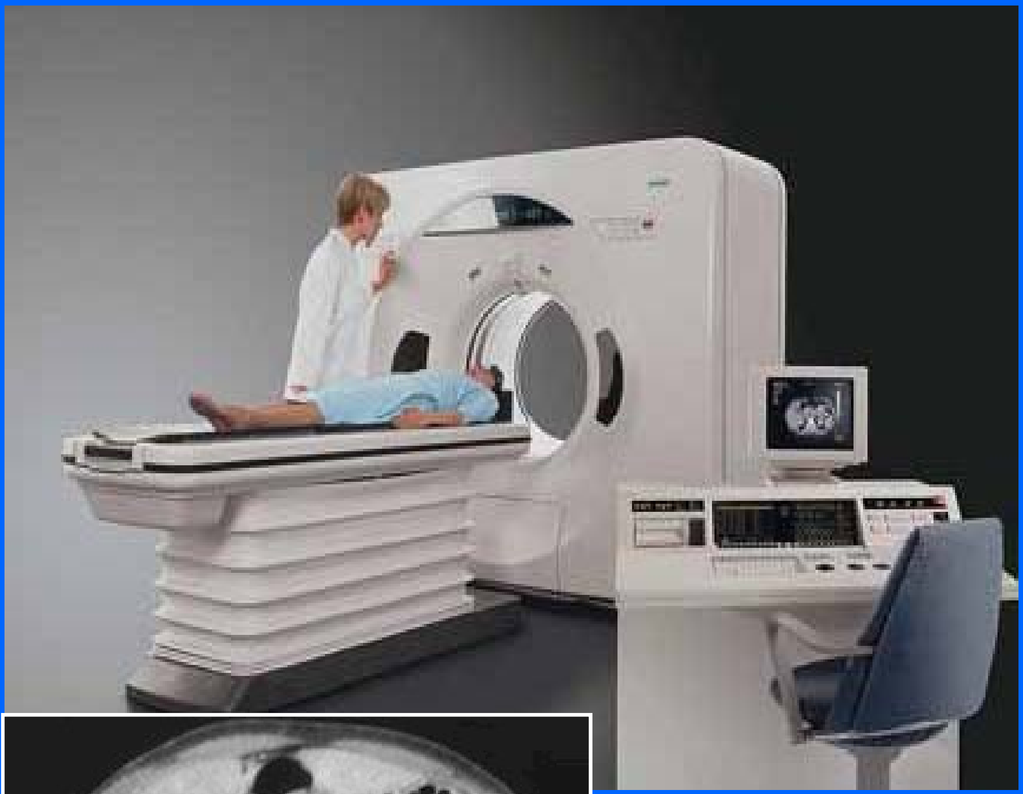
Outline

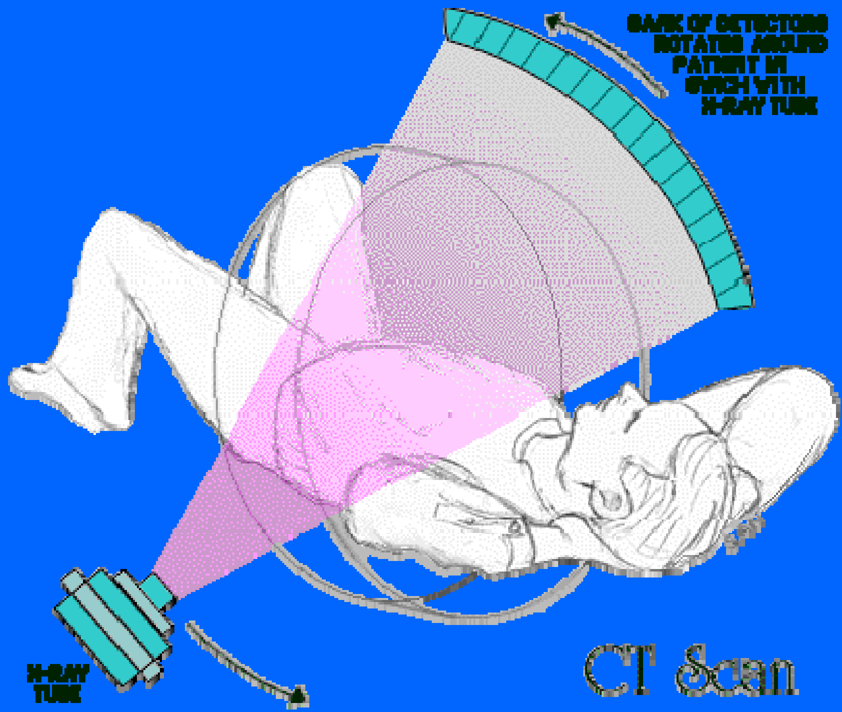
- Introduction: an historical review **I**
- Applications in medical diagnostics **II**
- Particle accelerators for medicine **III**
- Applications in conventional radiation therapy **IV**
- Hadrontherapy, the frontier of cancer radiation therapy **V**
  - Proton-therapy
  - Carbon ion therapy
  - Neutrons in cancer therapy

Diagnostics is essential!



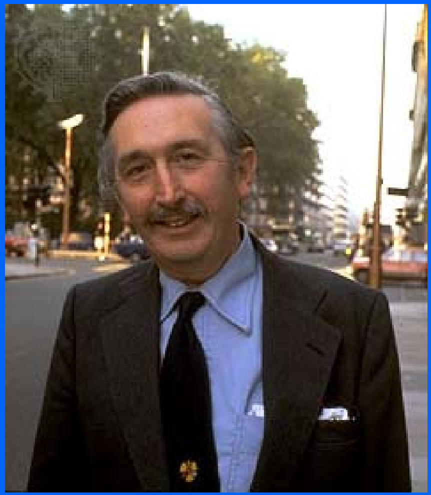
Abdomen

Computer Tomography (CT)



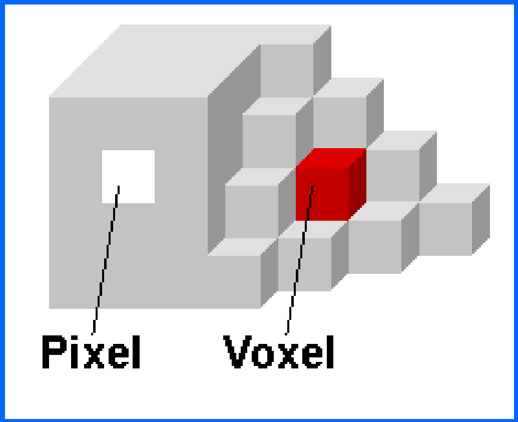
- **Measurement of the electron density**
- **Information on the morphology**

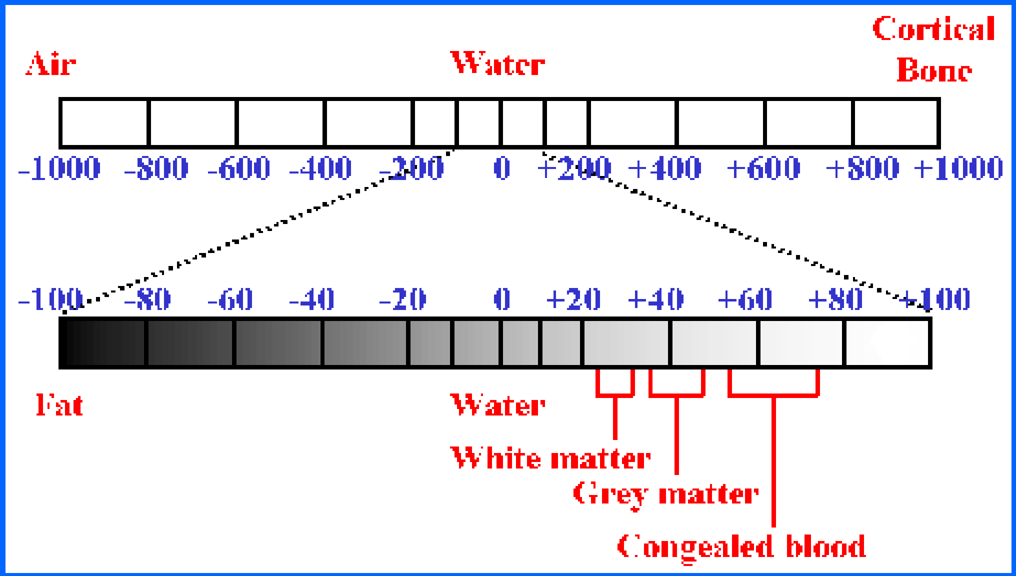
CT and Hounsfield numbers



G. Hounsfield

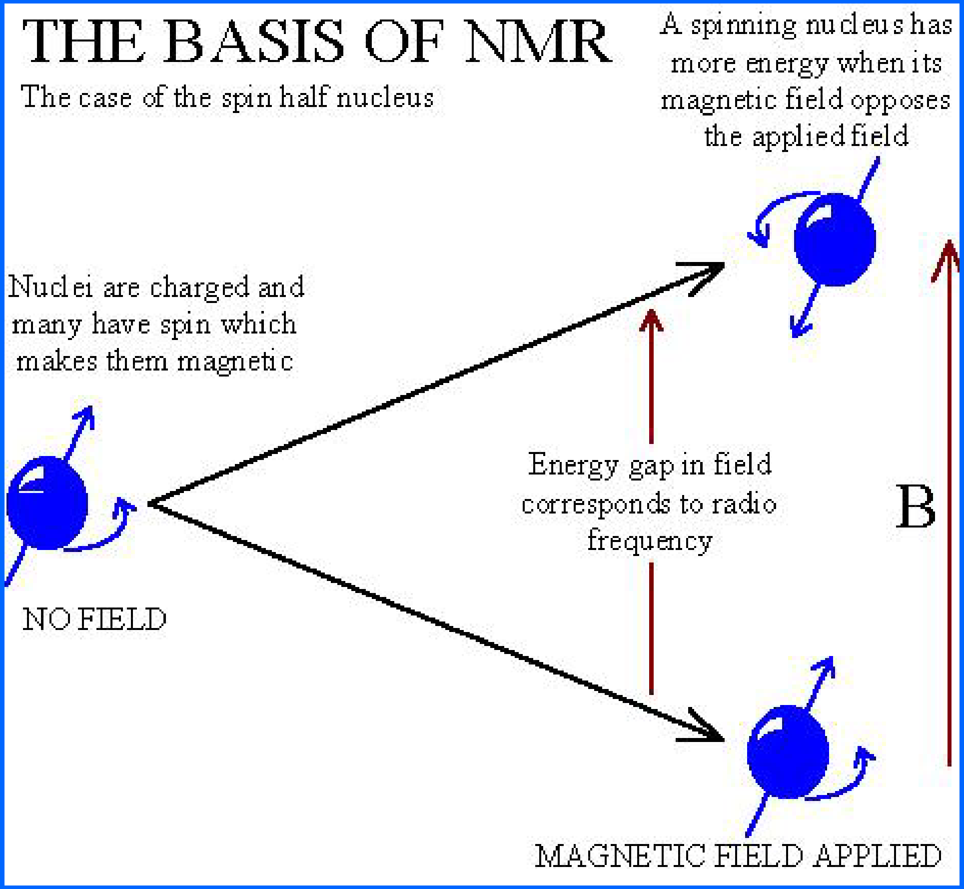
1979 Nobel Prize for Physiology or Medicine





Through the measurement of the attenuation coefficient in many directions and slices (i.e. many radiographies) the Hounsfield numbers are calculated for all the Voxels (=VOlume piXELS)

Nuclear Magnetic Resonance

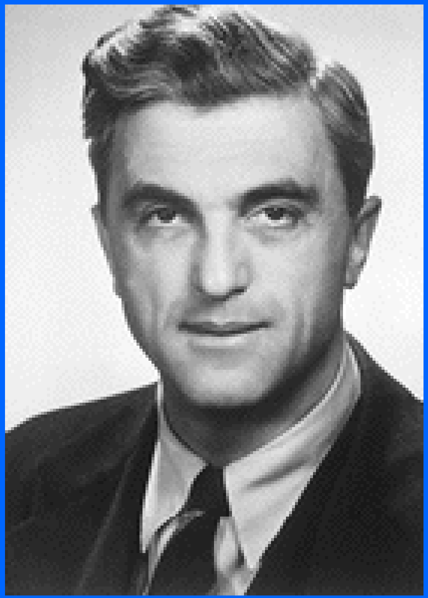


1938-1945

Felix Bloch and Edward Purcell

discover and study

NMR

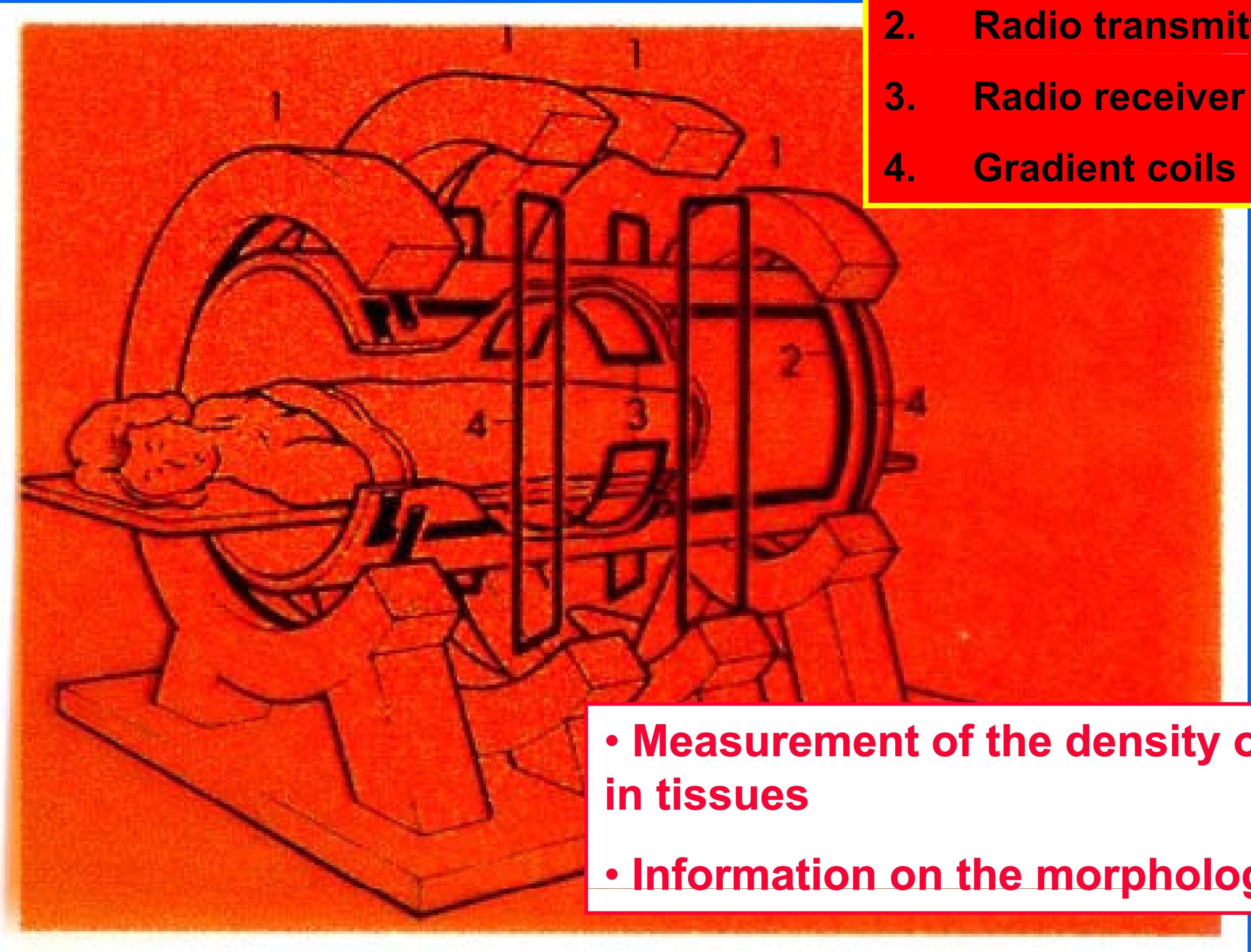


In 1954 Felix Bloch became

the first CERN Director General

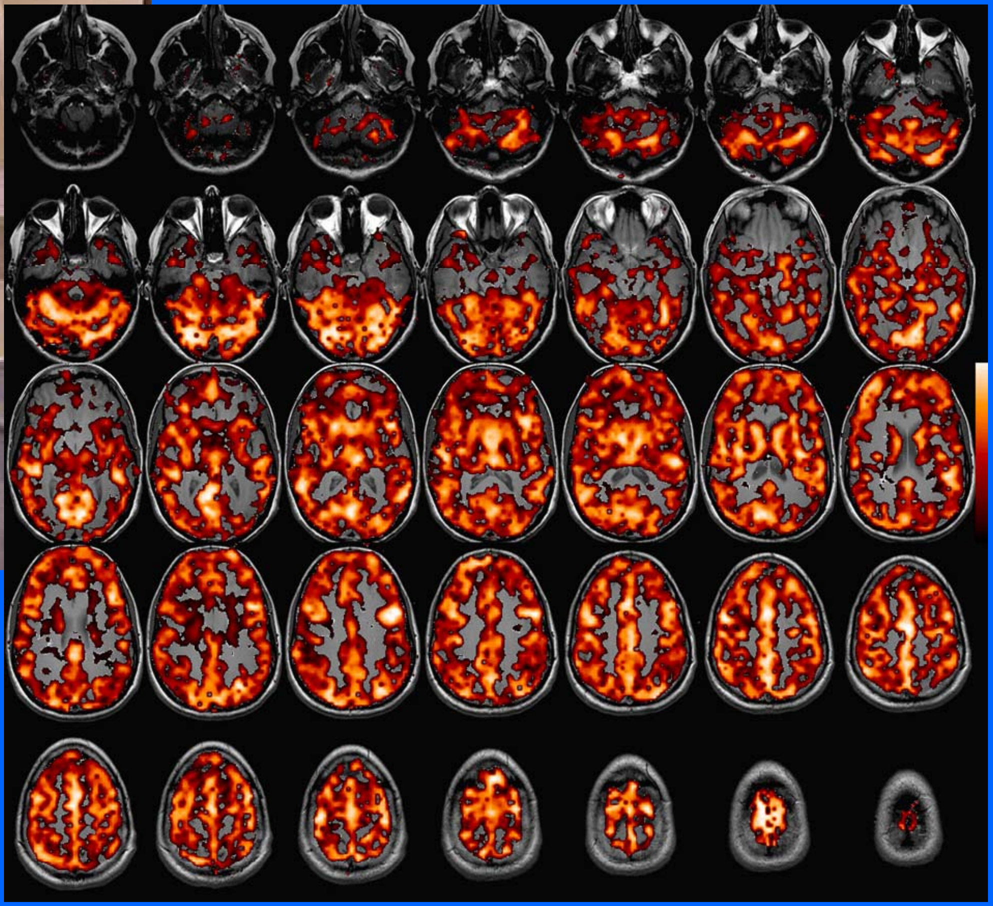
MRI = Magnetic Resonance Imaging

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

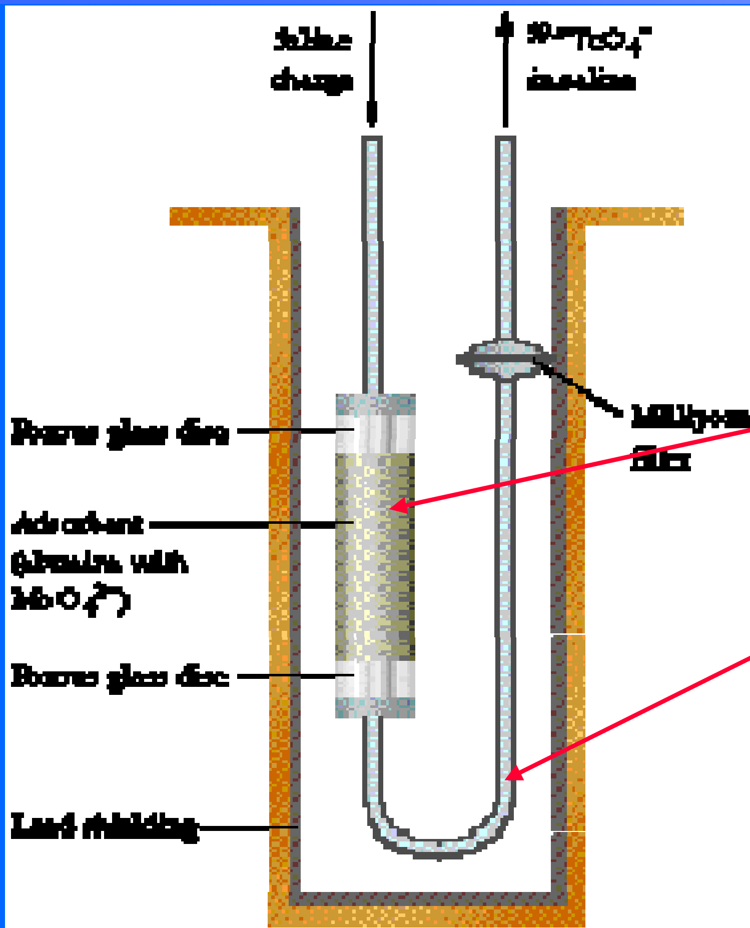


- **Measurement of the density of the protons (water) in tissues**
- **Information on the morphology**

A MRI scanner



SPECT = Single Photon Emission Computer Tomography

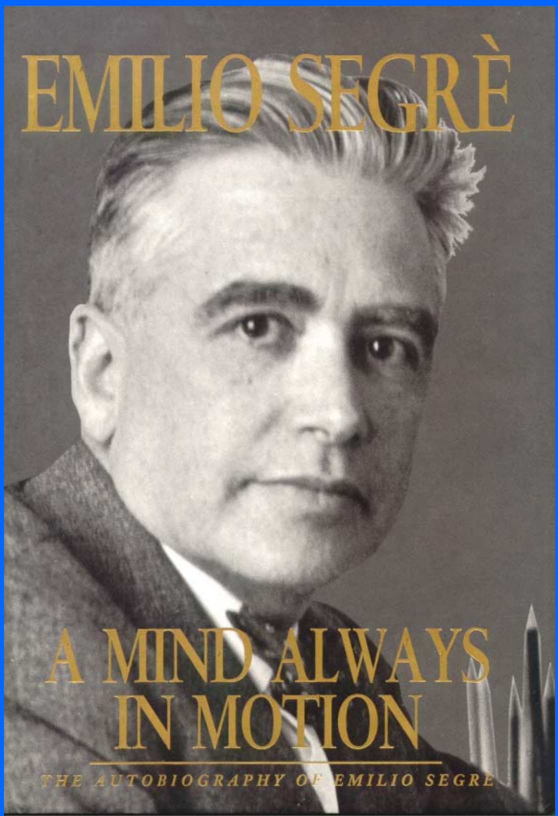


In reactors <u>slow neutrons</u> produce

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

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

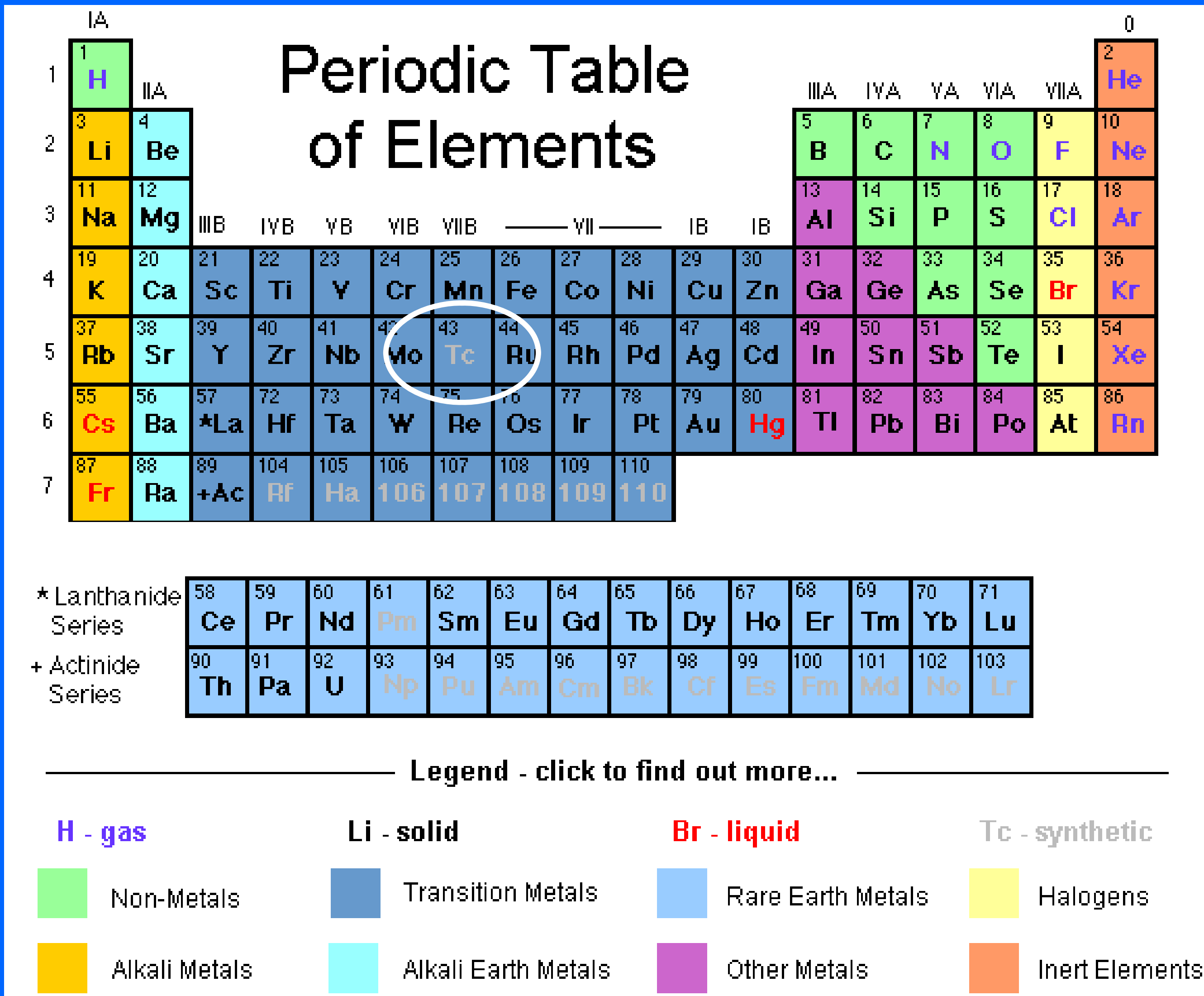
gamma of 0.14 MeV



Emilio Segrè

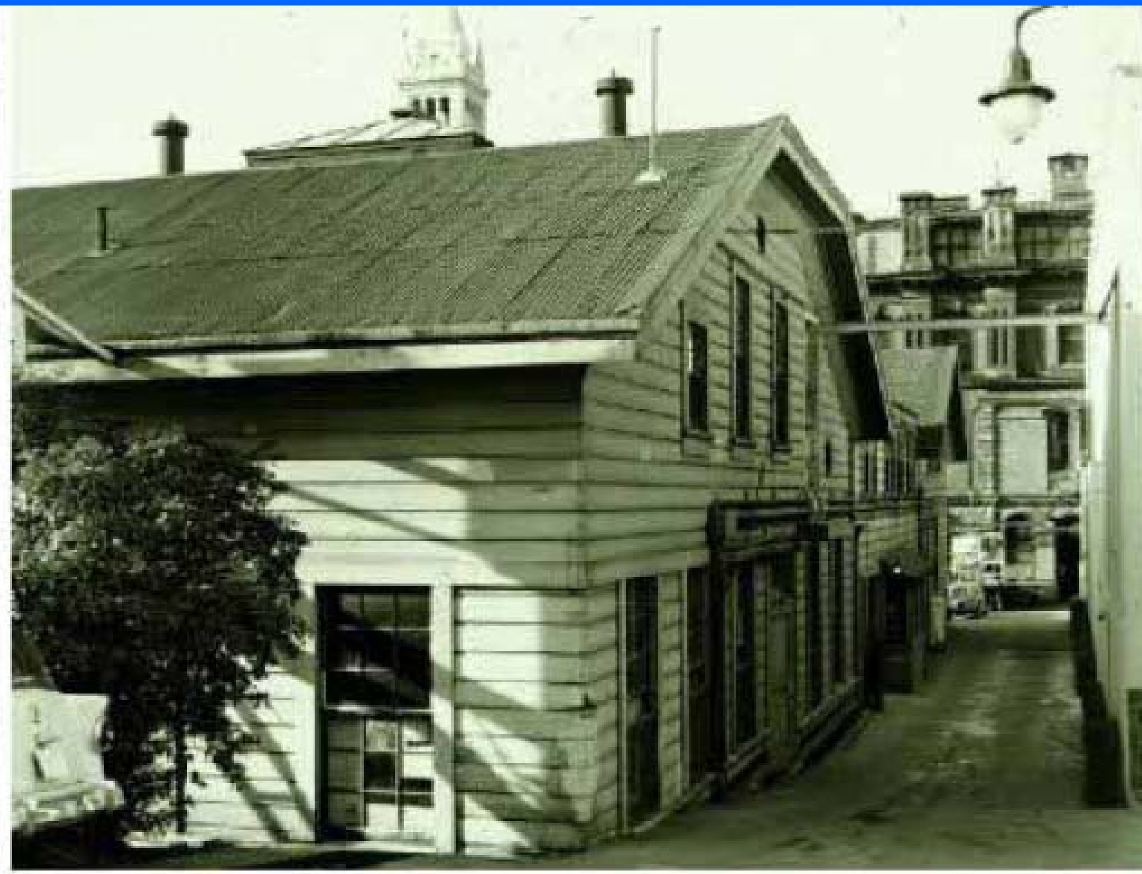
1937: Discovery of element 43 "Technetium" ^{97}Tc(2.6 My)

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



- **The element 43 was missing**
- **In 1925 W. Noddack and I. Tacke announced the discovery of Rhenium (75) and Masurium (43)**
- **In 1934 Fermi and his group were bombarding "all" the elemnts with slow neutrons and Segrè was in charge of procuring the different elements**
- **…but asking for a sample of Masurium he was answerd "Numquam vidi"…**

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.

The discovery of technetium

- Lawrence was using deflectors for the cyclotron made of Molybdenum (42)

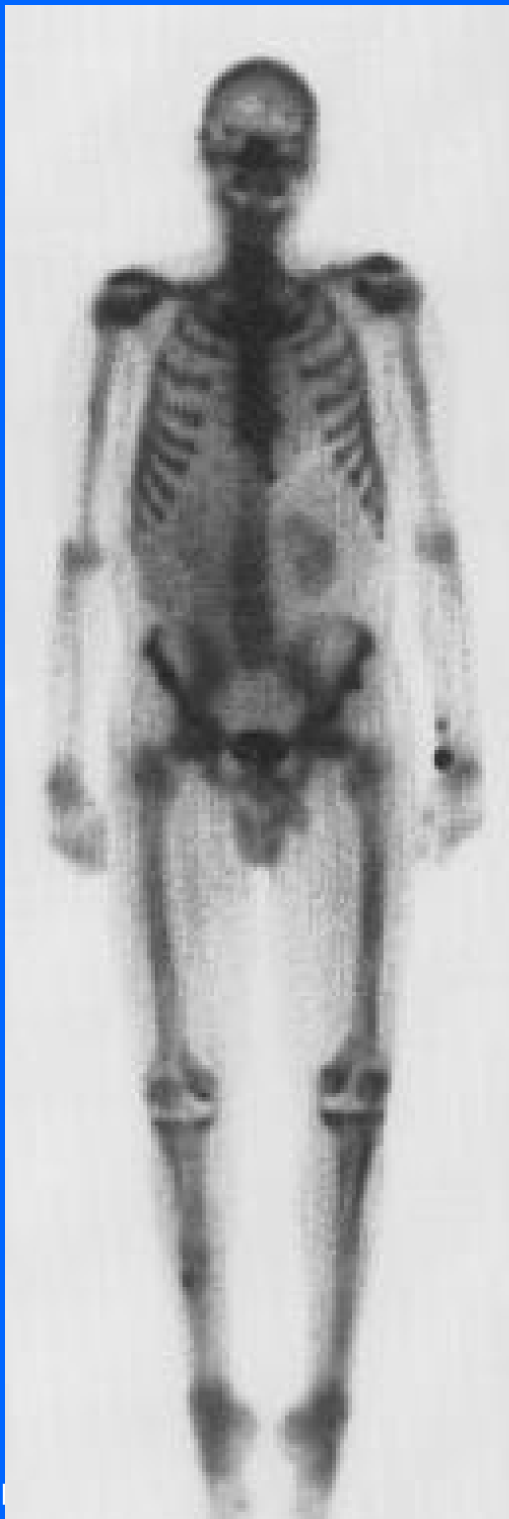
- Segrè thought : Molybdenum + proton… 42 + 1 = 43 !

- In February 1937 Segrè received a letter from Lawrence with some Molybdenum coming from the deflectors and…

- …the element 43 was identified with the help of a chemist (Carlo Perrier)

- The element 43 was called Technetium since it is the first element artificially produced (the most stable isotope has an half-life of 4.2×10^6 years)

SPECT scanner



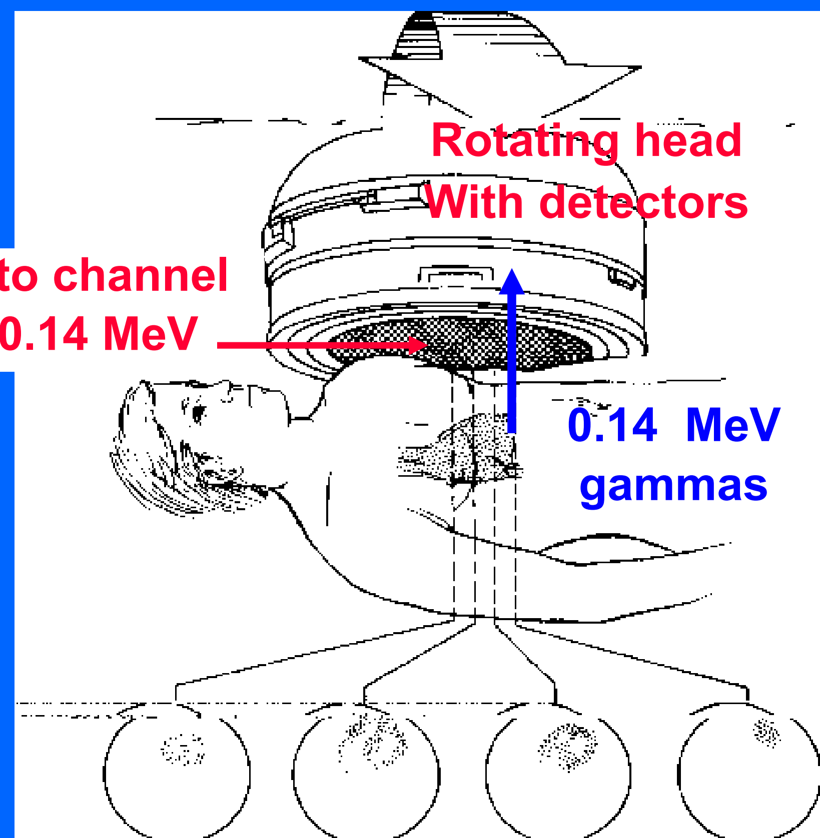
85% of all nuclear medicine examinations use technetium produced by slow neutrons in reactors

… liver

lungs

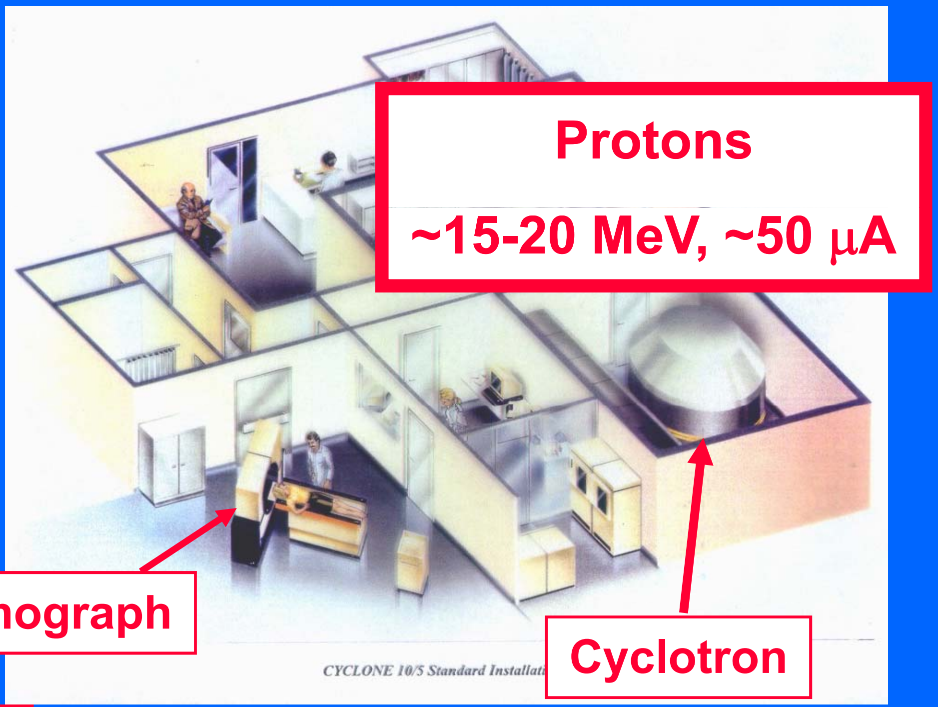
bones …

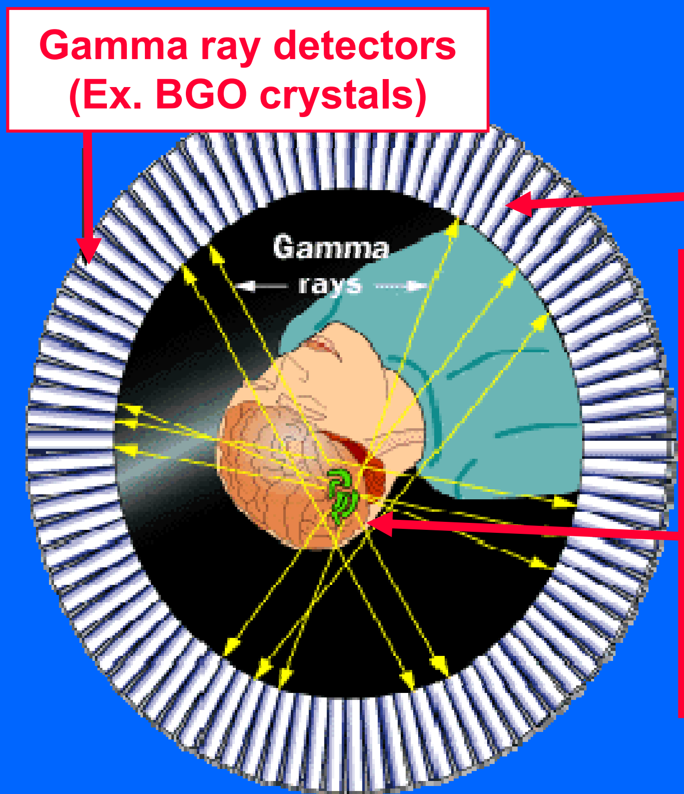
- Measurement of the density the molecules which contain technetium
- Information on morphology and/or metabolism

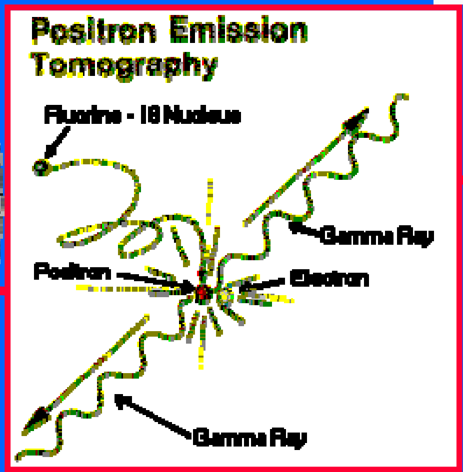


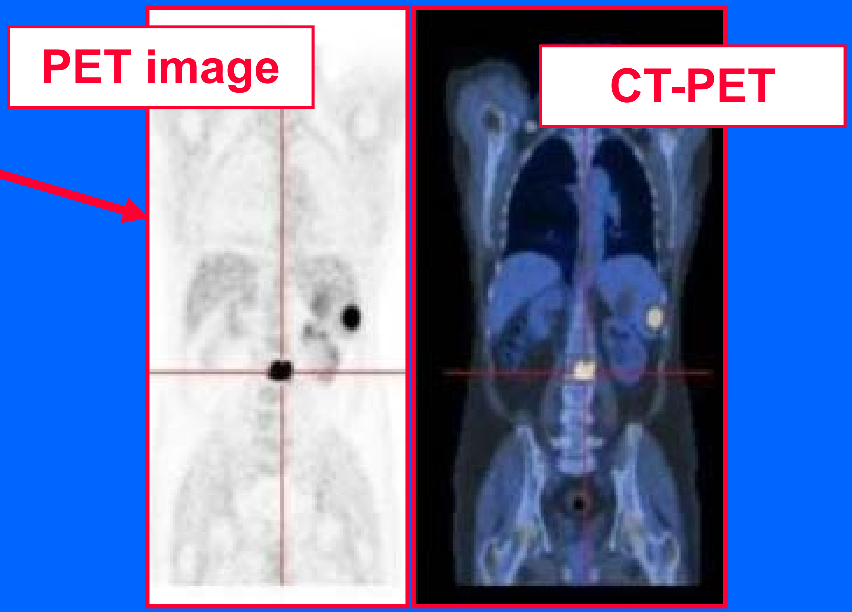
Positron Emission Tomography (PET)

- 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



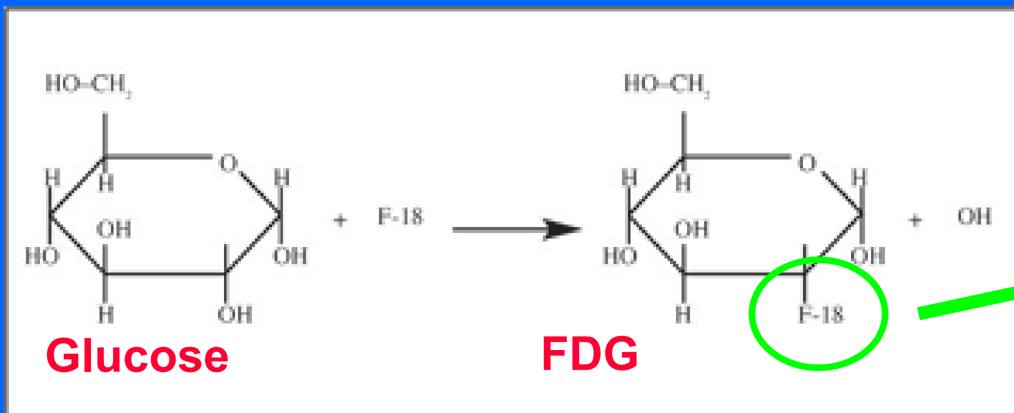


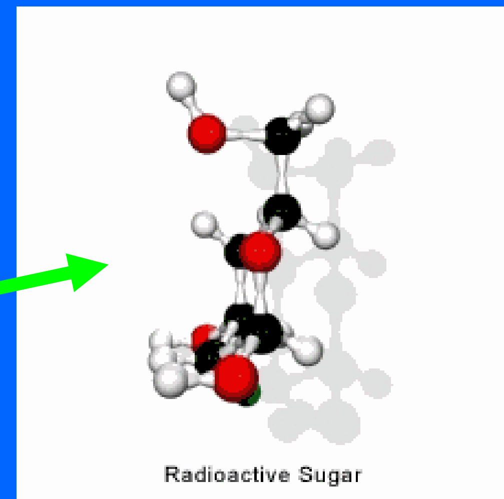




How does it work?

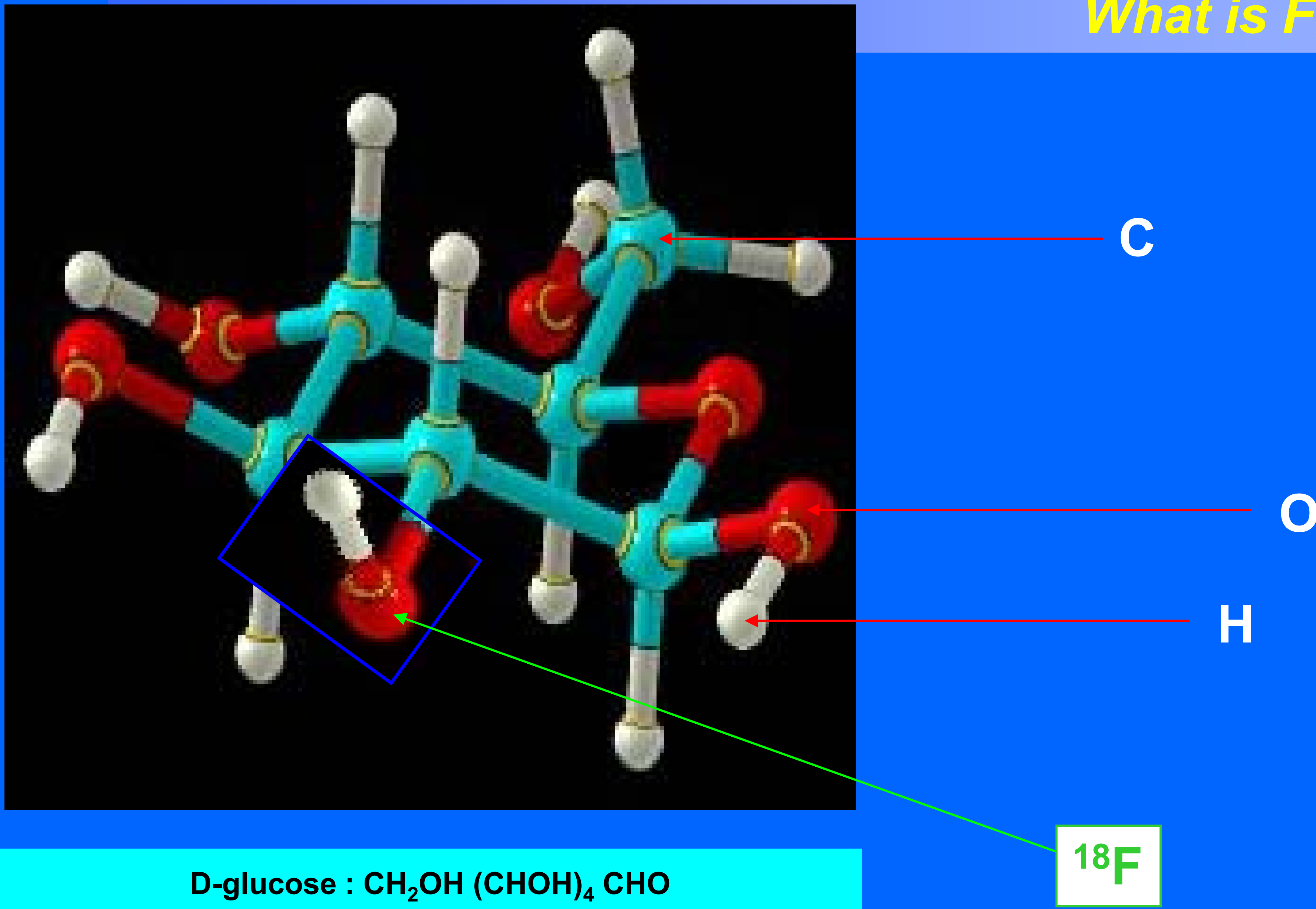
- $H_2{}^{18}O$ water is bombarded with protons to produce ^{18}F
- Fluoro-Deoxy-D-Glucose (FDG) is synthesized





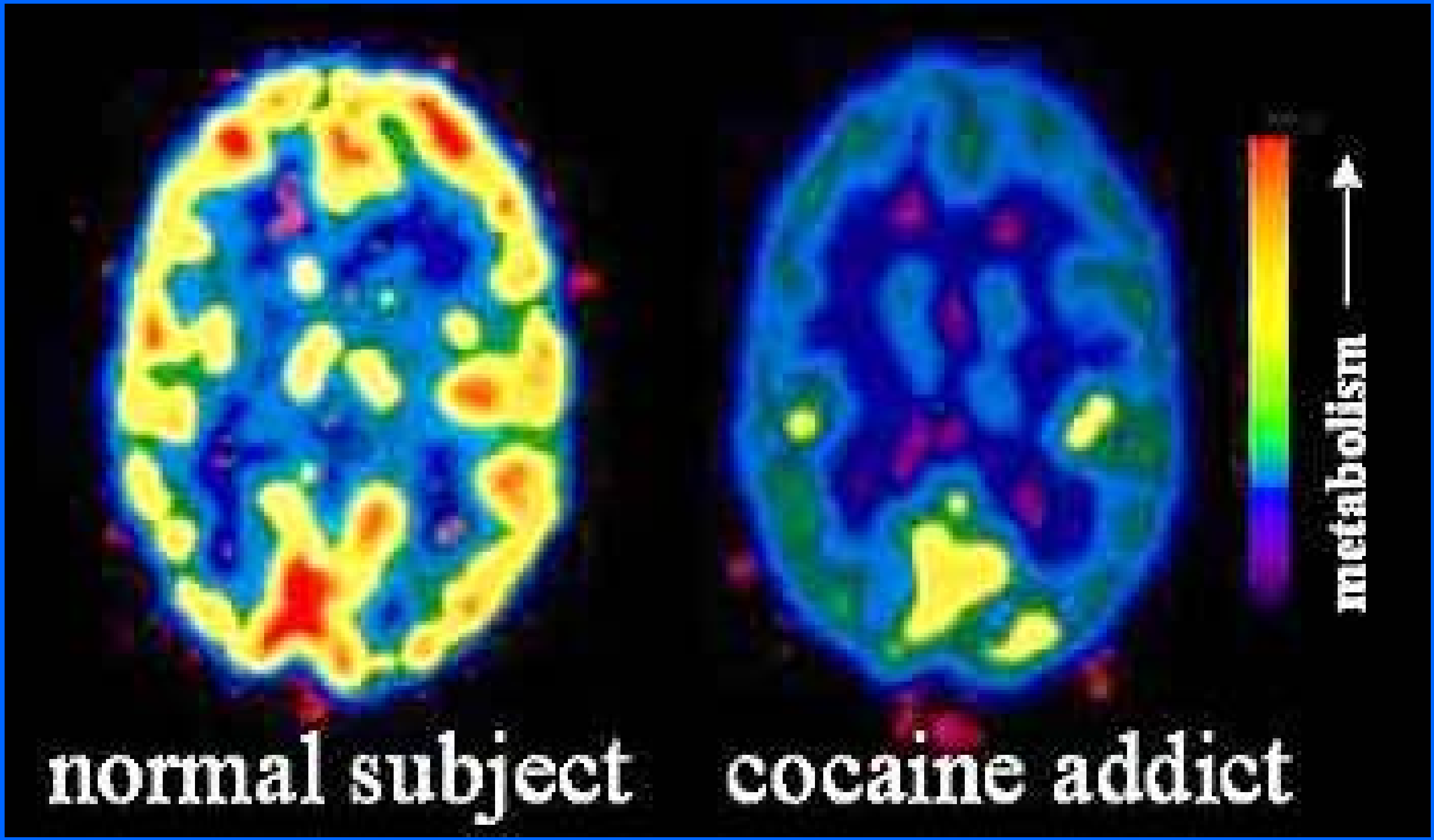
- FDG is transported to the hospital
- FDG is injected into the patient
- FDG is trapped in the cells that try to metabolize it
- Concentration builds up in proportion to the rate of glucose metabolism
- Tumors have a high rate of glucose metabolism and appear as “hot spots” in PET images

What is FDG?



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

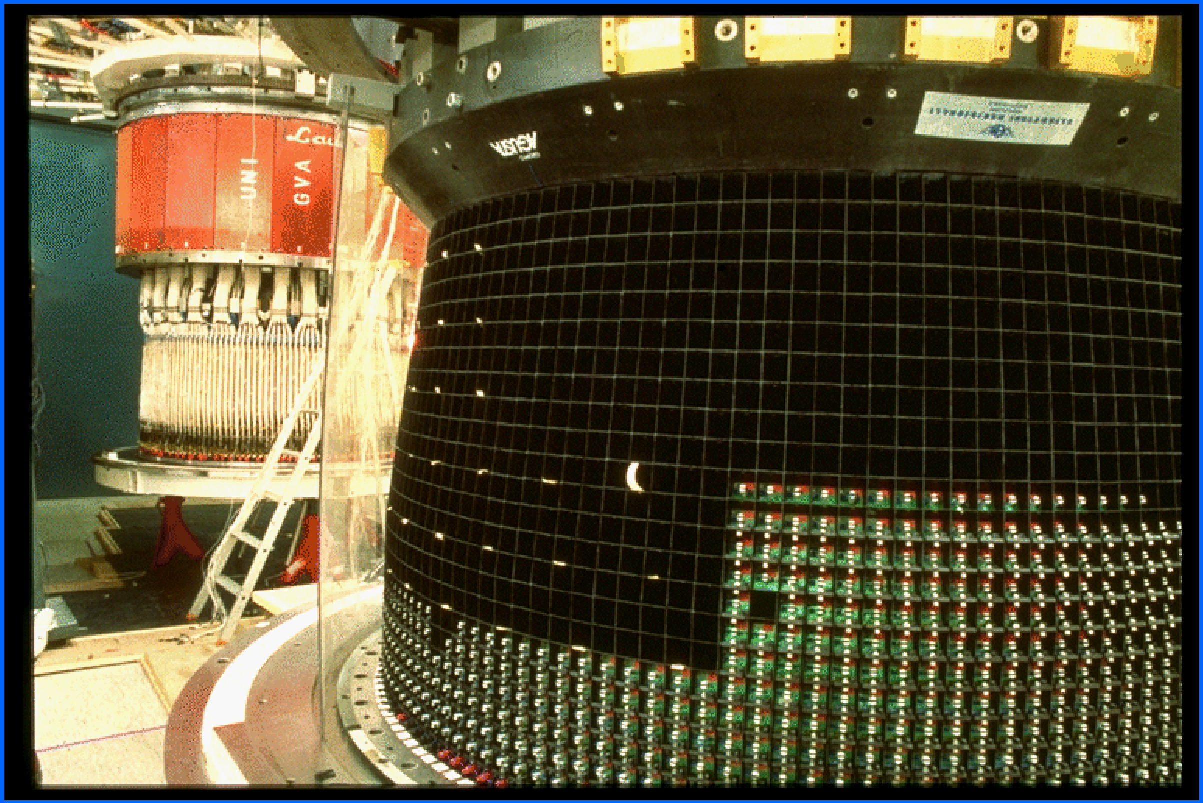
PET: one example

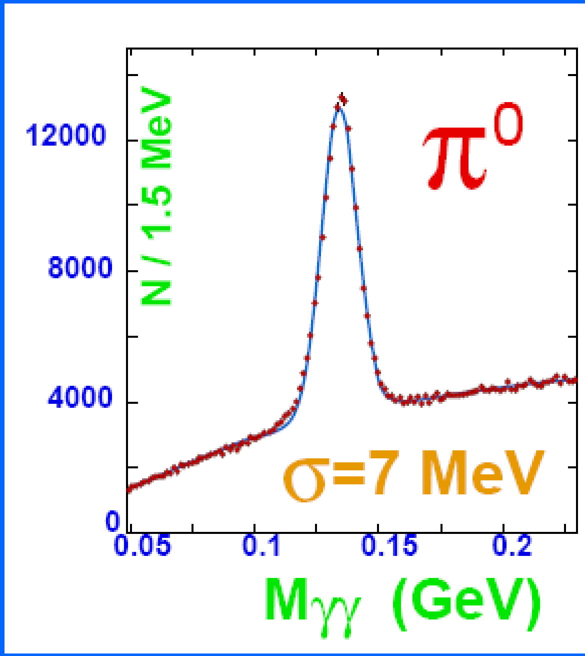


- **18FDG/PET images**
- **The cocaine addict has depressed metabolism !**

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

BGO crystals have been developed for detectors in particle physics

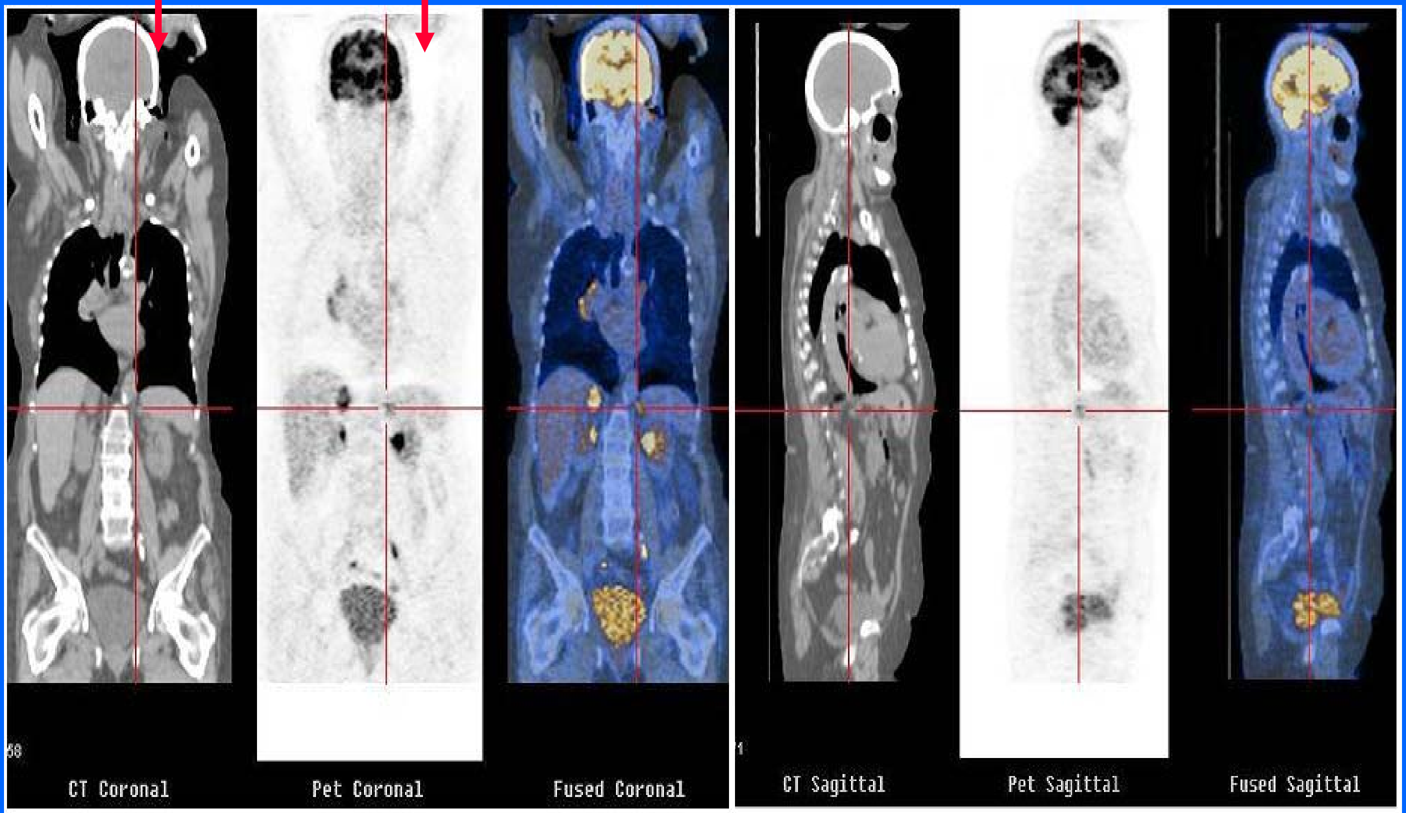




- 11000 BGO crystals
- Precise measurement of the energy deposited by the particles
- Almost 4 π coverage

The new diagnostics: CT/PET

morphology **metabolism**



David Townsend

CERN: 1970-78

Uni Ginevra

UPSM Pittsburgh

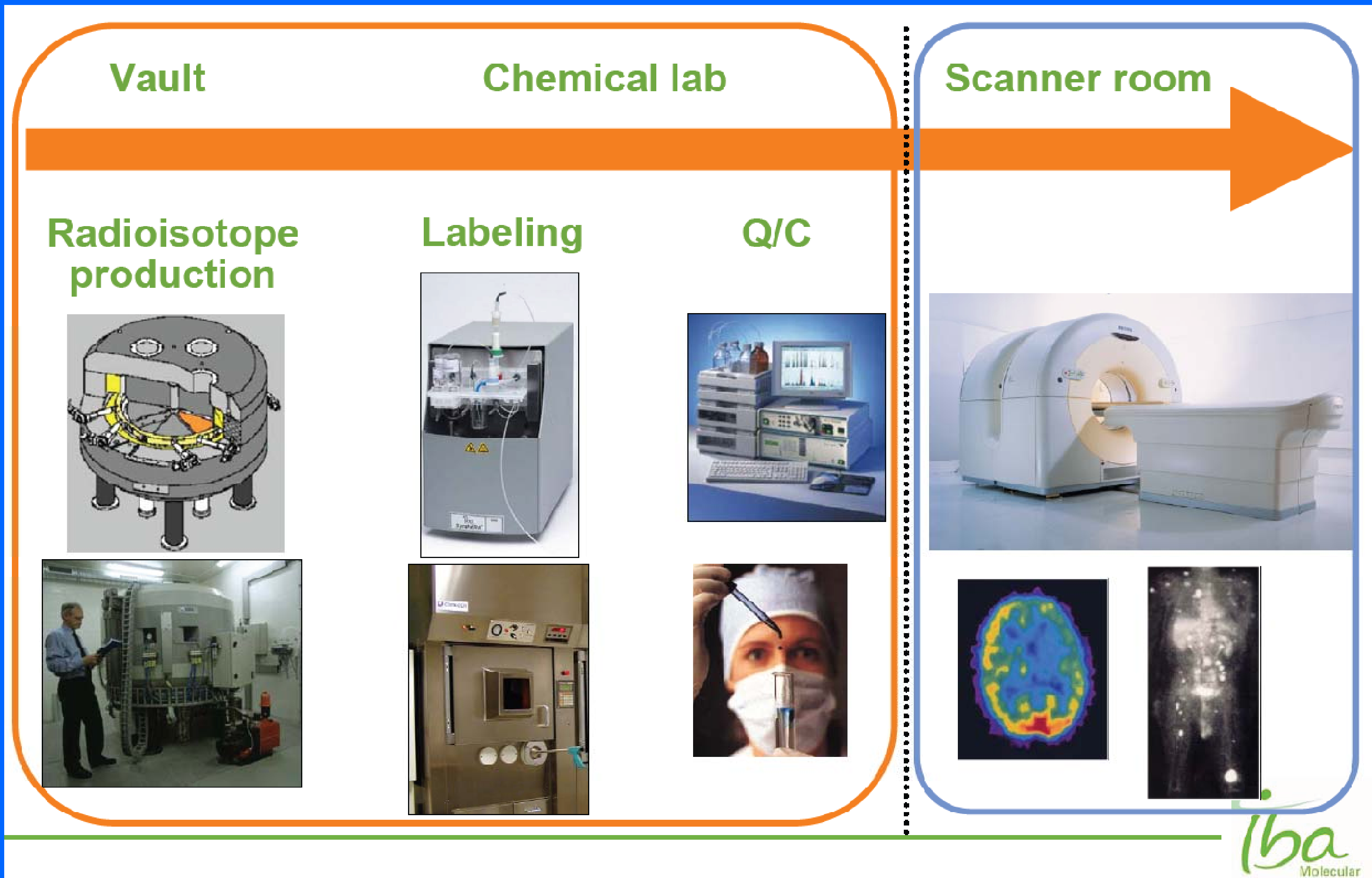
and

Ronald Nutt

(CTS – CTI)

Exercise: the production of FDG for PET

The full FDG-PET chain



Courtesy IBA

Basic data

- 20 MeV proton beam (cyclotron)
- Current : 50 μA
- FWHM : about 15 mm
- Target : 99% 18-O enriched water
- Reaction : 18-O (p,n) 18-F

- Fluorine 18 : half-life $t_{1/2}$=110 min.
- Irradiation time 60 min.

- What is the value of the 18-F activity produced?

One TR19 cyclotron by the company ACSI

(Vancouver, Canada) is installed at the Policlinico Gemelli in Rome

It is daily used for FDG production

The target

Courtesy

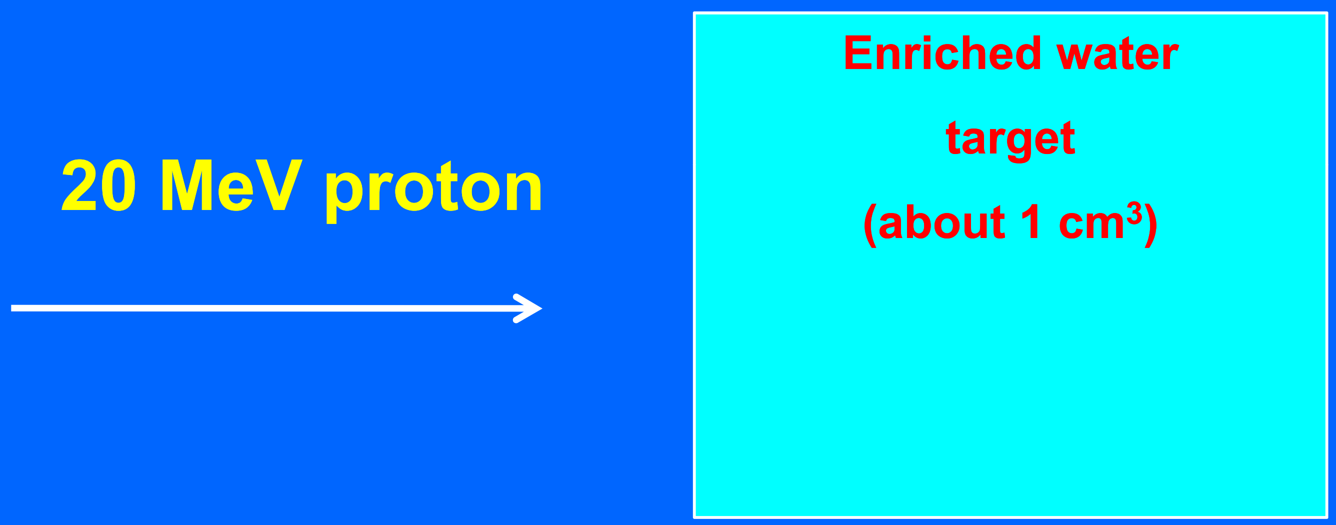
Pipes for cooling. Why?

Let's suppose that the beam completely stops in the target:

$$20 \text{ MeV} \times 50\ \mu\text{A} \times (1/e) = 1000 \text{ W}$$

1 cal = 4.18 J i.e. 1 cm^3 of water passes between 0 and 100 degrees

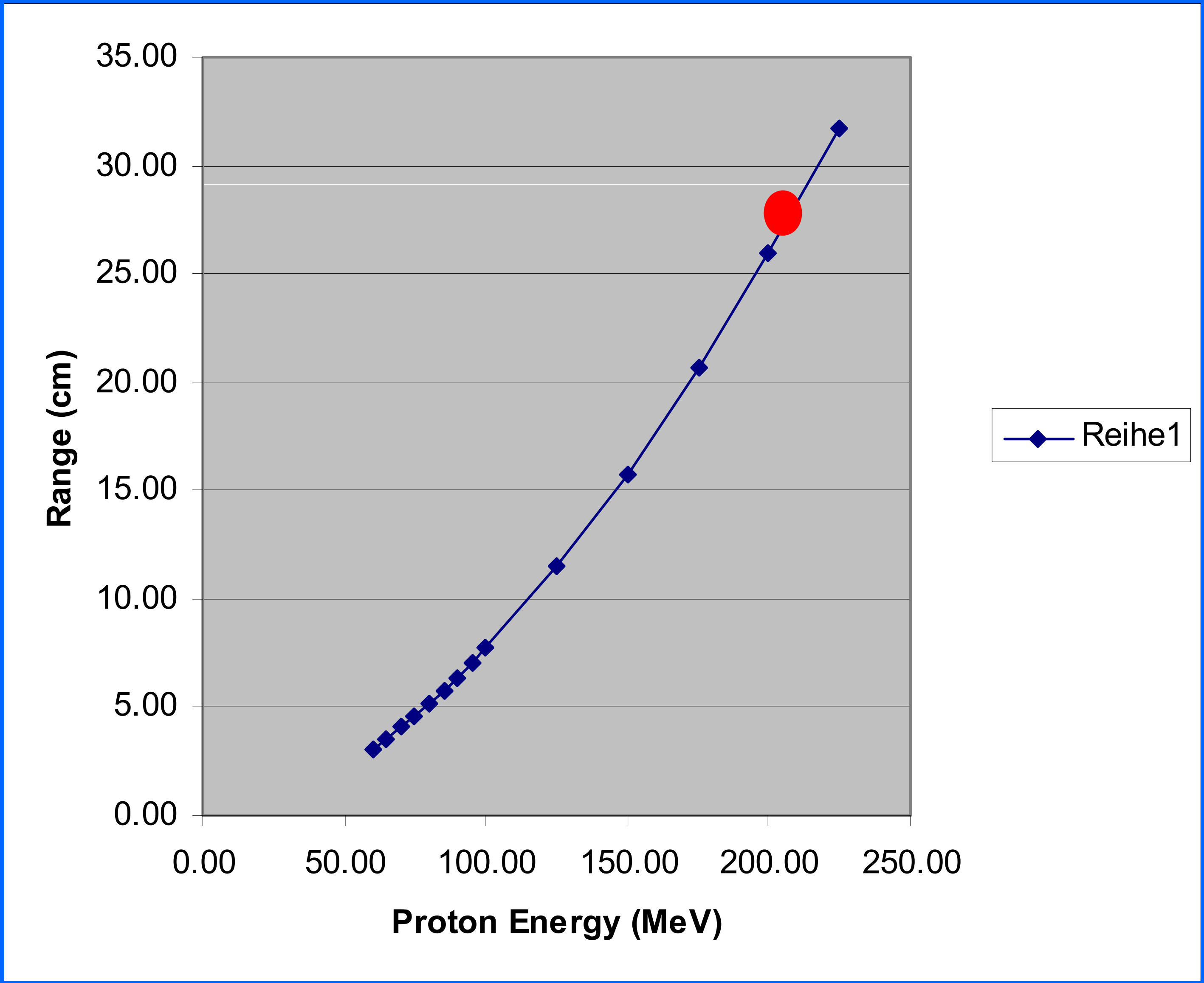
in less than 0.5 seconds !



- **The proton stops in water?**

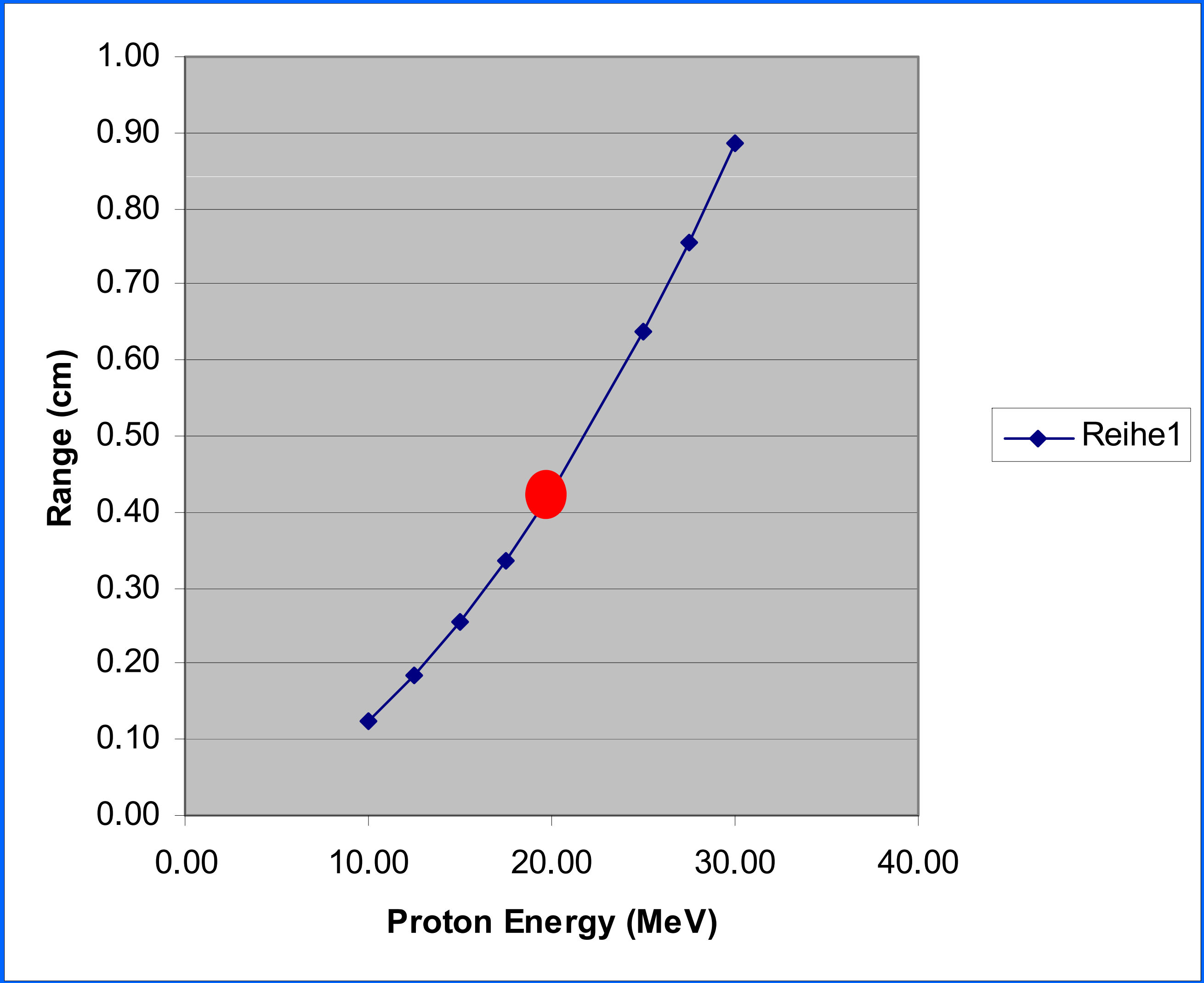
- **"Sometimes" the reaction 18-O (p,n) 18-F occurs. Probability?**

Range of the protons in water



Important to remember : 200 MeV → 27 cm

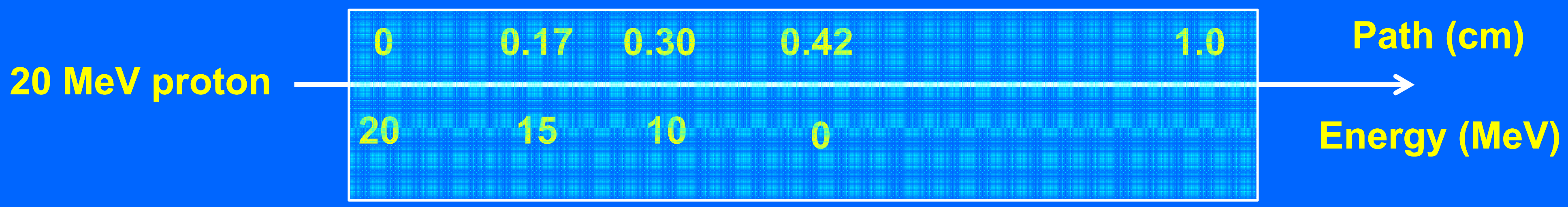
Range of protons in water



20 MeV → 0.4 cm – All protons stop in the target

Residual range

Energy (MeV)	Range (cm)
20	0.42
15	0.25
10	0.12
5	0.036



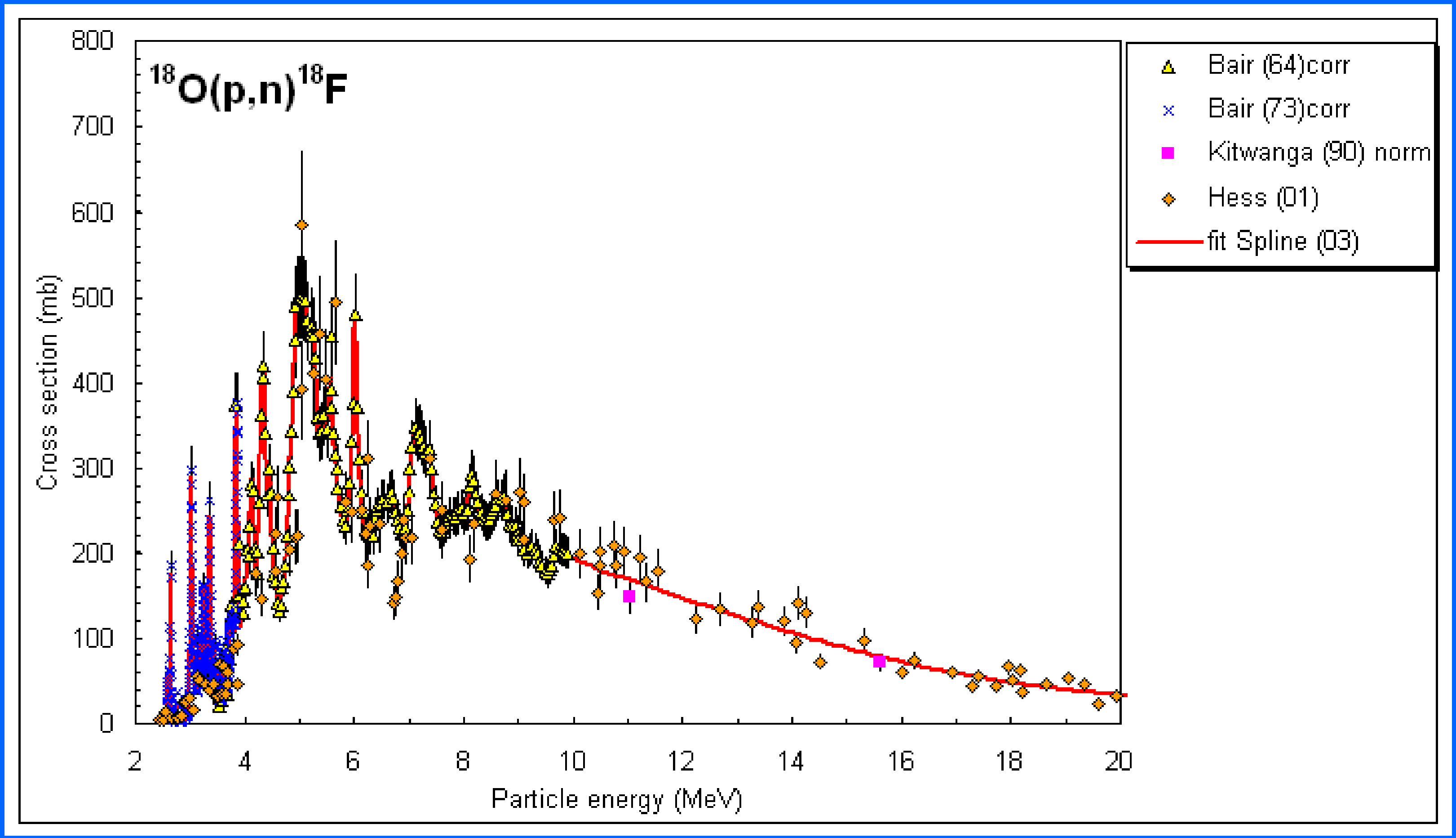
The reaction can take place in any point of the path

i.e. at different energies !

A useful link :

physics.nist.gov – NIST National Institute of Standards and technology

The cross section



For the exercise we will consider an average value of 100 mb for all the energies

(1 barn = 10^{-24} cm^2)

- How many 18-O targets are there?

20 g (18+1+1) of enriched H2O contain N_0 molecules

$\rightarrow$ 6.022 x 10^{23} / 20 $\rightarrow$ 3 x 10^{22} 18-O atoms/cm^3

- How many “bullets” per second?

Current / charge of the proton

$$N_R = \sigma \times \frac{I}{e} \times \frac{N_t}{V} \times L_t \times \Delta t$$

N_R	number of reactions i.e. number of 18-F nuclides produced
σ	cross section
I	beam current
e	charge of the electron
N_t	number of traget 18-O nuclei
V	volume of the target
L_t	thickness of the target **?**
Δt	Irradiation time interval

Calculations

- Thickness of the target → range = 0.42 cm

- <u>Result 1</u>
- In 60 minutes : $N_0 = 2 \times 10^{15}$ 18-F nuclei are produced

- Which is the corresponding activity?
- $N(t)=N_0 \times \exp(-t/\tau)$
- At t=0 the activity dN/dt is: N_0/τ
- F-18 : $t_{1/2} = 110$ min → $\tau = t_{1/2} / \ln 2 = 158$ min = 9480 s
- Activity : $A = 2 \times 10^{11}$ Bq (Bq → Bequerel)
- 1 Ci = 3.7×10^{10} Bq (Ci → Curie)

- <u>Result 2</u>
- The produced activity is about 6 Ci at the end of the irradiation

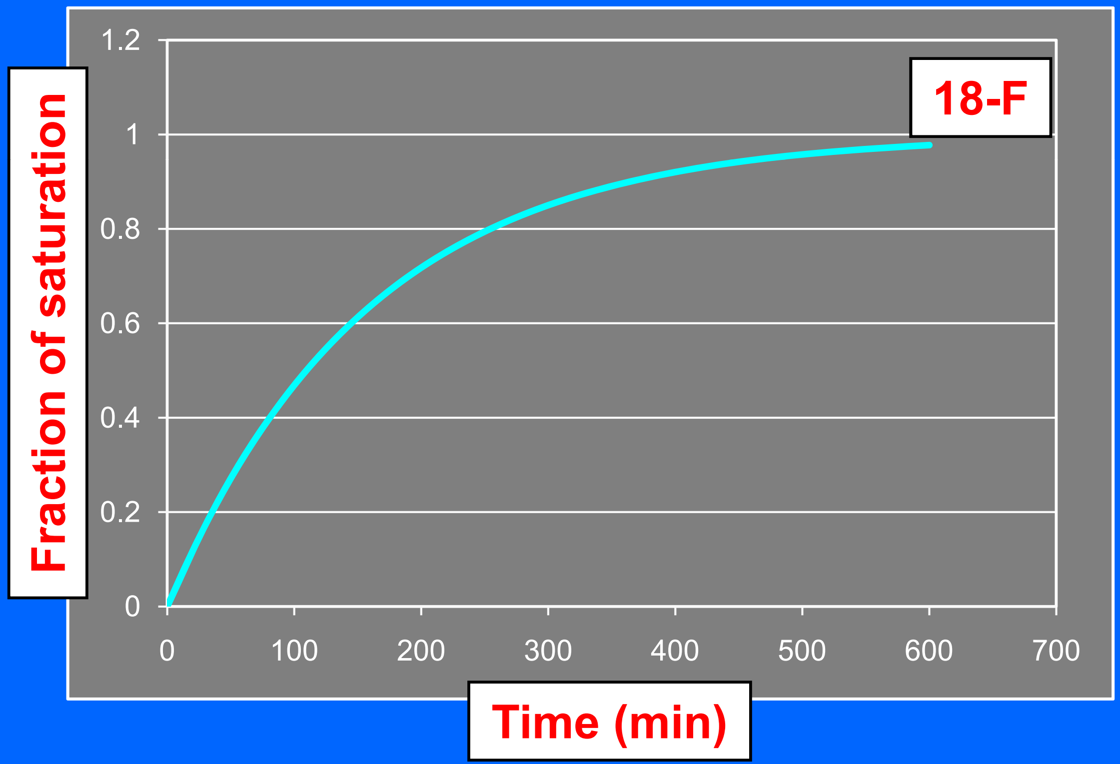
…but 18-F decays during irradiation

$$\Delta N = A \times \Delta t - N(t) \times \frac{\Delta t}{\tau}$$

Irradiation

Decay

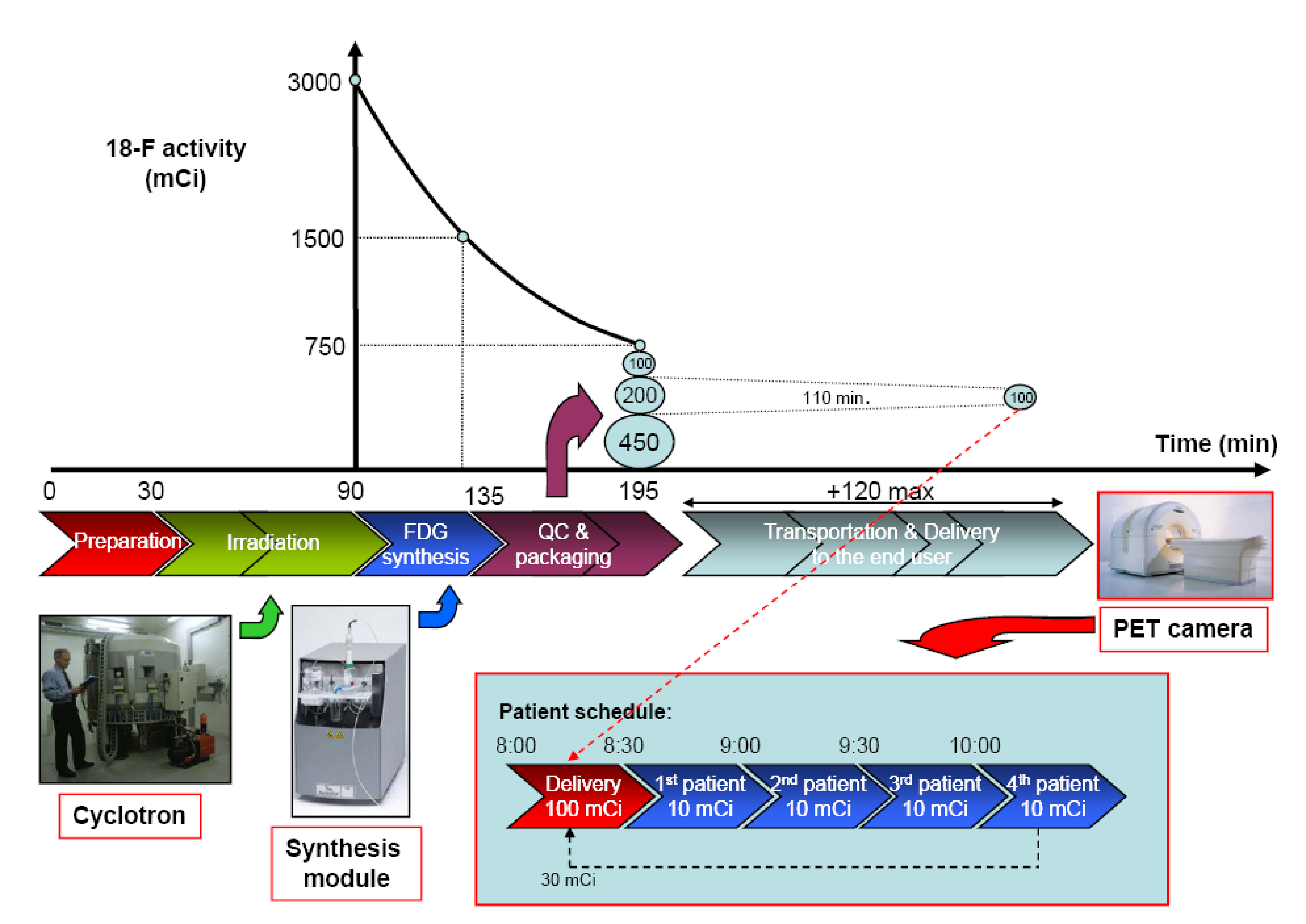
$$N(t) = A\tau \times (1 - e^{-t/\tau})$$



- If $t \ll \tau$ the effect can be neglected
- If $t \gg \tau$ saturation effect : production ~ decay
- For 18-F : the regime is far from saturation for t<120 min.

- Exercise – Taking this effect into account about 4.5 Ci of activity are produced in 60 min. irradiation

A realistic supply chain



End of part II