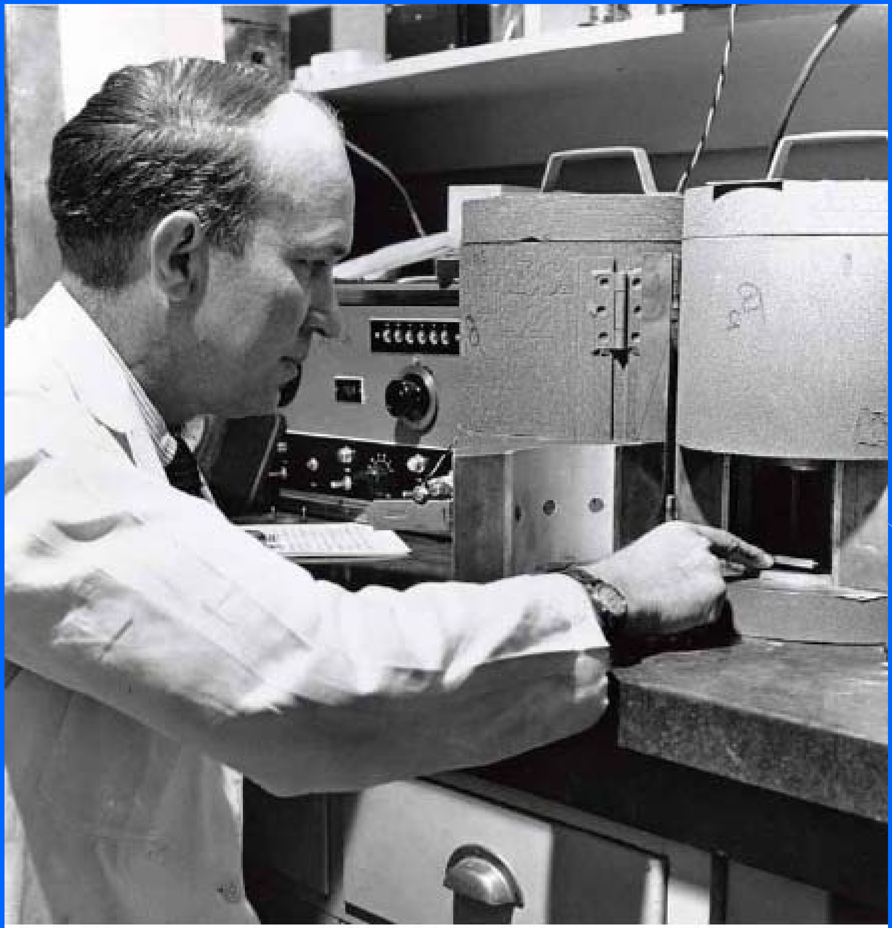
Modern cyclotron

Ernest Lawrence

(1901 – 1958)

A copy is on display at CERN Microcosm

The Lawrence brothers



John H. Lawrence made the first clinical therapeutic application of an artificial radionuclide when he used phosphorus-32 to treat leukemia. (1936)

- John Lawrence, brother of Ernest, was a medical doctor
- They were both working in Berkley
- First use of artificially produced isotopes for medical diagnostics
- Beginning of nuclear medicine

An interdisciplinary environment helps innovation!

Discovery of the neutron

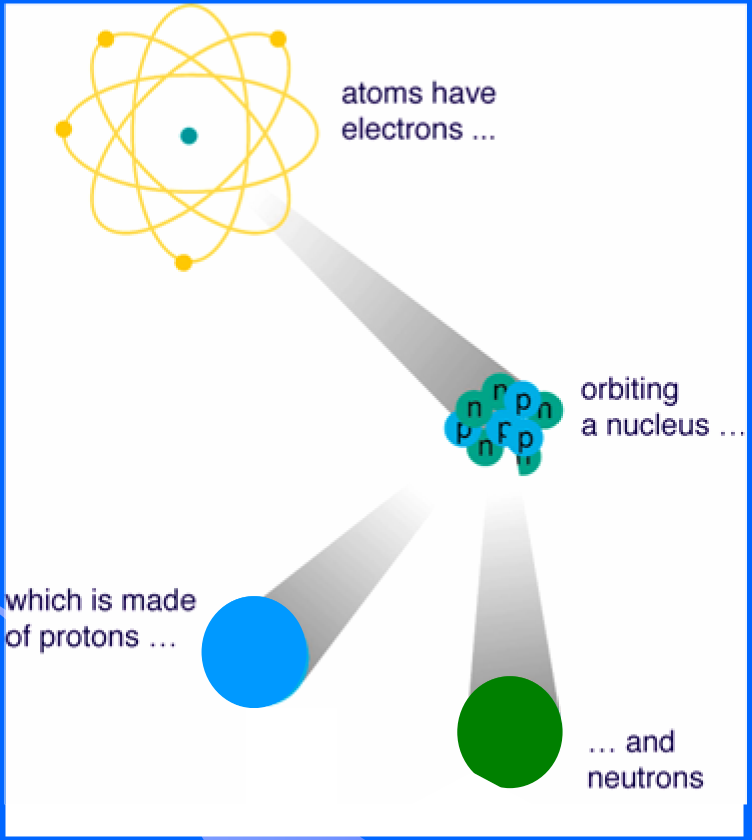
1932

James Chadwick

(1891 – 1974)

Student of

Ernest Rutherford

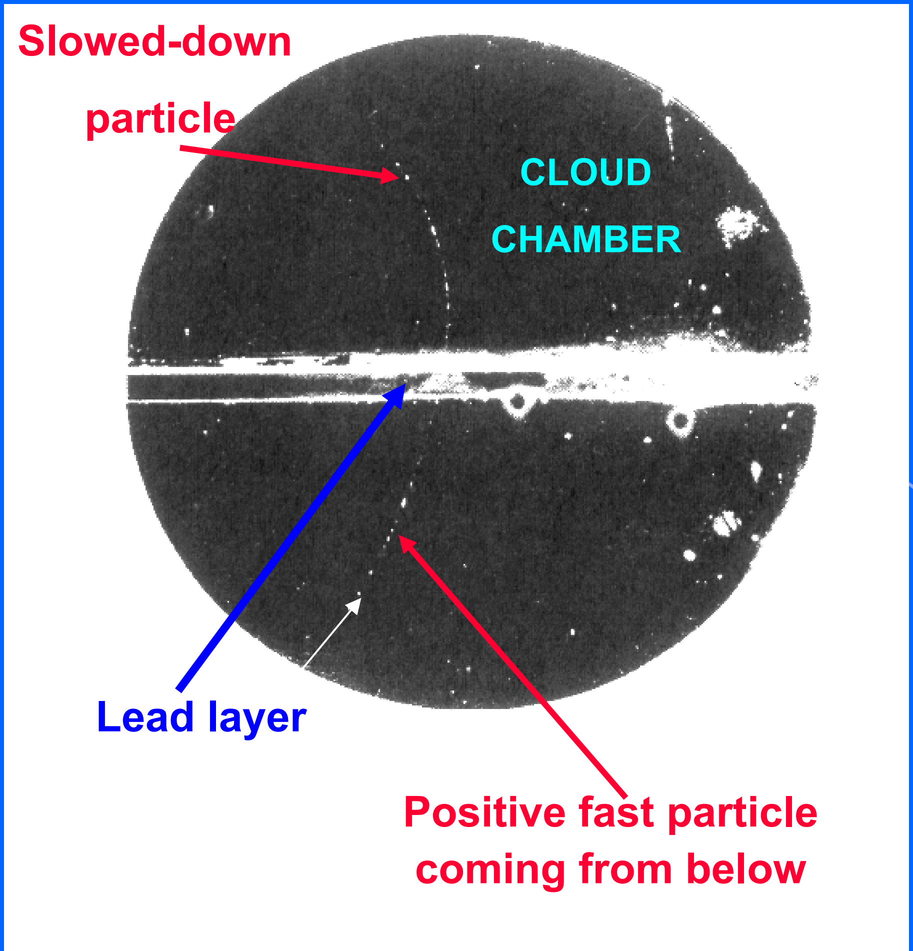


Neutrons are used today to

- Produce isotopes for medical diagnostics and therapy
- Cure some kind of cancer

Matter and antimatter...

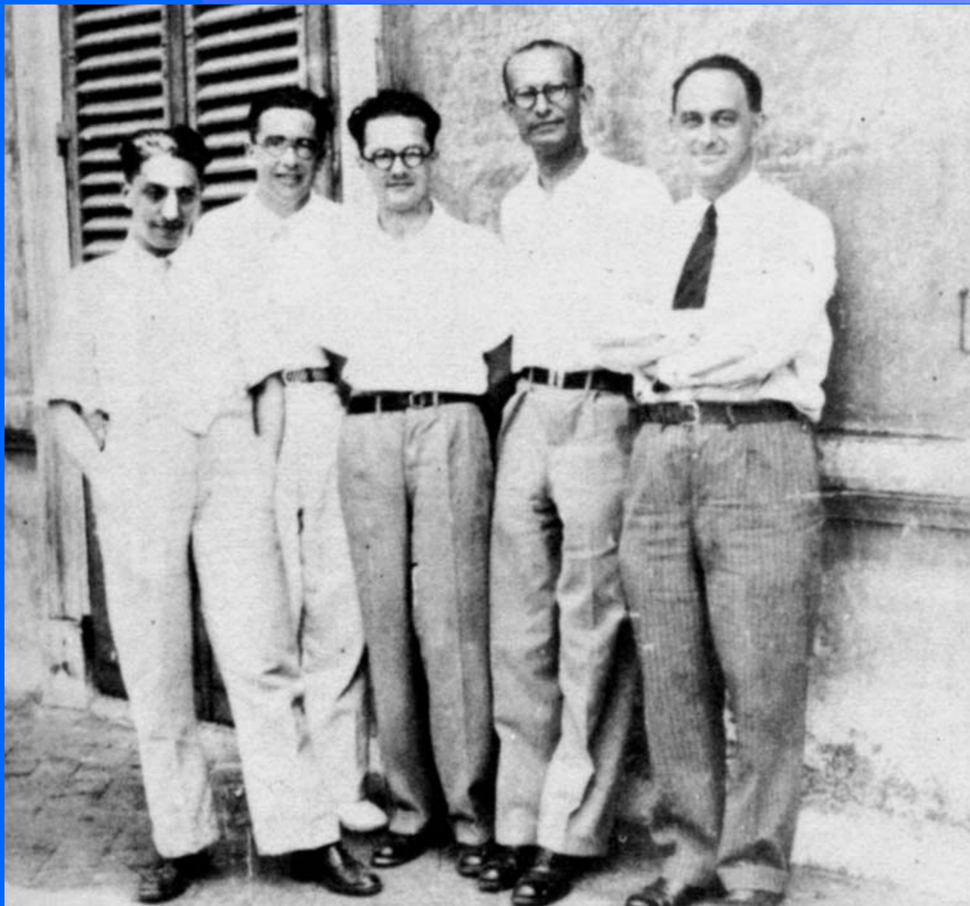
1932 – discovery of antimatter: the positron



Carl D. Anderson - Caltech

The positron is at the basis of Positron Emission Tomography (PET)

Discovery of the effectiveness of slow neutrons



O. D'Agostino E. Segrè E. Amaldi F. Rasetti E. Fermi

1934

First radioisotope of Iodine

among fifty new artificial species

RADIOATTIVITÀ « BETA » PROVOCATA
DA BOMBARDAMENTO DI NEUTRONI. — III.

E. AMALDI, O. D'AGOSTINO, E. FERMI, F. RASETTI, E. SEGRÈ

« Ric. Scientifica », 5 (1), 452–453 (1934).

Sono state proseguite ed estese le esperienze di cui alle Note precedenti [1] coi risultati che ricordiamo appresso.

Idrogeno – Carbonio – Azoto – Ossigeno. – Non dànno effetto apprezzabile. Sono stati esaminati paraffina irradiata al solito modo per 15 ore con una sorgente di 220 mC, acqua irradiata per 14 ore con 670 mC e carbonato di guanidina irradiato per 14 ore con 500 mC.

Fluoro. – Il periodo del Fluoro è sensibilmente minore di quanto indicato precedentemente e cioè di pochi secondi.

Magnesio. – Il Magnesio ha due periodi, uno di circa 40 secondi e uno più lungo.

Alluminio. – Oltre al periodo di 12 minuti segnalato precedentemente ve ne è anche un altro dell'ordine di grandezza di un giorno. L'attività corrispondente a questo secondo periodo segue le reazioni chimiche caratteristiche del Sodio. Si tratta probabilmente di un Na^{24}.

Zolfo. – Il periodo dello S è assai lungo, certamente di molti giorni. L'attività si separa con le reazioni caratteristiche del Fosforo.

Cloro. – Si comporta analogamente allo S. Anche qui si può separare

corrispondente a questo secondo periodo segue le reazioni chimiche caratteristiche del Sodio. Si tratta probabilmente di un Na^{24}.

Zolfo. – Il periodo dello S è assai lungo, certamente di molti giorni. L'attività si separa con le reazioni caratteristiche del Fosforo.

Cloro. – Si comporta analogamente allo S. Anche qui si può separare
un principio attivo; probabilmente si tratta di un P^{32} identico a quello che si ricava dallo S.

Manganese. – Ha un effetto debole con un periodo di circa 15 minuti.

Cobalto. – Ha un effetto di 2 ore. Il principio attivo si comporta come Mn. Data l'identità di periodo e di comportamento chimico si tratta quasi certo di un Mn^{56} identico a quello che si forma irradiando il Fe.

Zinco. – Ha due periodi, uno di 6 minuti e uno assai più lungo.

Gallio. – Periodo 30 minuti.

Bromo. – Ha due periodi, uno di 30 minuti e l'altro di 6 ore. L'attività corrispondente al periodo lungo e probabilmente anche l'altra, seguono chimicamente il Br.

Palladio. – Periodo di alcune ore.

Jodio. – Periodo 30 minuti. L'attività segue chimicamente lo Jodio.

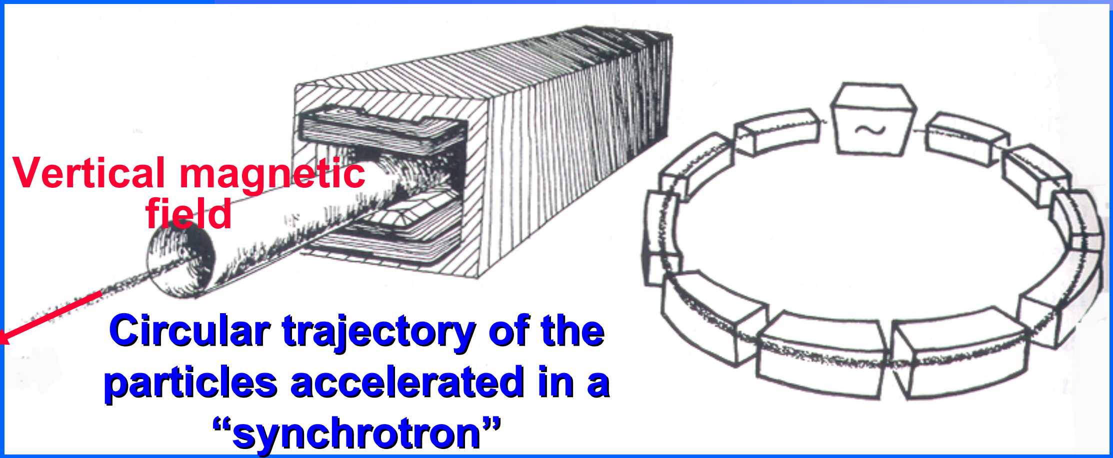
Praseodimio. – Ha due periodi. Uno di 5 minuti e l'altro più lungo.

Neodimio. – Periodo 55 minuti.

Samario. – Ha due periodi uno di 40 minuti e uno più lungo.

Oro. – Periodo dell'ordine di grandezza di 1 o 2 giorni.

Four other crucial years: the synchrotron



1944

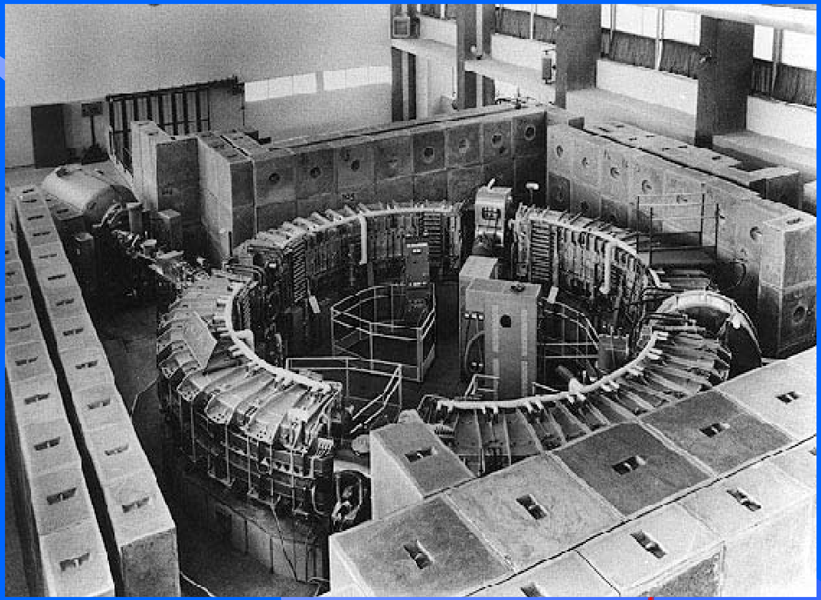
principle of phase stability

1 GeV electron synchrotron

Frascati - INFN - 1959

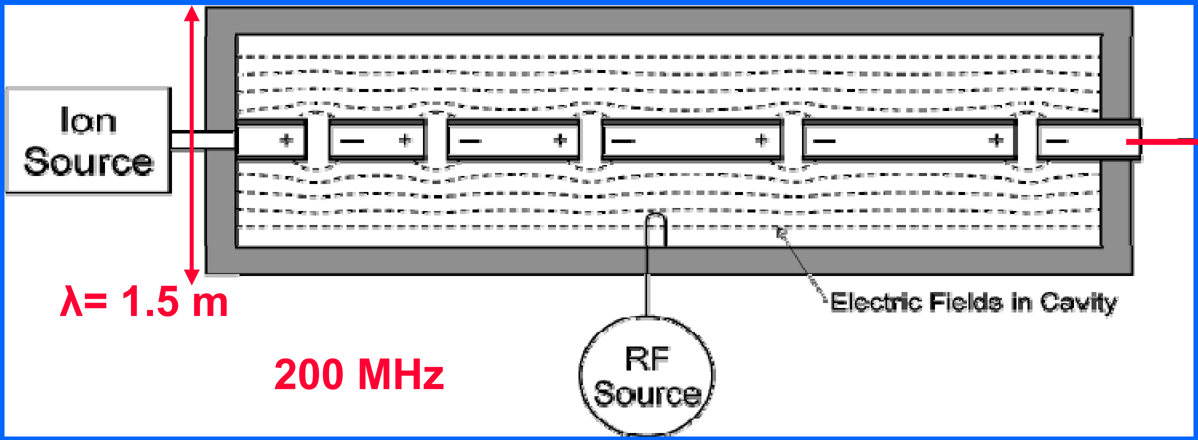
Veksler visits McMillan

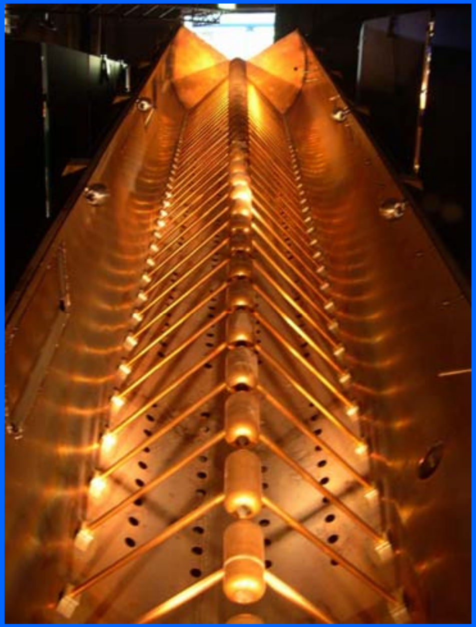
1959 - Berkeley



Radio-frequency linacs for protons and ions

Linear accelerator (linac)





100 MeV linac on display
at CERN Microcosm

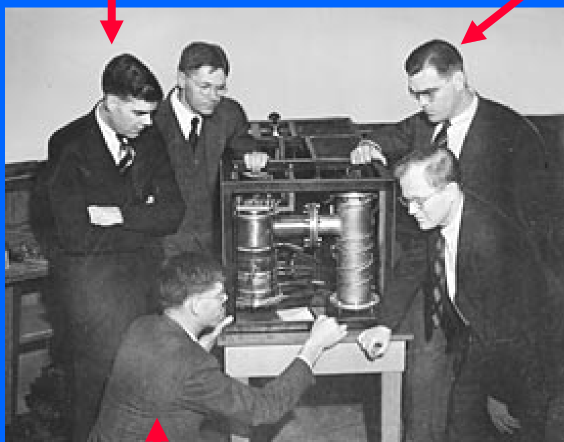
L. Alvarez

1946 – Drift Tube Linac

The electron linac

Sigurd Varian

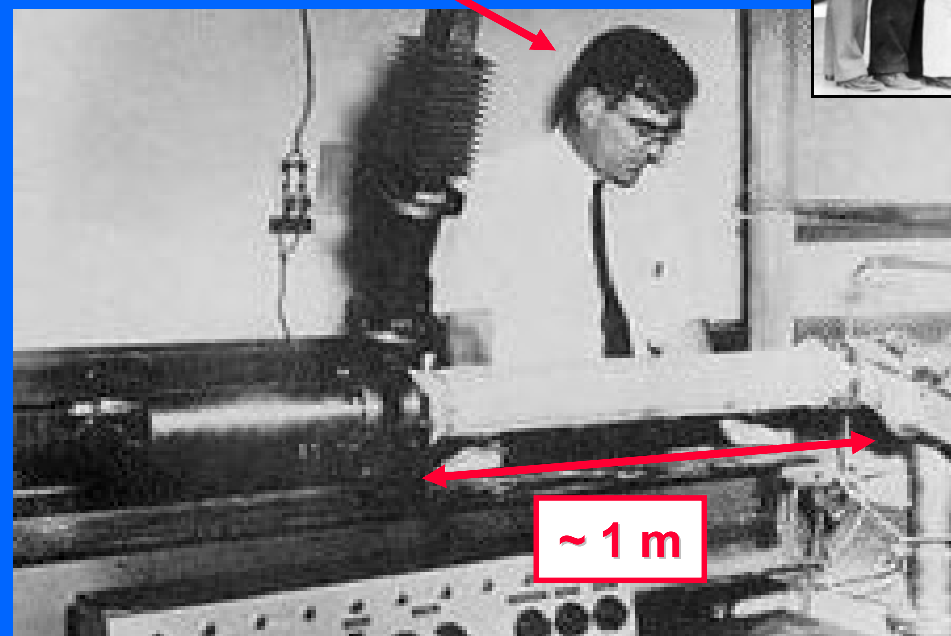
William W. Hansen



Russell Varian

1939

Invention of the klystron



The electron linac is used today in hospital based conventional radiation therapy facilities

1947
first linac for electrons
4.5 MeV and 3 GHz

The beginning of CERN 50 years ago

Isidor Rabi

UNESCO talk in 1950

1952: Pierre Auger

Edoardo Amaldi

Secretary General

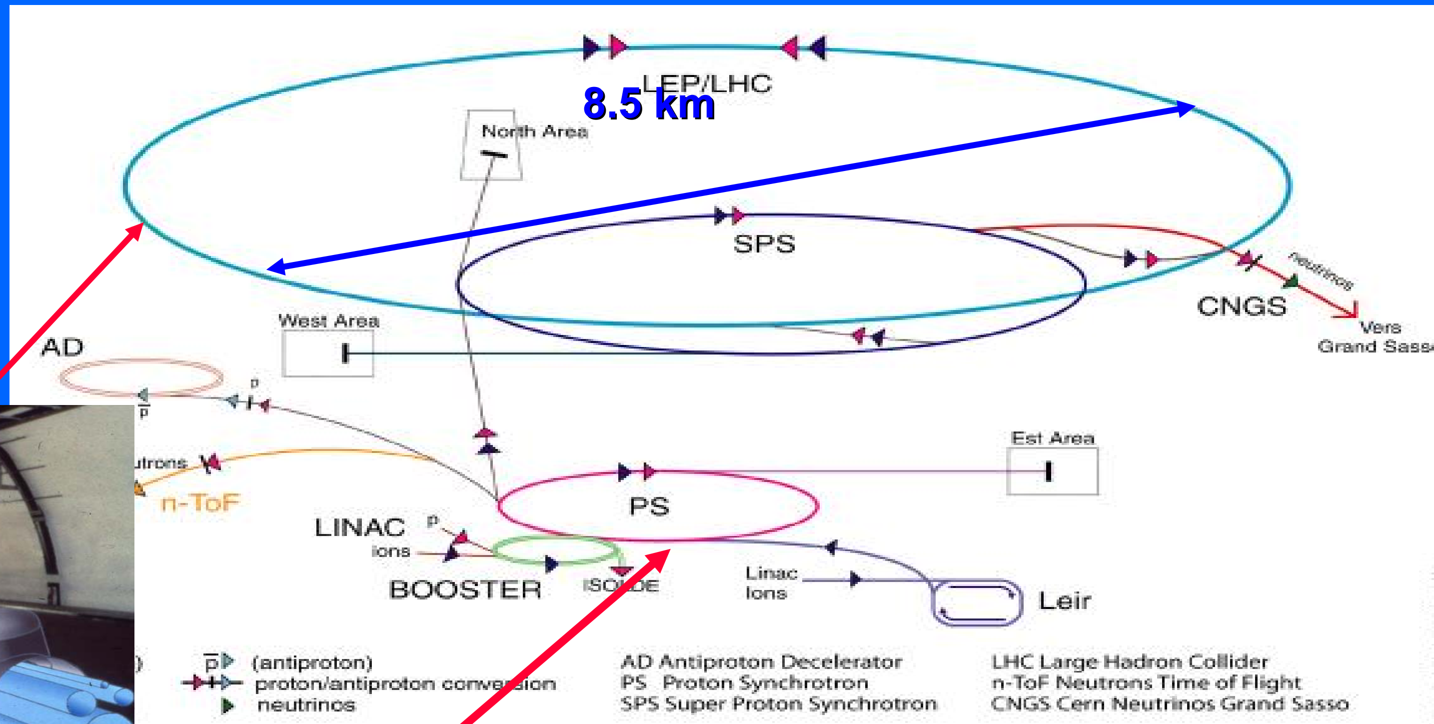
1952-54

at the meeting that created the provisional CERN

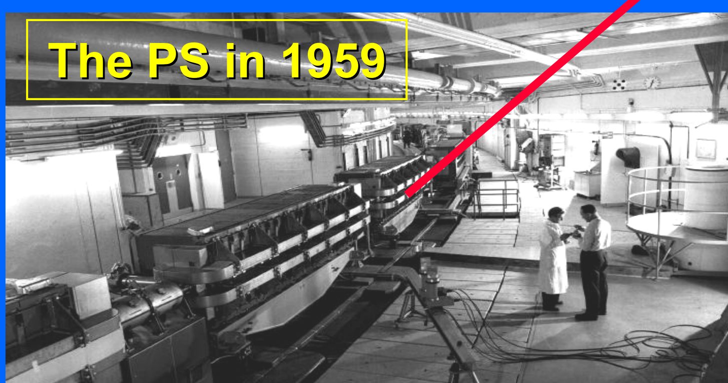
At CERN we have linacs and strong-focusing synchrotrons

Large Hadron Collider (7+7) TeV

2007



The PS in 1959



In 1952 the "strong-focusing" method invented at BNL (USA) was chosen for the CERN PS

Accelerators running in the world

CATEGORY OF ACCELERATORS	NUMBER IN USE (*)
High Energy acc. (E >1GeV)	~120
Synchrotron radiation sources	>100
Medical radioisotope production	~200
Radiotherapy accelerators	> 7500
Research acc. included biomedical research	~1000
Acc. for industrial processing and research	~1500
Ion implanters, surface modification	>7000
TOTAL	> 17500

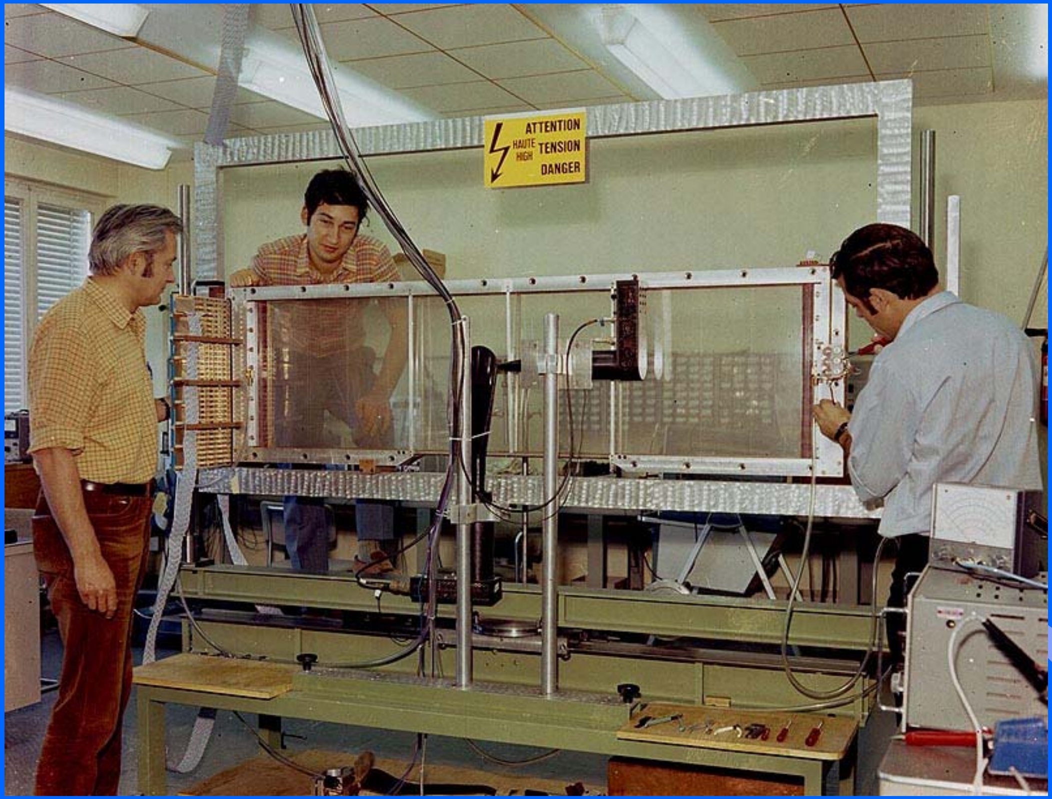
9000

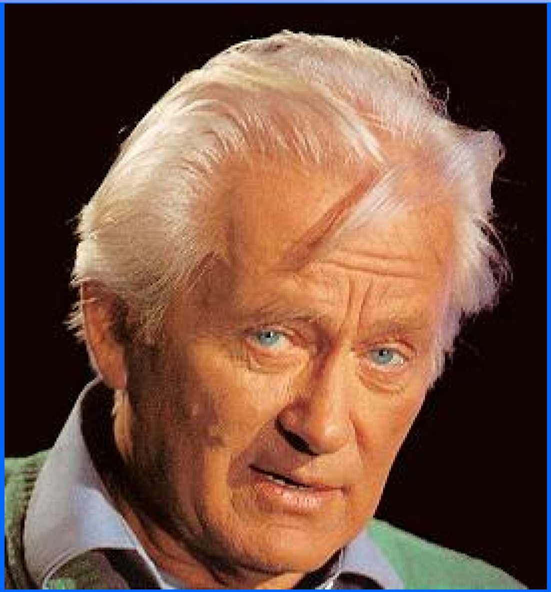
(*) W. Maciszewski and W. Scharf: Int. J. of Radiation Oncology, 2004

- **About half are used for bio-medical applications**

- They are the “eyes” of particle physicists
- A very impressive development in the last 100 years
  - From the Geiger counter to ATLAS and CMS !
- Crucial in many medical applications

One example: the multiwire proportional chamber





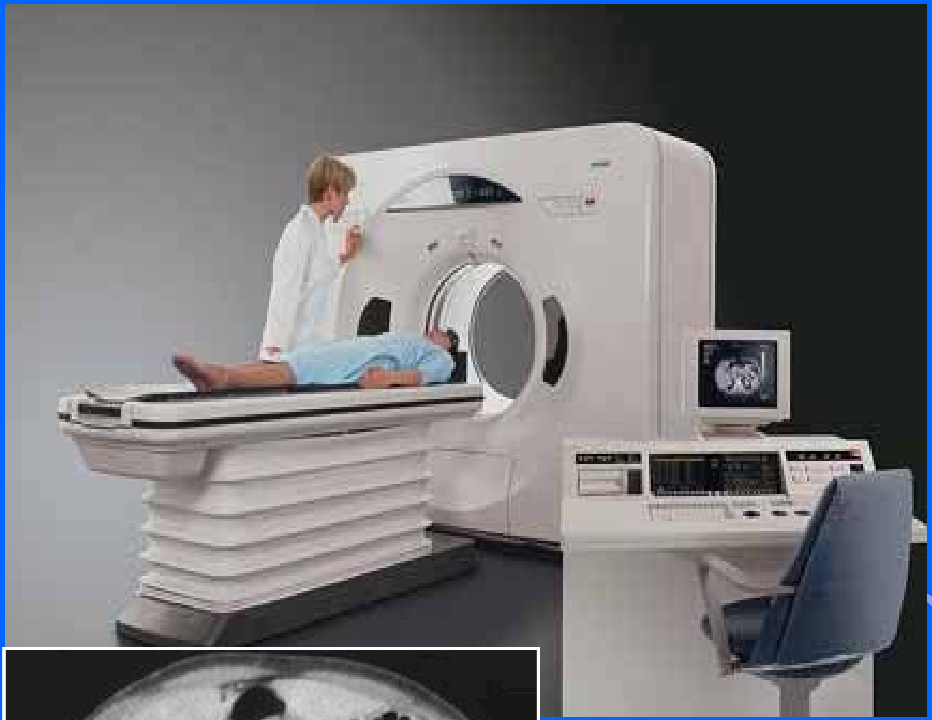
Georges Charpak, CERN physicist since 1959,

Nober prize 1992

- Invented in 1968, launched the era of fully electronic particle detection
- Used for biological research and could eventually replace photographic recording in applied radio-biology
- The increased recording speeds translate into faster scanning and lower body doses in medical diagnostic tools based on radiation or particle beams

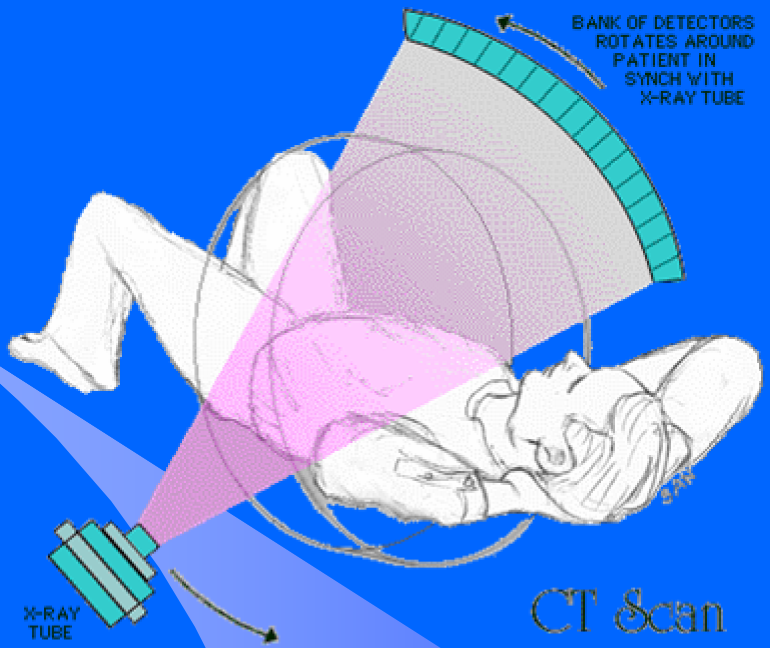
Applications in medical diagnostics

Diagnostics is essential!



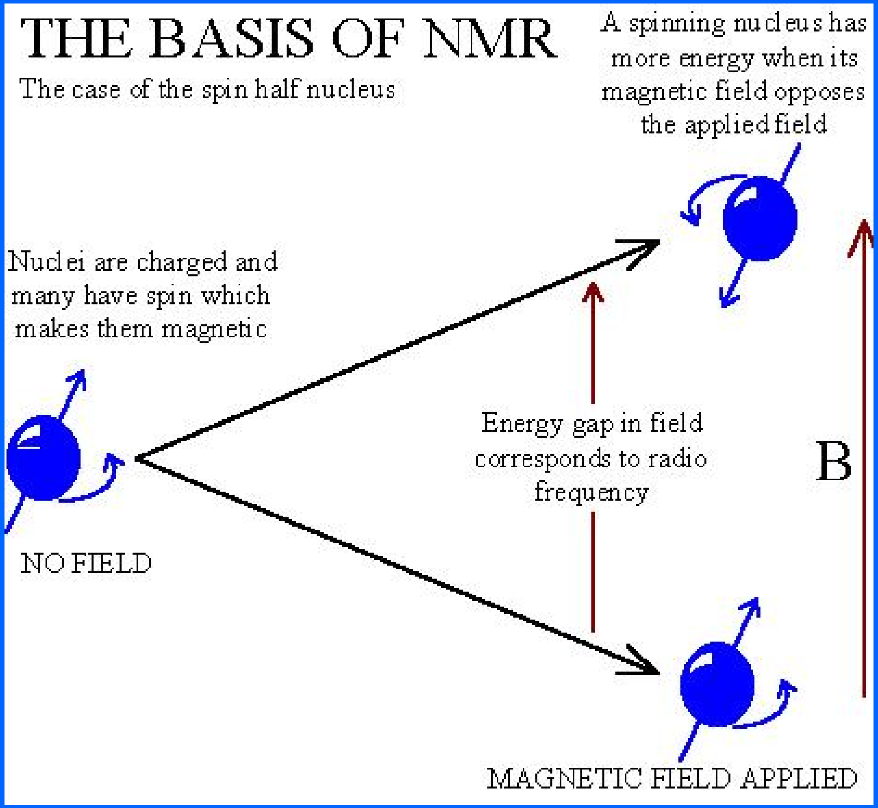
Abdomen

Computer Tomography (CT)



- Measurement of the electron density
- Information on the morphology

Nuclear Magnetic Resonance

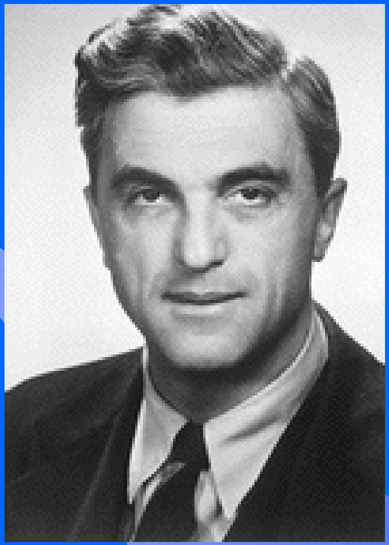


1938-1945

Felix Bloch and Edward Purcell

discover and study

NMR

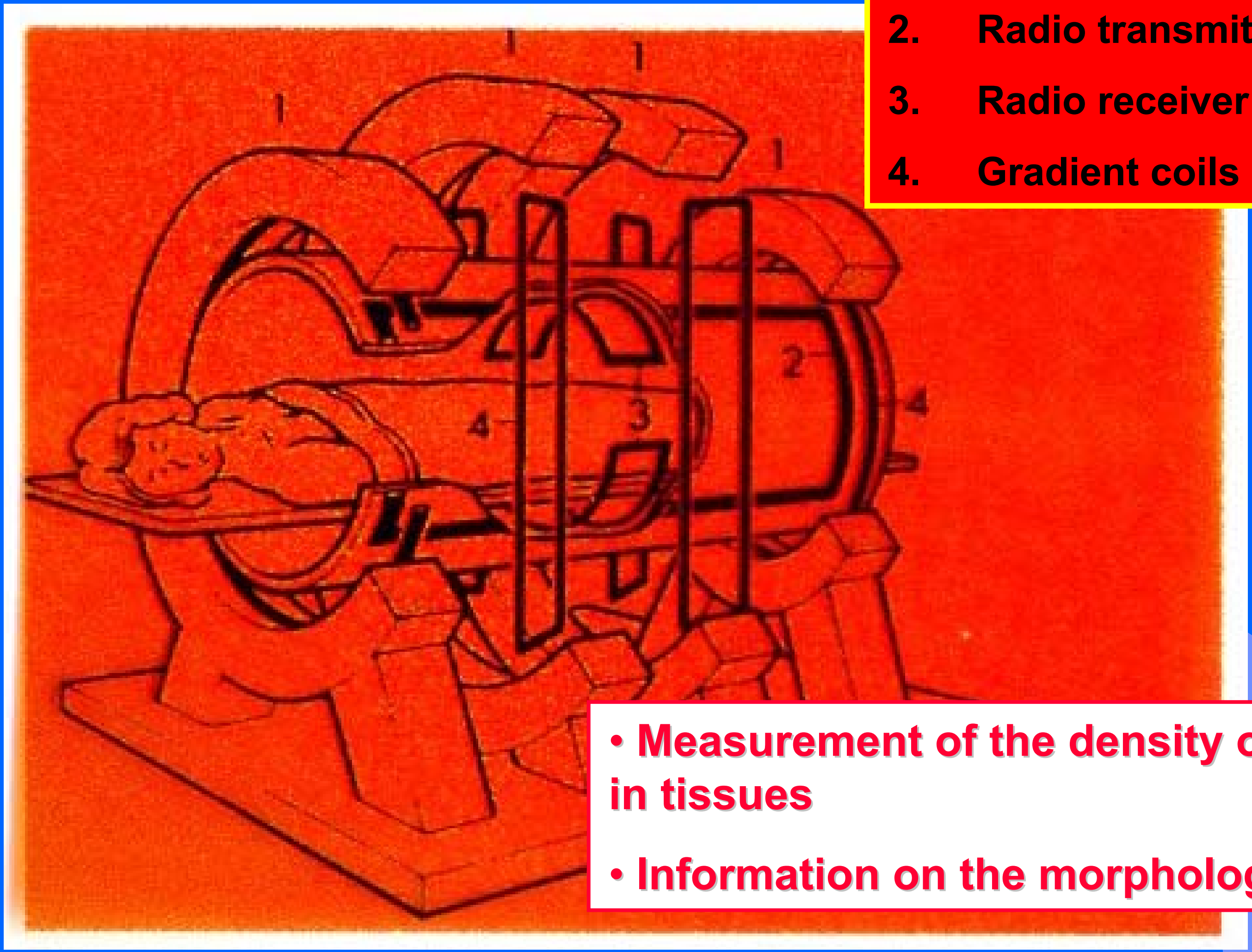


In 1954 Felix Bloch became

the first CERN Director General

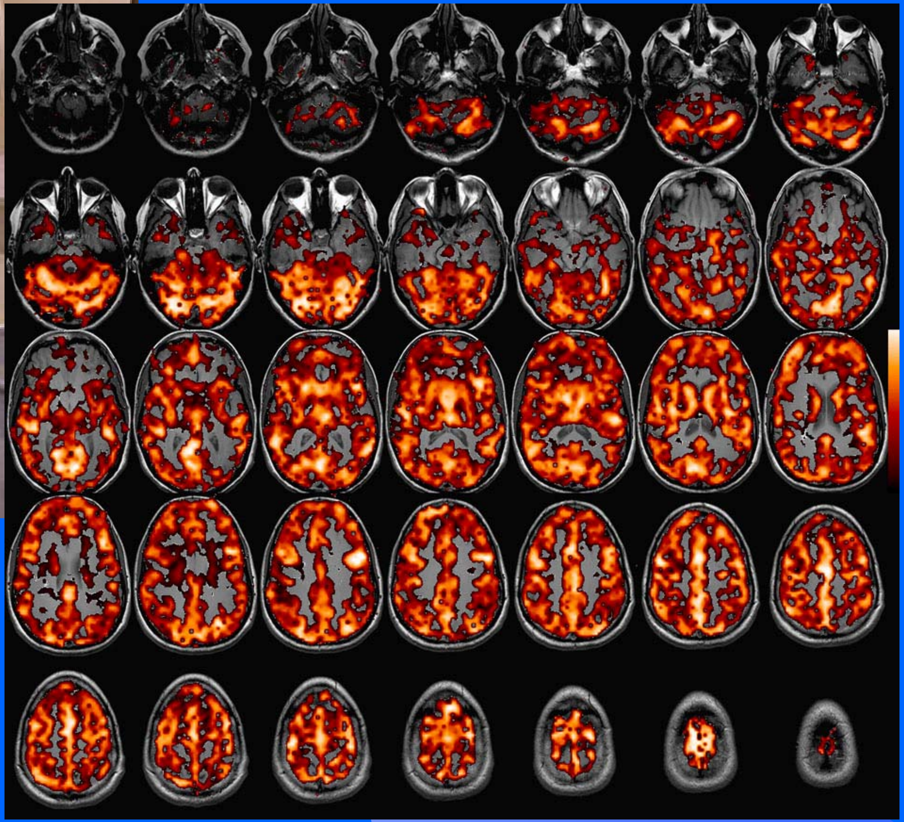
MRI = Magnetic Resonance Imaging

1. Main magnet (0.5-1 T)
2. Radio transmitter coil
3. Radio receiver coil
4. Gradient coils

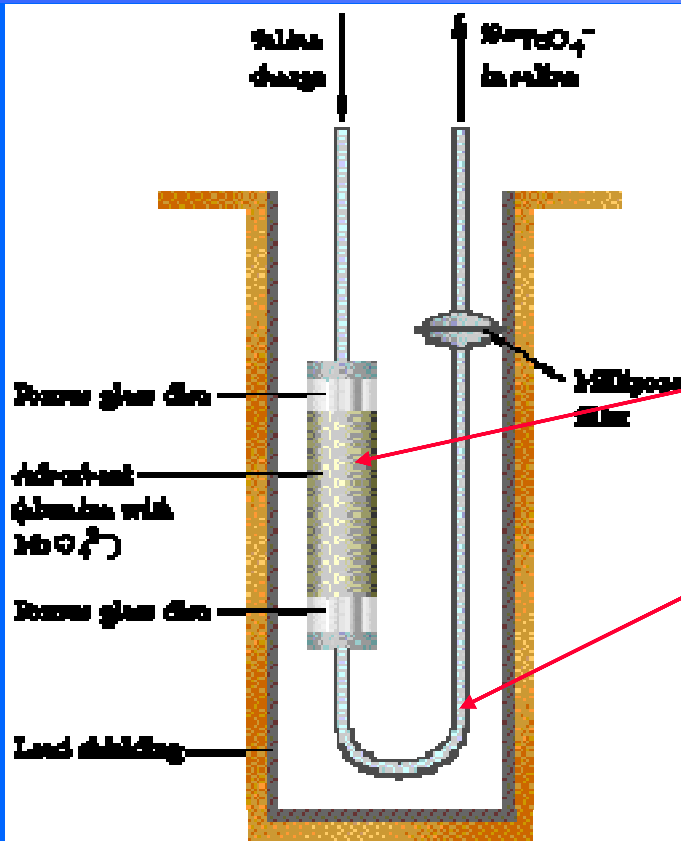


- Measurement of the density of the protons (water) in tissues
- Information on the morphology

A MRI scanner



SPECT = Single Photon Emission Computer Tomography

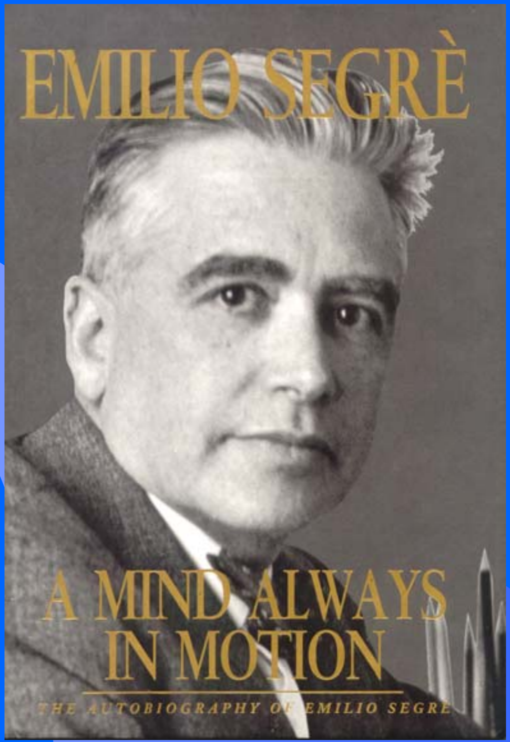


In reactors <u>slow neutrons</u> produce

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

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

gamma of 0.14 MeV

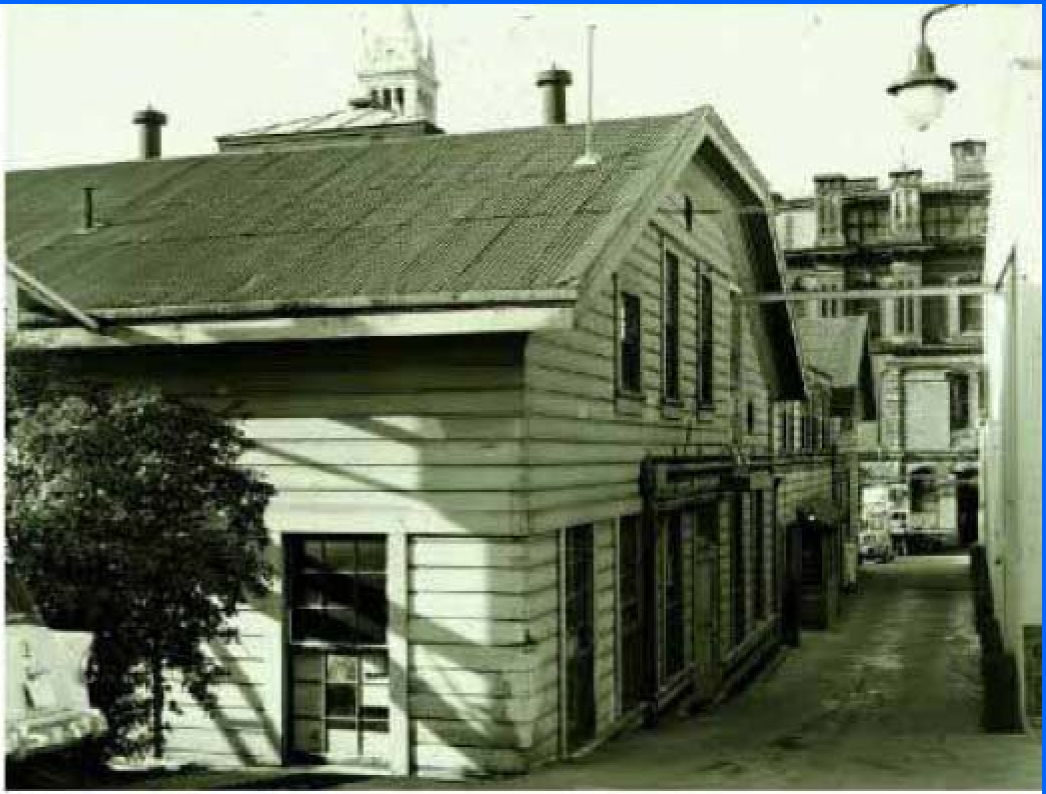


Emilio Segrè

1937: Discovery of element 43 “Technetium” ^{97}Tc(2.6 My)

1938: discovery of ^{99m}Tc with E. McMillan

The discovery of technetium



The Rad Lab is officially established within the UC Physics Department with Lawrence as director; in Italy, Segrè examines an "invaluable gift" of material irradiated by the 27-inch cyclotron and discovers the first artificial element, later named technetium.

SPECT scanner

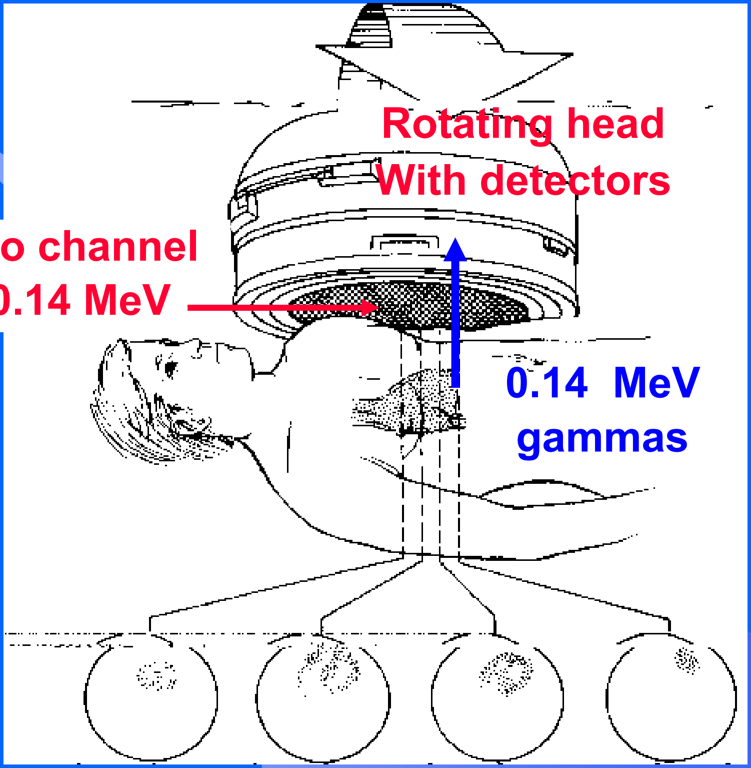
85% of all nuclear medicine examinations use technetium produced by slow neutrons in reactors

- Measurement of the density the molecules which contain technetium
- Information on morphology and/or metabolism

… liver

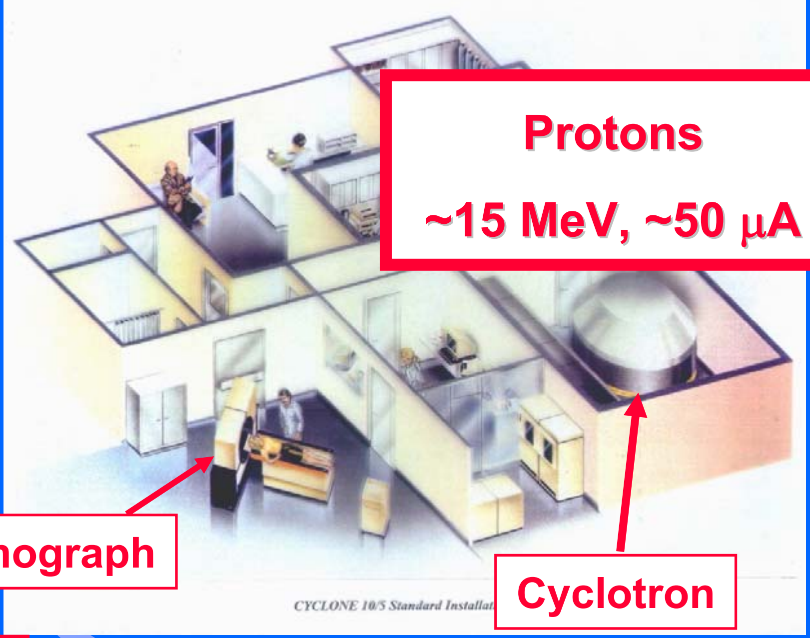
lungs

bones …



Positron Emission Tomography (PET)

- FDG with ^{18}F is the most used drug (half life 110 minutes)
- Measurement of the density of ^{18}F through back-to-back gamma detection
- Information on metabolism



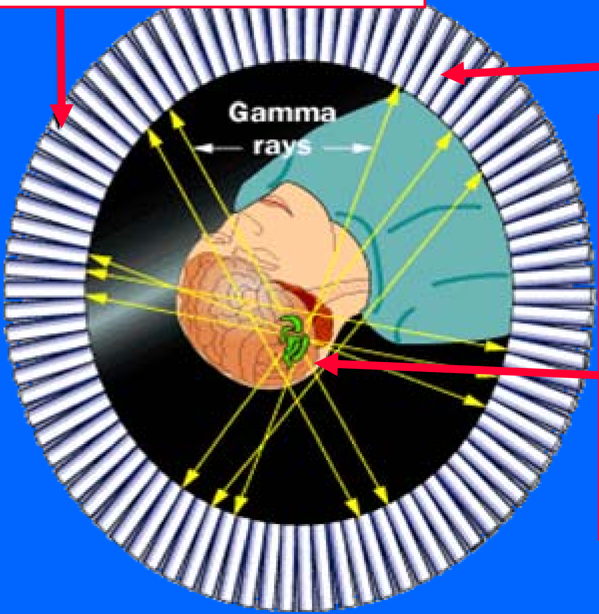
Protons

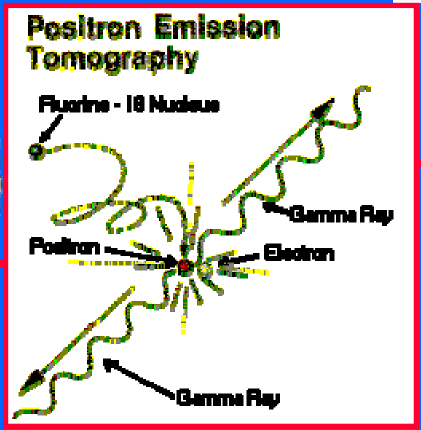
~15 MeV, ~50 μA

PET tomograph

Cyclotron

Gamma ray detectors (Ex. BGO crystals)

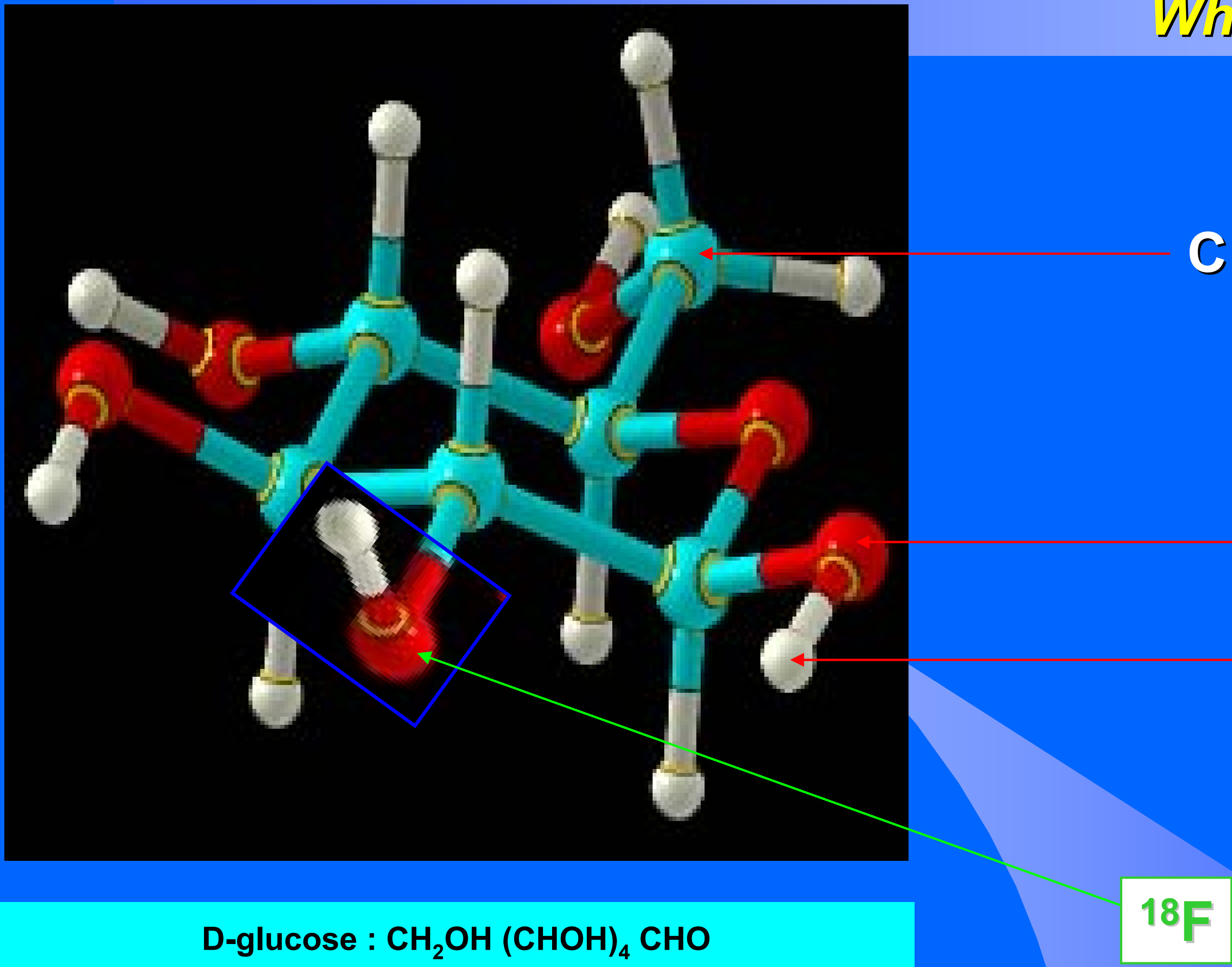




PET image

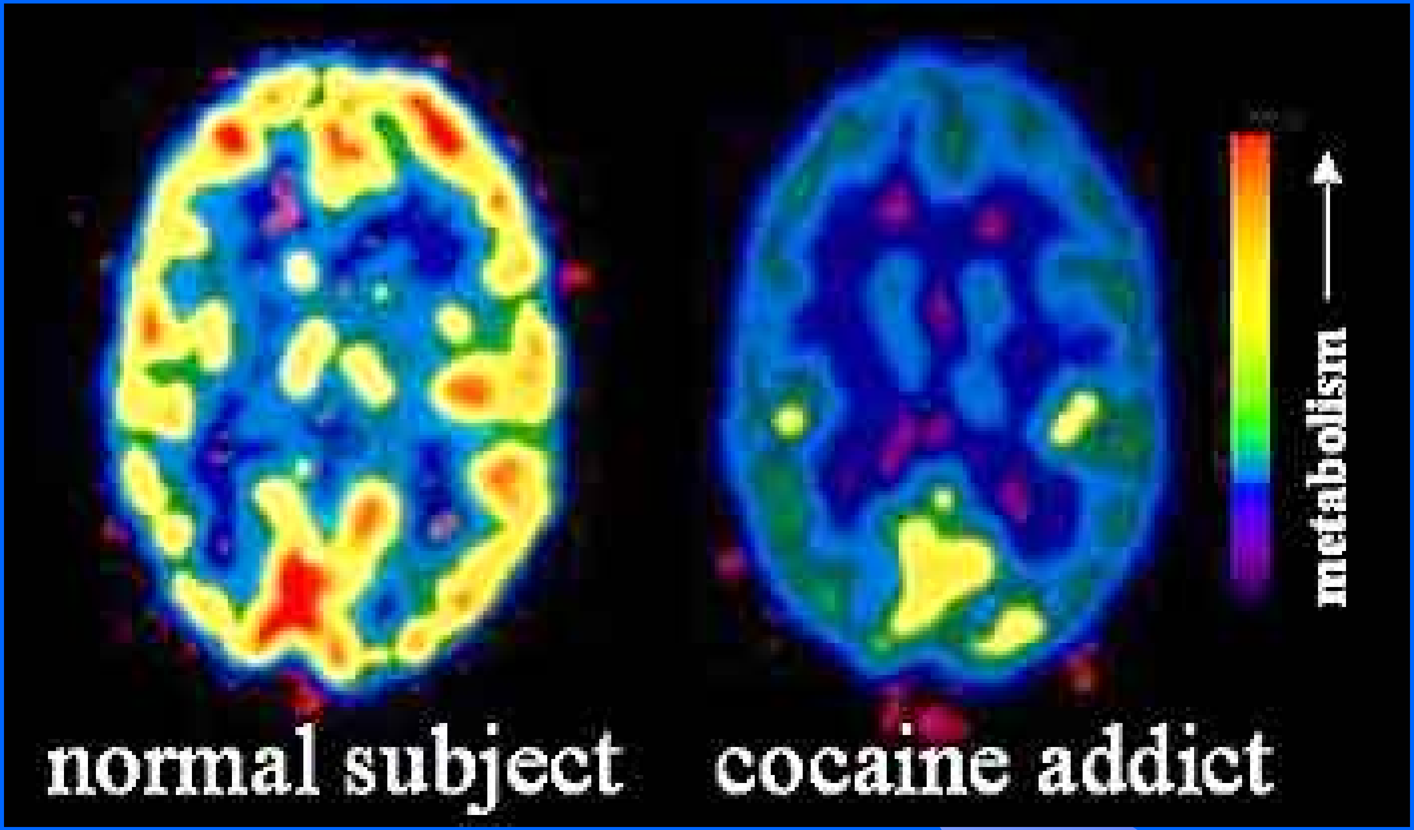
CT-PET

What is FDG?



D-glucose : $CH_2OH\ (CHOH)_4\ CHO$

PET: one example

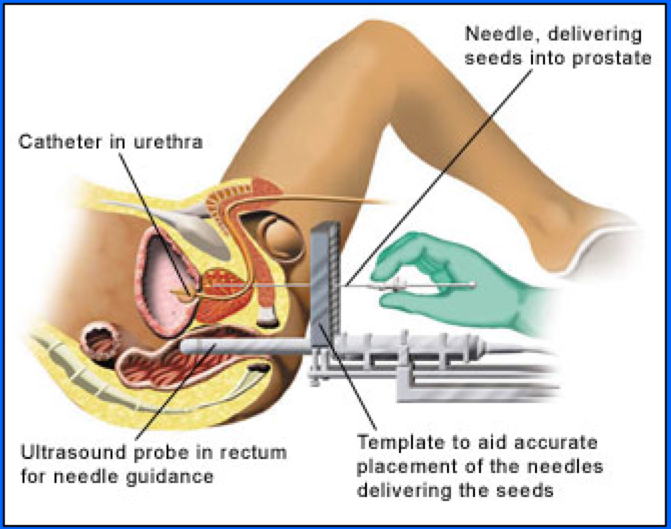


- 18FDG/PET images
- The cocaine addict has depressed metabolism !

Applications in cancer radiation therapy

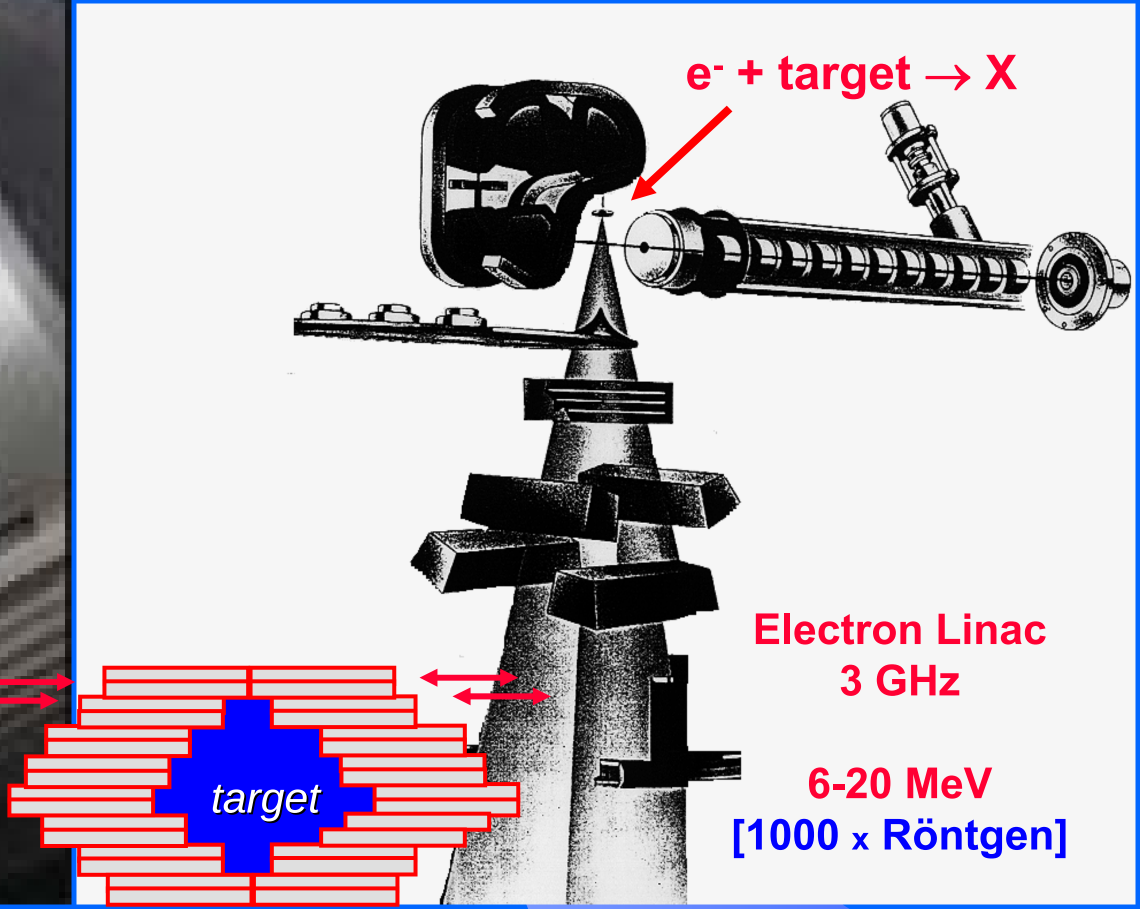
Methods

- Brachitherapy
  - Insertion of radiation sources in the body



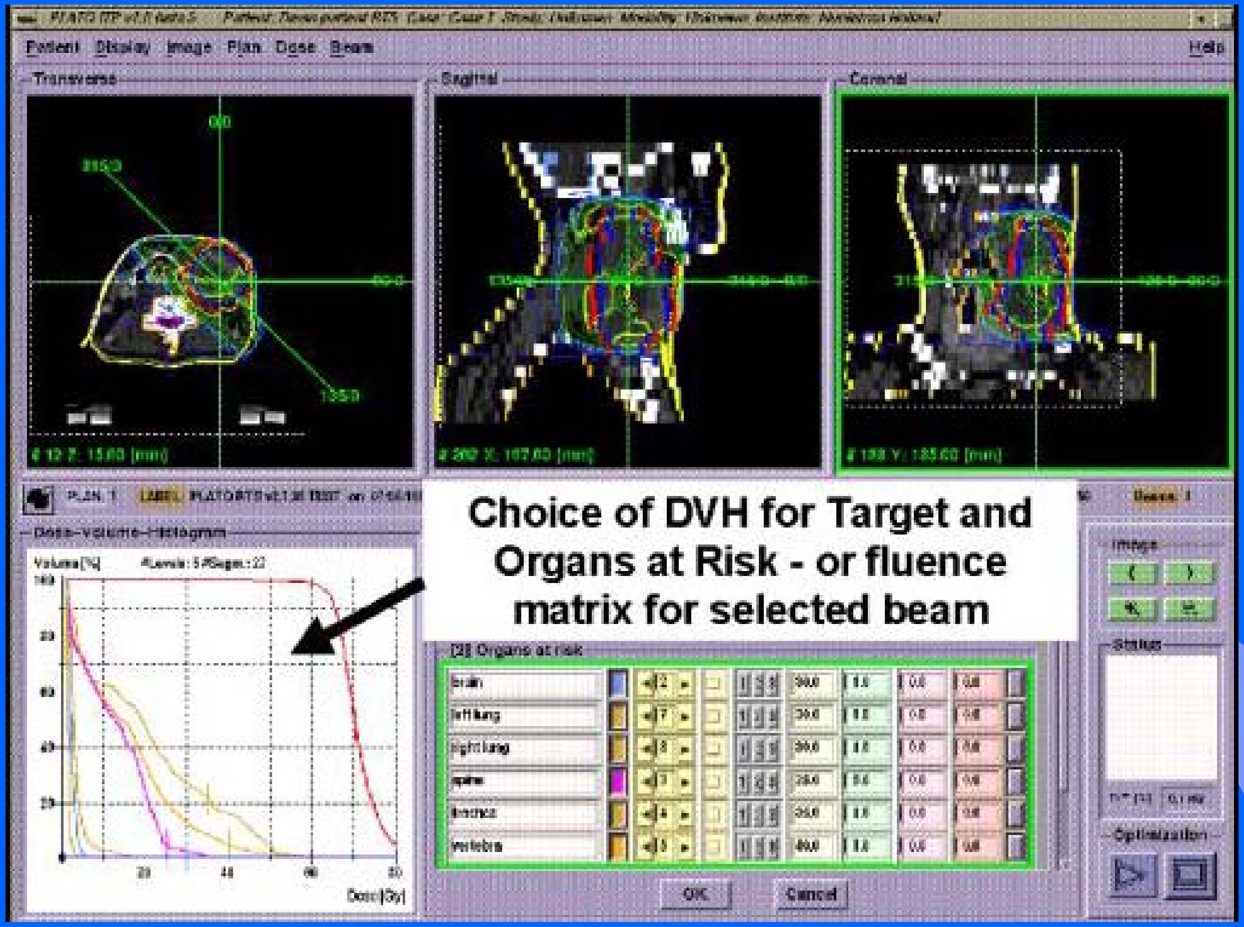
- Radio immunotherapy
  - The radiation is brought by a radioisotope attached to a specifically selective vector
- Teletherapy
  - Bombardment of the tumour tissues with radiation coming from outside the body of the patient

Conventional radiation therapy with X-rays



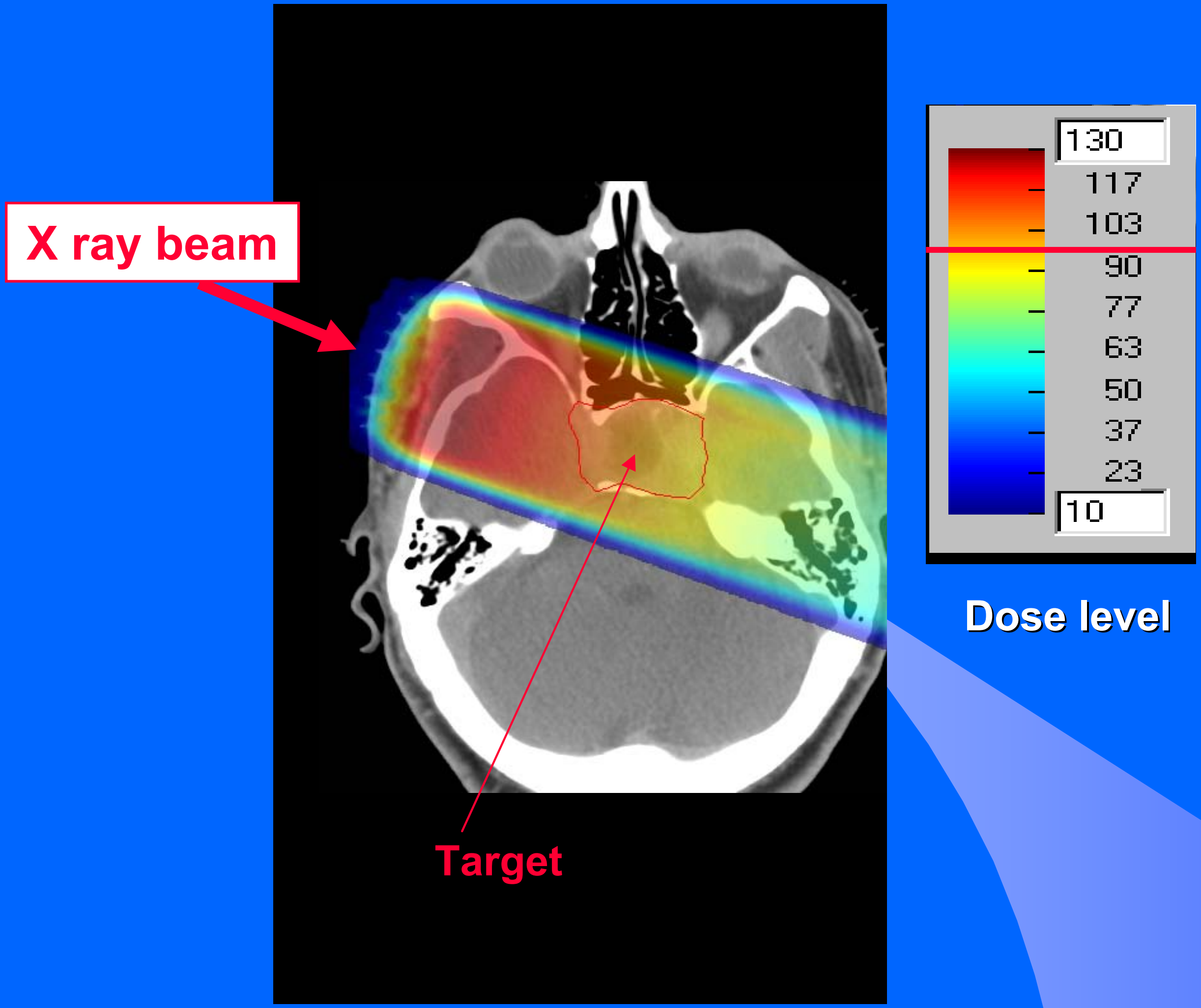
- Electron linacs to produce gamma rays (called X-rays by medical doctors)
- 20'000 patients/year every 10 million inhabitants

Computerized Treatment Planning System (TPS)

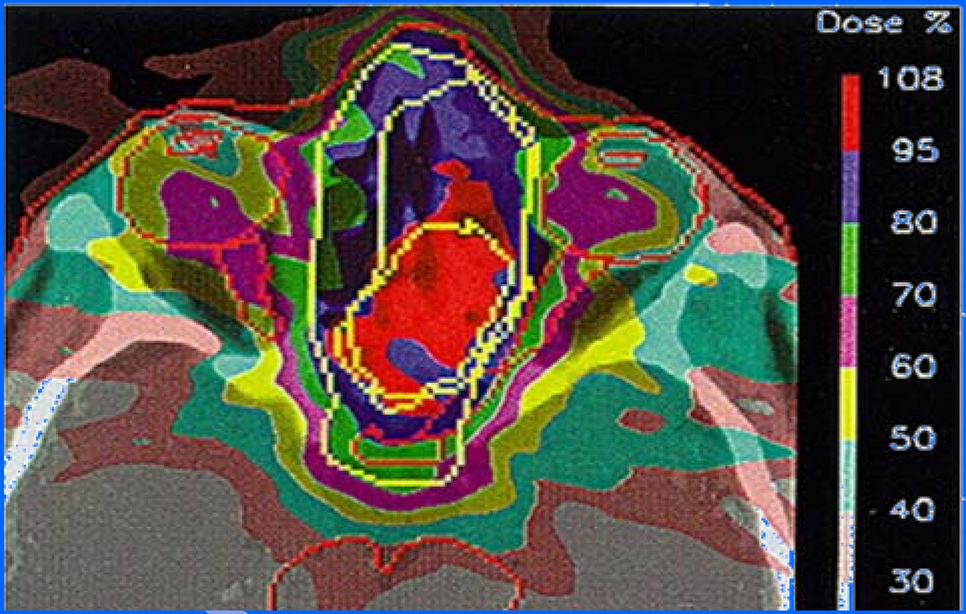


- TC scan data are used to
  - design the volume to be irradiated
  - choose the radiation fields
  - calculate the doses to the target and to healthy tissues
- The dose is given in about 30-40 fractions of about 2 Gray

The problem of X ray therapy



The problem of X ray therapy



9 different photon beams

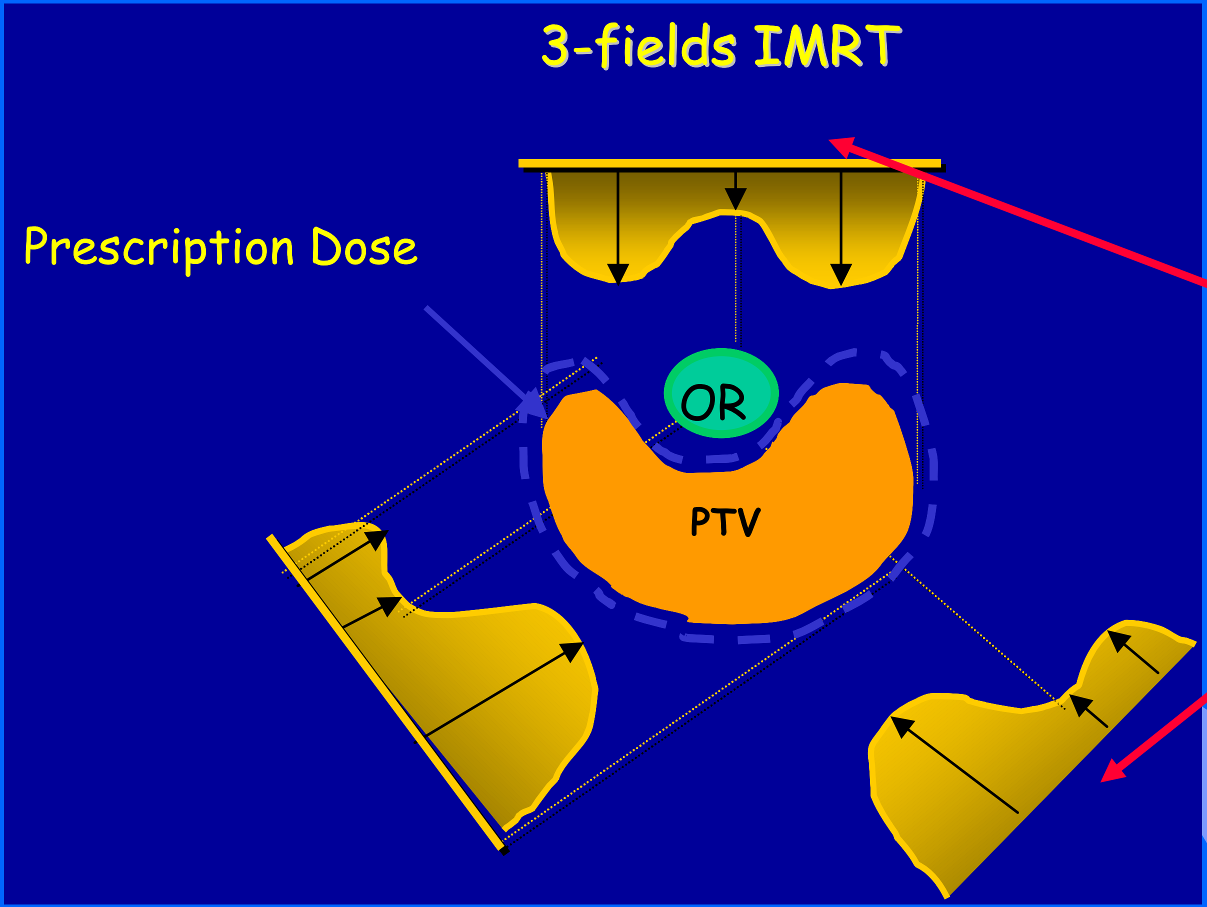
Solution:

- **Use of many crossed beams**
- **Intensity Modulation Radiation Therapy (IMRT)**

The limit is due to the dose given to the healthy tissues!

Especially near organs at risk (OAR)

Multi leaf collimators and IMRT

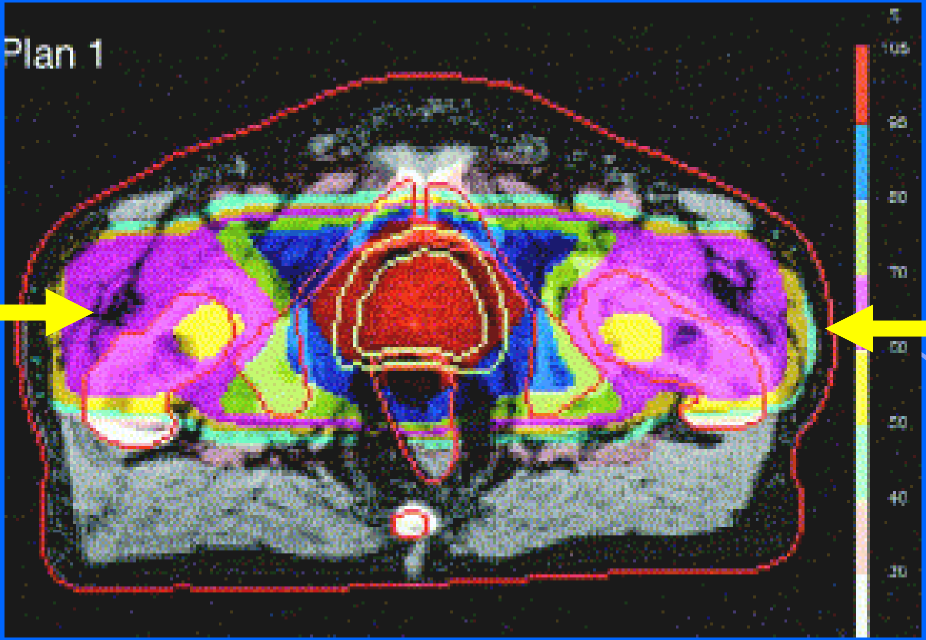


Multi leaf collimator which moves during irradiation

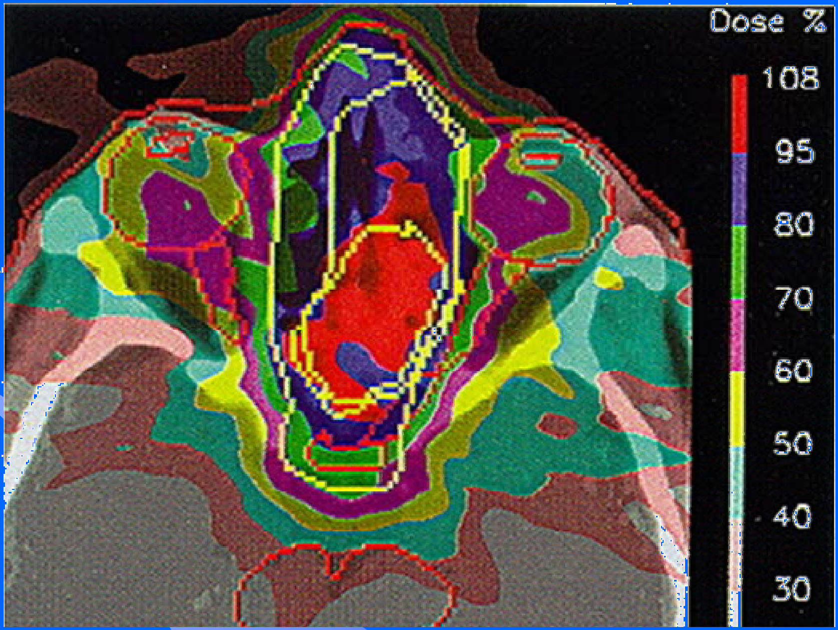
- It is possible to obtain concave dose volumes
- Time consuming (used for selected cases)

Can we do better ?

2 X ray beams



9 X ray beams (IMRT)



A question for a particle physicist

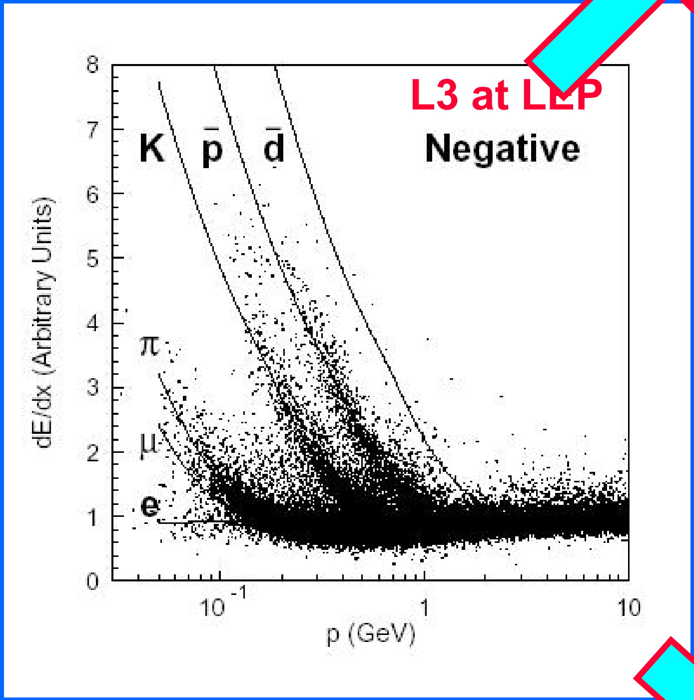
Are there better radiations to attack the tumour and spare at best the healthy tissues?

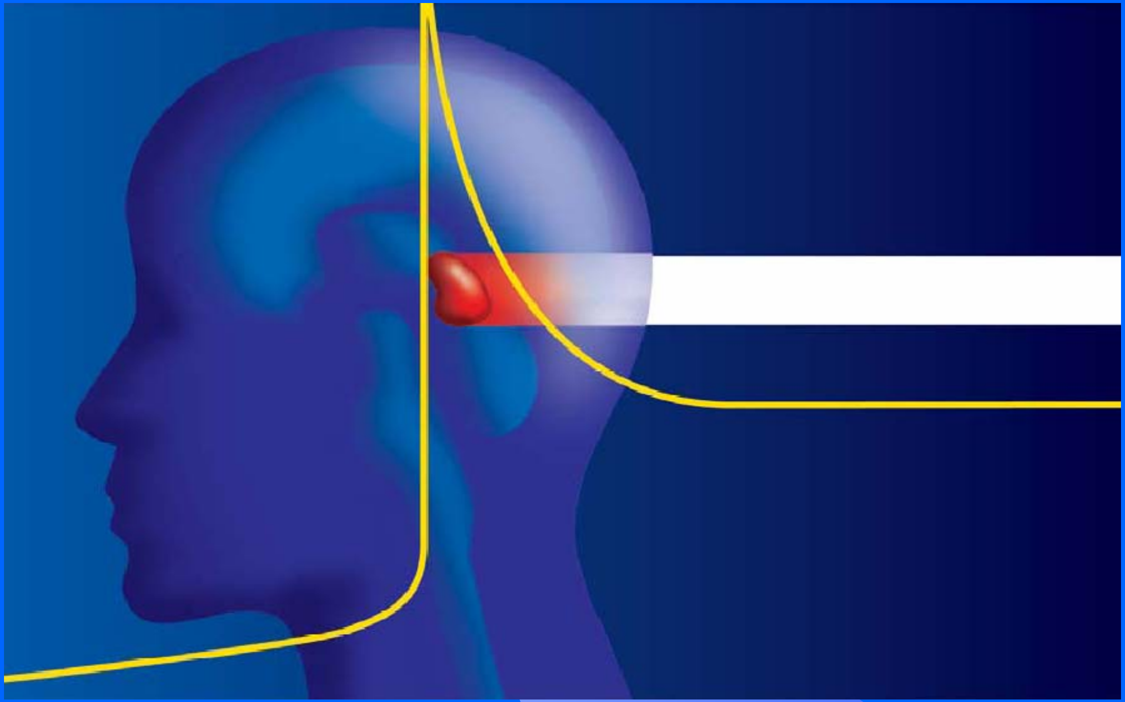
Answer : BEAMS OF CHARGED HADRONS

Let's go back to physics...

Fundamental physics

Particle identification

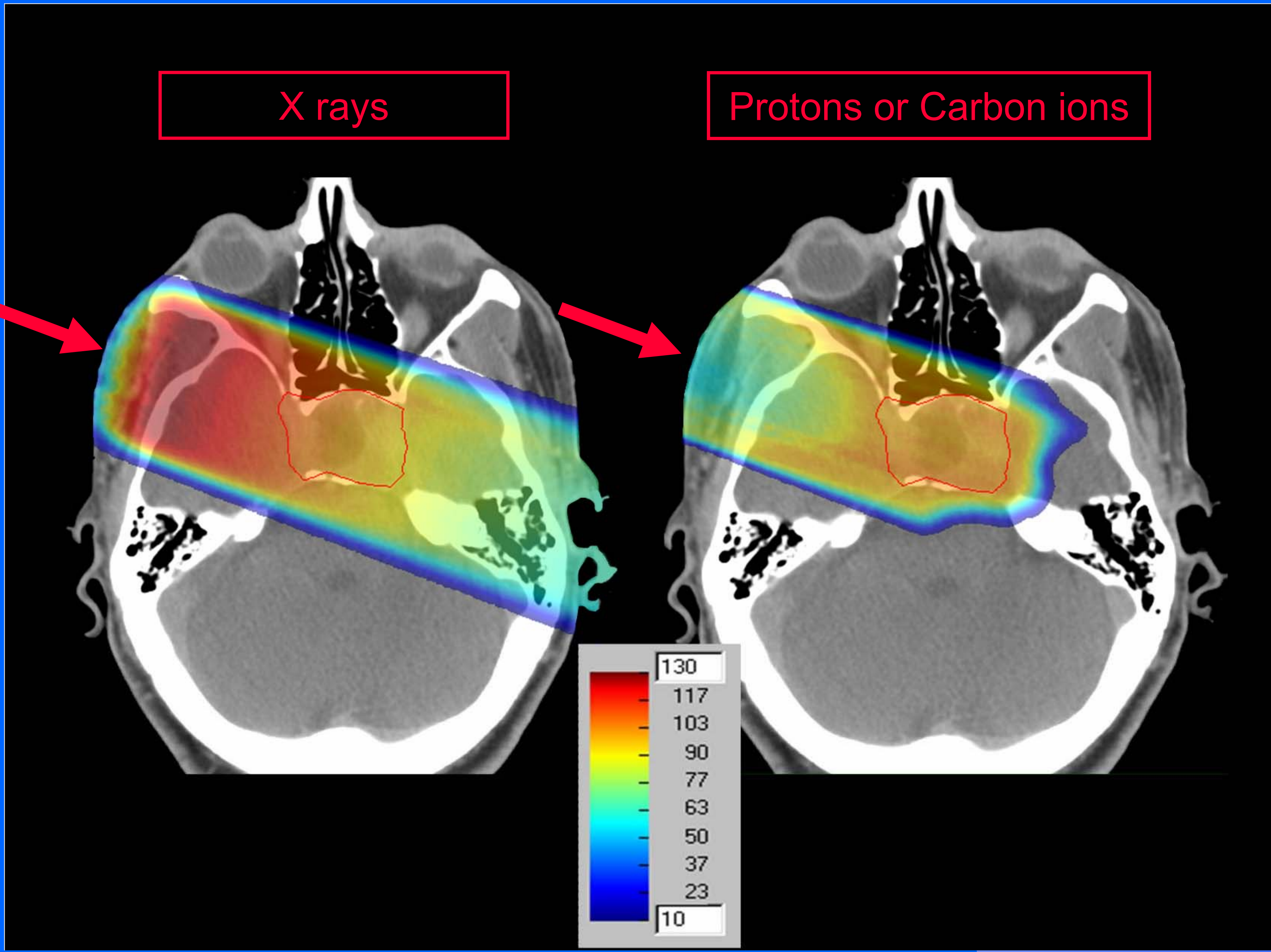




Medical applications

Cancer hadrontherapy

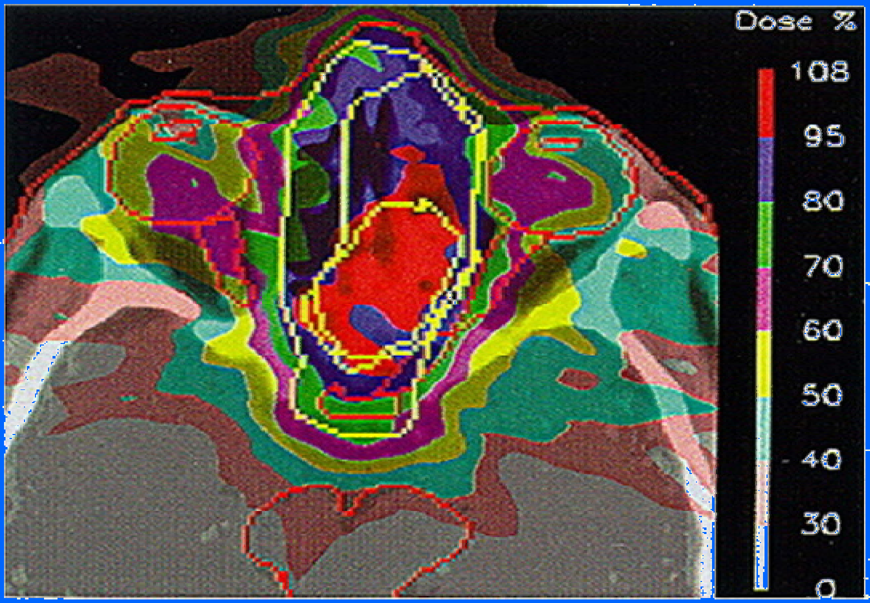
Single beam comparison



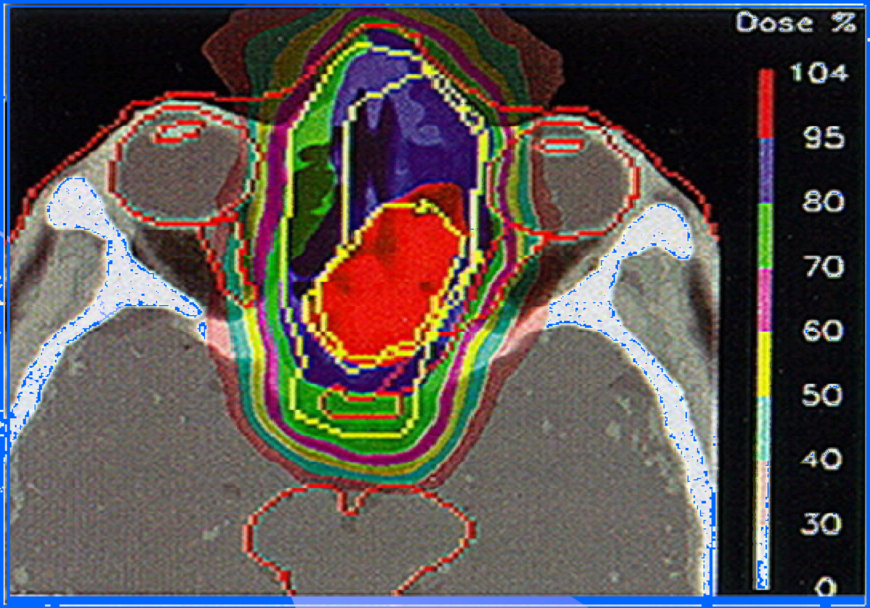
Protons and ions are more precise than X-rays

Tumour between the eyes

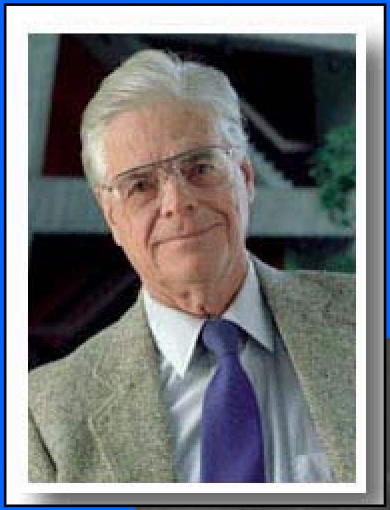
9 X ray beams



1 proton beam



The first idea – Bob Wilson, 1946



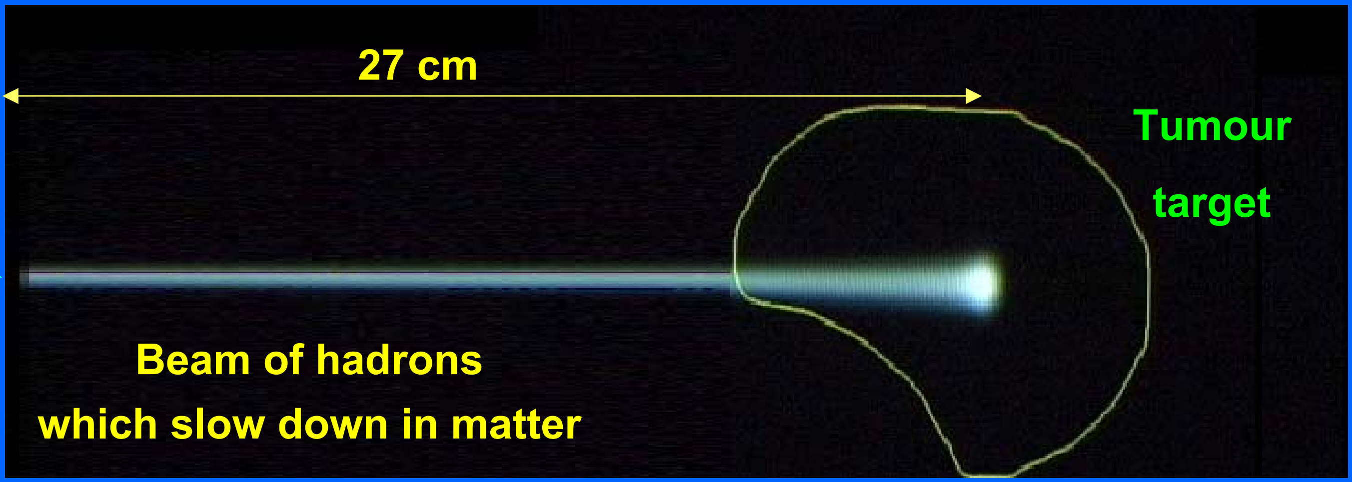
- Bob Wilson was student of Lawrence in Berkley
- Study of the shielding for the new cyclotron
- Interdisciplinary environment = new ideas!
- Use of protons and charged hadrons to better distribute the dose of radiation in cancer therapy

R.R. Wilson, Radiology 47 (1946) 487

The basic principles of hadrontherapy

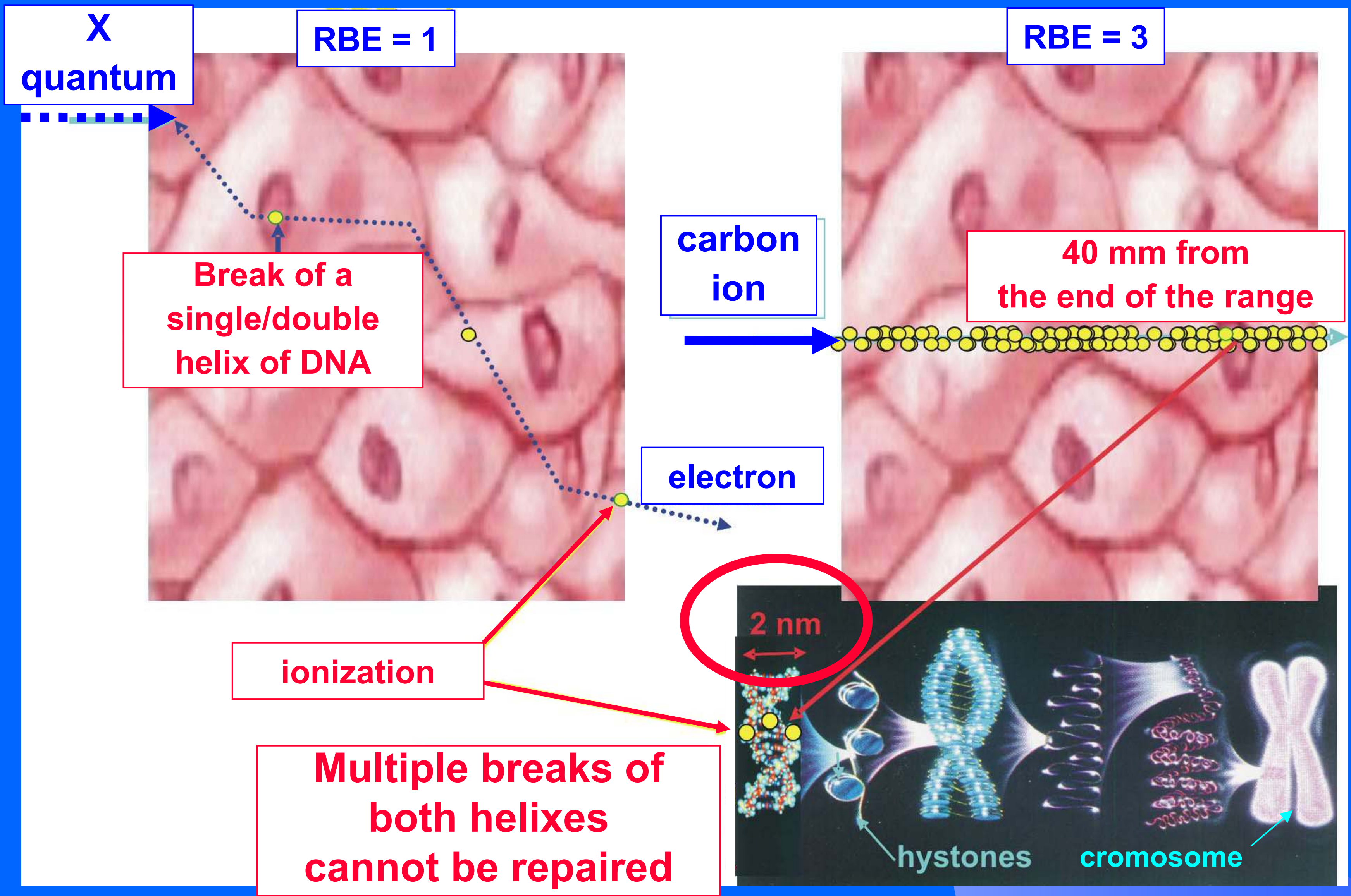
Protons
200 MeV
1 nA

Carbon ions
4800 MeV
0.1 nA



- Bragg peak
  - Better conformity of the dose to the target → healthy tissue sparing
- Hadrons are charged
  - Beam scanning for dose distribution
- Heavy ions
  - Higher biological effectiveness

Why ions have a large biological effectiveness?



Ions have high LET (Linear Energy Transfer)

Number of potential patients

Study by AIRO, 2003

Italian Association for Oncological Radiotharapy

X-ray therapy 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 tumours

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

Every 50 M inhabitants

• Proton-therapy

4-5 centres

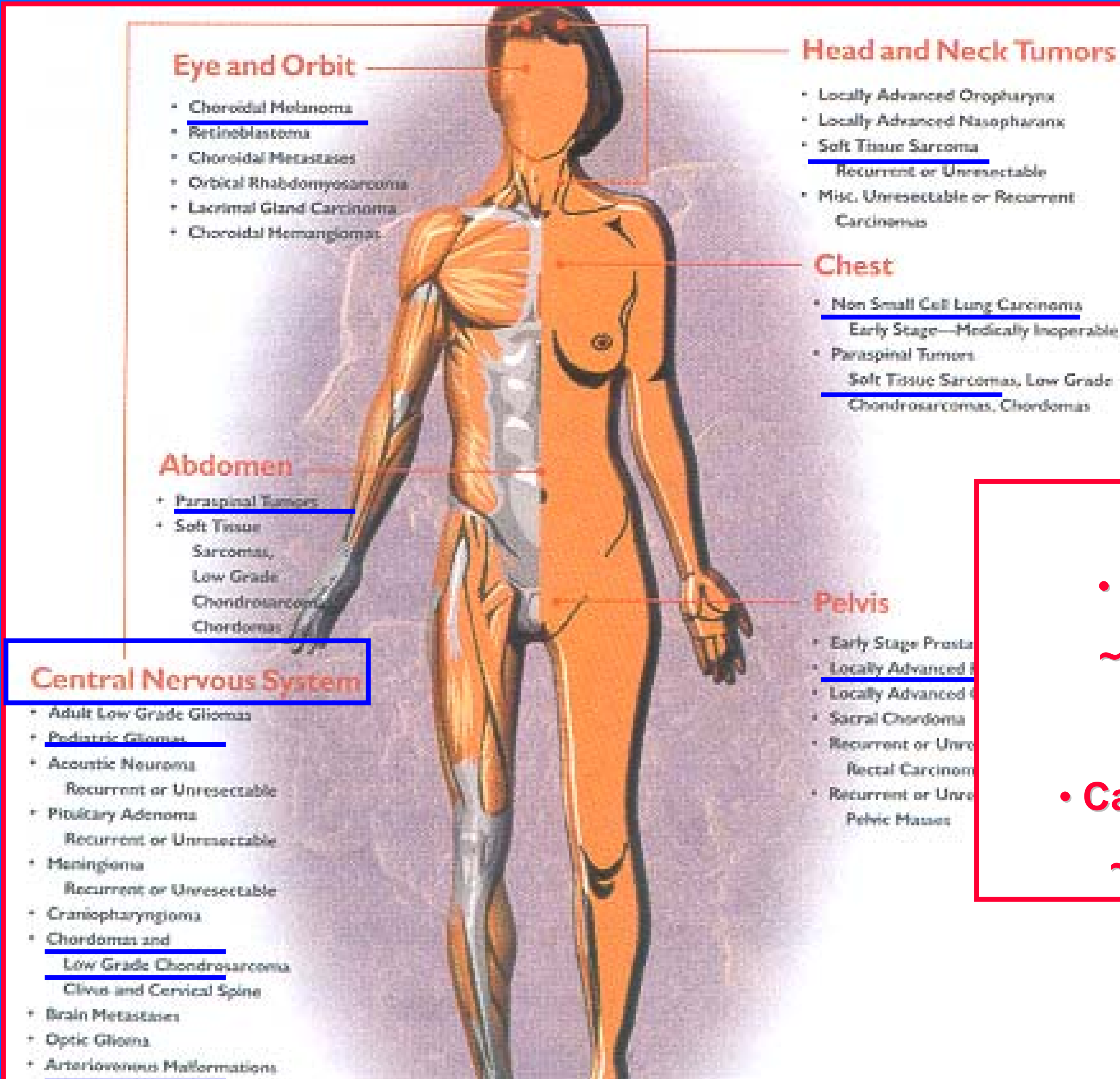
• Carbon ion therapy

1 centre

TOTAL about 3'000 pts/year

every 10 M

The sites



Up to present

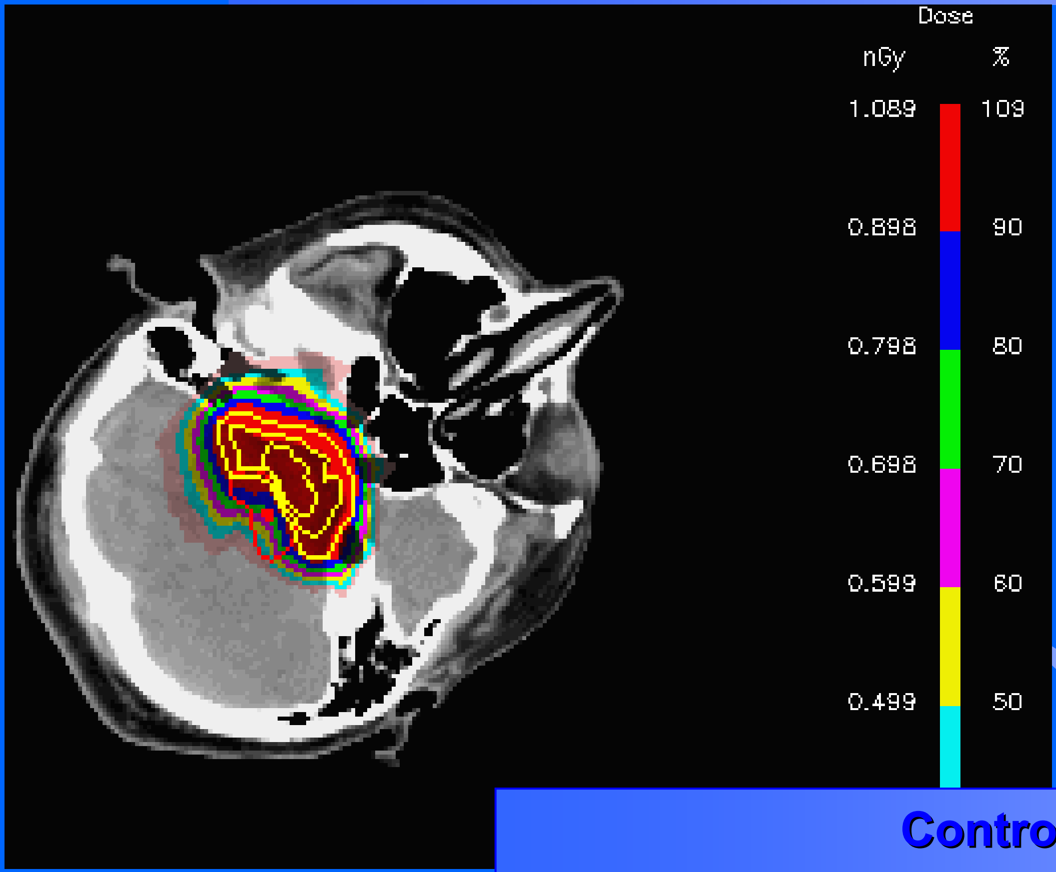
• Proton-therapy:

~ 45 000 patients

• Carbon ion therapy:

~ 2 200 patients

Example: tumours of the central nervous system



Control at 5 years

	RT	Protons
Chordomas	17-50%	73-83%
Chondrosarcomas	50-60%	90-98%

Present and “near” future of hadrontherapy

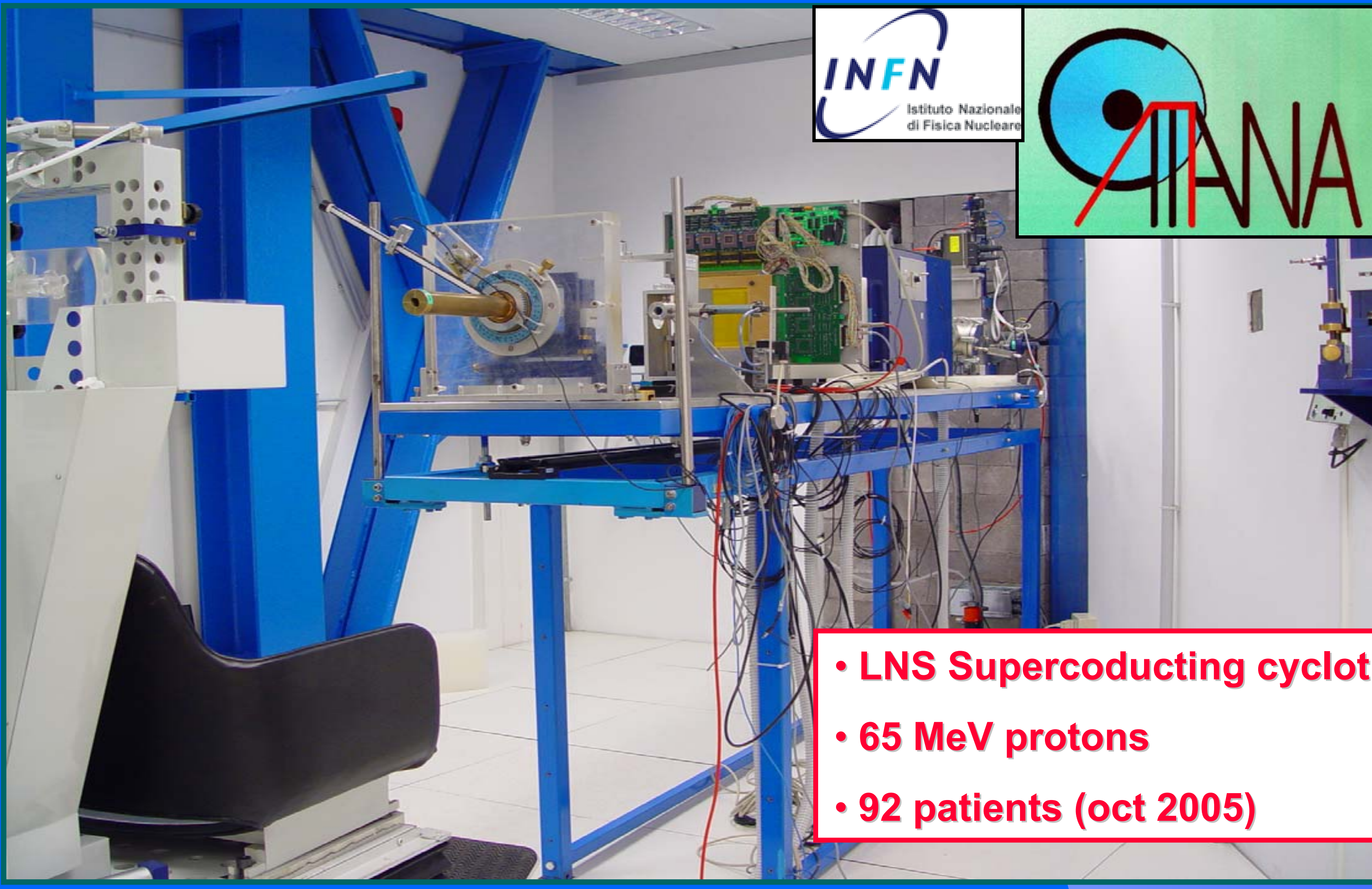
- **Proton-therapy is “booming”!** *(for more information see PTCOG, www.ptcog.com)*
  - Laboratory based centres: Orsay, PSI, INFN-Catania, …
  - Hospital based centres: 3 in USA, 4 in Japan and many under construction (USA, Japan, Germany, China, Korea, Italy, …)
  - Companies offer “turn-key” centres (cost: 50-60 M Euro)

- **Carbon ion therapy**
  - 2 hospital based centres in Japan
  - Pilot project at GSI
  - 2 hospital based centres under construction in Germany and Italy
  - 2 projects approved (France and Austria)
  - European network ENLIGHT

The map of hadrontherapy

TERA

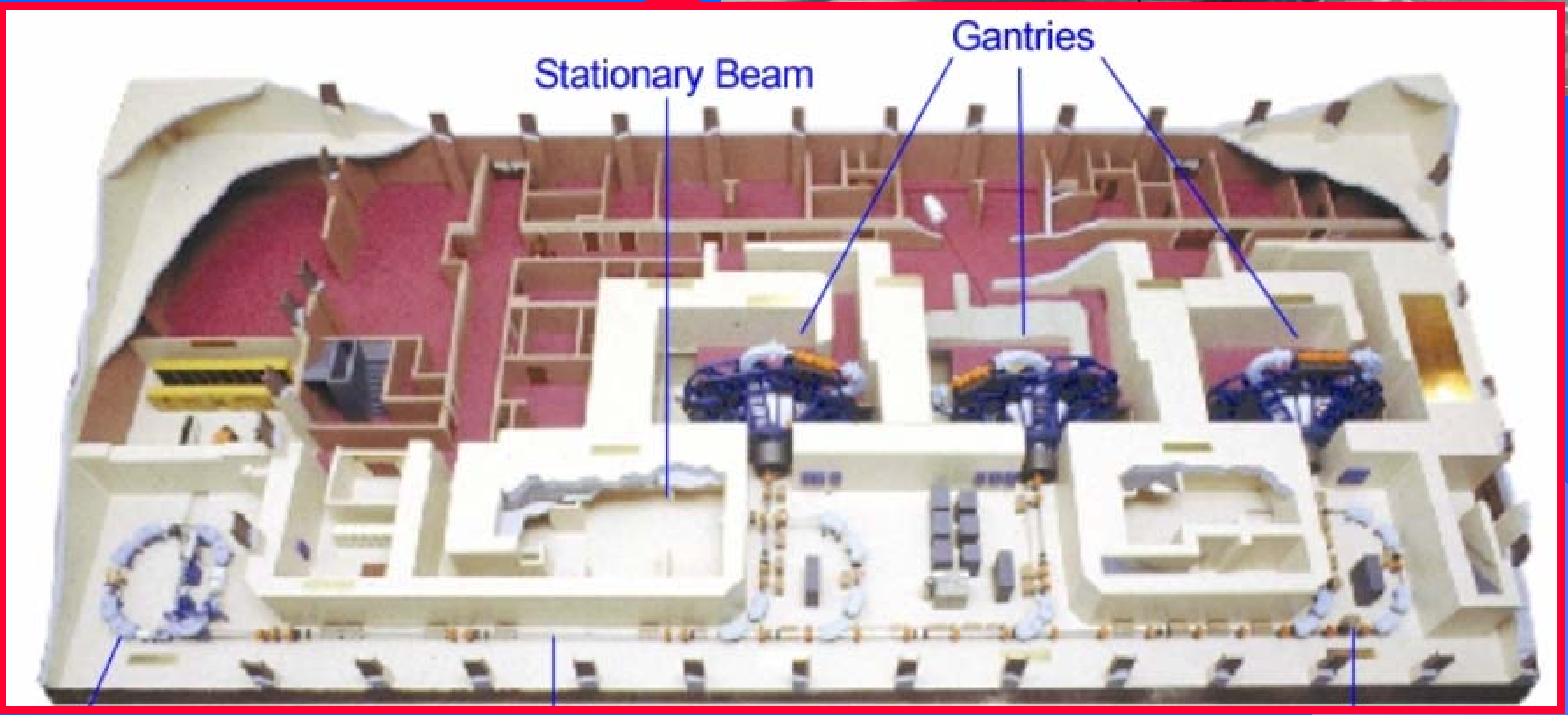
The eye melanoma treatment at INFN-LNS in Catania



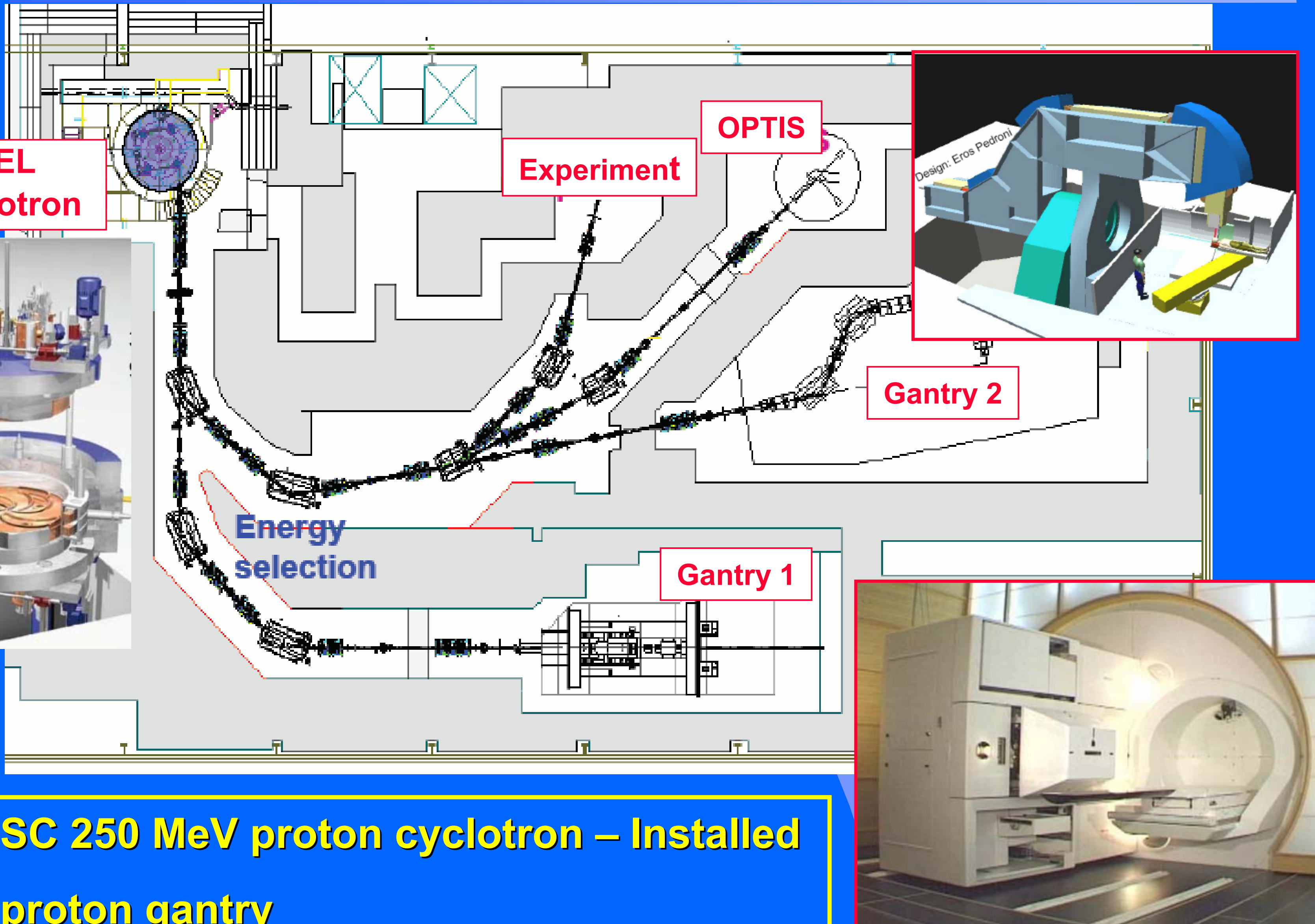
- LNS Supercoducting cyclotron
- 65 MeV protons
- 92 patients (oct 2005)

The Loma Linda University Medical Center (USA)

- First hospital-based proton-therapy centre, built in 1993
- ~160/sessions a day
- ~1000 patients/year



PROSCAN project at PSI



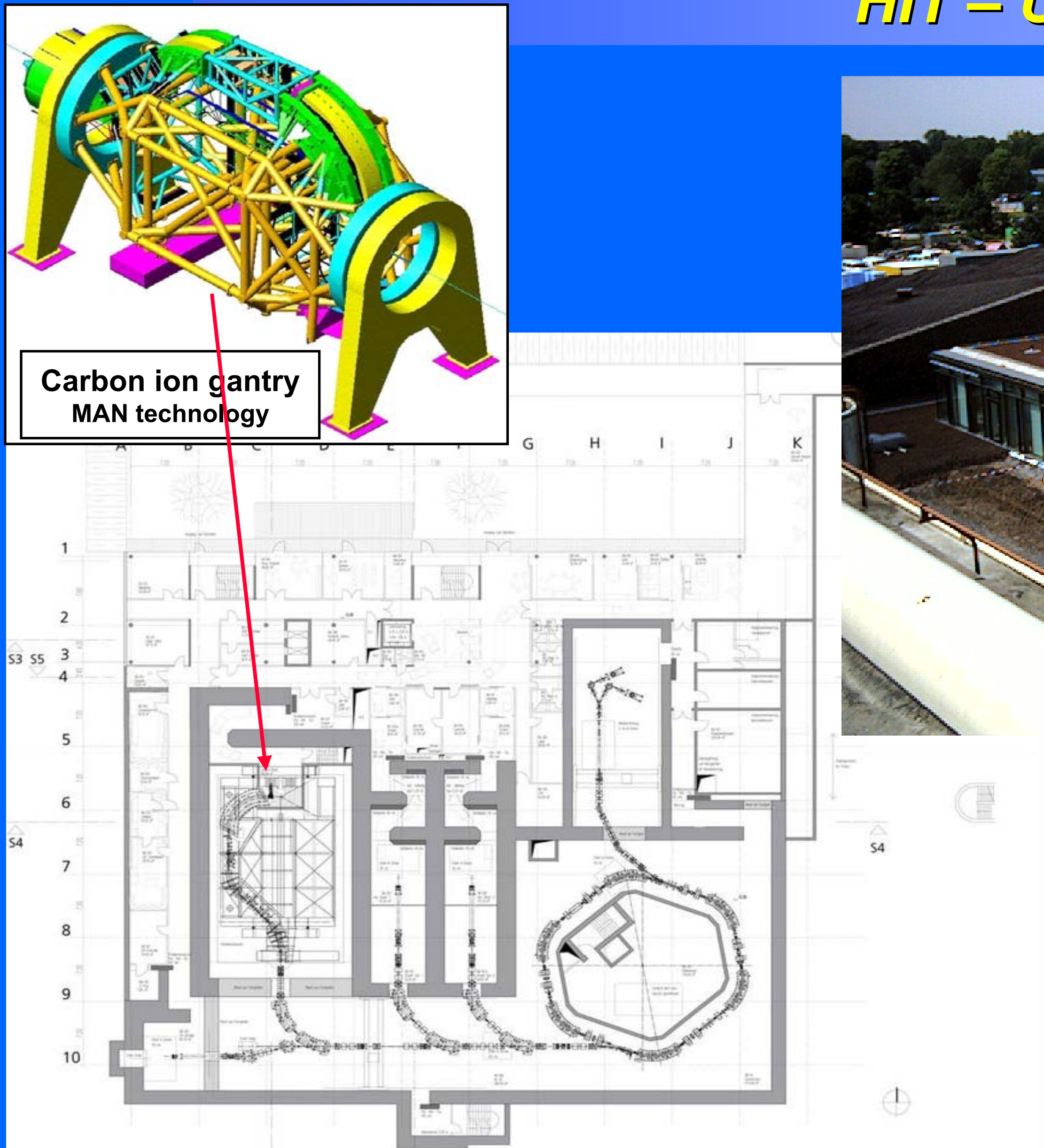
- New SC 250 MeV proton cyclotron – Installed
- New proton gantry

1998 - GSI pilot project (G. Kraft)

200 patients treated with carbon ions

PET on-beam

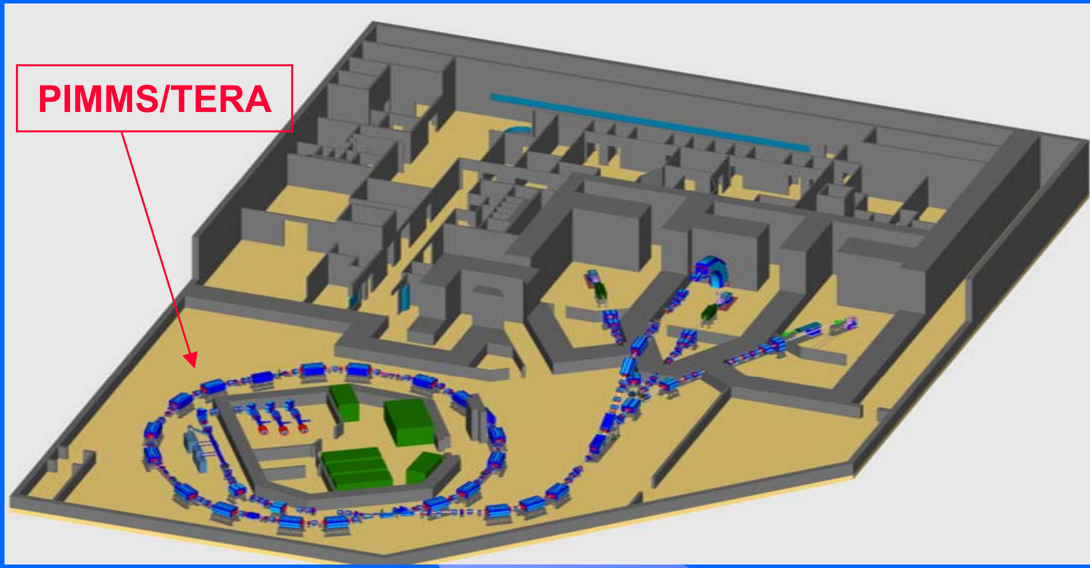
HIT – University of Heidelberg



- Hospital based centre
- Project started in 2001
- First patient treatment foreseen in 2007

The TERA Foundation

- Not-for-profit foundation created in 1992 by Ugo Amaldi and recognized by the Italian Ministry of Health in 1994
- Research in the field of particle accelerators and detectors for hadron-therapy
- First goal: the Italian National Centre (CNAO) now under construction in Pavia



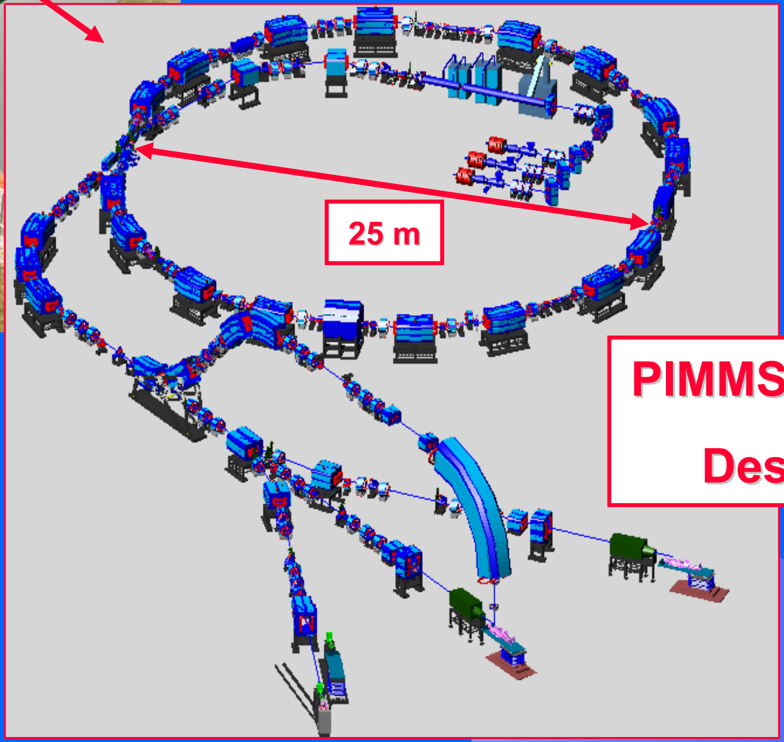
- Collaborations with many research institutes and universities
  - in particular CERN, INFN, PSI, GSI, JRC, Universities of Milan, Turin and Piemonte Orientale

CNAO on the Pavia site

- Investment: 75 M€
- Main source of funds:

Italian Health Ministry

- Ground breaking: March 2005
- Treatment of the first patient foreseen by the end of 2007



PIMMS/TERA

Design

- Hospital based centre
- Protons and carbon ions

CNAO

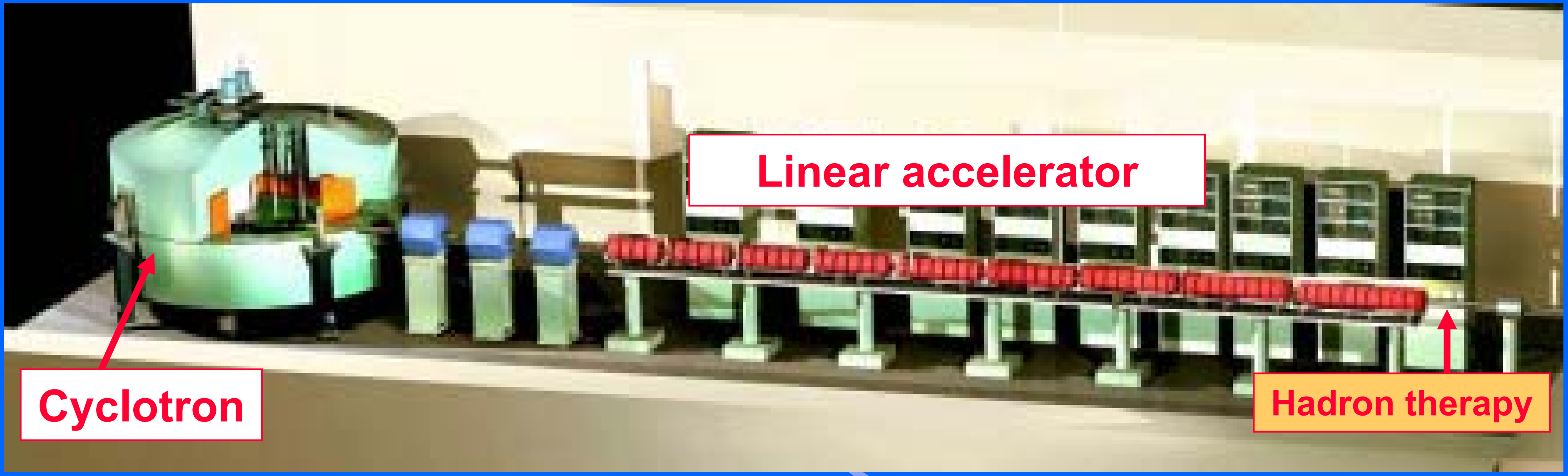
January 21st, 2006

June 1st, 2006

Courtesy S. Rossi (CNAO Foundation)

What does a patient see?

The CYCLINAC: a new idea for the future



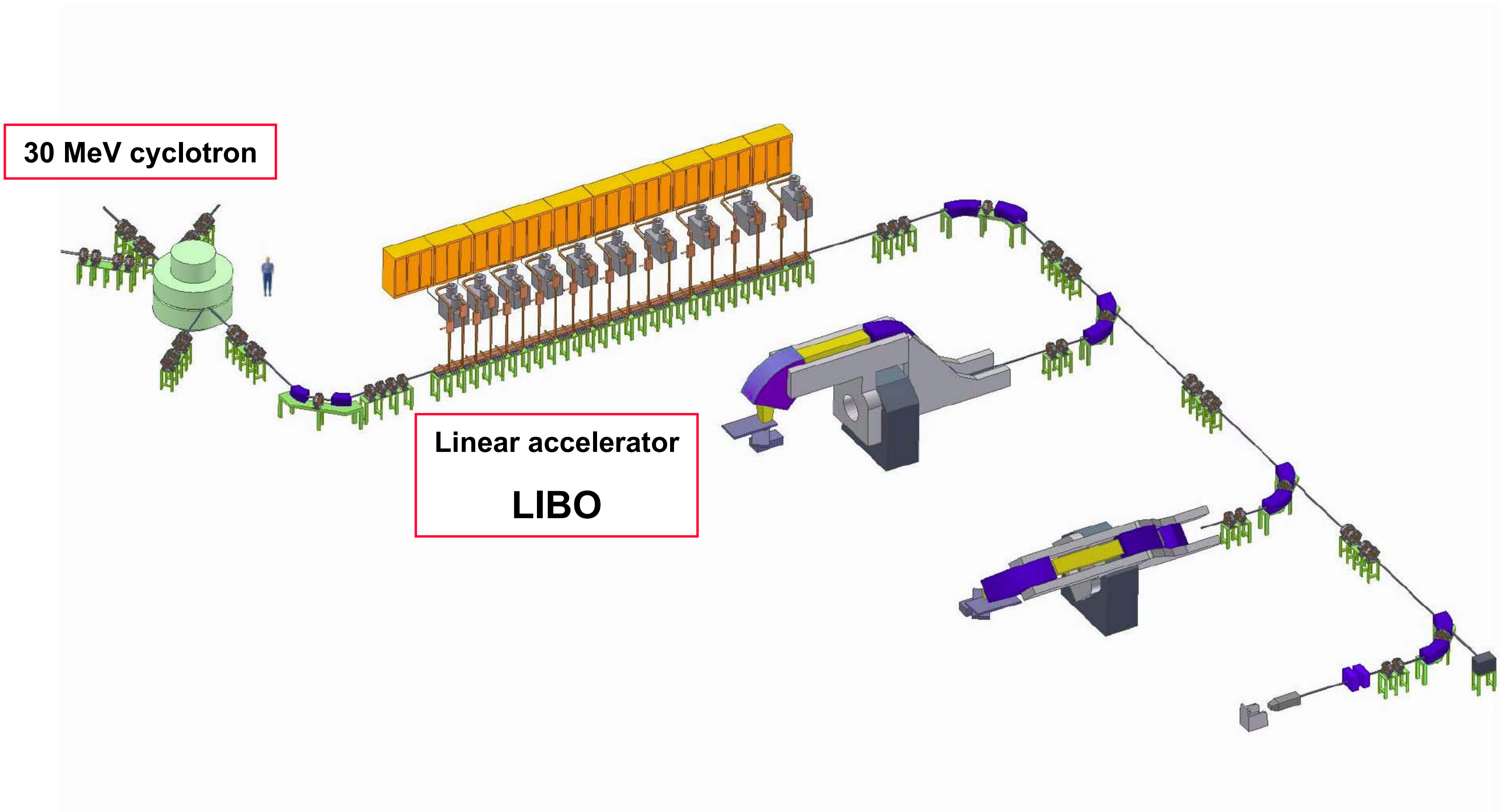
- CYCLINAC = CYClotron + LINAC
- Commercial cyclotron for the production of radioisotopes
- Linac to boost the beam energy for hadron-therapy

Two main functions

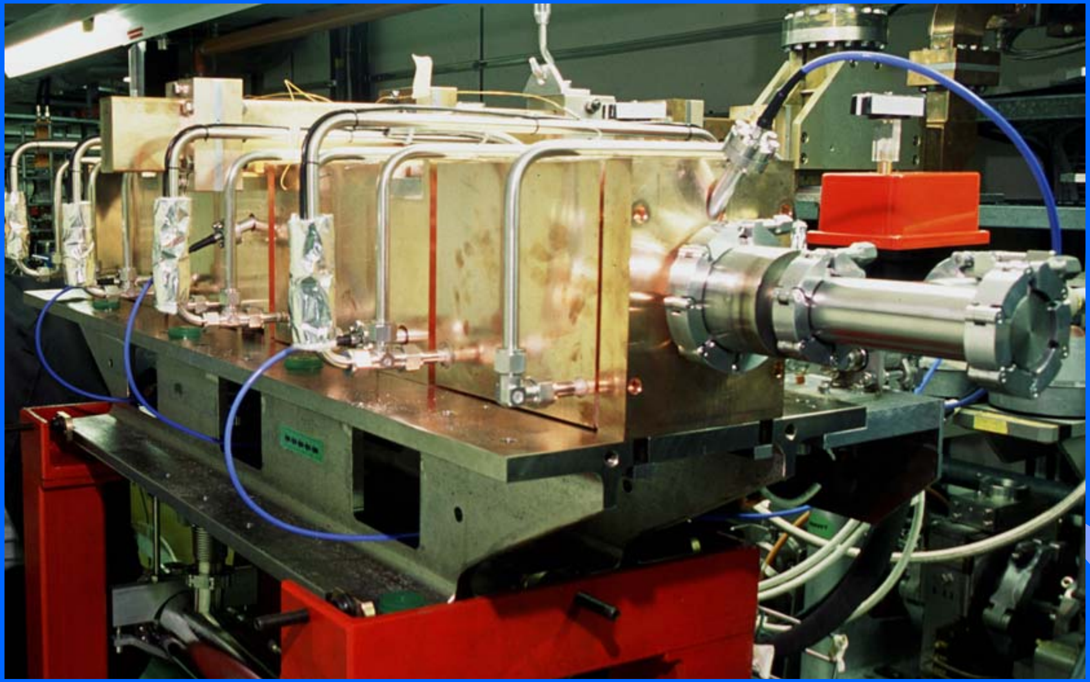
DIAGNOSTICS + THERAPY

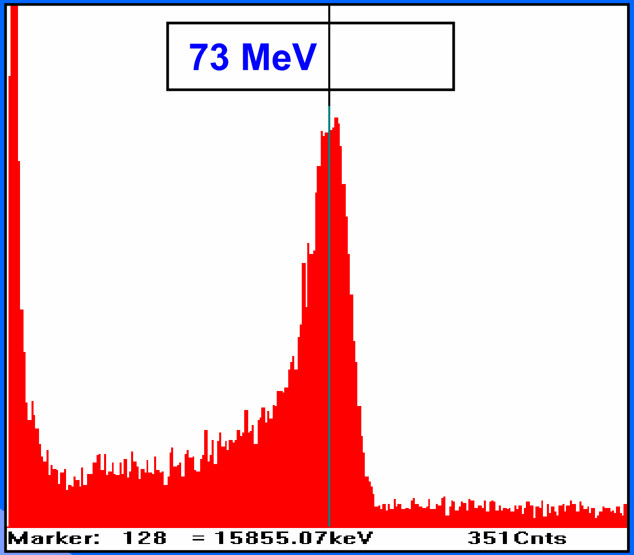
IDRA

Institute for Diagnostics and RAdiotherapy



Prototype of LIBO (on display at CERN Microcosm)





Collaboration INFN-CERN-TERA 1999-2002

Module tested at LNS of INFN, Catania

NIM A 521 (2004) 512

Accelerated beam from the 60 MeV cyclotron of LNS

- **Since the beginning of particle physics, more than one-hundred years go…**

Particle physics offers medicine and biology very powerful tools and techniques to study, detect and attack the disease

To fully exploit this large potentiality, all these sciences must work together!

Work is in progress…

Physics is beautiful…

…and useful !