Medical Applications of Particle Physics

Saverio Braccini

TERA
Foundation for Oncological Hadrontherapy

Outline

- Introduction: a short historical review
- Applications in medical diagnostics
- Applications in conventional cancer radiation therapy

I

- Hadrontherapy, the new frontier of cancer radiation therapy
  - Proton-therapy
  - Carbon ion therapy
- Neutrons in cancer therapy
- Conclusions and outlook

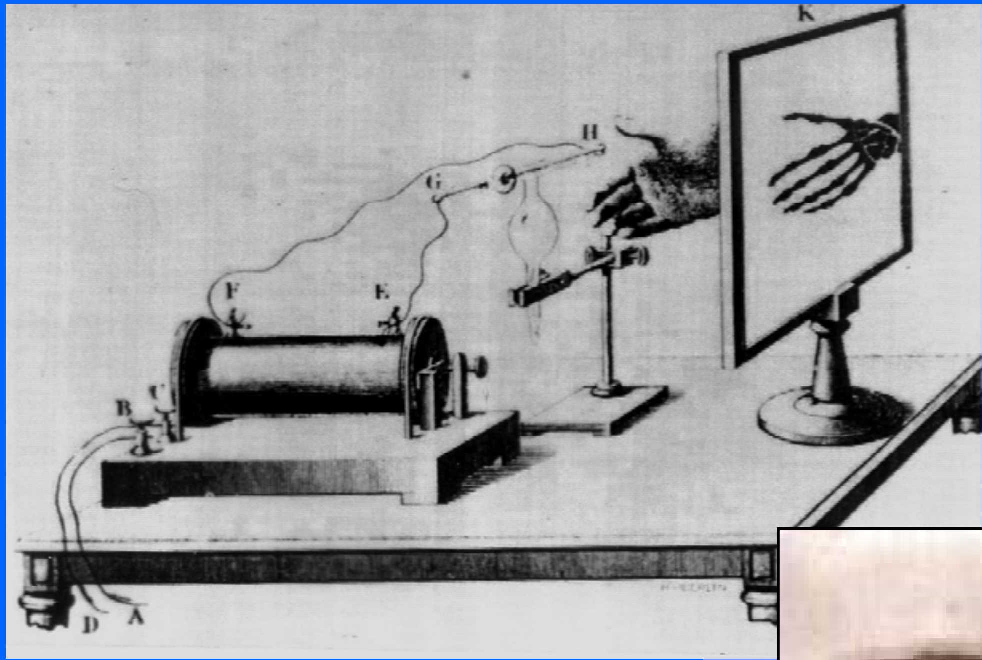
II

Introduction

Fundamental research in particle physics and medical applications

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

Wilhelm Conrad Röntgen



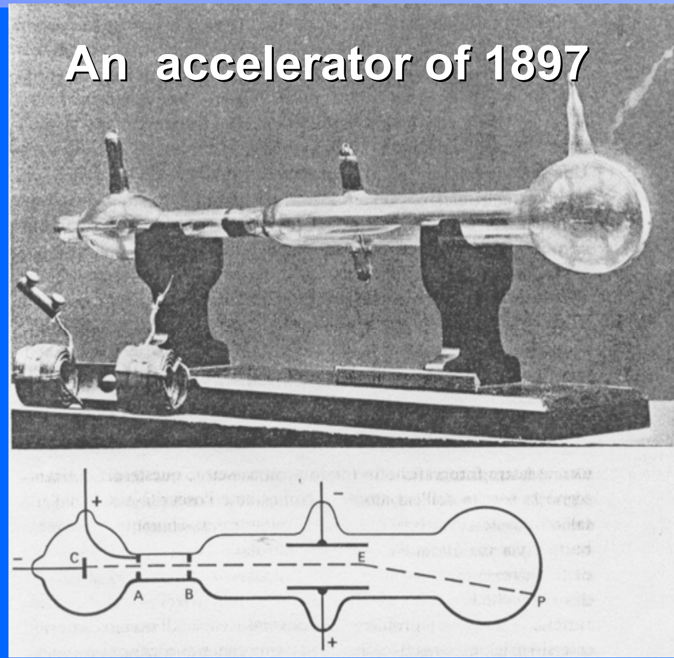
- **December 1895 : first radiography**

The beginning of modern physics and medical physics

Wilhelm Conrad Röntgen

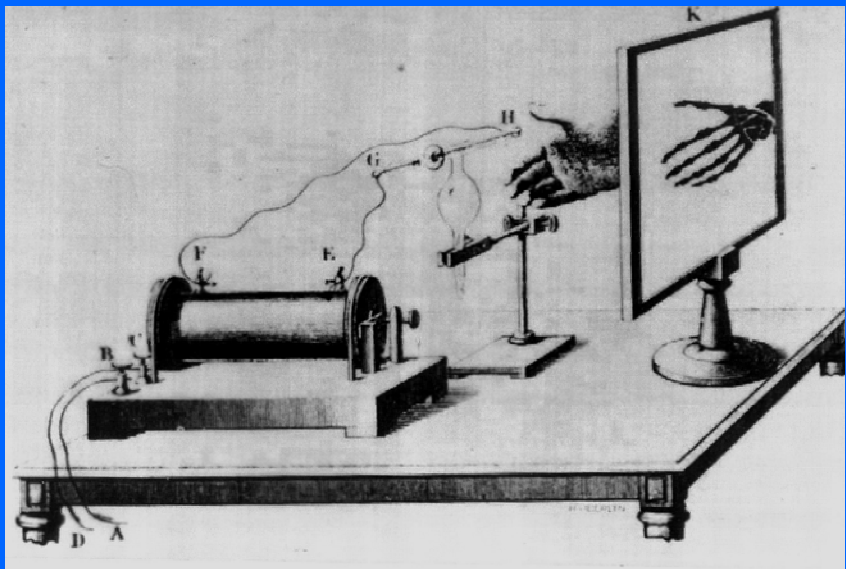
1895

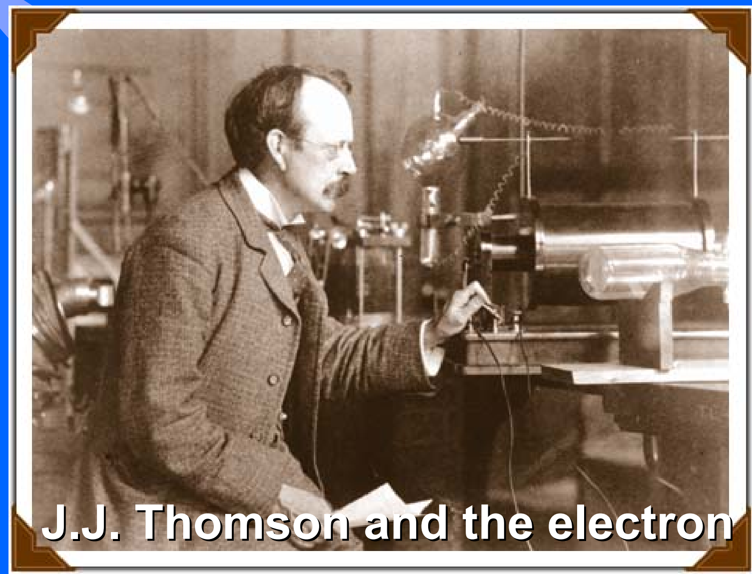
discovery of X rays



An accelerator of 1897

1895 – starting date of four magnificent years in experimental physics





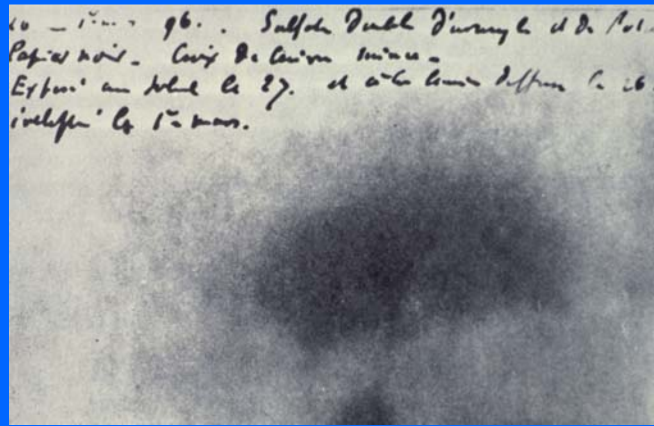
J.J. Thomson and the electron

The beginning of modern physics and medical physics

Henri Becquerel
(1852-1908)

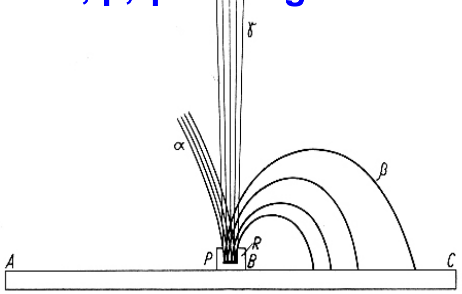
1896:

Discovery of natural radioactivity



Thesis of Mme. Curie – 1904

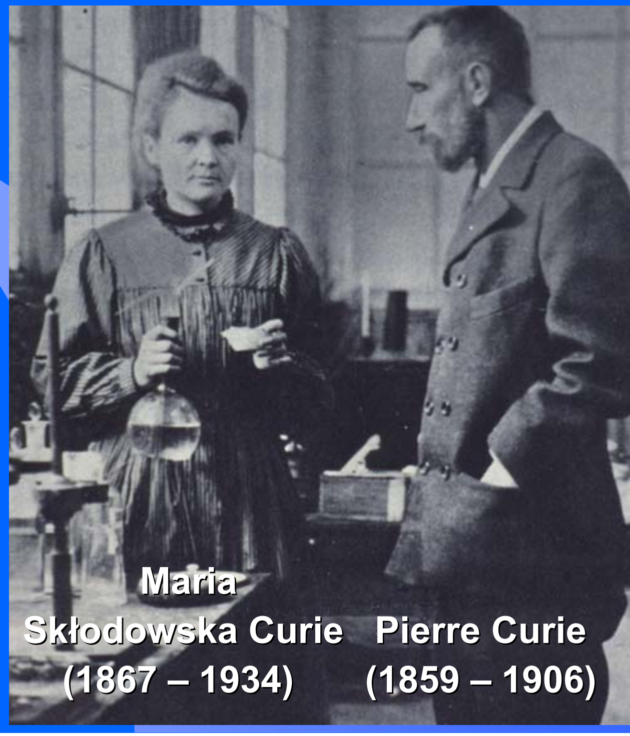
α, β, γ in magnetic field



About one hundred years ago

1898

Discovery of radium



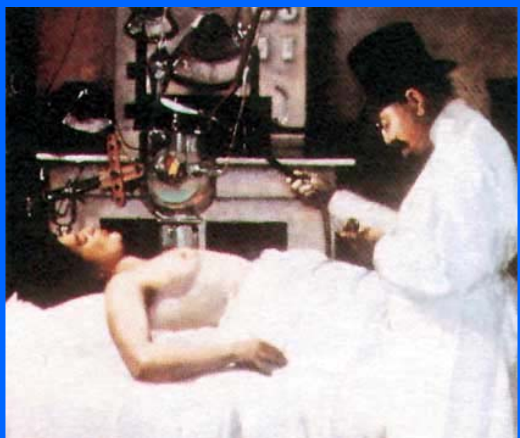
Maria Skłodowska Curie (1867 – 1934)

Pierre Curie (1859 – 1906)

First applications in cancer therapy

<u>Basic concept</u>

Local control of the tumour



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

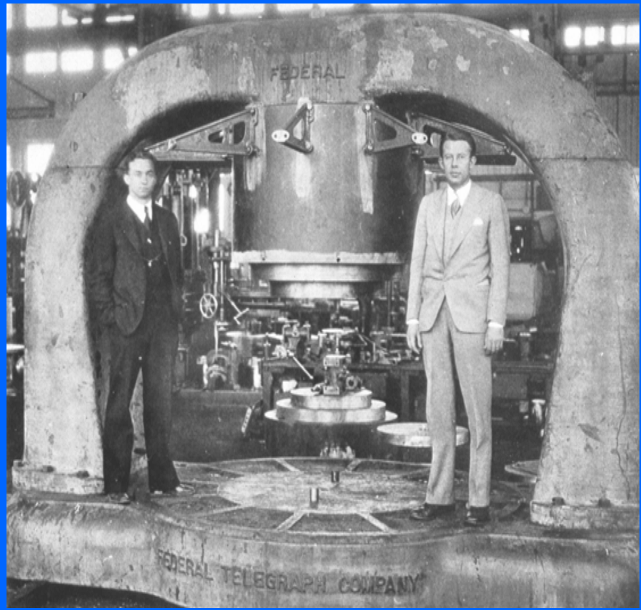
A big step forward…

…in physics and in

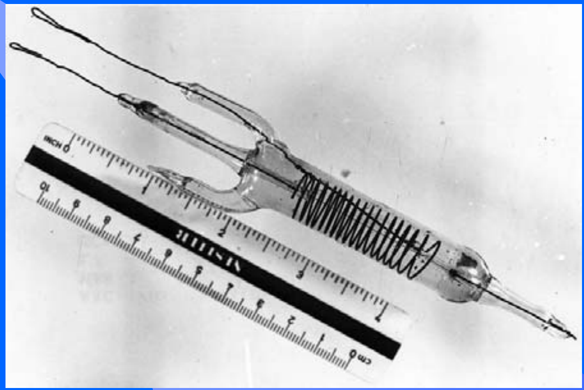
- **Medical diagnostics**
- **Cancer radiation therapy**

due to the development of three fundamental tools

- **Particle accelerators**
- **Particle detectors**
- **Computers**



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

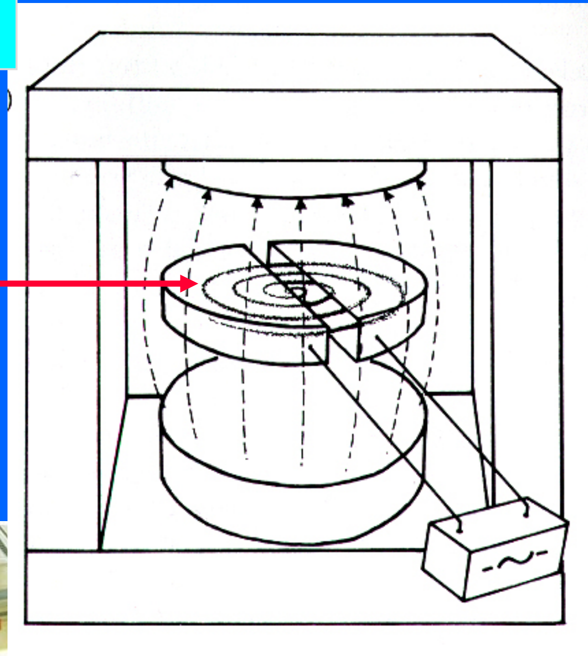


Geiger-Müller counter built by E. Fermi and his group in Rome

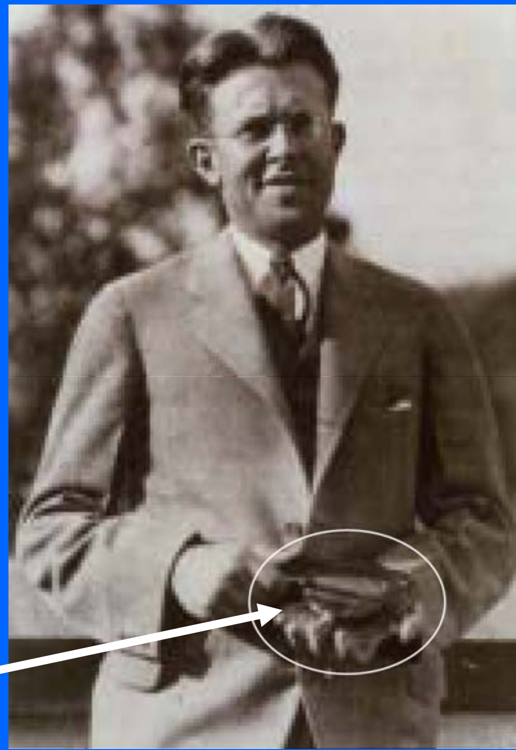
1930: the beginning of four other magnificent years

1930: invention of the cyclotron

Spiral trajectory of an accelerated nucleus



Modern cyclotron

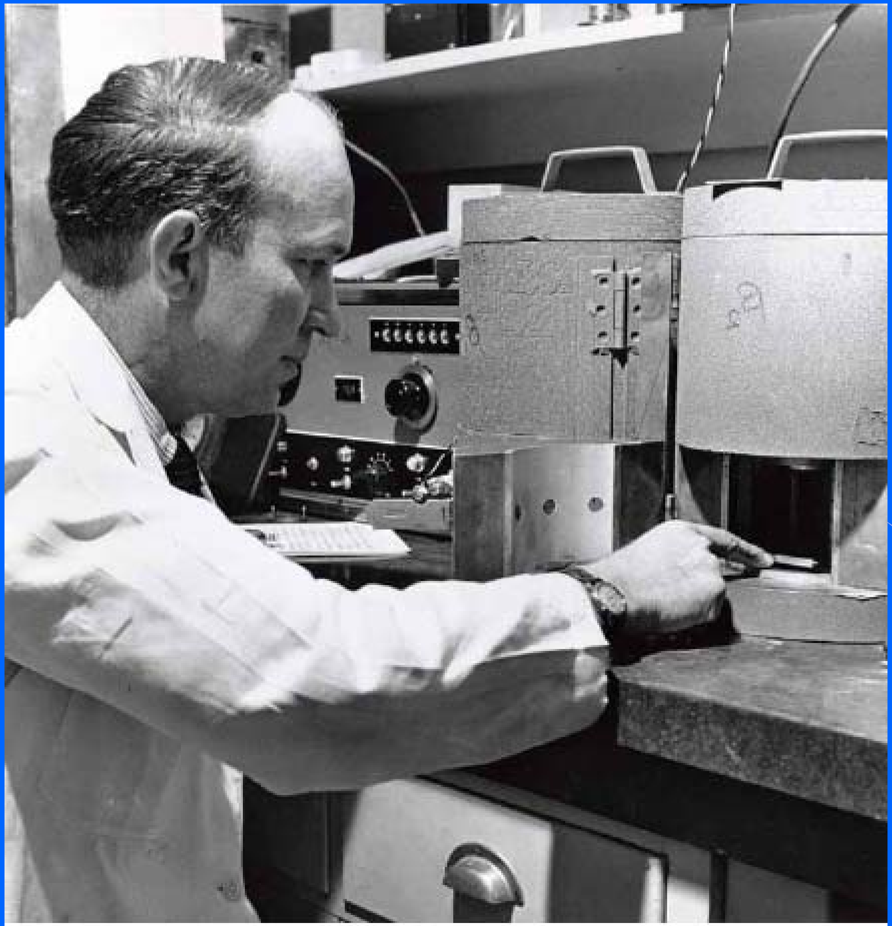


Ernest Lawrence

(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

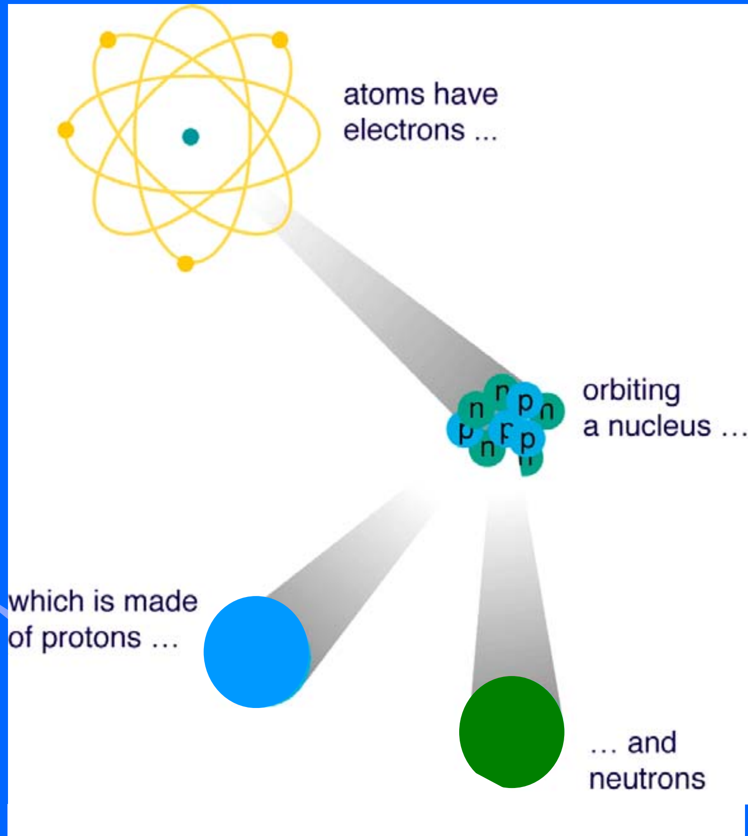
1932

James Chadwick

(1891 – 1974)

Student of

Ernest Rutherford

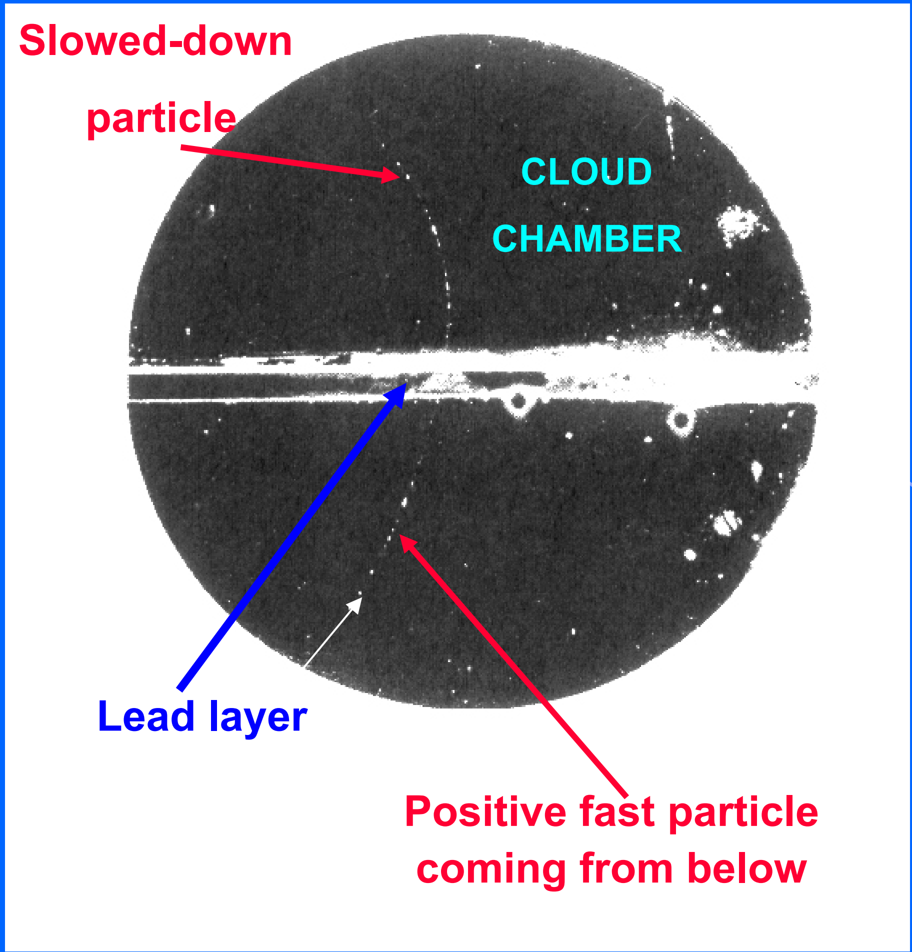


Neutrons are used today to

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

Matter and antimatter...

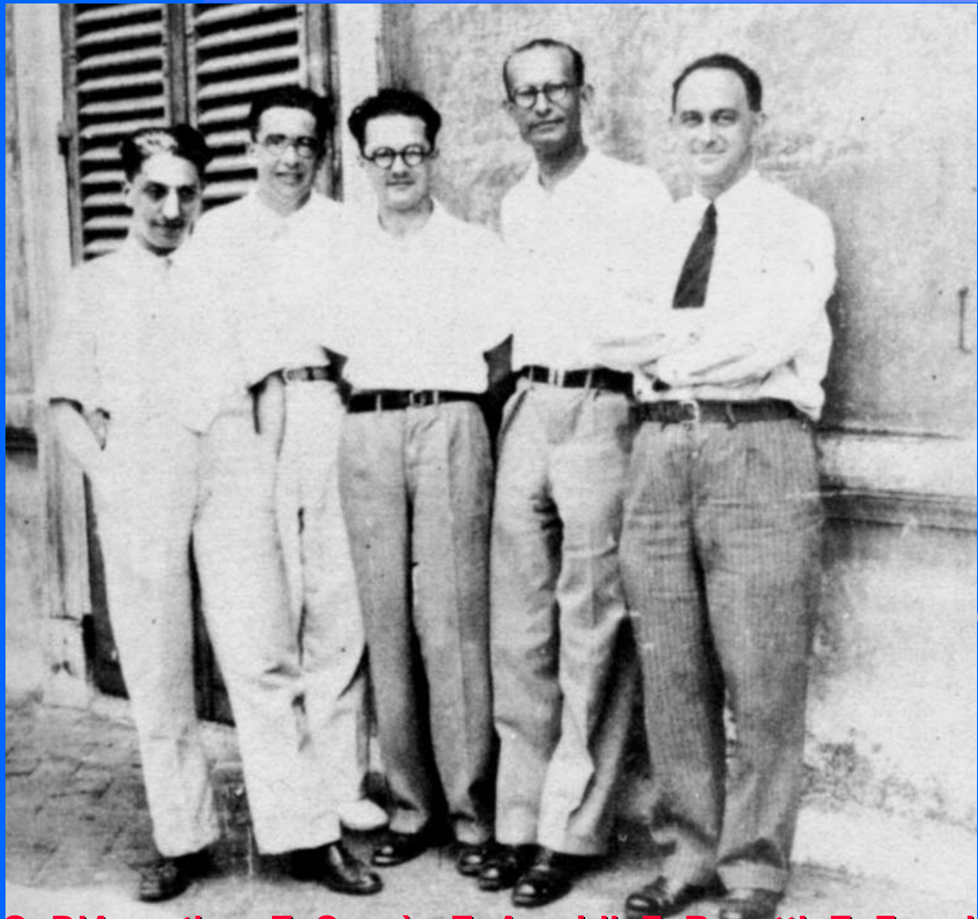
1932 – discovery of antimatter: the positron



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.

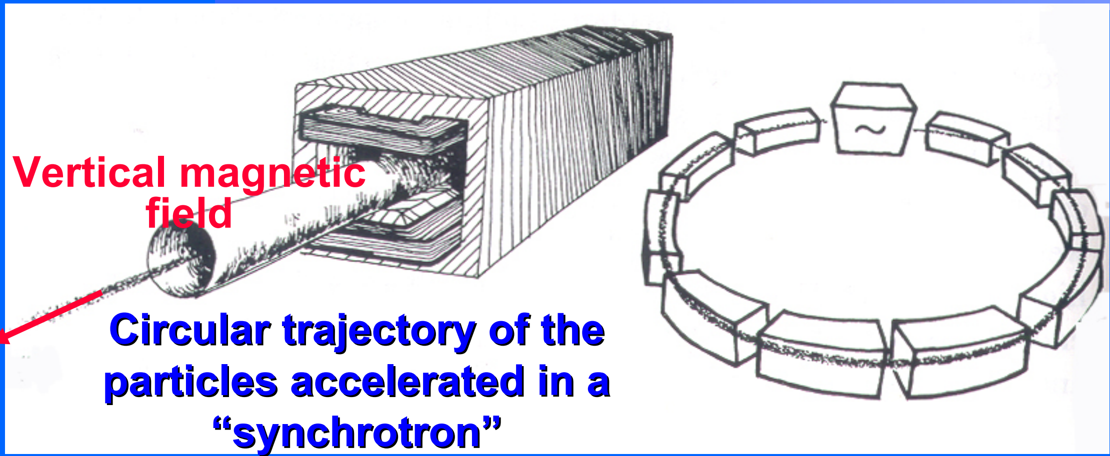
Praseodimio. – Ha due periodi. Uno di 5 minuti e l'altro più lungo.

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

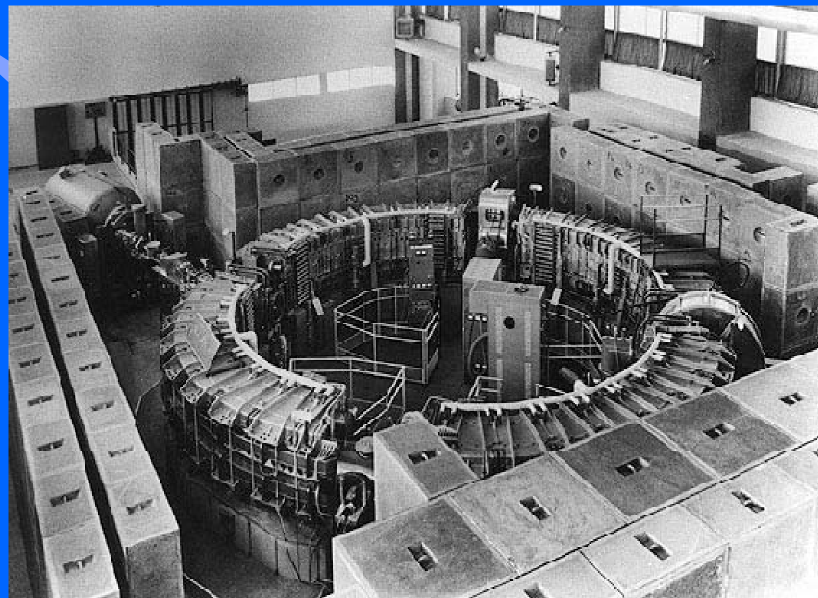
principle of phase stability

1 GeV electron synchrotron

Frascati - INFN - 1959

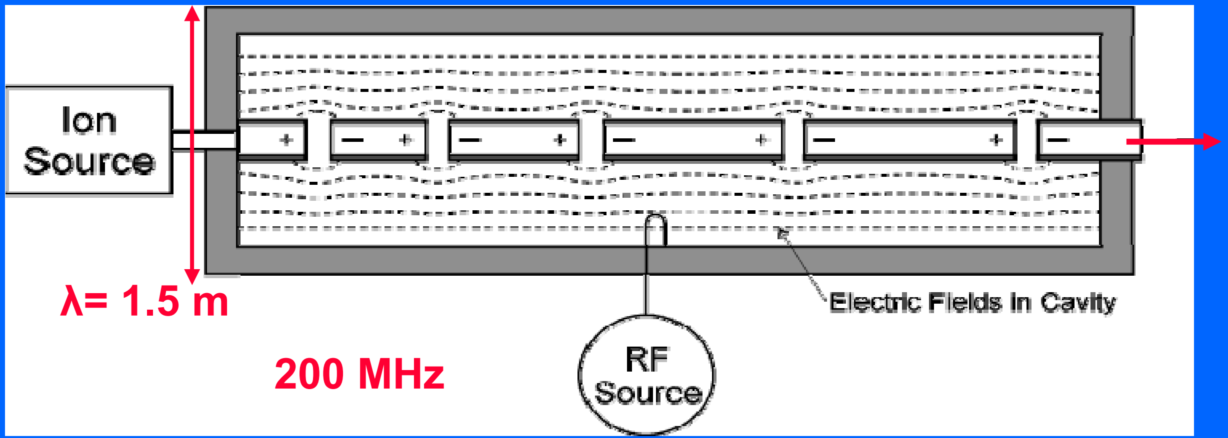
Veksler visits McMillan

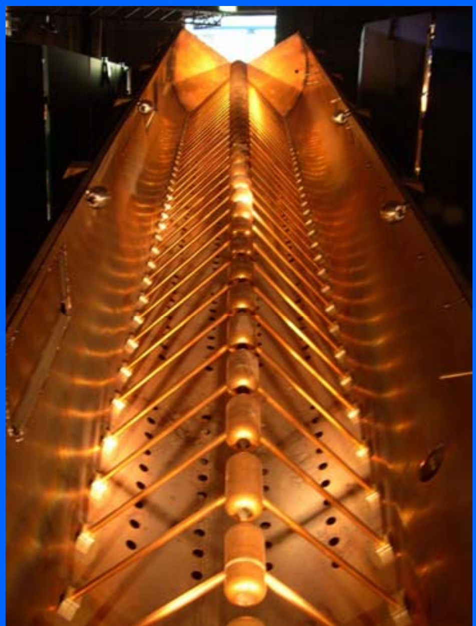
1959 - Berkeley



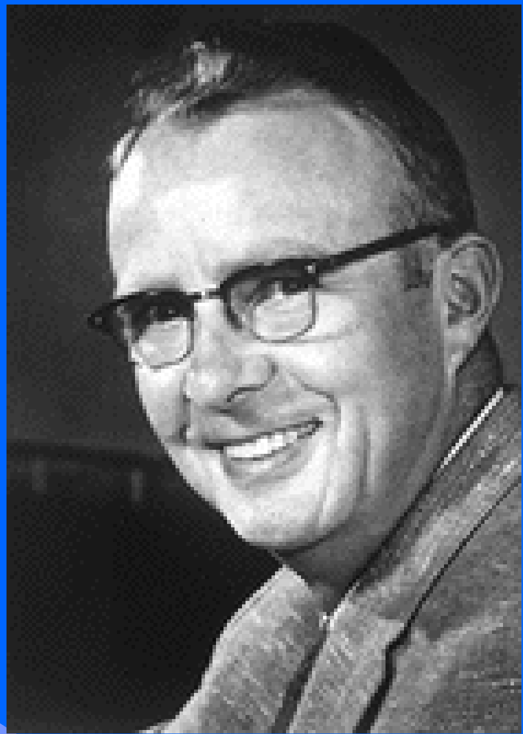
Radio-frequency linacs for protons and ions

Linear accelerator (linac)





100 MeV linac on display
at CERN Microcosm



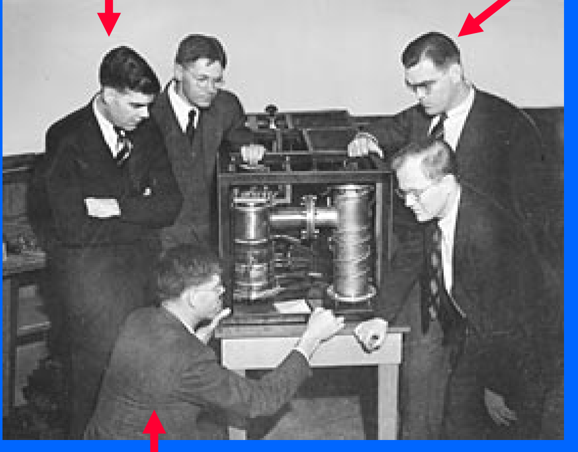
L. Alvarez

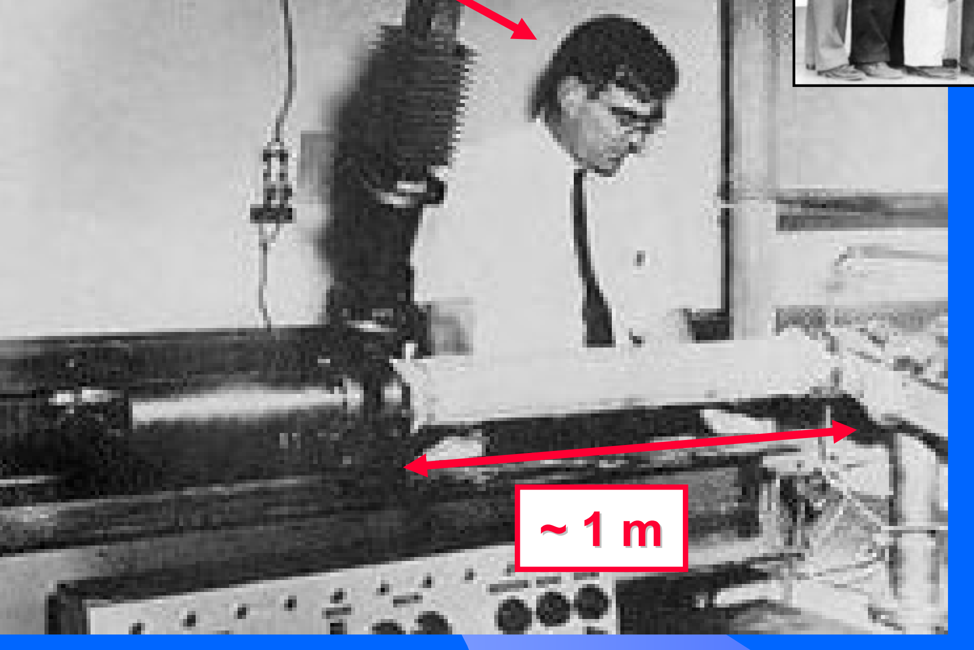
1946 – Drift Tube Linac

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**

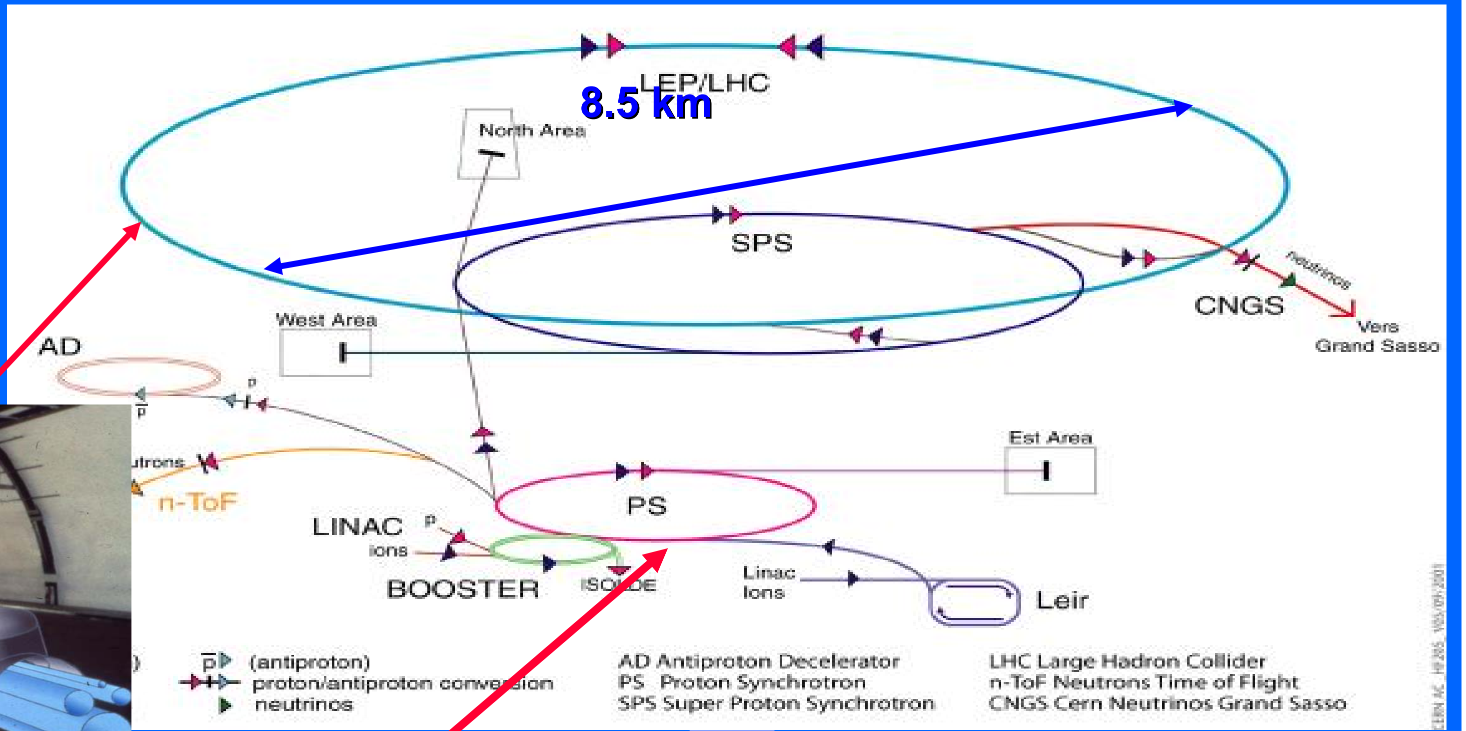
Secretary General

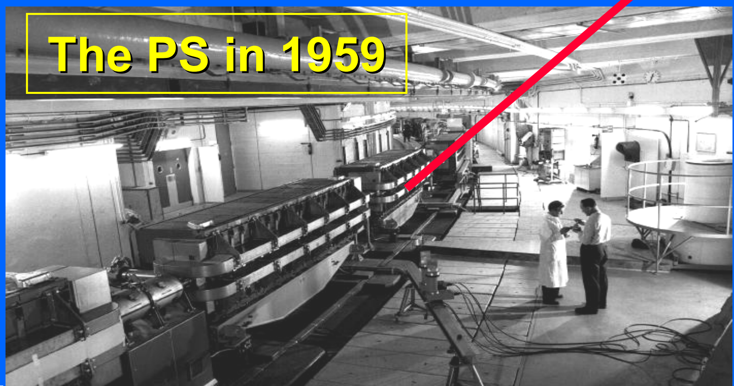
1952-54

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

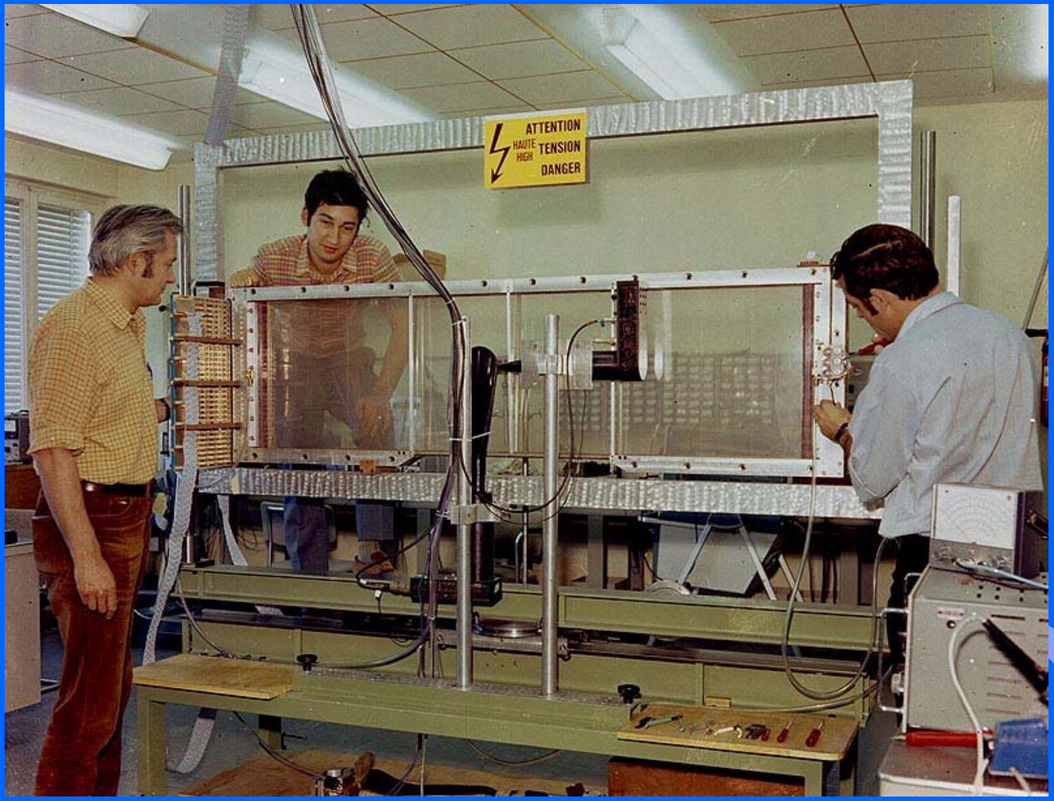
- **About half are used for bio-medical applications**

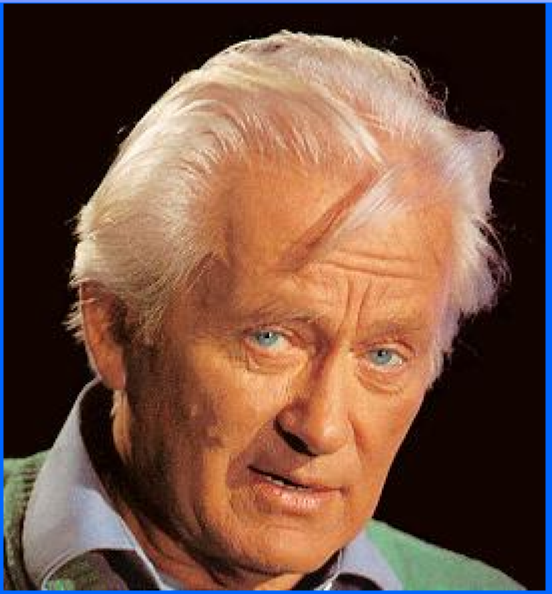
- They are the “eyes” of particle physicists

- 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





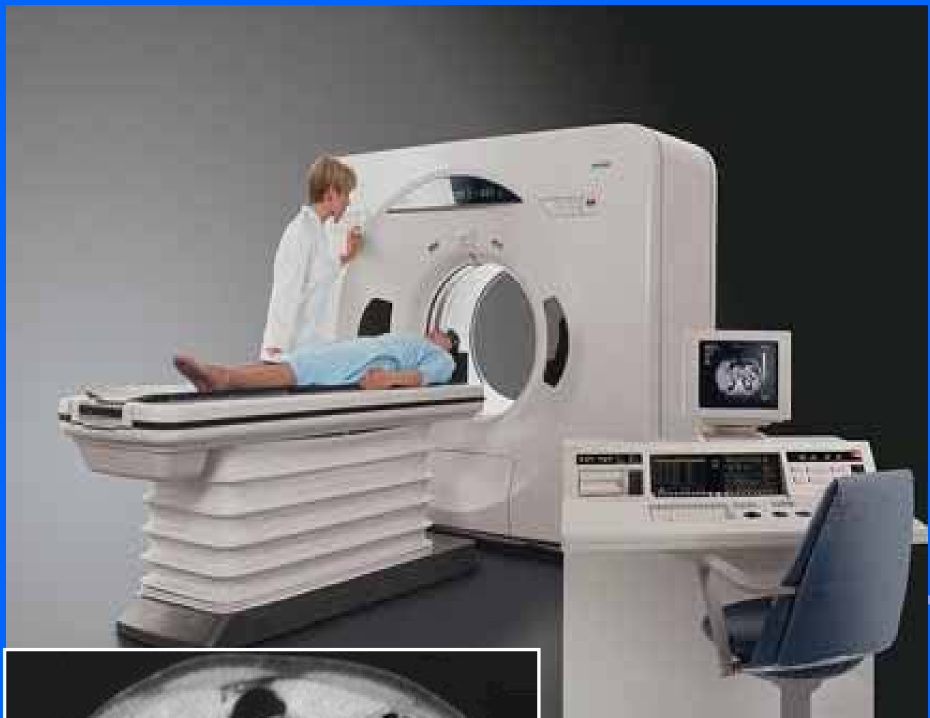
Georges Charpak, CERN physicist since 1959,

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

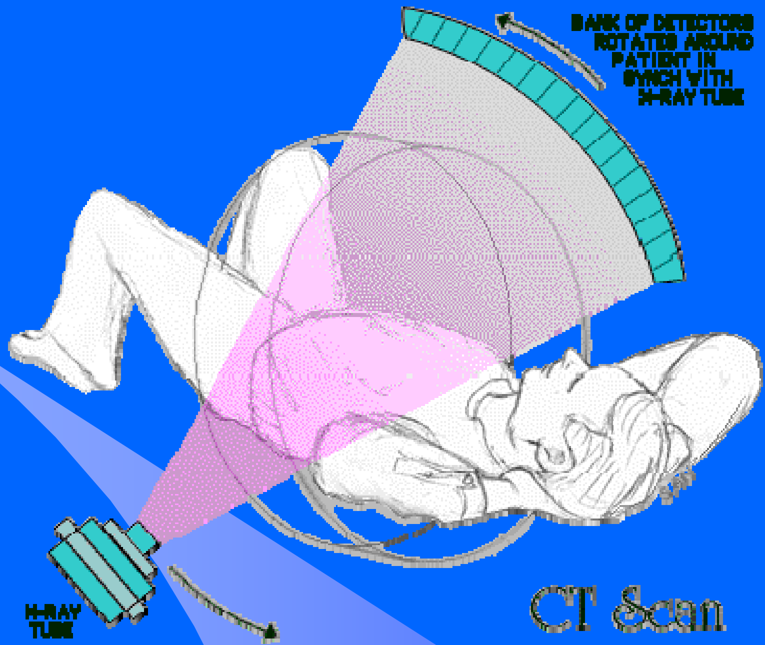
Applications in medical diagnostics

Diagnostics is essential!



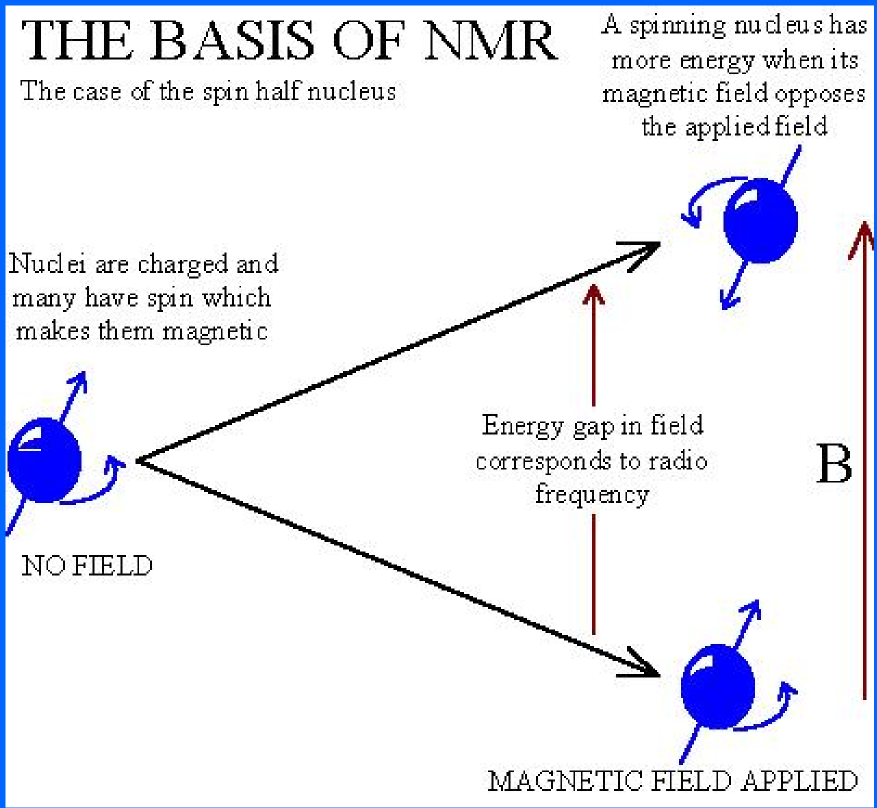
Abdomen

Computer Tomography (CT)



- Measurement of the electron density
- Information on the morphology

Nuclear Magnetic Resonance

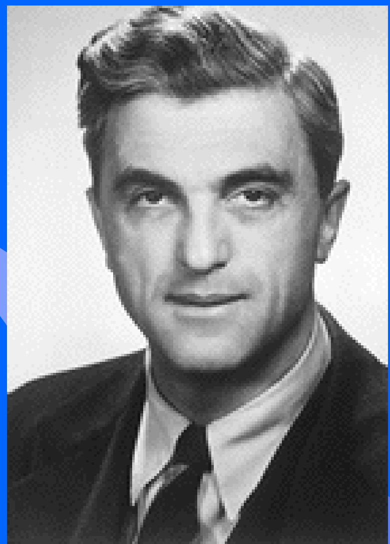


1938-1945

Felix Bloch and Edward Purcell

discover and study

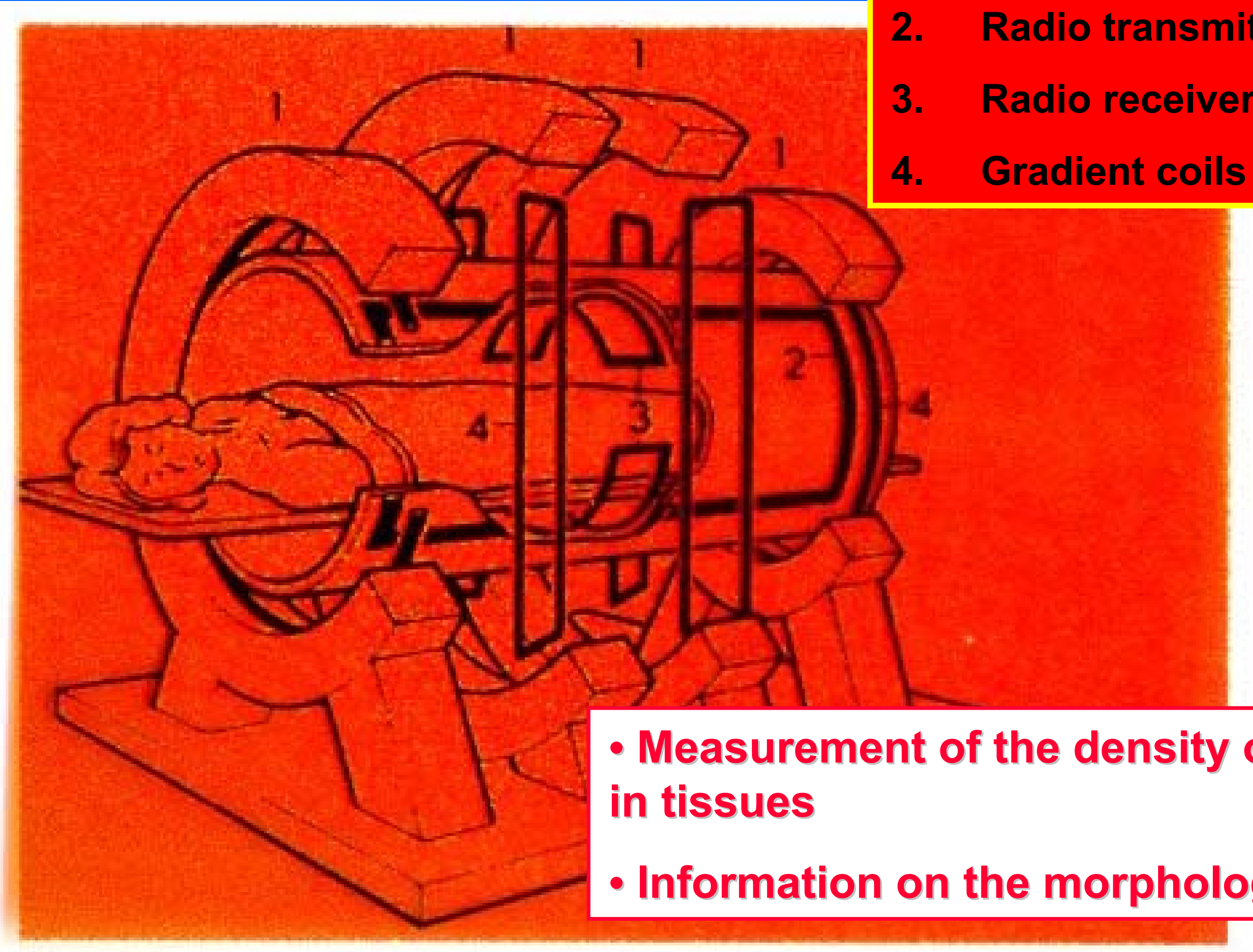
NMR



In 1954 Felix Bloch became

the first CERN Director General

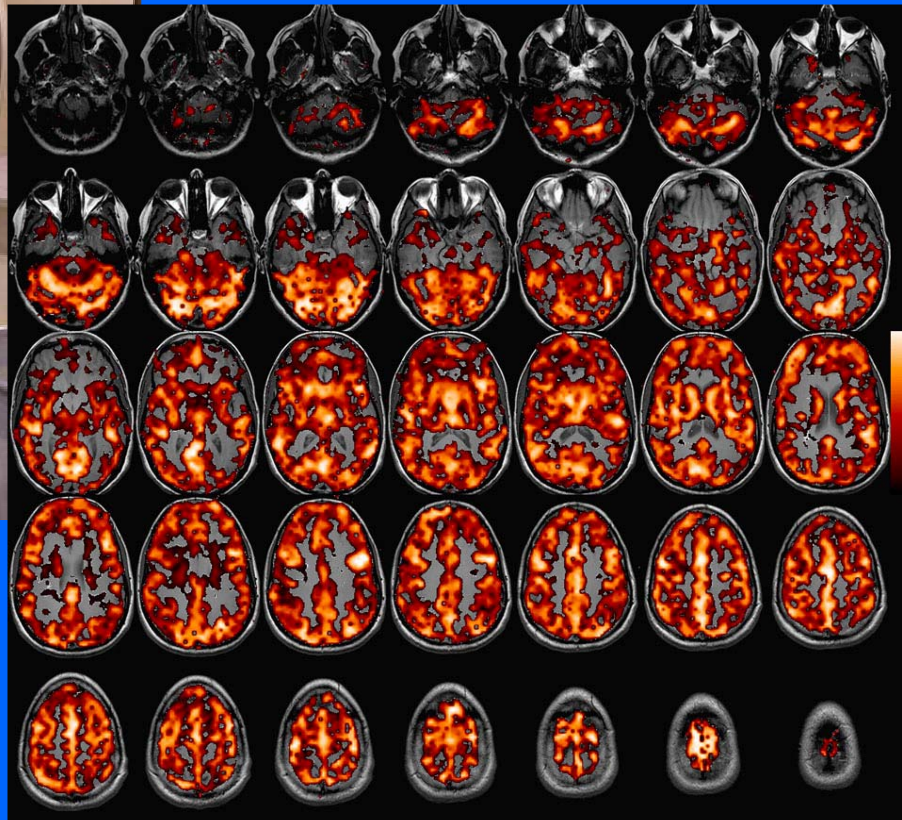
MRI = Magnetic Resonance Imaging



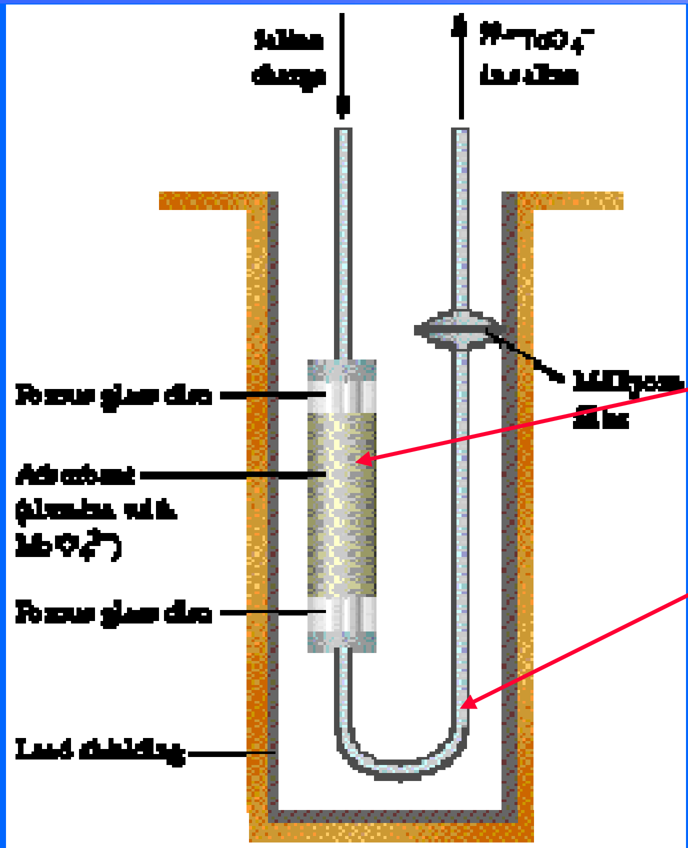
1. Main magnet (0.5-1 T)
2. Radio transmitter coil
3. Radio receiver coil
4. Gradient coils

- 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 slow neutrons produce

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

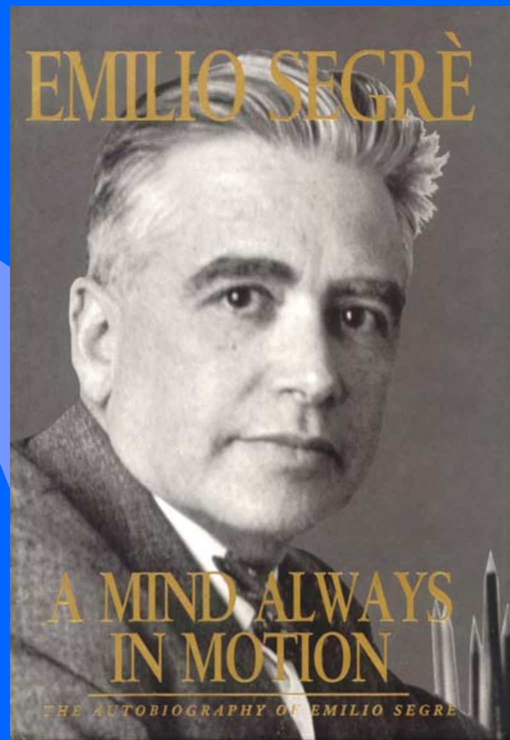
^{99}Mo (66 h) = ^{99m}Tc (6 h) + e^- + $\overline{\nu}$

gamma of 0.14 MeV

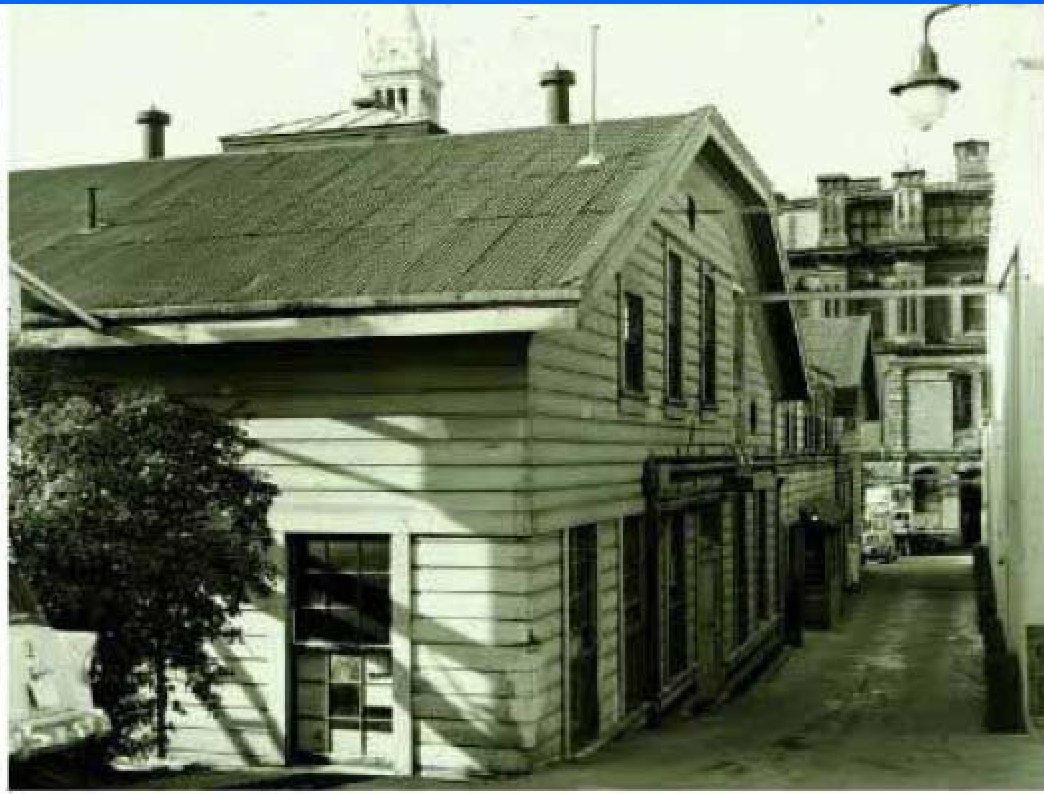
Emilio Segrè

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

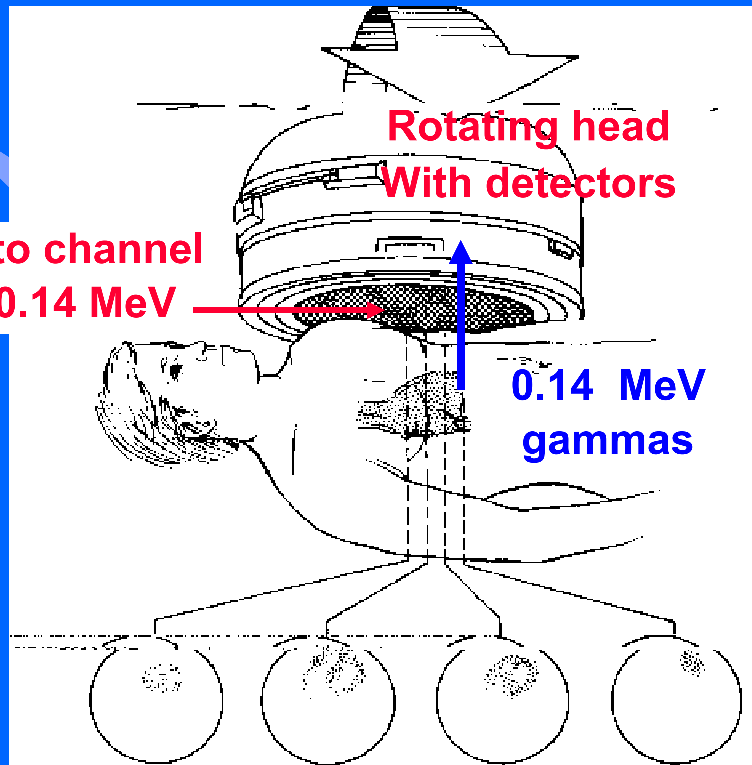
85% of all nuclear medicine examinations use technetium produced by slow neutrons in reactors

… liver

lungs

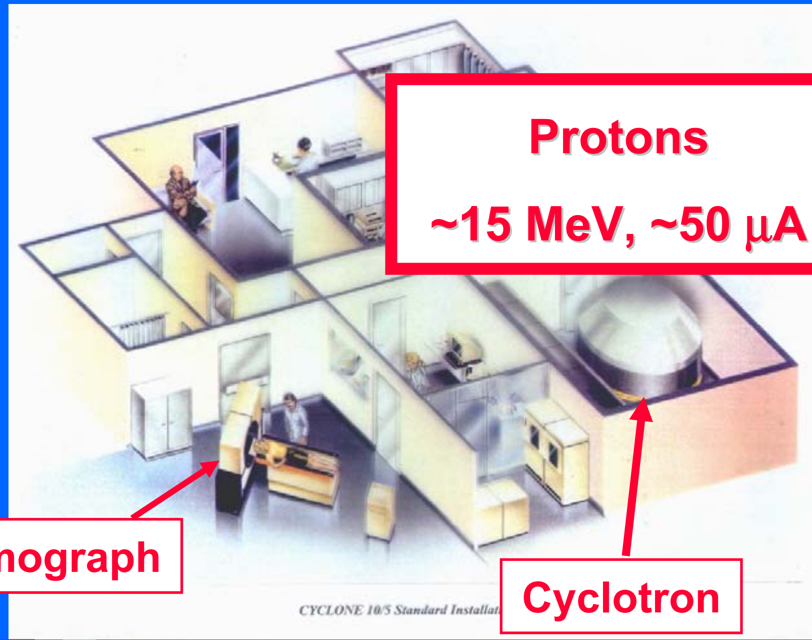
bones …

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



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**



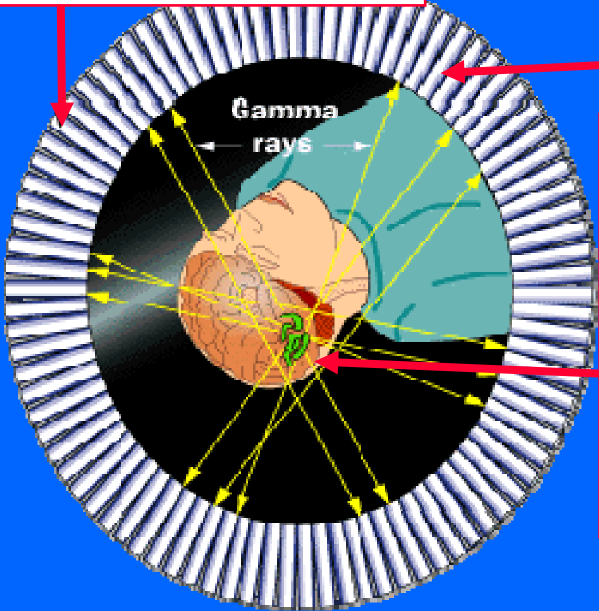
Protons

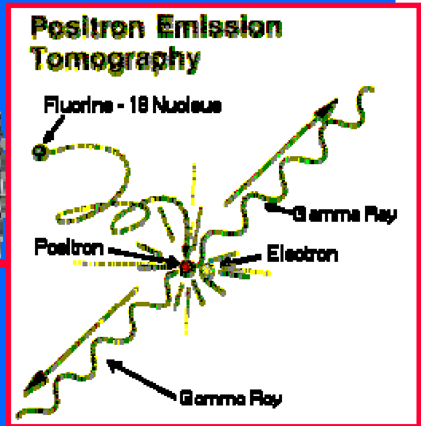
~15 MeV, ~50 μA

PET tomograph

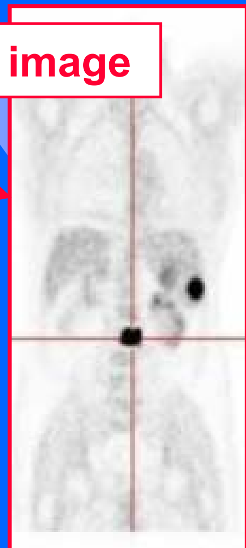
Cyclotron

Gamma ray detectors (Ex. BGO crystals)





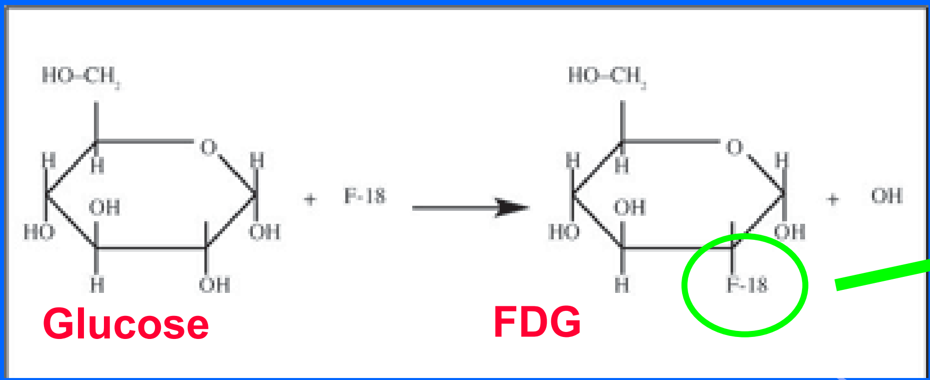
PET image

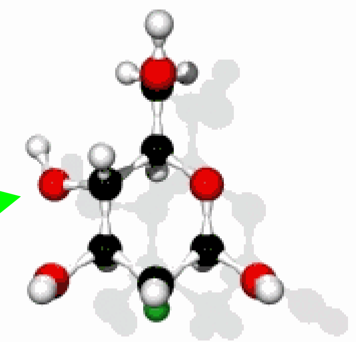


CT-PET

How does it work?

- $H_2{}^{18}O$ water is bombarded with protons to produce ^{18}F
- Fluoro-Deoxy-D-Glucose (FDG) is synthesized



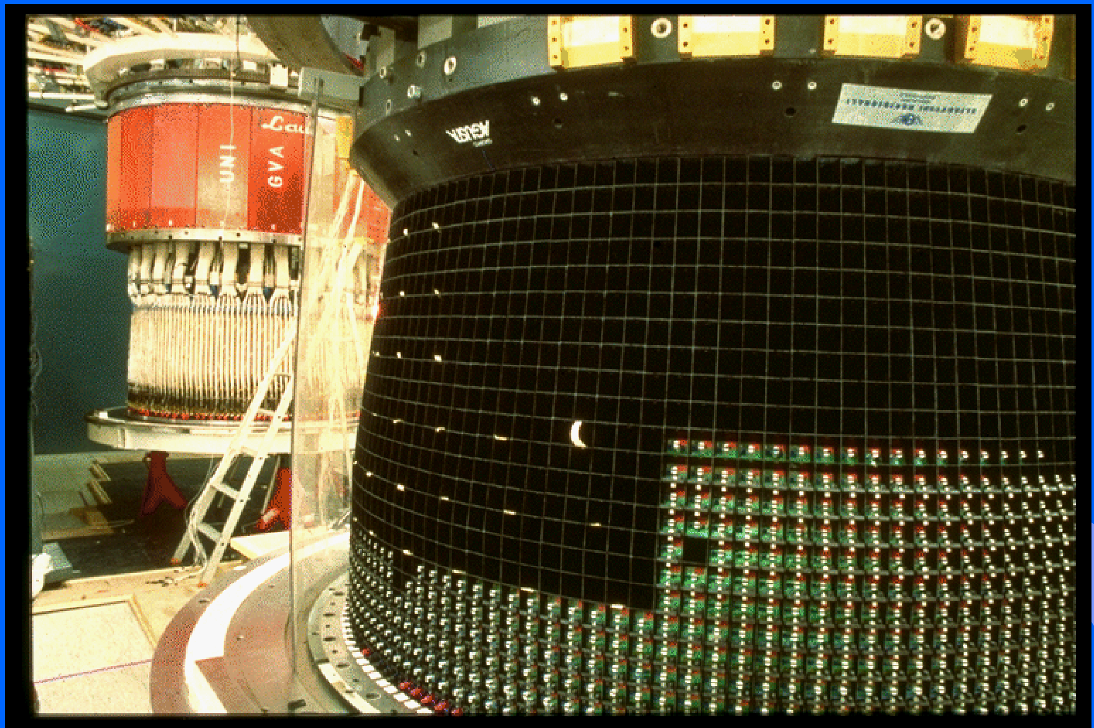


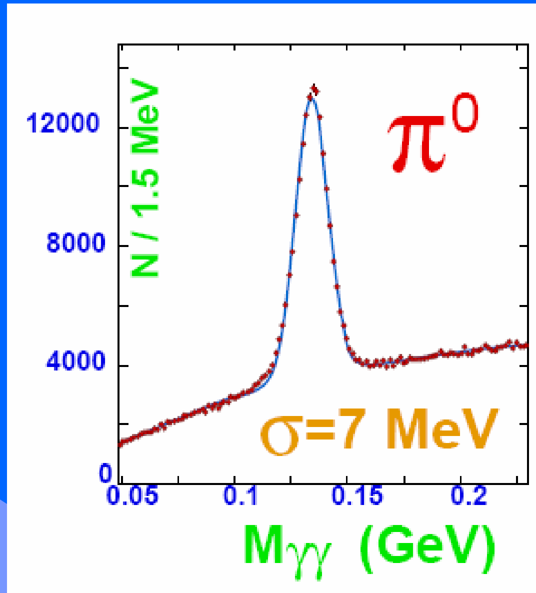
Radioactive Sugar

- FDG is transported to the hospital
- FDG is injected into the patient
- FDG is trapped in the cells that try to metabolize it
- Concentration builds up in proportion to the rate of glucose metabolism
- Tumors have a high rate of glucose metabolism and appear as “hot spots” in PET images

The BGO calorimeter of the L3 experiment at LEP (CERN 1989-2000)

BGO crystals have been developed for detectors in particle physics

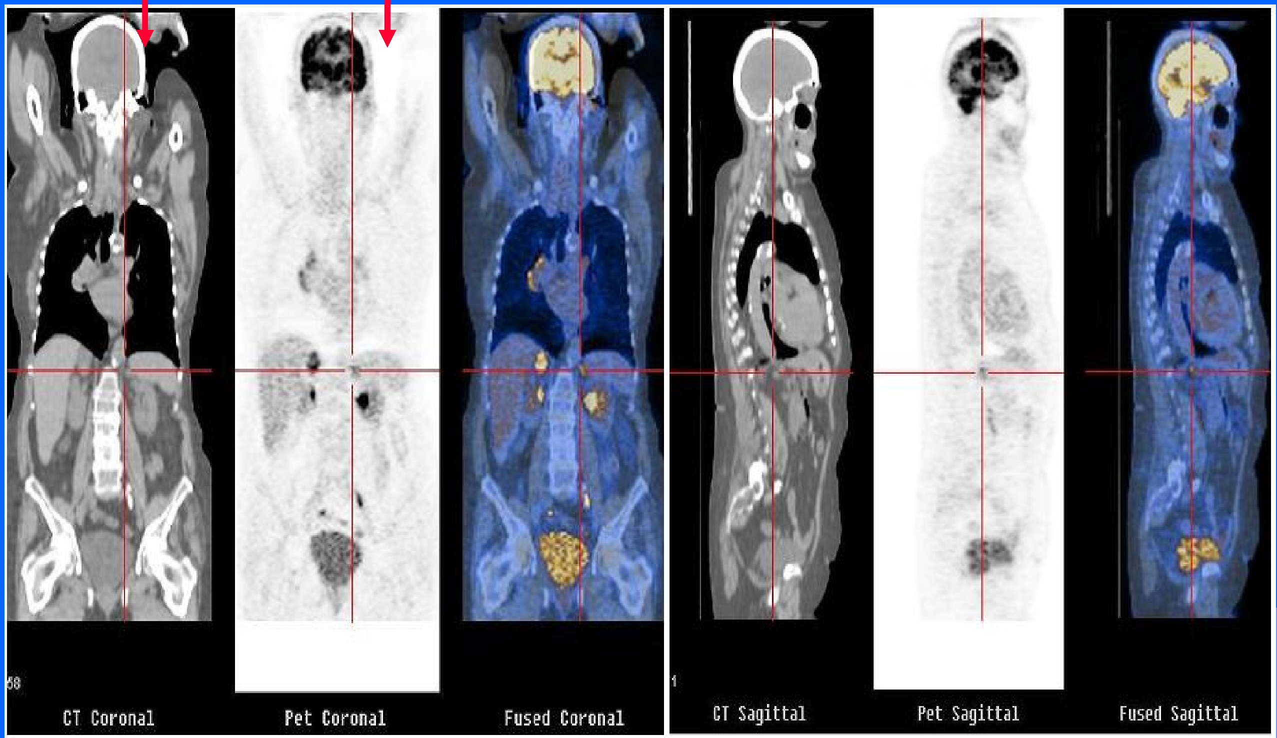




- 11000 BGO crystals
- Precise measurement of the energy deposited by the particles
- Almost 4 π coverage

The new diagnostics: CT/PET

morphology metabolism



David Townsend

CERN: 1970-78

Uni Ginevra

UPSM Pittsburgh

and

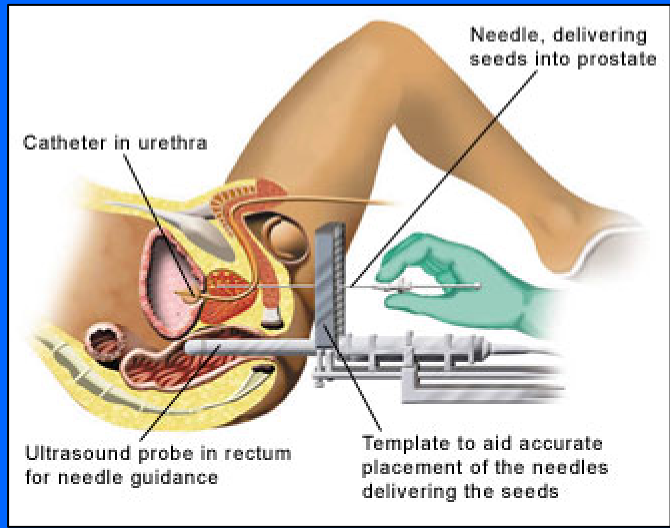
Ronald Nutt

(CTS – CTI)

Applications in conventional cancer radiation therapy

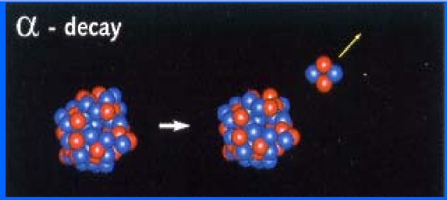
Methods

- Brachitherapy
  - Insertion of radiation sources in the body



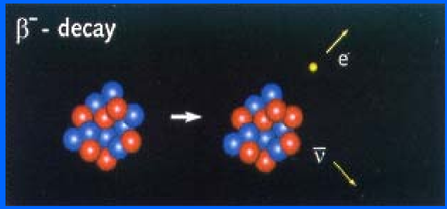
- Teletherapy
  - Bombardment of the tumour tissues with radiation coming from outside the body of the patient
- Radio immunotherapy
  - The radiation is brought by a radioisotope attached to a specifically selective vector

Radioactivity in cancer therapy



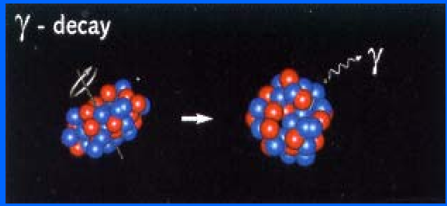
targeted radioimmunotherapy

α particles from Bismuth-213 **for leukaemia**



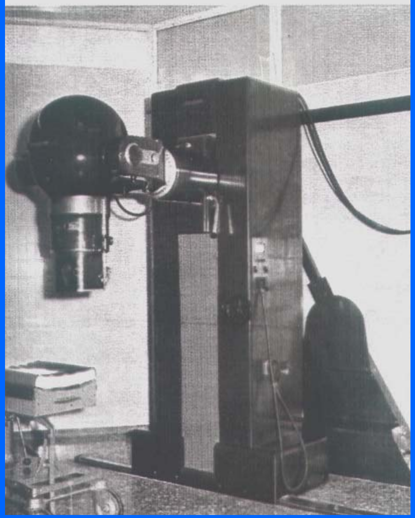
β particles from Yttrium-90 **for glioblastoma**

teletherapy



gammas from Cobalt-60 **for deep tumours**

COBALT "BOMB" - PICKER (1960)



Cobalt source 2000

Cobalt-60

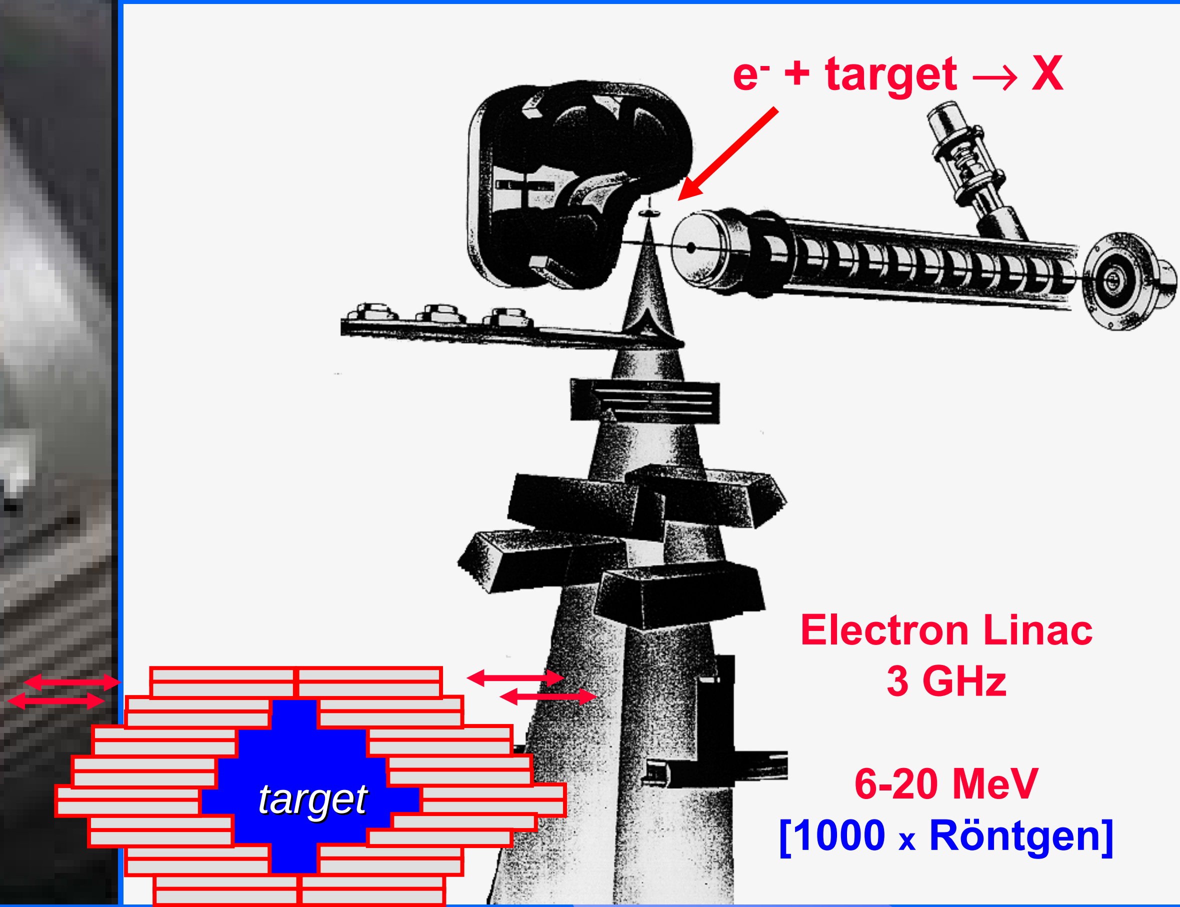
(1 MeV gammas)

is produced in reactors

by slow neutrons

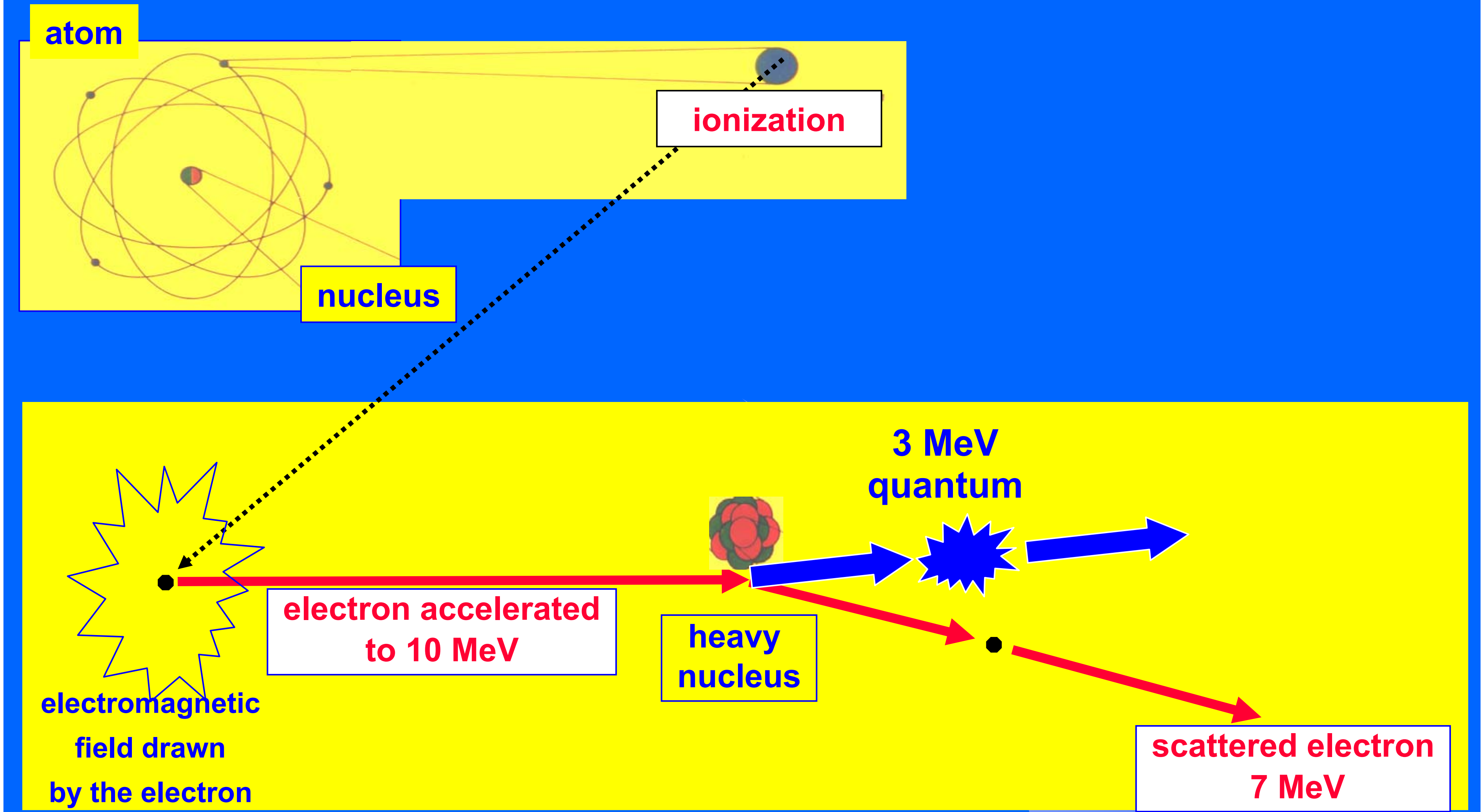
TERA

Teletherapy with X-rays

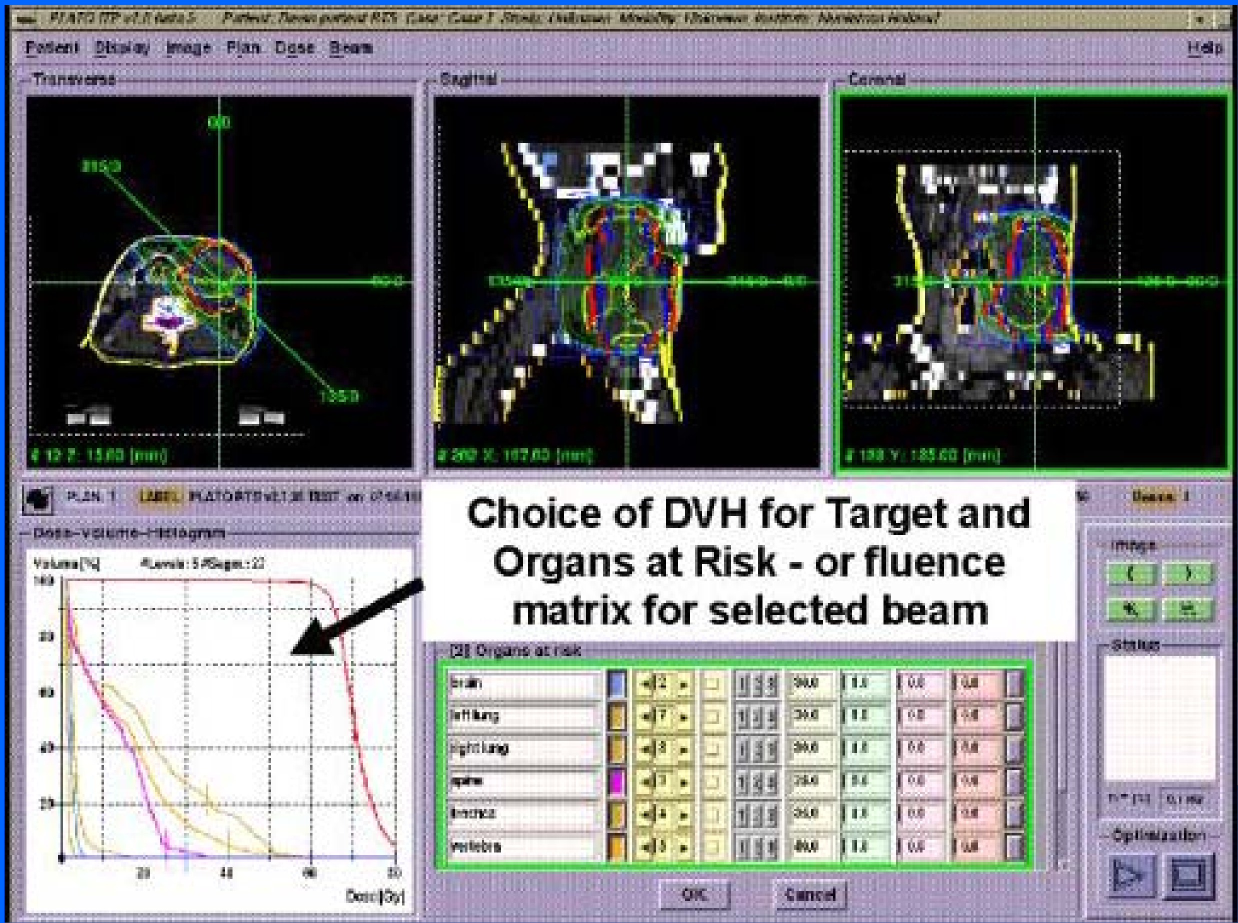


- Electron linacs to produce gamma rays (called X-rays by medical doctors)
- 20'000 patients/year every 10 million inhabitants

Production of X "quanta"

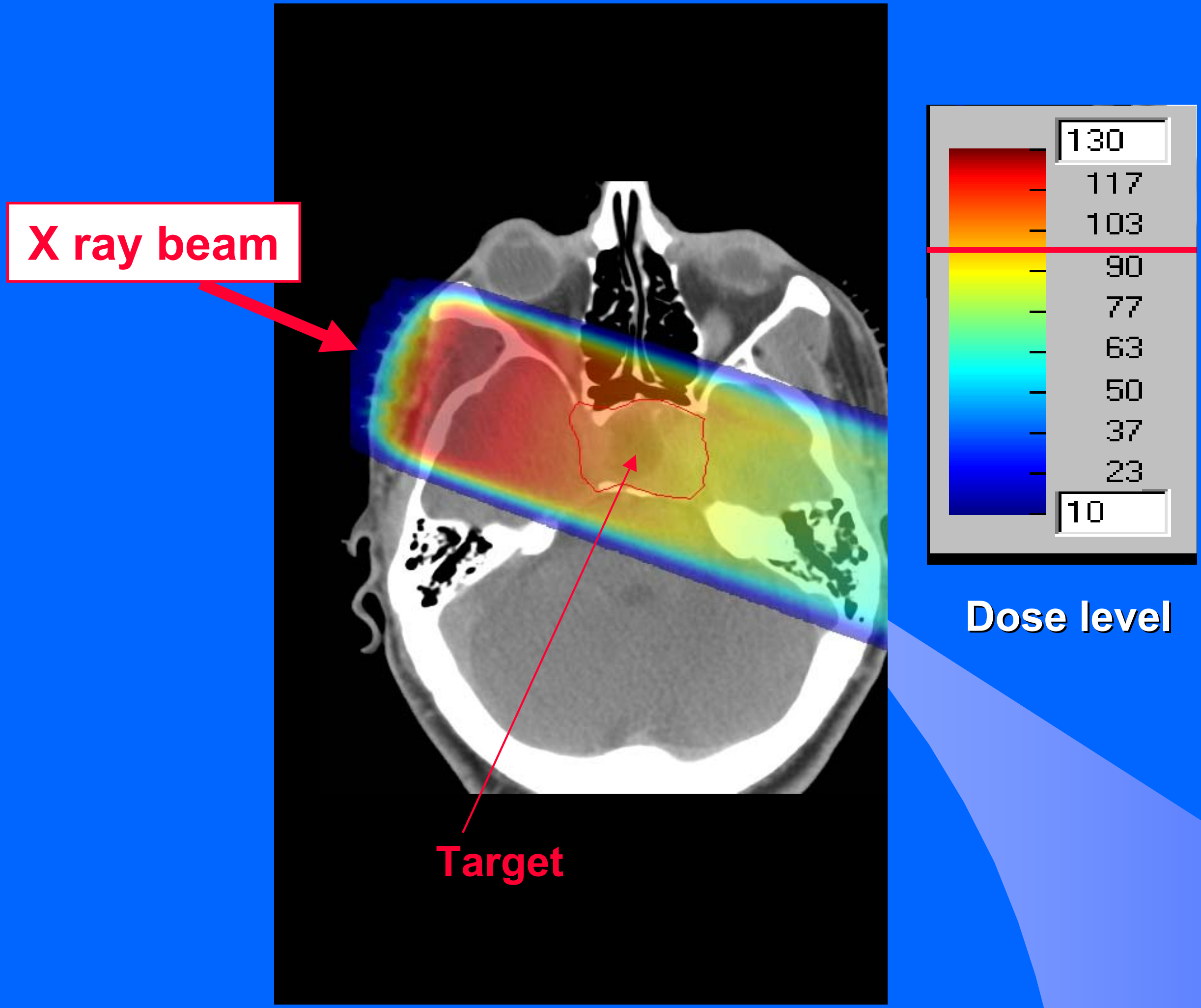


Computerized Treatment Planning System (TPS)



- 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

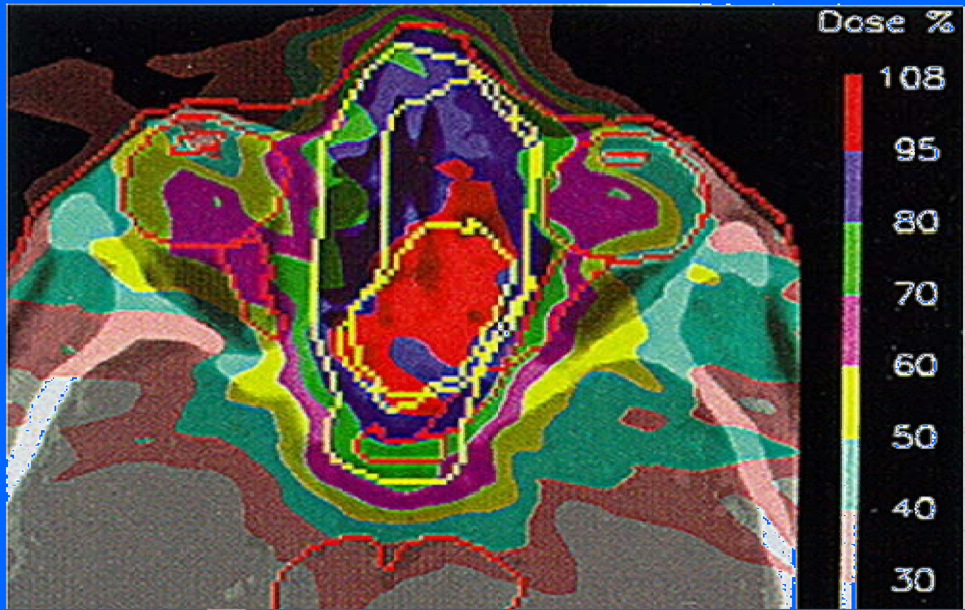
The problem of X ray therapy



The problem of X ray therapy

Solution:

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

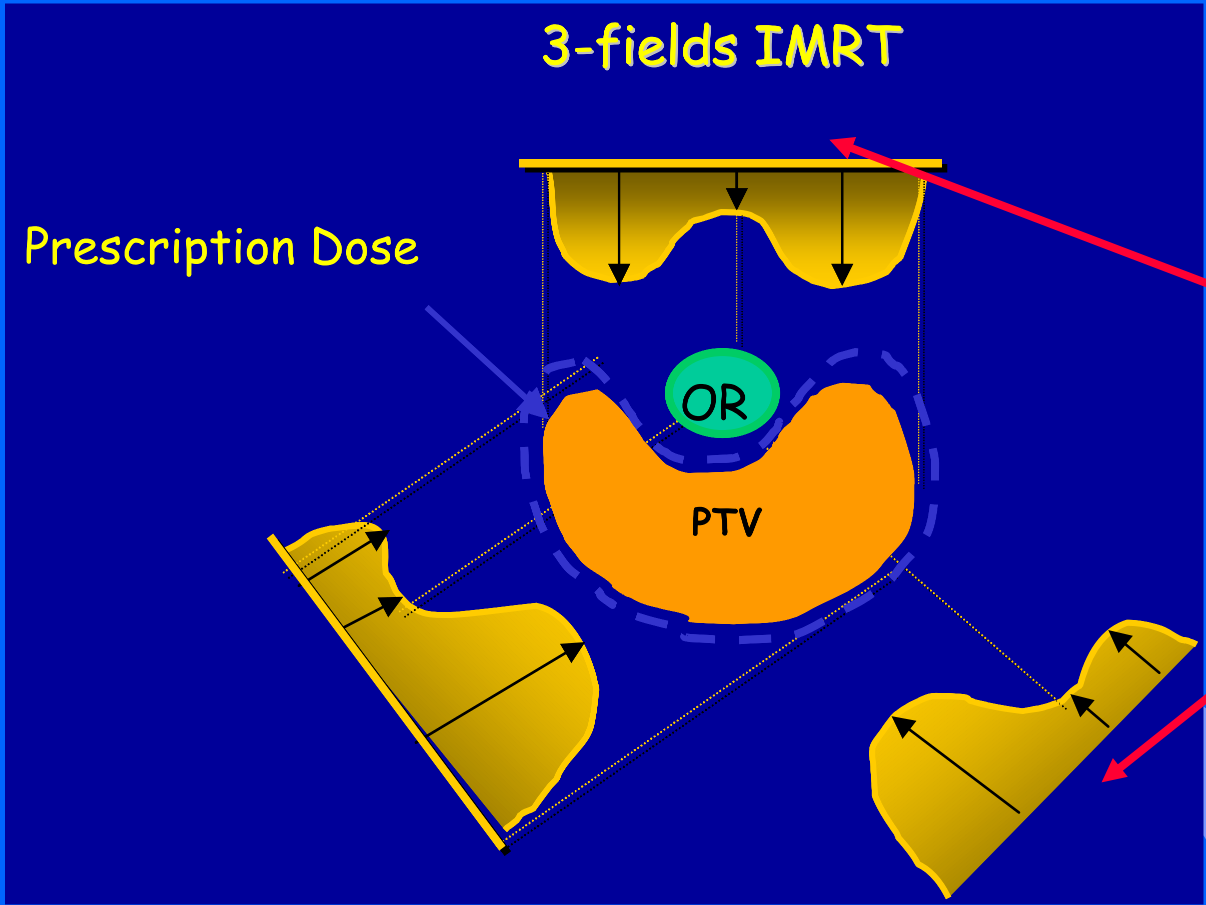


9 different photon beams

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

Especially near organs at risk (OAR)

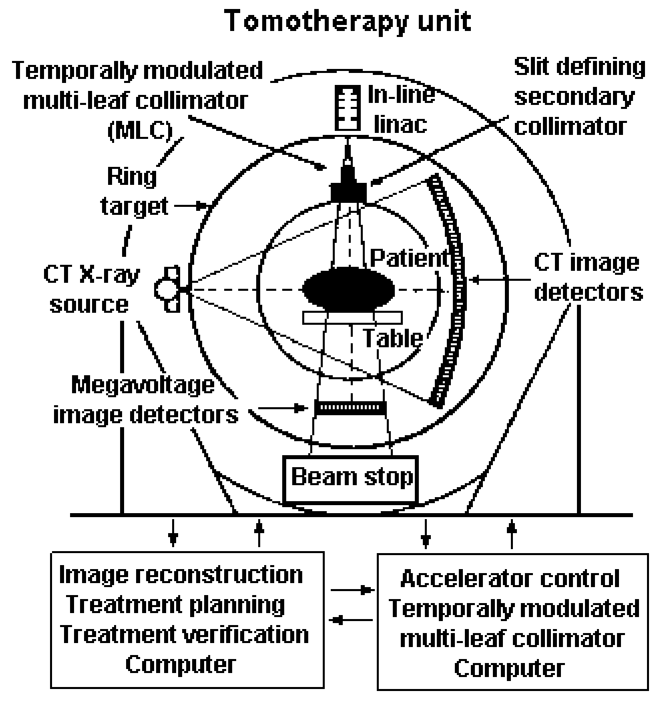
Multi leaf collimators and IMRT

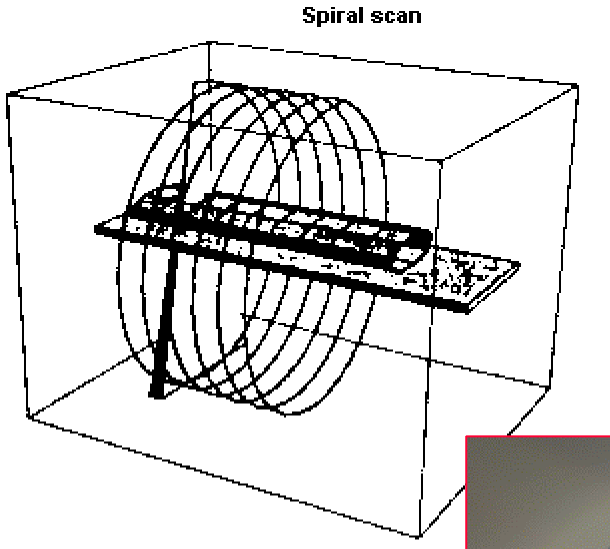


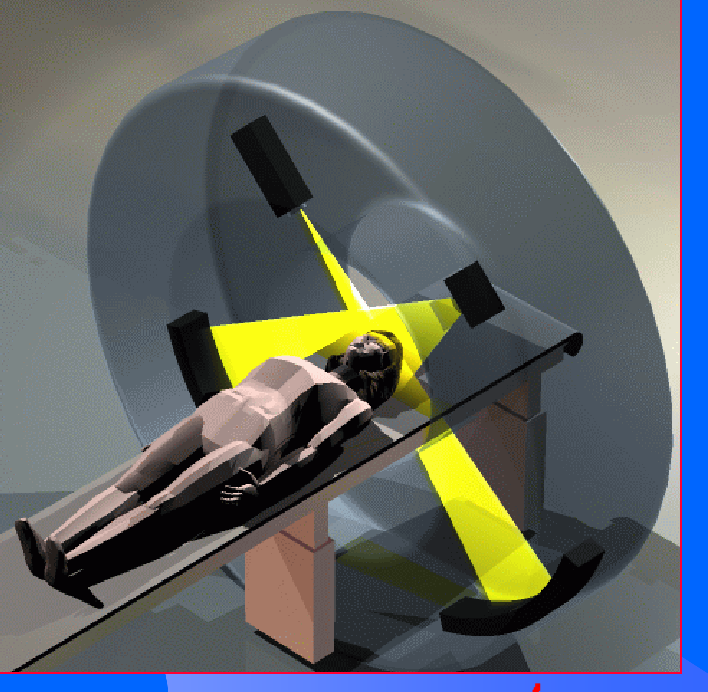
Multi leaf collimator which moves during irradiation

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

Tomotherapy







- The tumour is irradiated as the accelerator rotates and the patient is moved (spiral pattern)
- The intensity is modulated through the use of a multi-leaf collimator
- CT imaging integrated within the device itself

The “gamma knife”

- Proposed in 1967 by Lars Leksell (neurosurgeon) and Borje Larsson (physicist) at Karolinska Institutet, Stockholm
- Treatment of selected brain tumors, arteriovenous malformations and brain dysfunctions
- Small volume diseases (located in the head) treated in one session only (“stereo-tactic radio-surgery”)
- Today, more than 30000 patients every year

Lars Leksell poses with his Gamma Knife head frame

The original 1967 Leksell Gamma Knife

Today's Leksell Gamma Knife

201 ^{60}Co radiation sources

- Lightweight 6 MV linear accelerator to produce X-rays mounted on a robotic arm
- Use of X-rays taken during treatment to establish the position of the lesion and monitor the treatment
- Possibility of multiple fractions
- Used to treat small volume tumours (ex . Brain, head & neck, lung, spine, abdomen and pelvis) and lesions throughout the spine

Intra Operative Radiation Therapy (IORT)

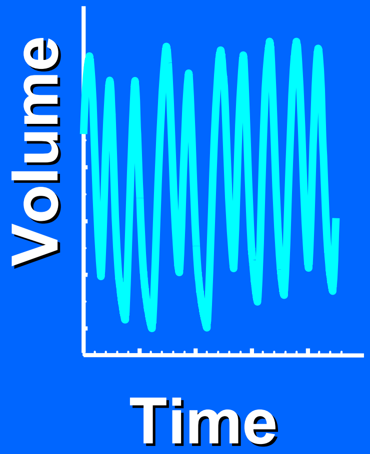
Irradiation with an electron beam during surgery

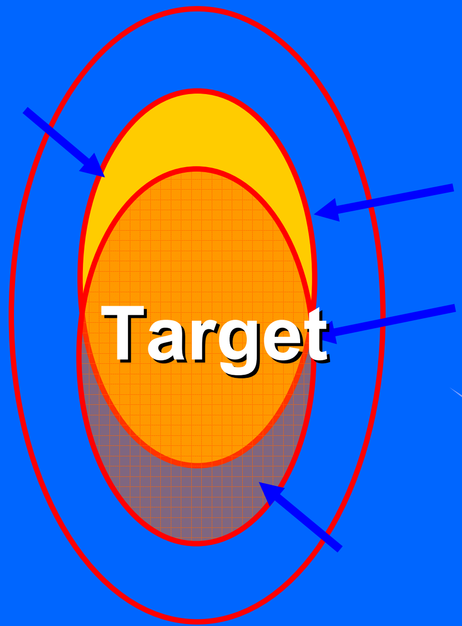
Electron energies: 3 – 9 MeV

Mean dose rate: 6 – 30 Gy/min

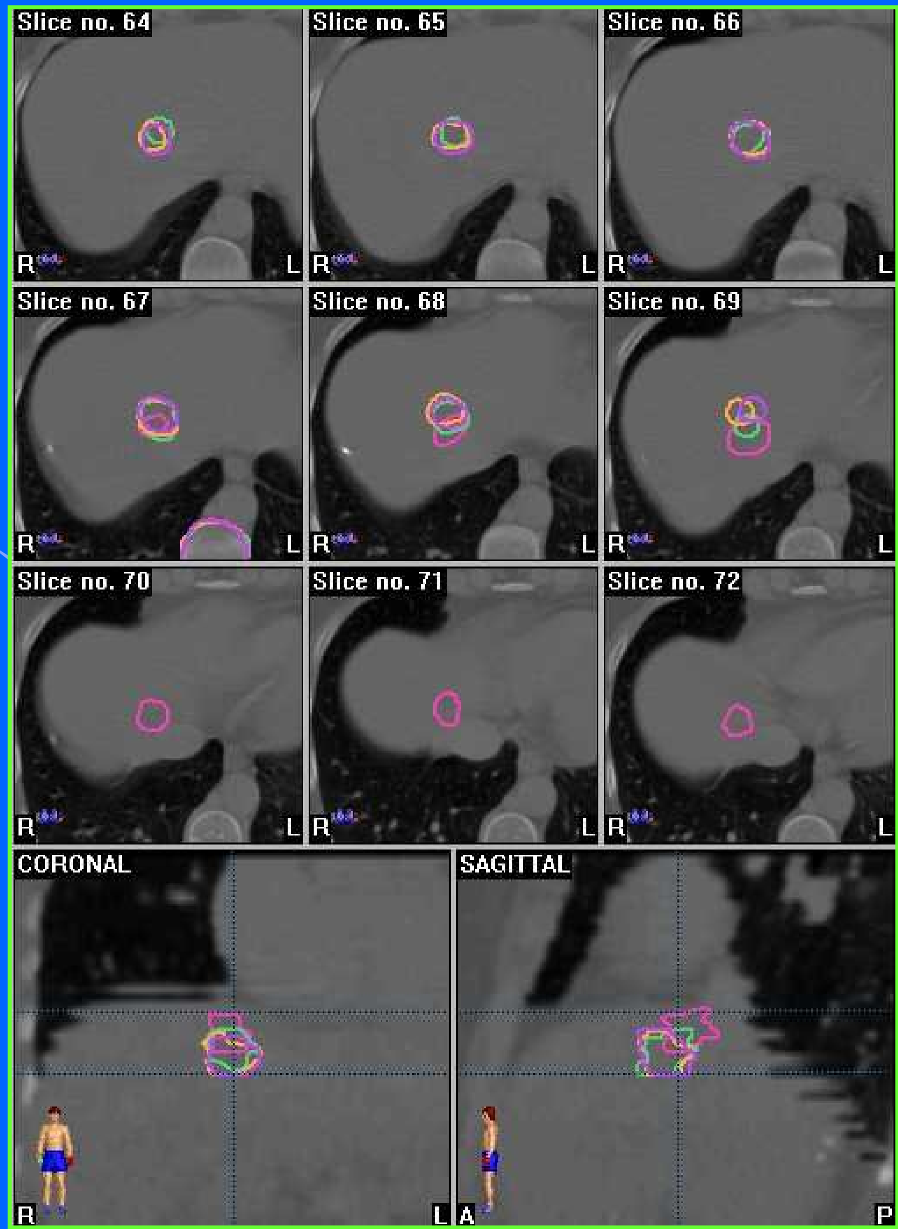
Irradiation time (21 Gy): 0.7 – 3.5 min

The problem of organ motion





Liver CT images

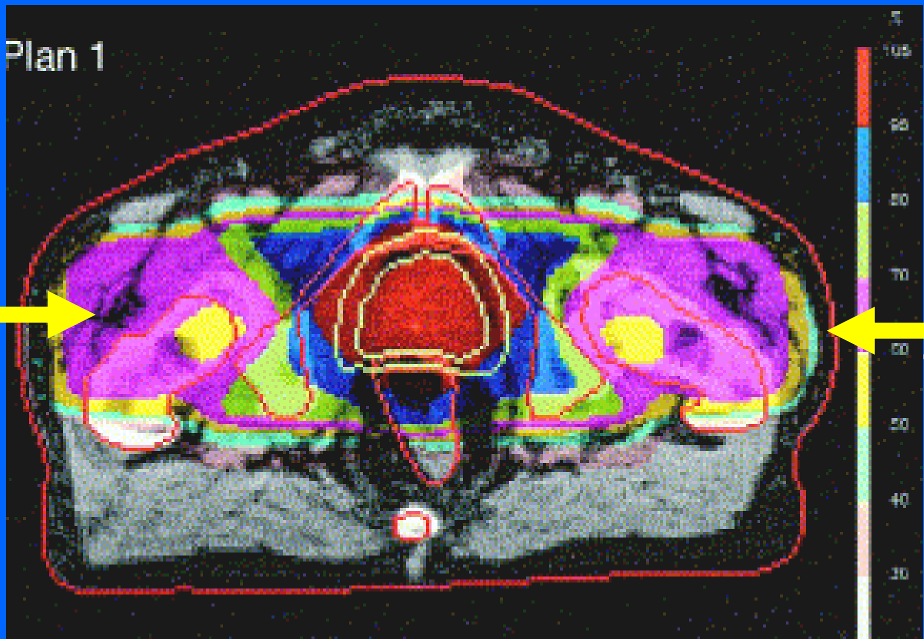


Possible solutions:

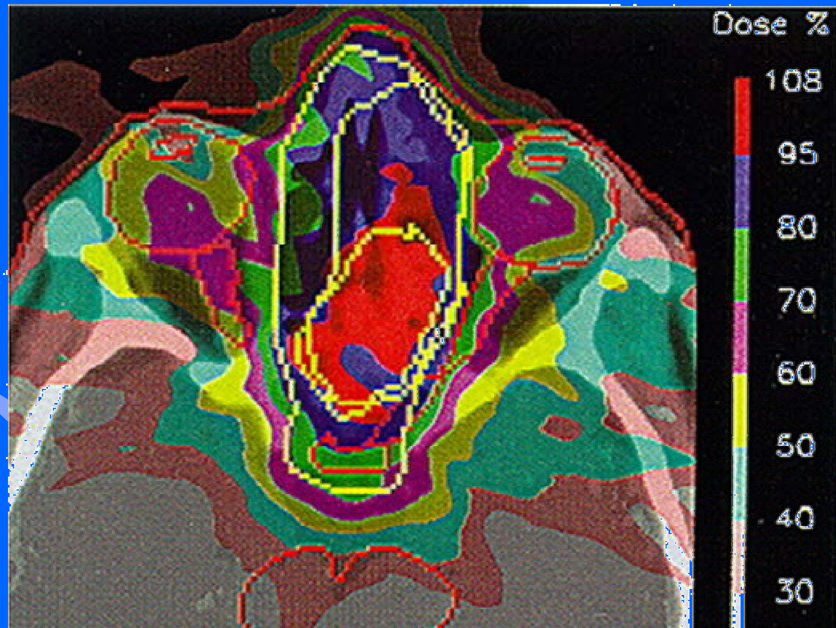
- Respiratory gating

- Image Guided Radiation Therapy (IGRT)

2 X ray beams



9 X ray beams (IMRT)



A question for a particle physicist

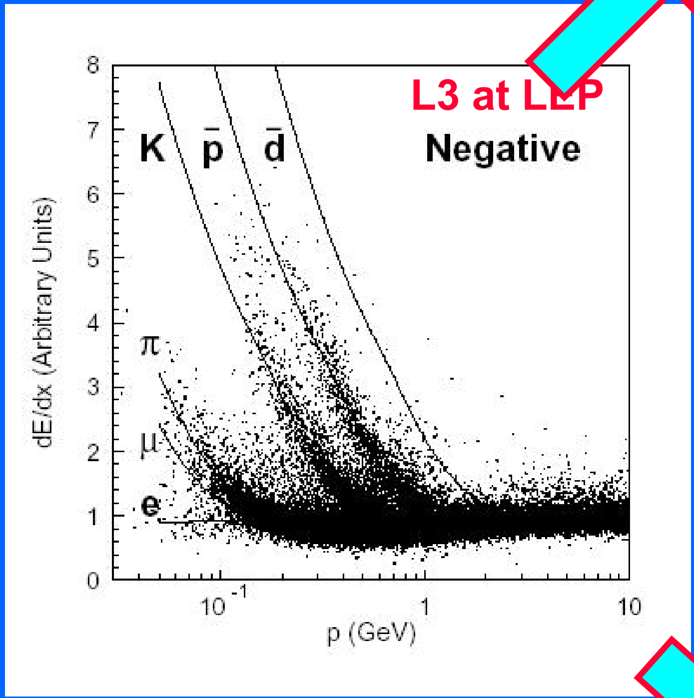
Are there better radiations to attack the tumour and spare at best the healthy tissues?

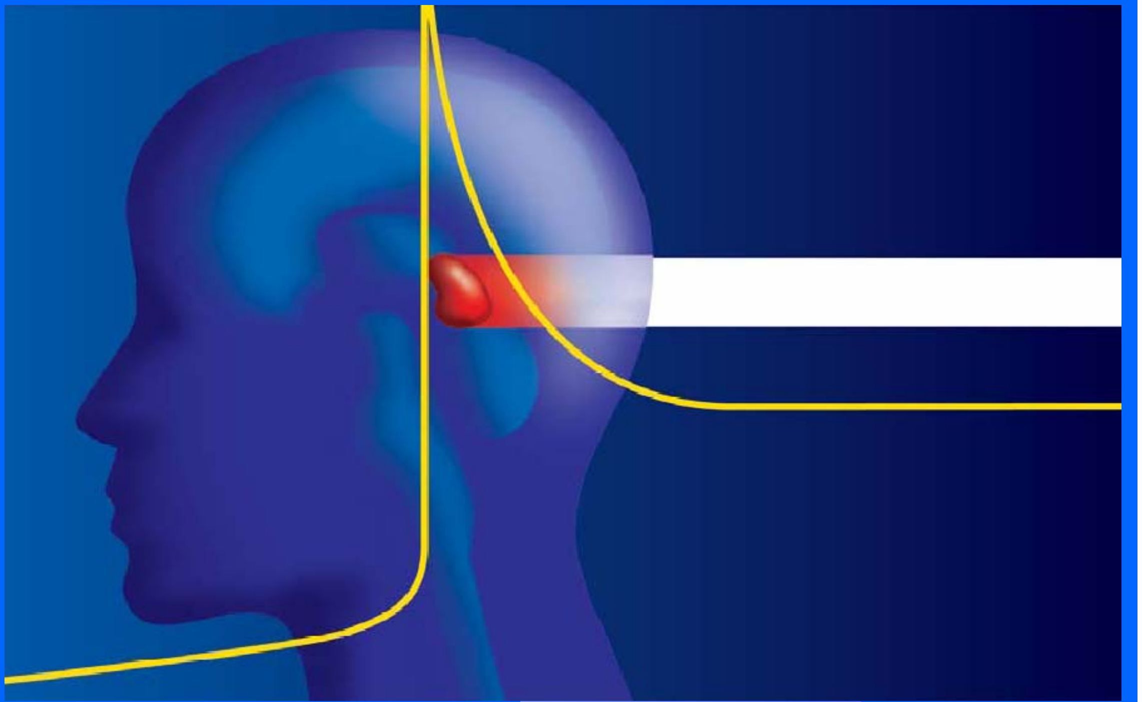
Answer : BEAMS OF CHARGED HADRONS

Let's go back to physics...

Fundamental physics

Particle identification





Medical applications

Cancer hadrontherapy

End of lecture I