Present and Future of Hadrontherapy

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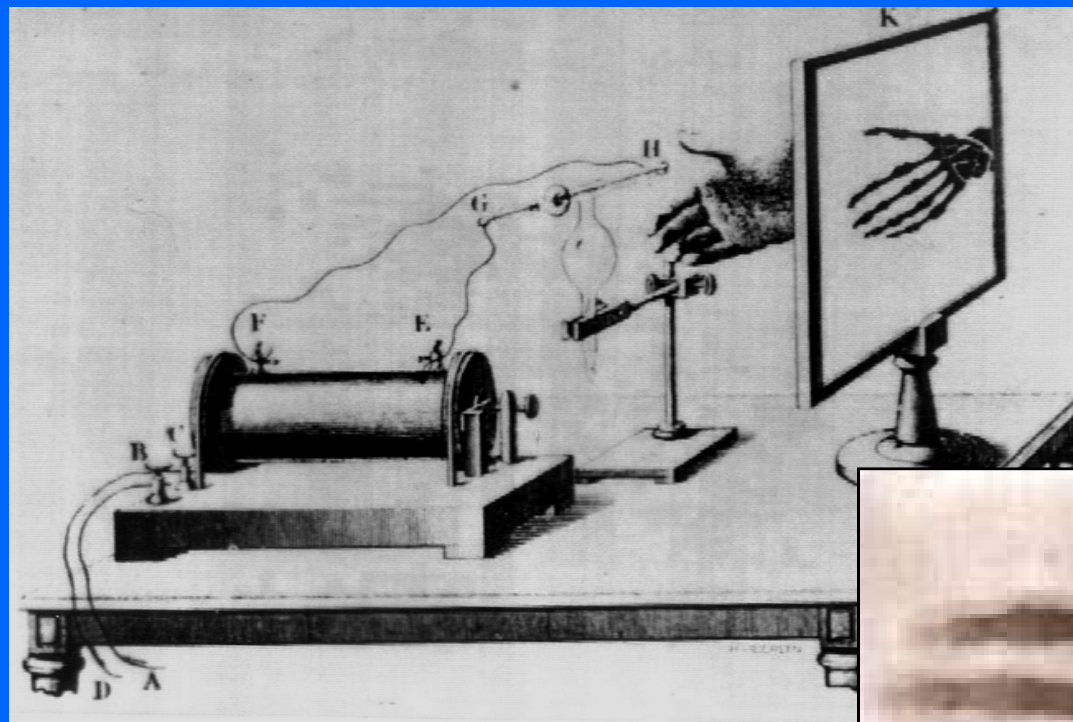
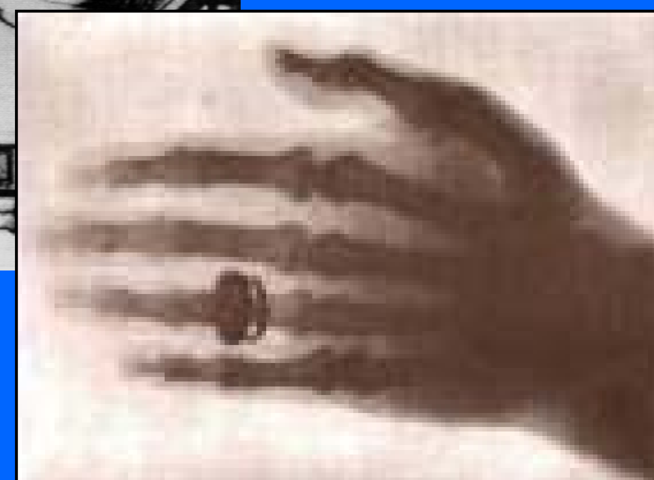
Outline

- Introduction
  - Fundamental research in physics and medical applications
- Diagnostics and conventional radiation therapy
- Hadrontherapy, the new frontier of cancer radiation therapy
  - Proton-therapy
  - Carbon ion therapy
- Some new ideas for the future of hadrontherapy
- Conclusions and outlook

- November 1895 : discovery of X rays

Wilhelm Conrad Röntgen

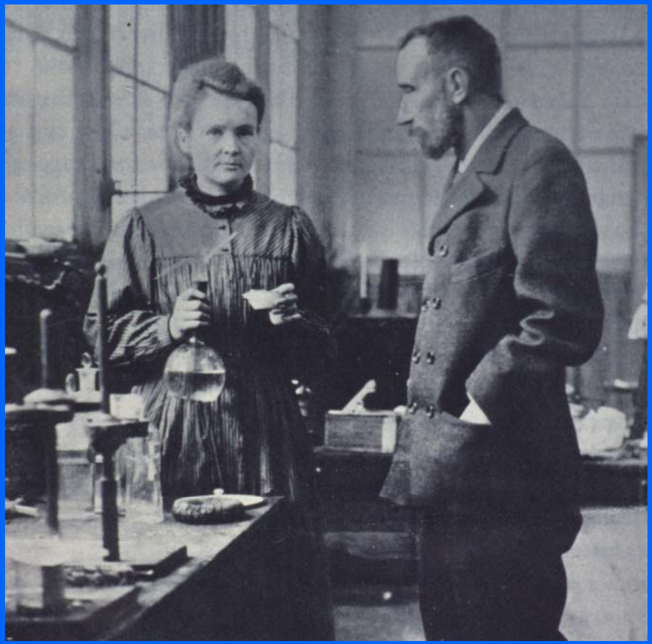




- December 1895 : first radiography
- First application of *photons* to medicine much before 1905 and light quanta! …and gamma-gamma interactions!!

- **1896 : discovery of natural radioactivity**

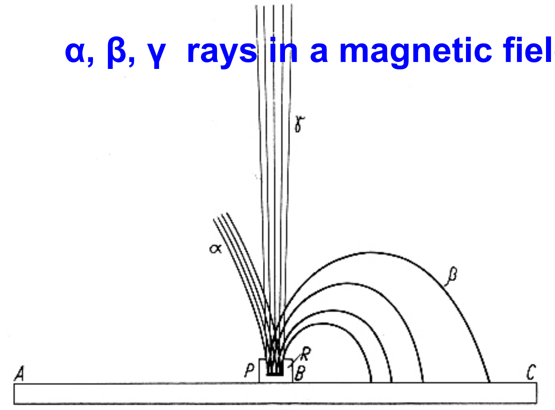
Henri Bequerel

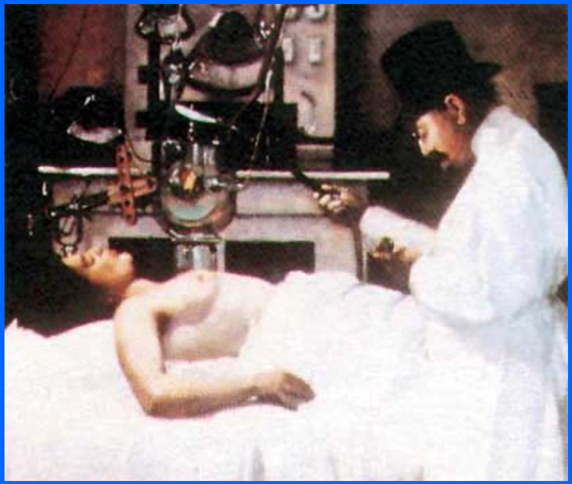


Maria Skłodowska-Curie and Pierre Curie

From the thesis of Mme Curie – 1904

α, β, γ rays in a magnetic field





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

STOCKHOLM

1902 1912

Courtesy J.P. Jerard, MD, Nice (France)

- **Basic concept: Local control of the tumour!**

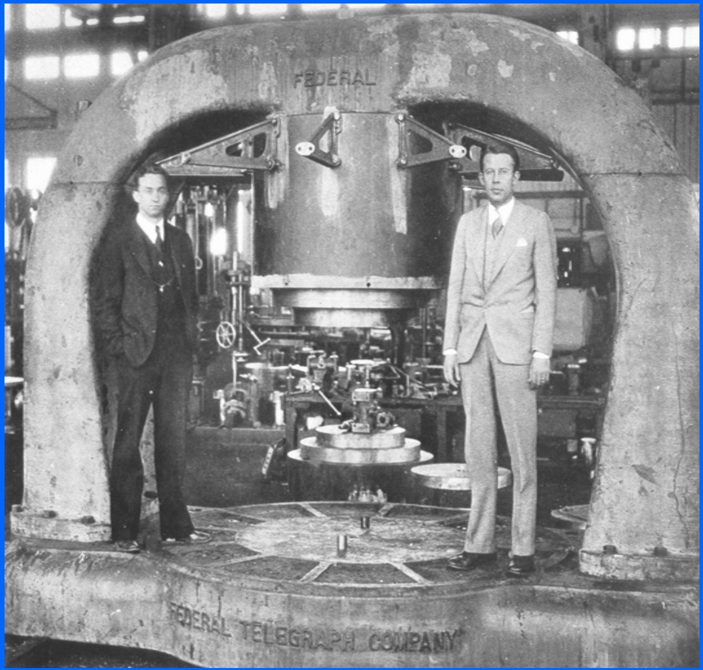
A big step forward…

…in high energy physics and in

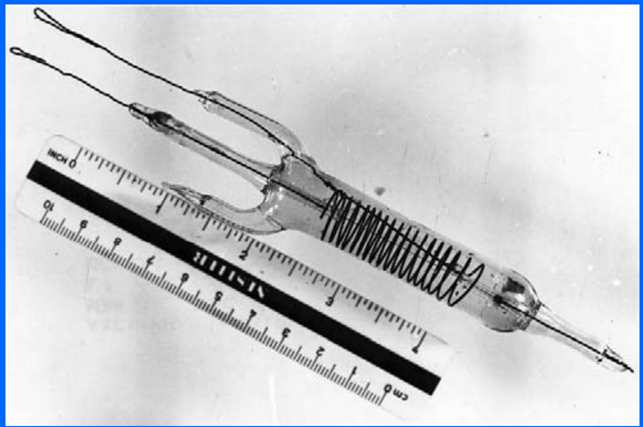
- Medical diagnostics
- Cancer radiation therapy

is due to the development of three fundamental tools

- Particle accelerators
- Particle detectors
- Computers

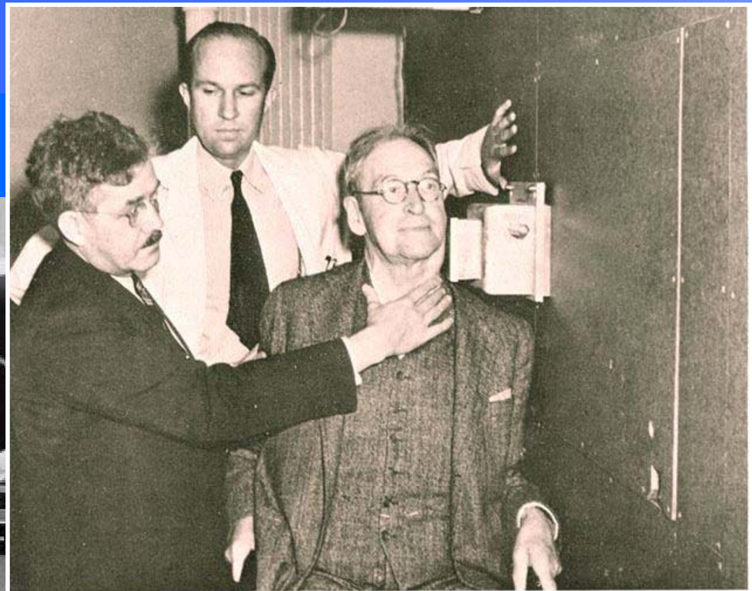


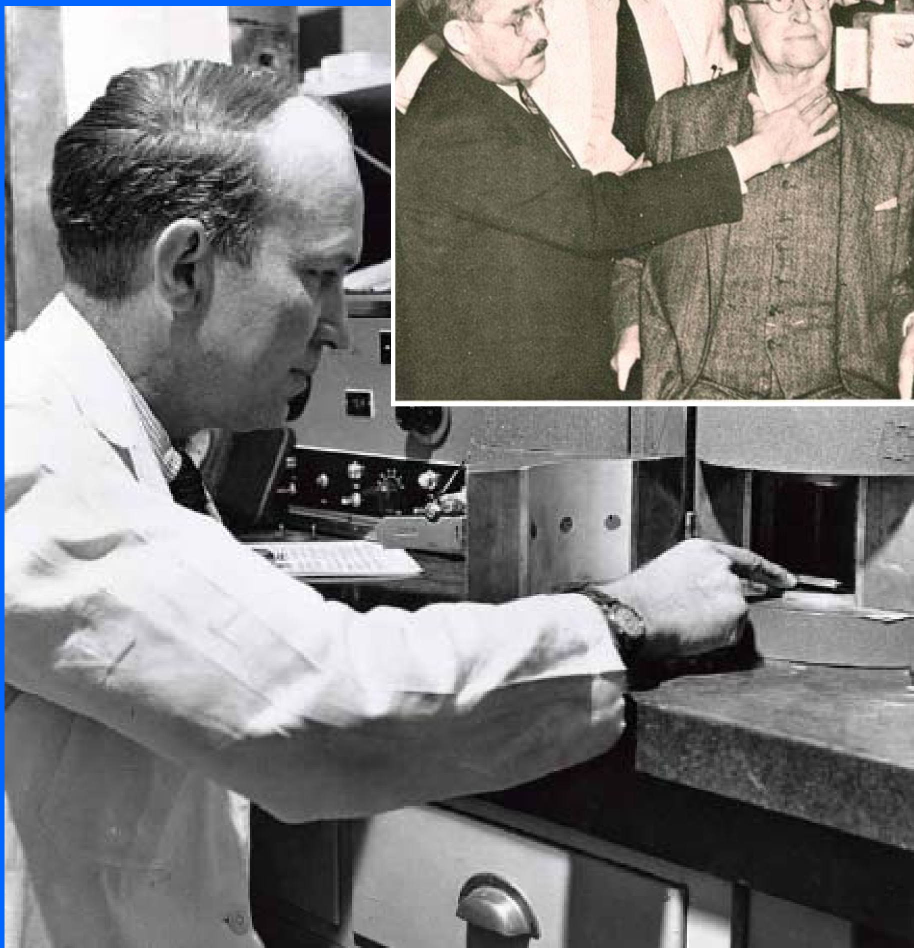
M. S. Livingston and E. Lawrence
with the 25 inches cyclotron



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

The Lawrence brothers and interdisciplinary research





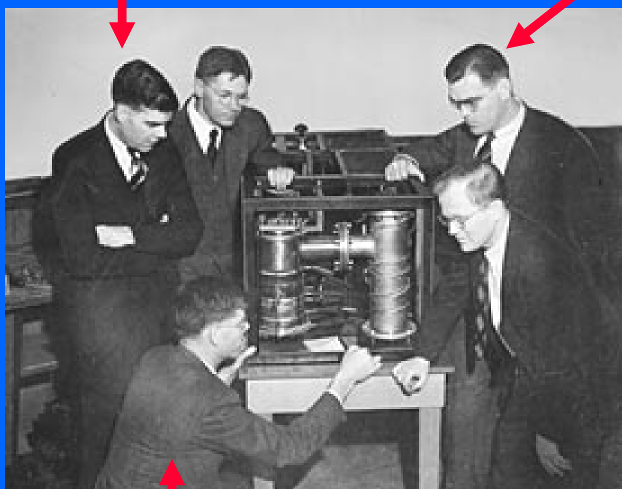
John H. Lawrence made the first clinical therapeutic application of an artificial radionuclide when he used phosphorus-32 to treat leukemia. (1936)

- John Lawrence, brother of Ernest, was a medical doctor
- They were both working in Berkeley
- First use of artificially produced isotopes for medical diagnostics
- First irradiations of salivary gland tumours with neutron beams

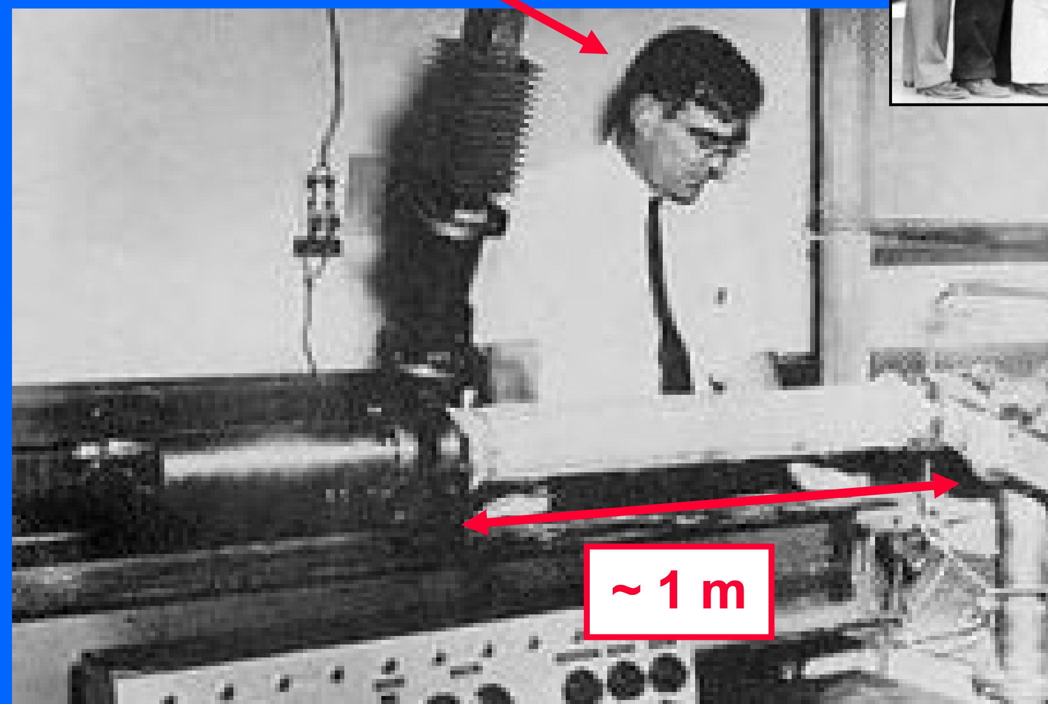
An interdisciplinary environment helps innovation!

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

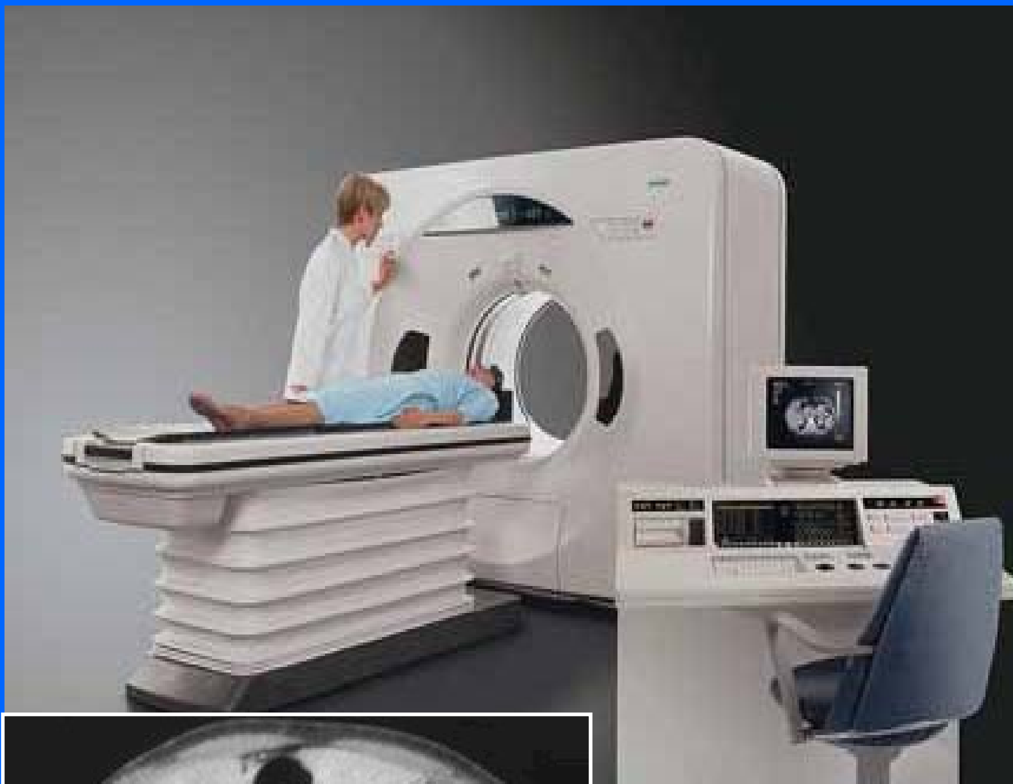
Accelerators running in the world

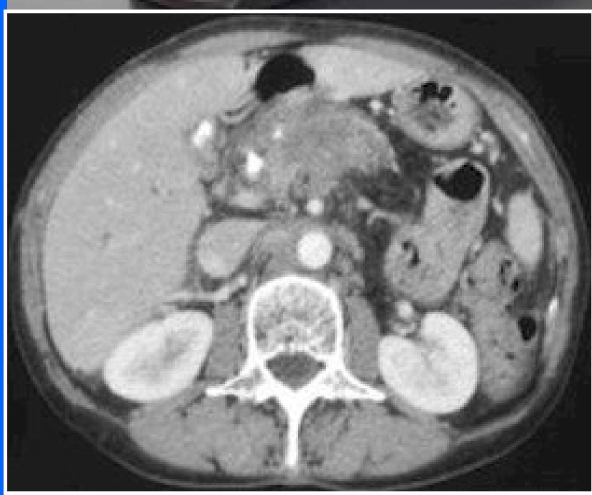
CATEGORY OF ACCELERATORS	NUMBER IN USE (*)
High Energy acc. (E >1GeV)	~120
Synchrotron radiation sources	>100
Medical radioisotope production	~200
Radiotherapy accelerators	> 7500 } 9000
Research acc. included biomedical research	~1000
Acc. for industrial processing and research	~1500
Ion implanters, surface modification	>7000
TOTAL	> 17500

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

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

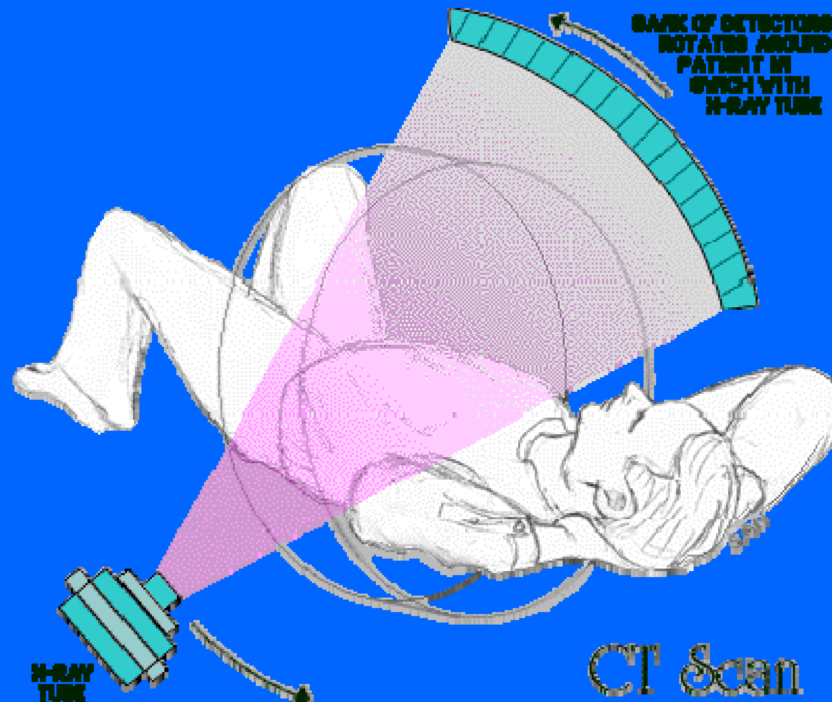
Diagnostics is essential!





Abdomen

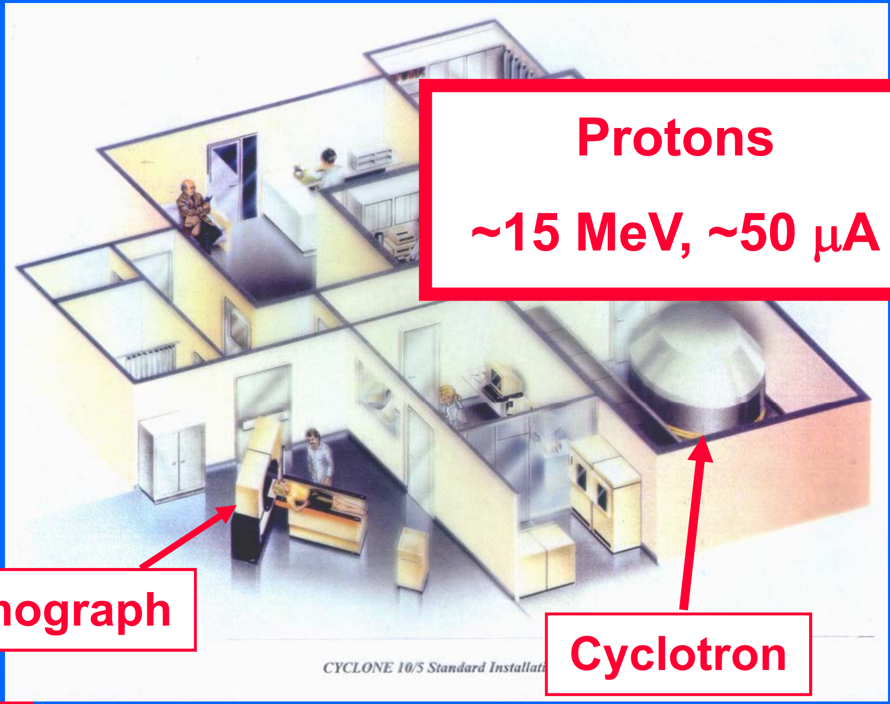
Computer Tomography (CT)



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

Positron Emission Tomography (PET)

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



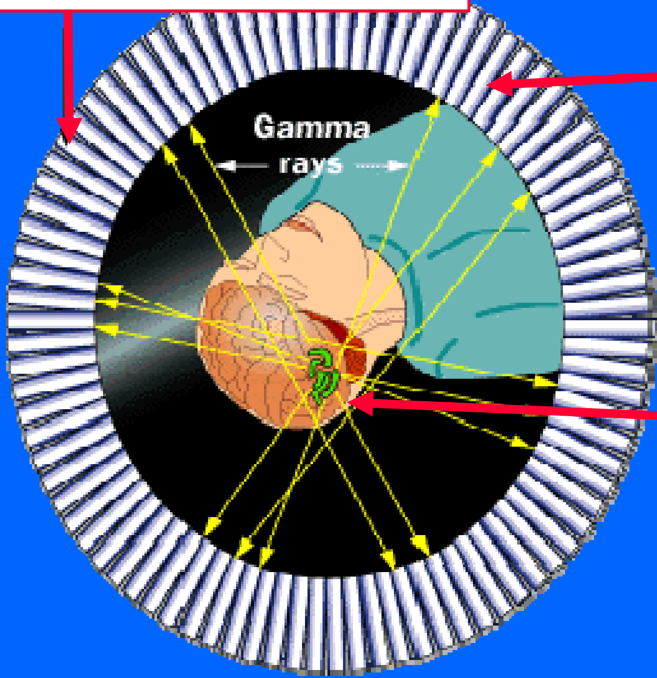
Protons

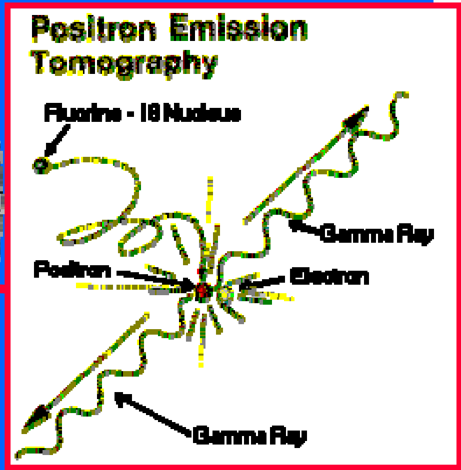
~15 MeV, ~50 μA

PET tomograph

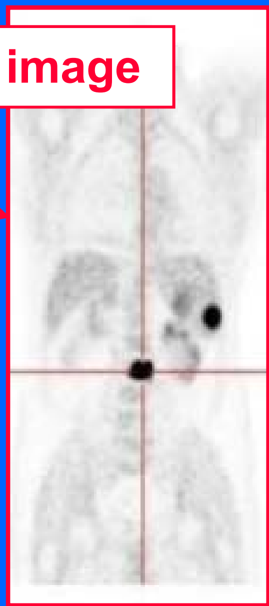
Cyclotron

Gamma ray detectors (Ex. BGO crystals)



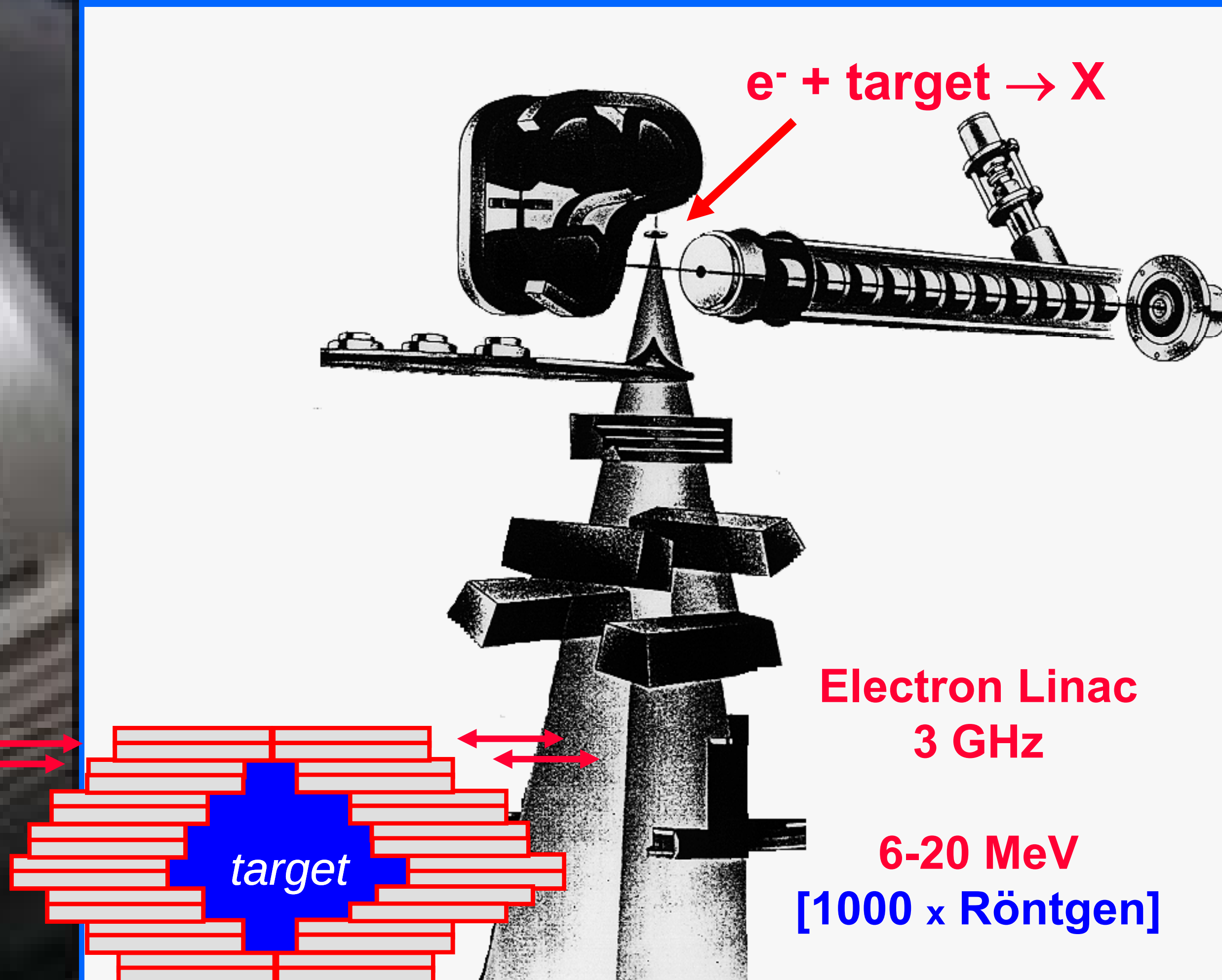


PET image



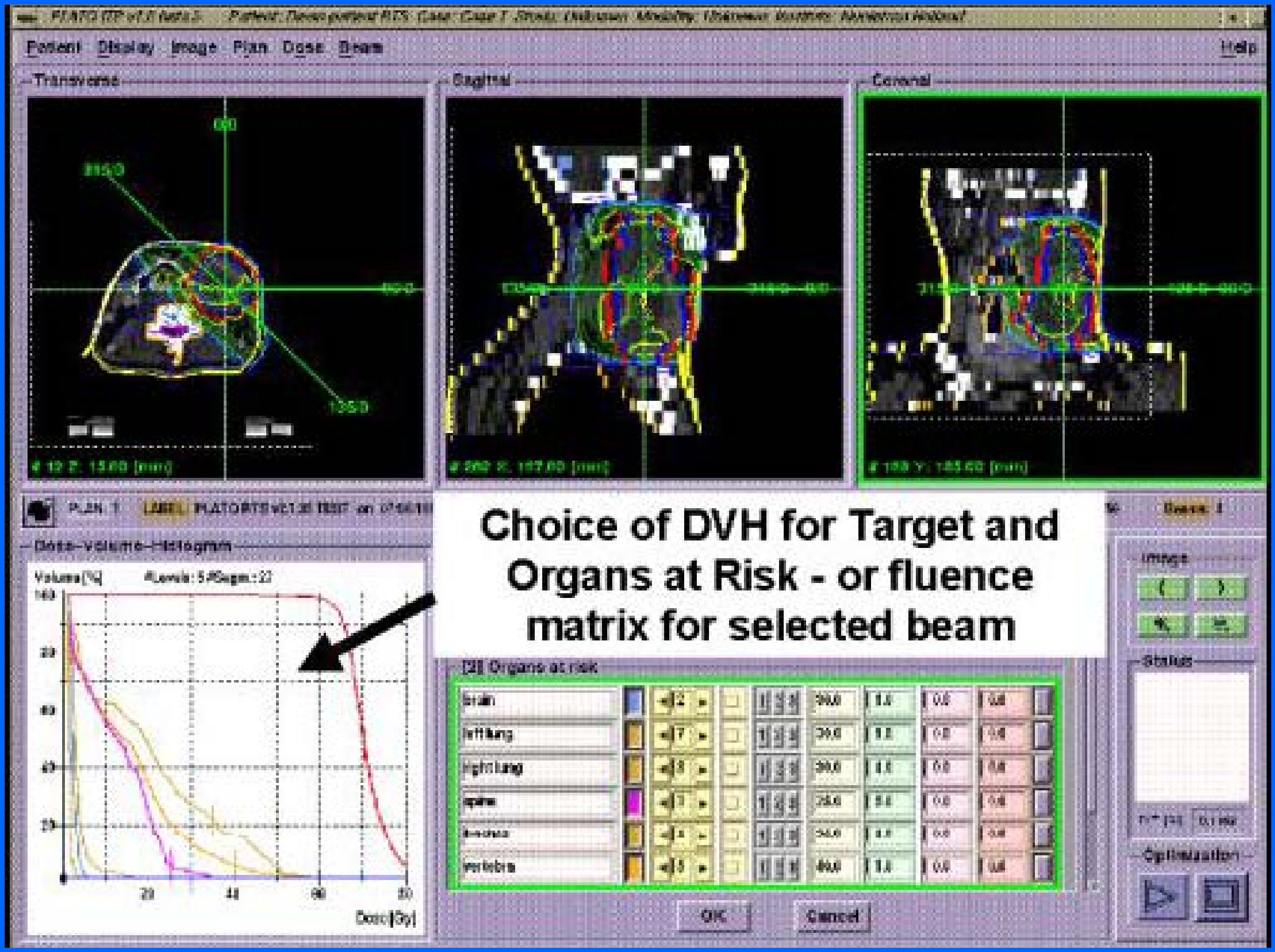
CT-PET

Radiotherapy with X-rays

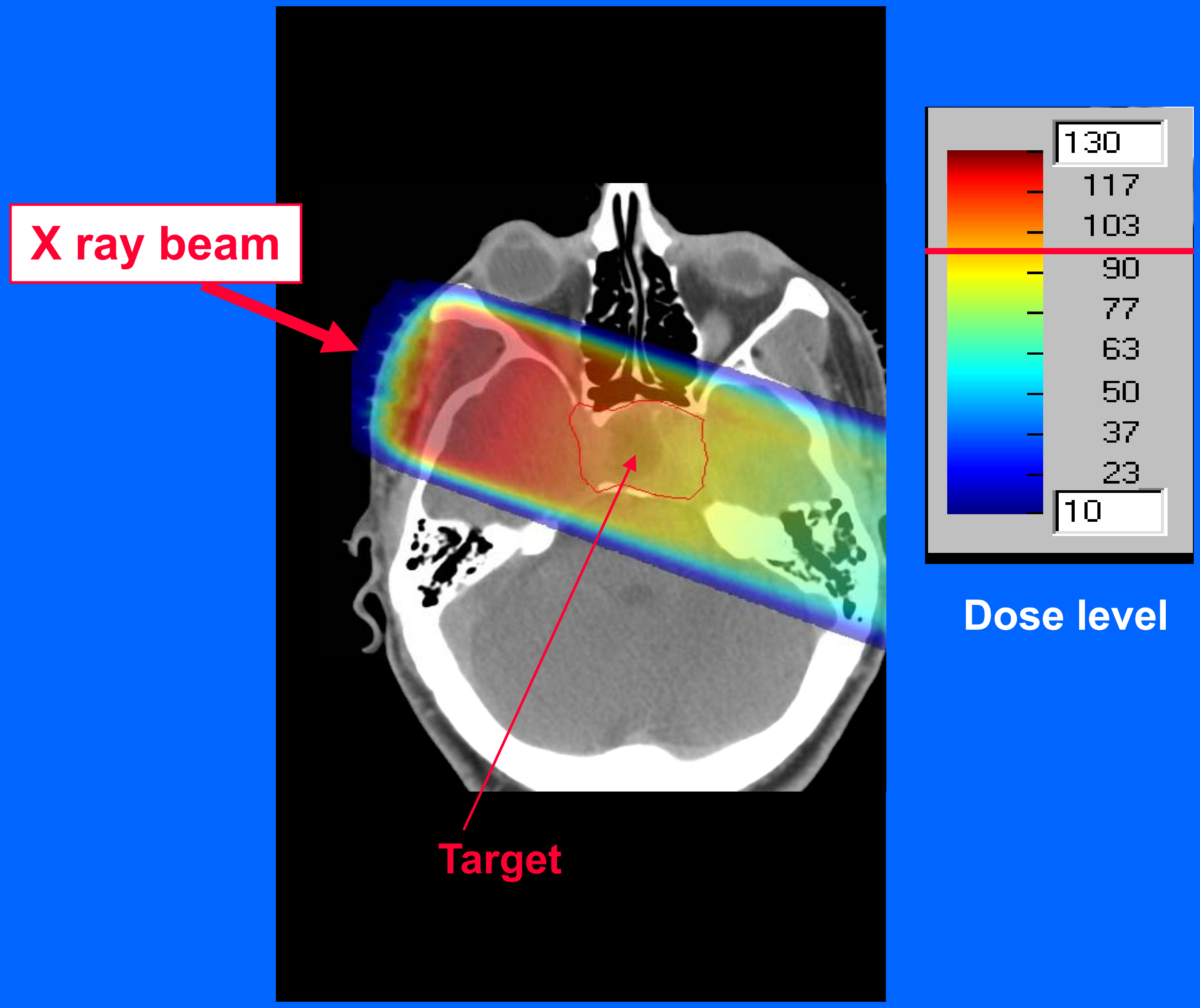


- **Electron linacs to produce gamma rays (called X-rays by medical doctors)**
- **20'000 patients/year every 10 million inhabitants**

How does it work?



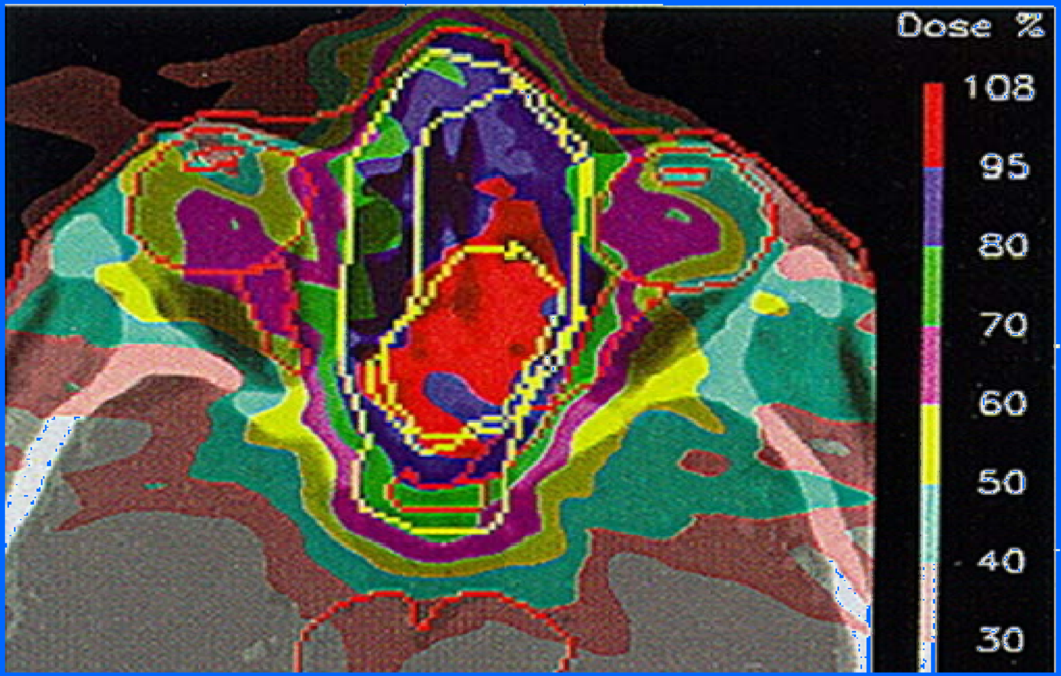
- TC scan data are used to
  - design the volume to be irradiated
  - choose the radiation fields
  - calculate the doses to the target and to healthy tissues
- The dose is given in about 30-40 fractions of about 2 Gray


X ray beam
Target
130
117
103
90
77
63
50
37
23
10
Dose level

The problem of X ray therapy

Solution:

- **Use of many crossed beams**
- **Intensity modulation (IMRT)**



9 different photon beams

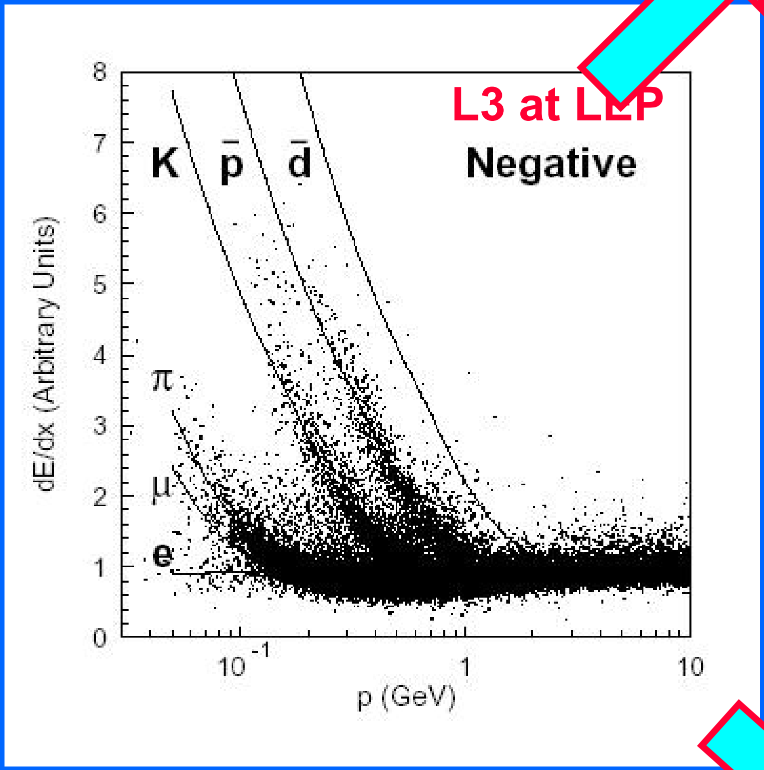
The limit is due to the dose given to the healthy tissues!

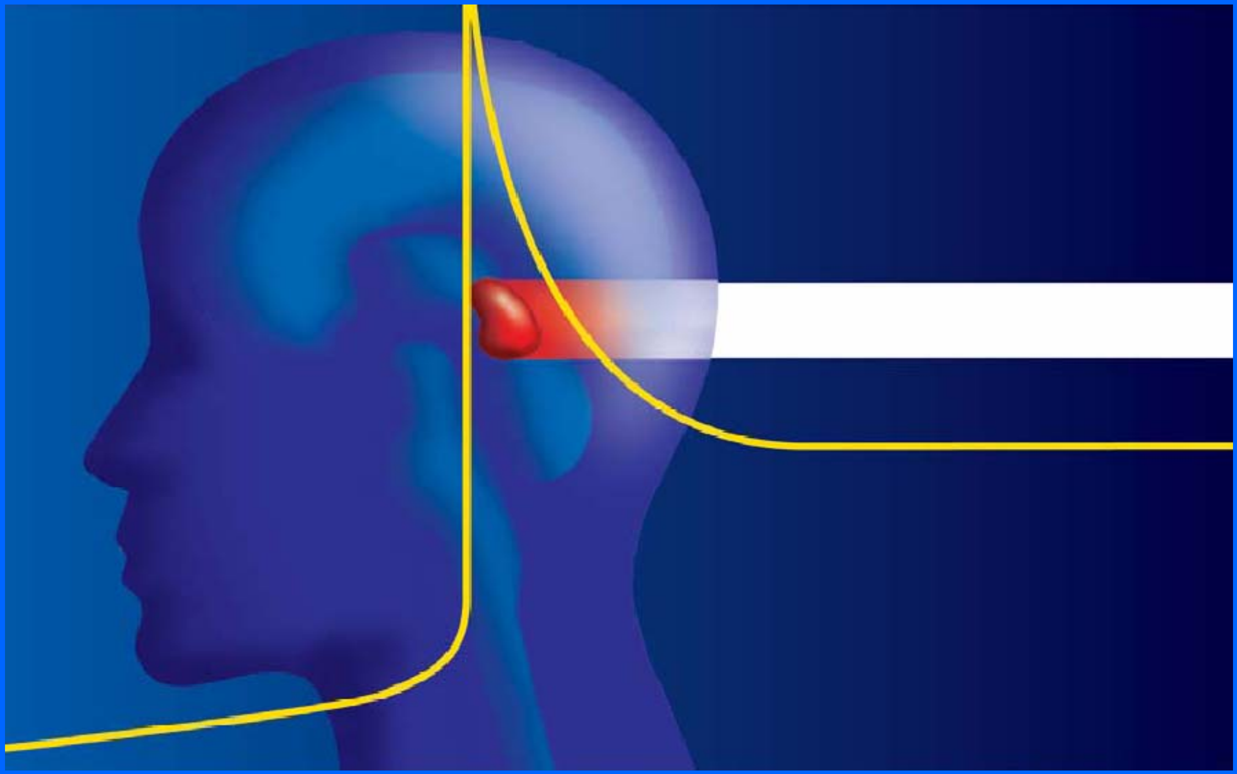
Especially near organs at risk (OAR)

Let's go back to physics...

Fundamental physics

Particle identification

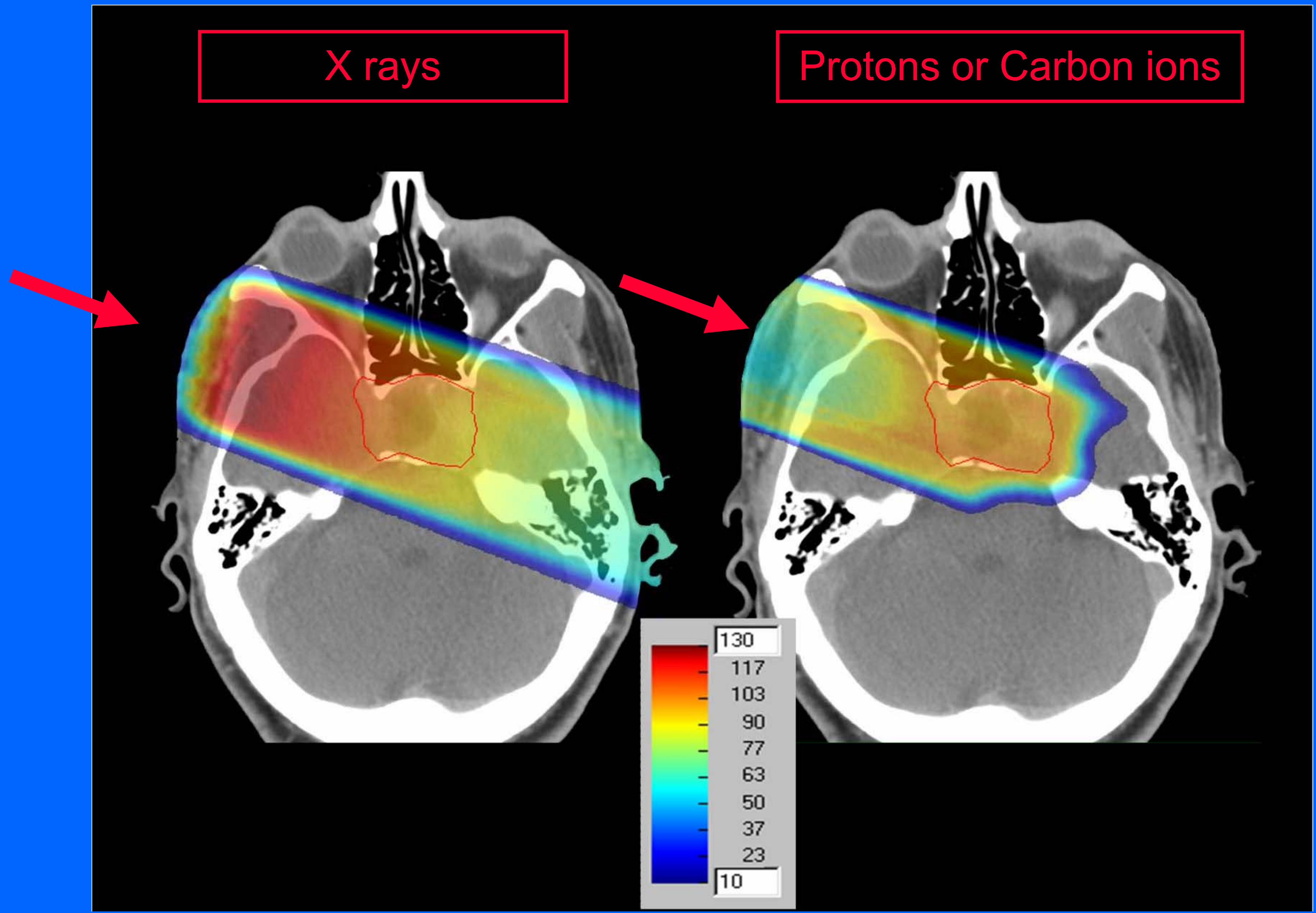




Medical applications

Cancer hadrontherapy

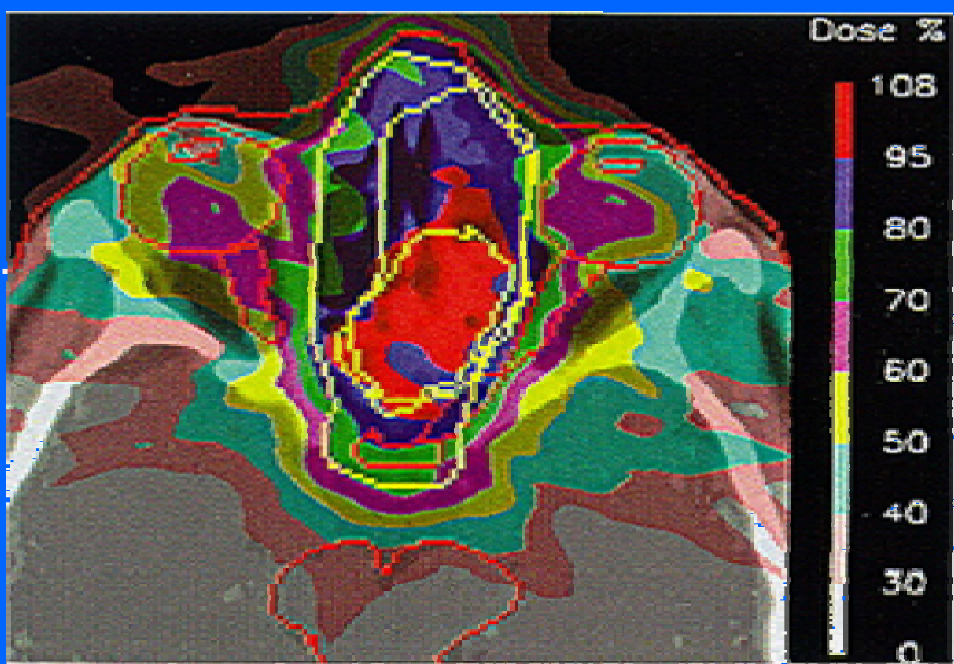
Single beam comparison



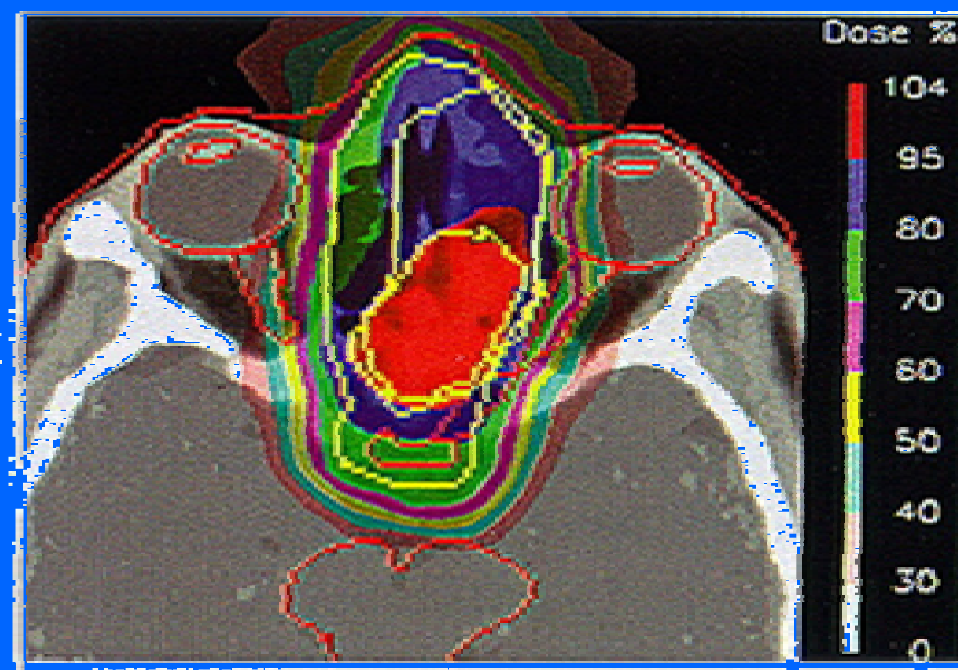
Protons and ions are more precise than X-rays

Tumour between the eyes

9 X ray beams



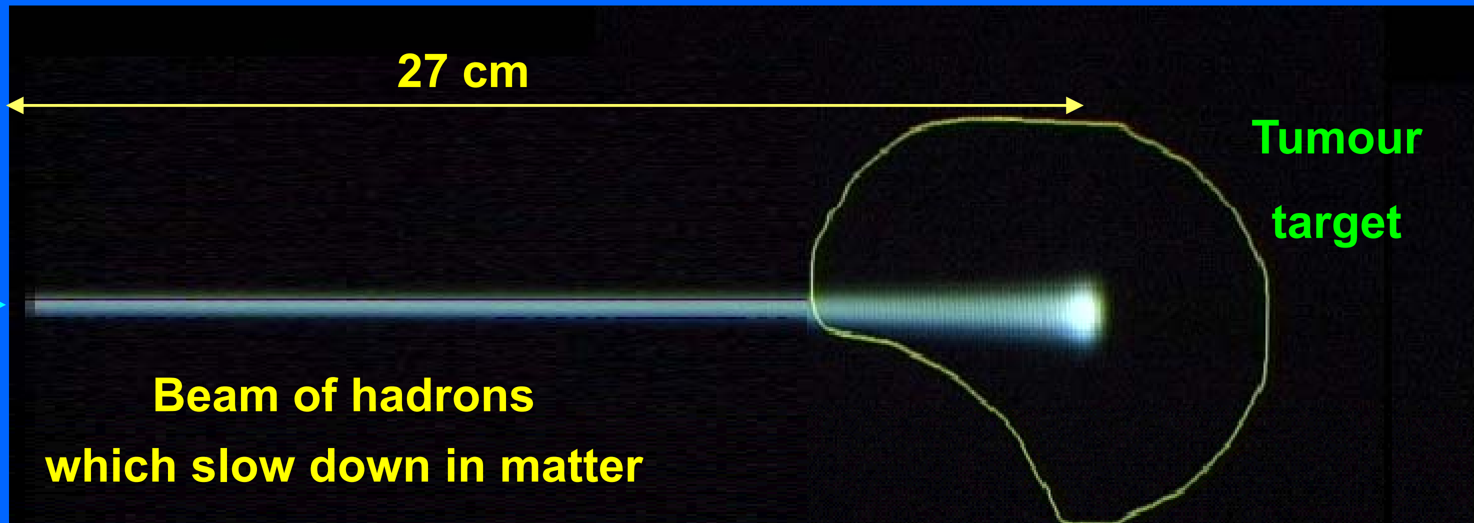
1 proton beam



The basic principles of hadrontherapy

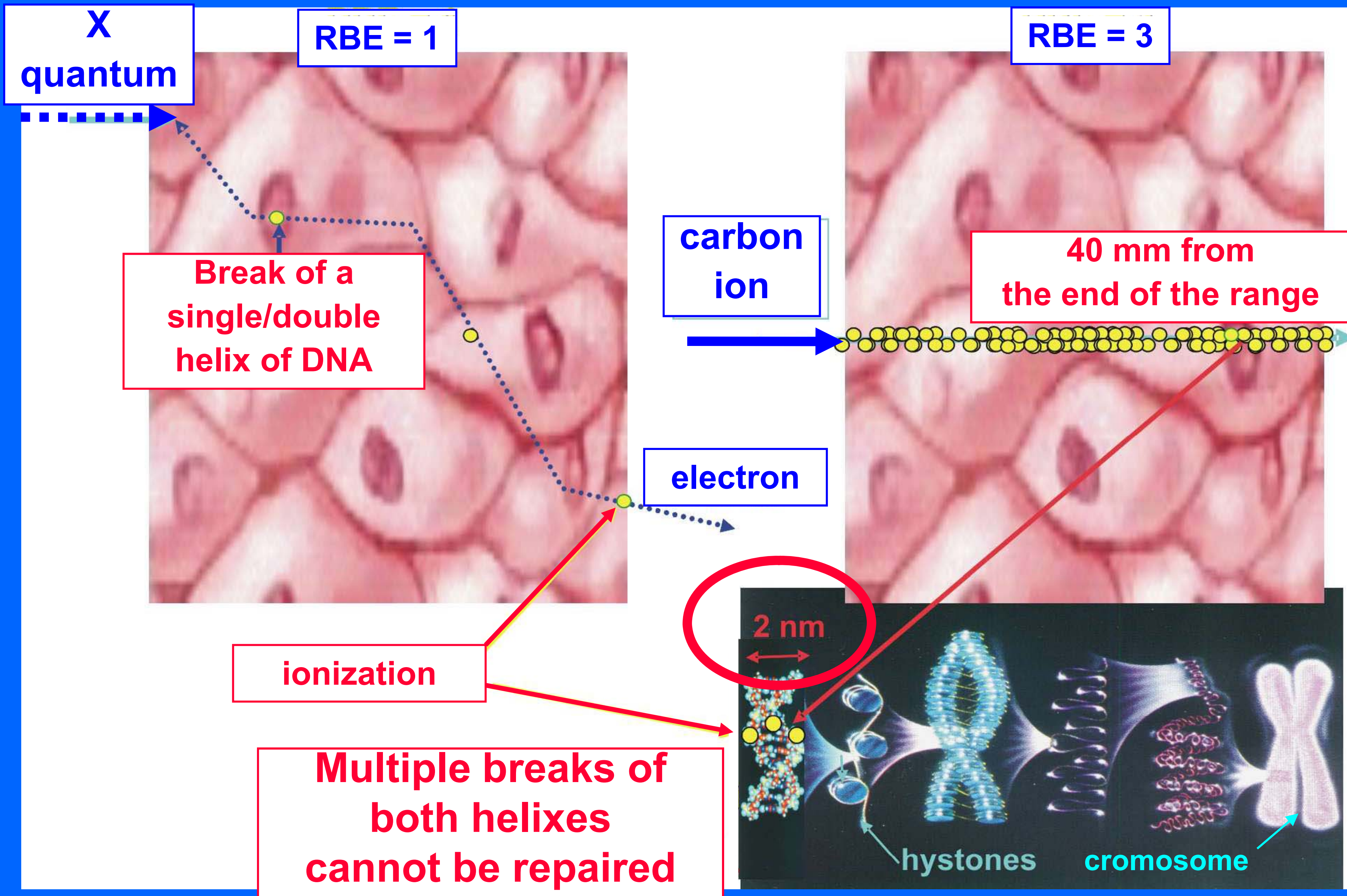
Protons
200 MeV
1 nA

Carbon ions
4800 MeV
0.1 nA

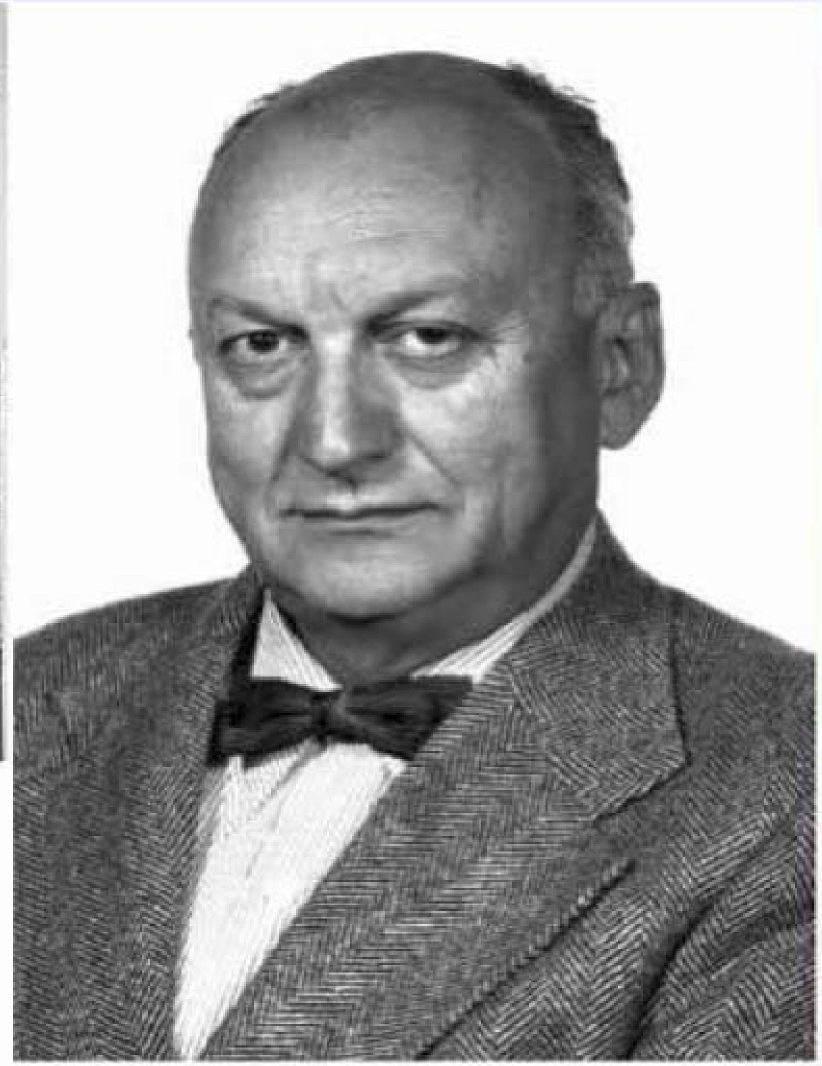


- First idea:
  - Bob Wilson, 1946
- Bragg peak
  - Better conformity of the dose to the target → healthy tissue sparing
- Hadrons are charged
  - Beam scanning for dose distribution
- Heavy ions
  - Higher biological effectiveness

Why ions have a large biological effectiveness?



The beginning of hadrontherpay 1954 at Berkeley

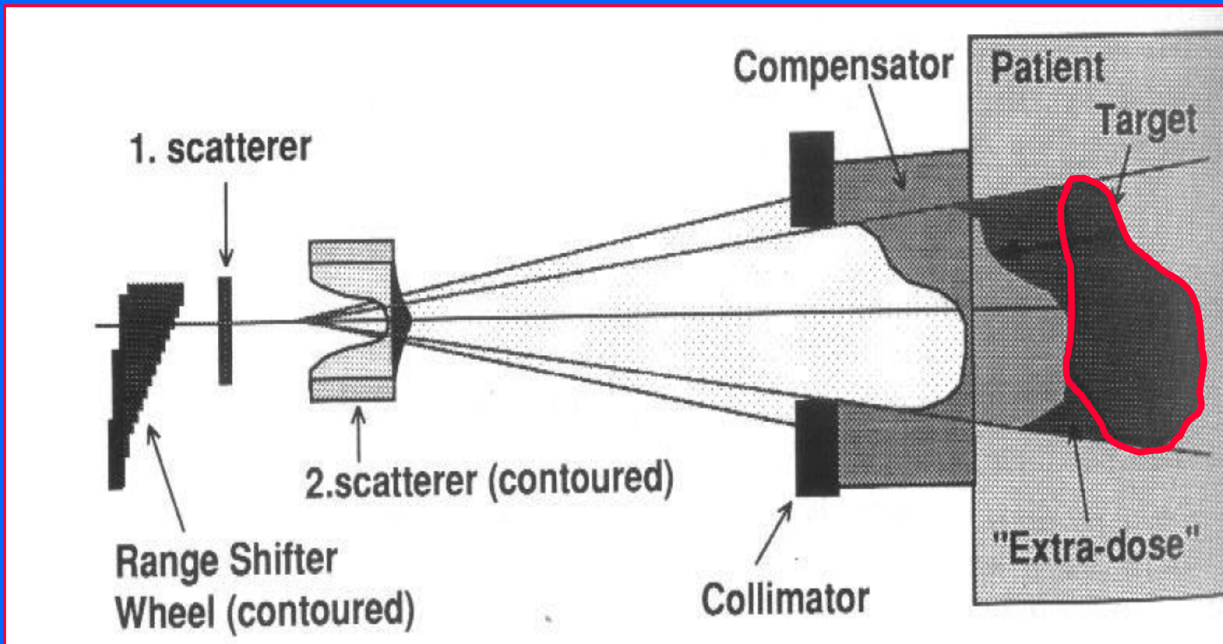


- 1948- Biology experiments using protons
- 1954- Human exposure to accelerated protons and alphas
- 1956 - 1986: Clinical Trials– 1500 patients treated

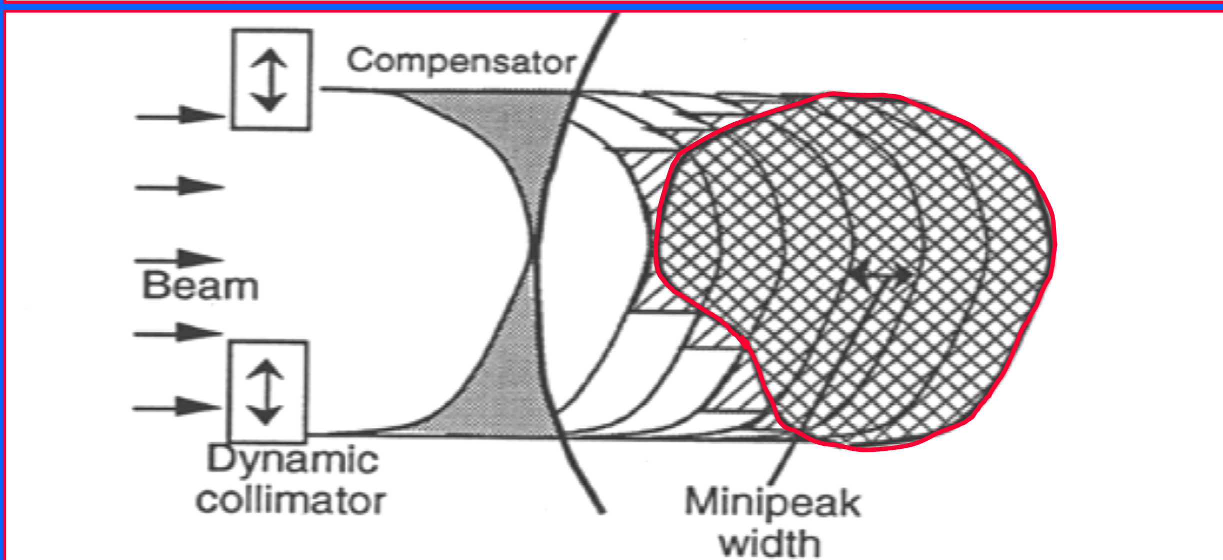
Cornelius A. Tobias

C.A. Tobias, J.H. Lawrence et al., Cancer Research 18 (1958) 121

Dose distribution: passive spreading



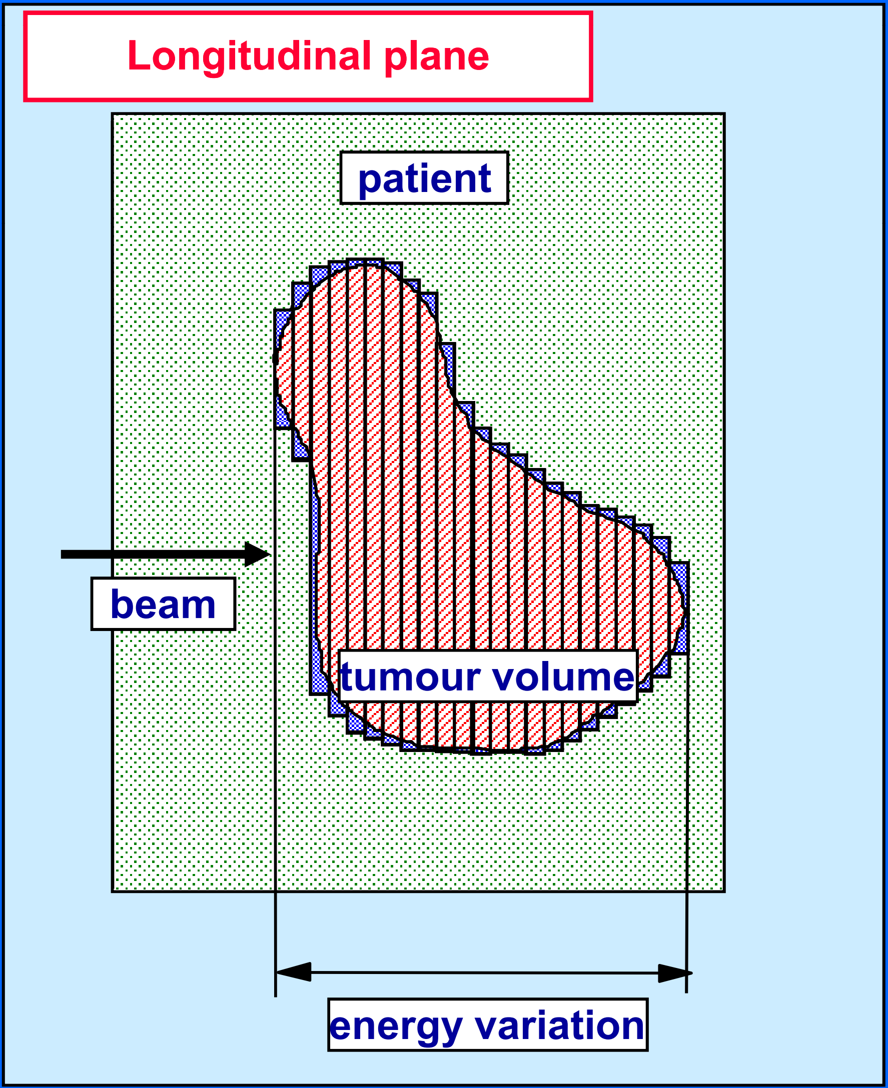
'Double scattering'

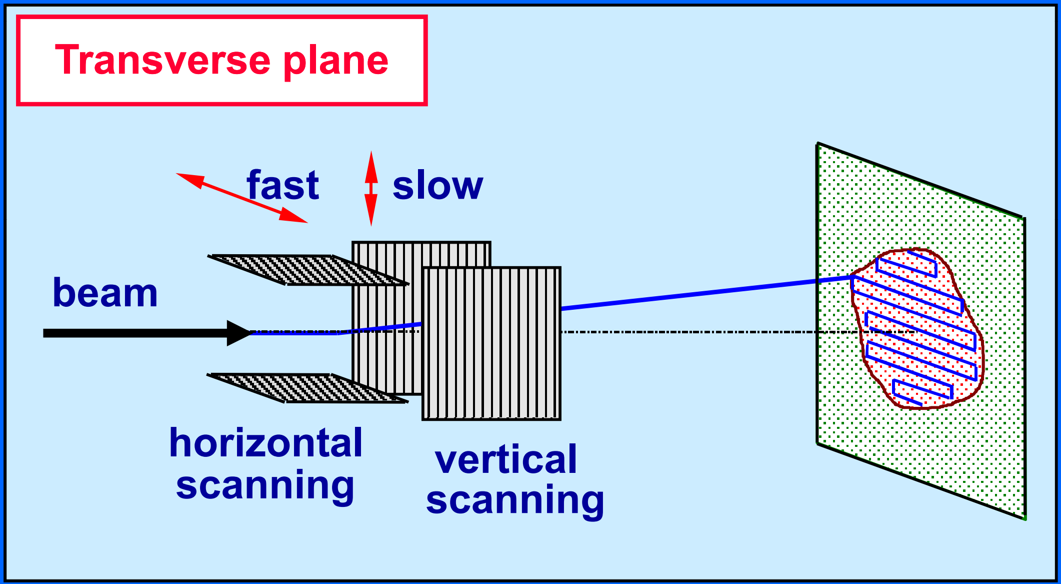


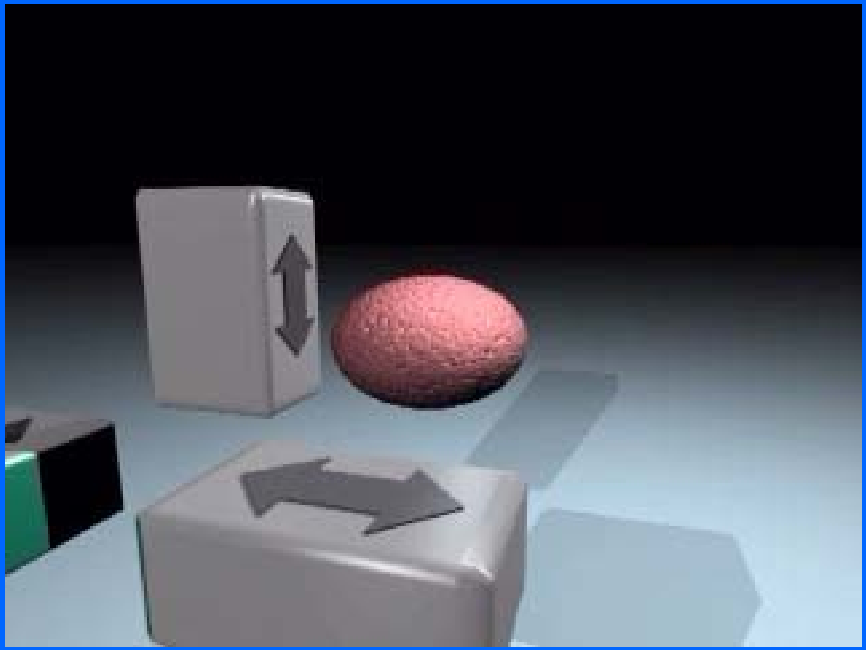
'Layer stacking'

These are the systems uses today in clinical practice!

Dose distribution: active scanning





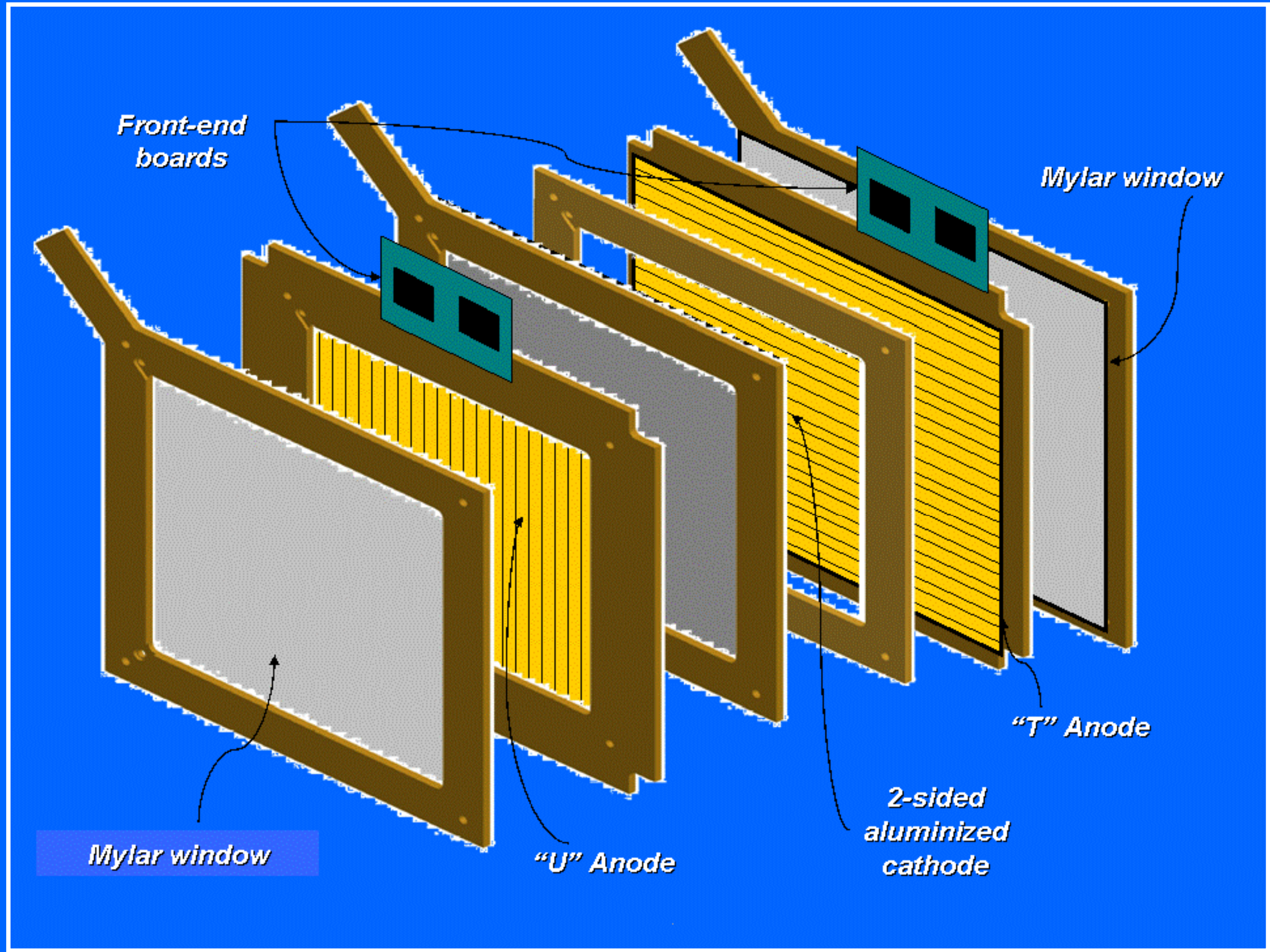


New technique developed mainly at GSI and PSI

SAMBA: an innovative detector

GOAL:
- **On-line monitoring**
- **Position and intensity**
- **Active spot scanning**

- Strip ionization chamber
- Orthogonal strips of 2 mm
- Very sensitive electronics (detection of charges of the order of 100 fC)

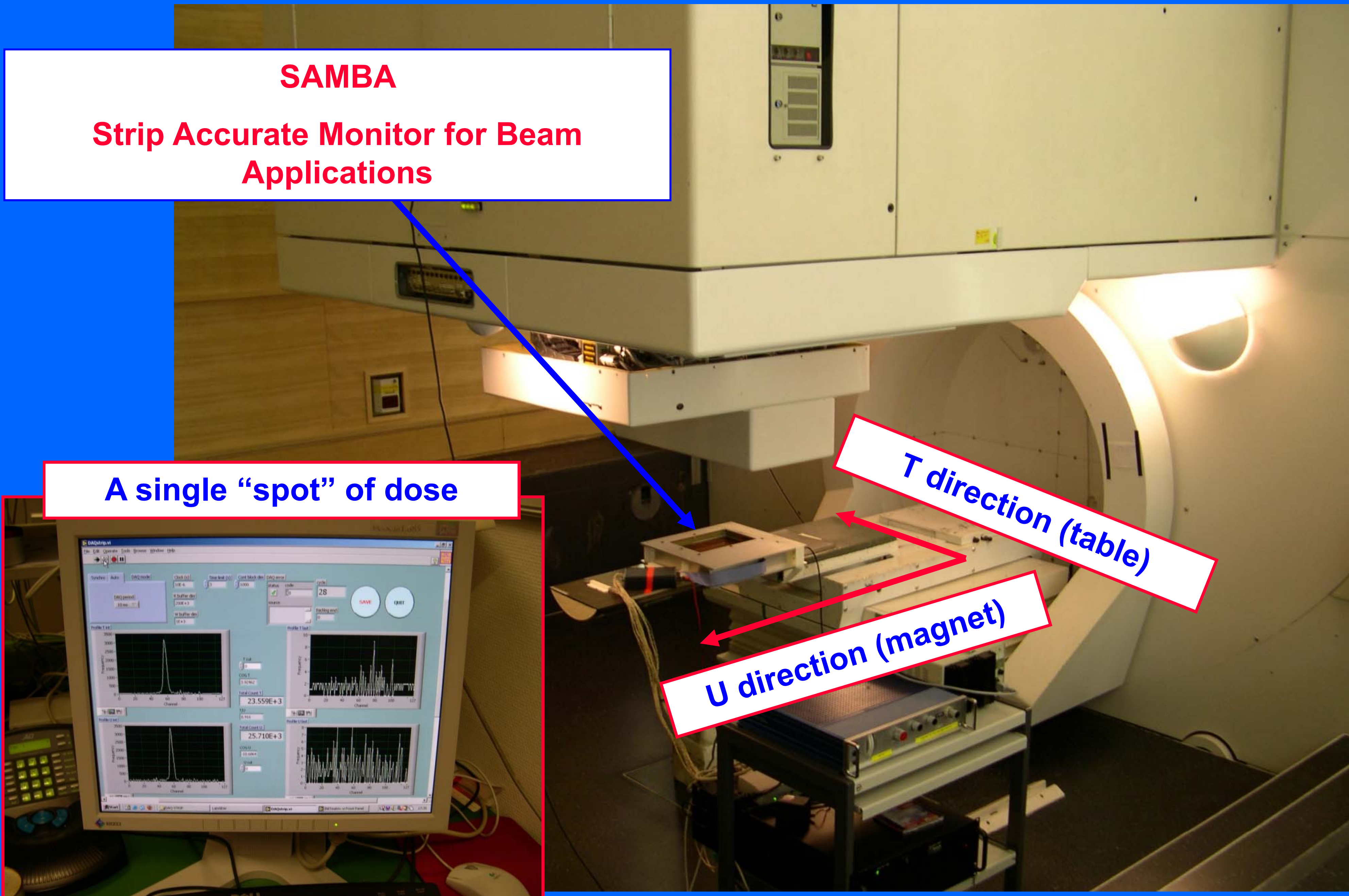


Collaboration TERA – PSI – INFN Torino

Beam tests on Gantry1 at PSI

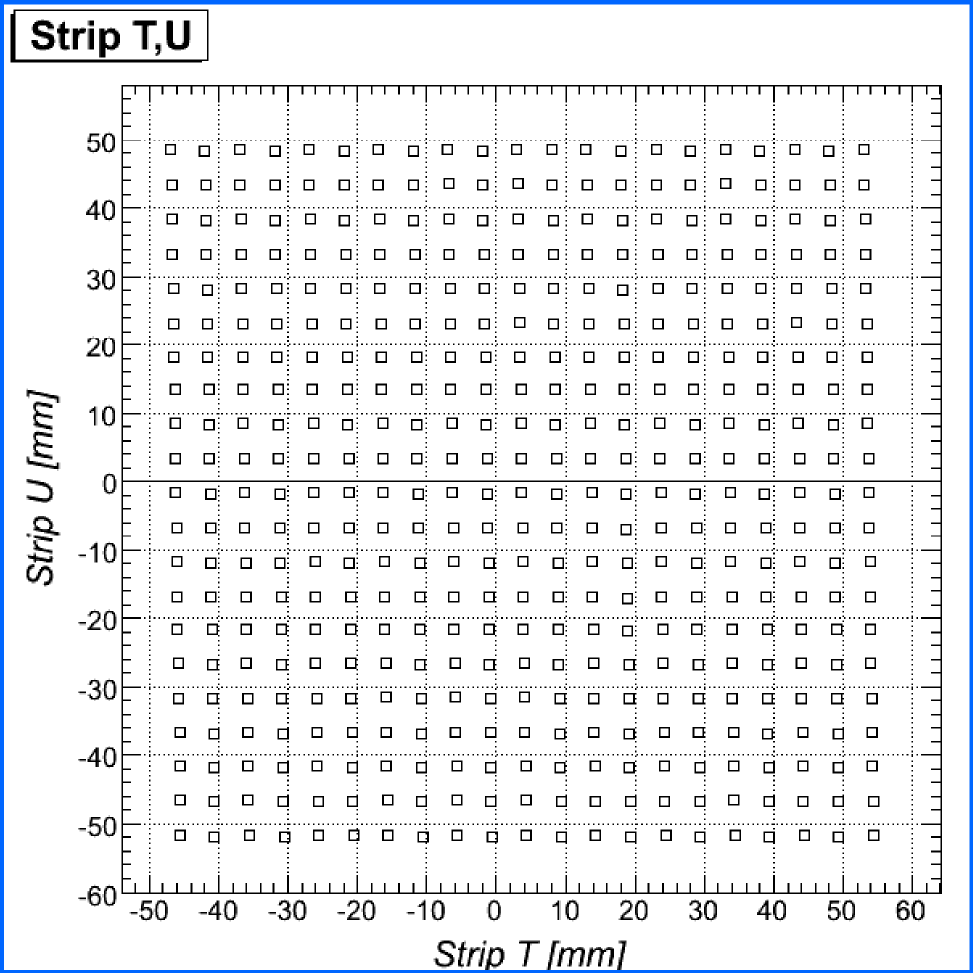
SAMBA

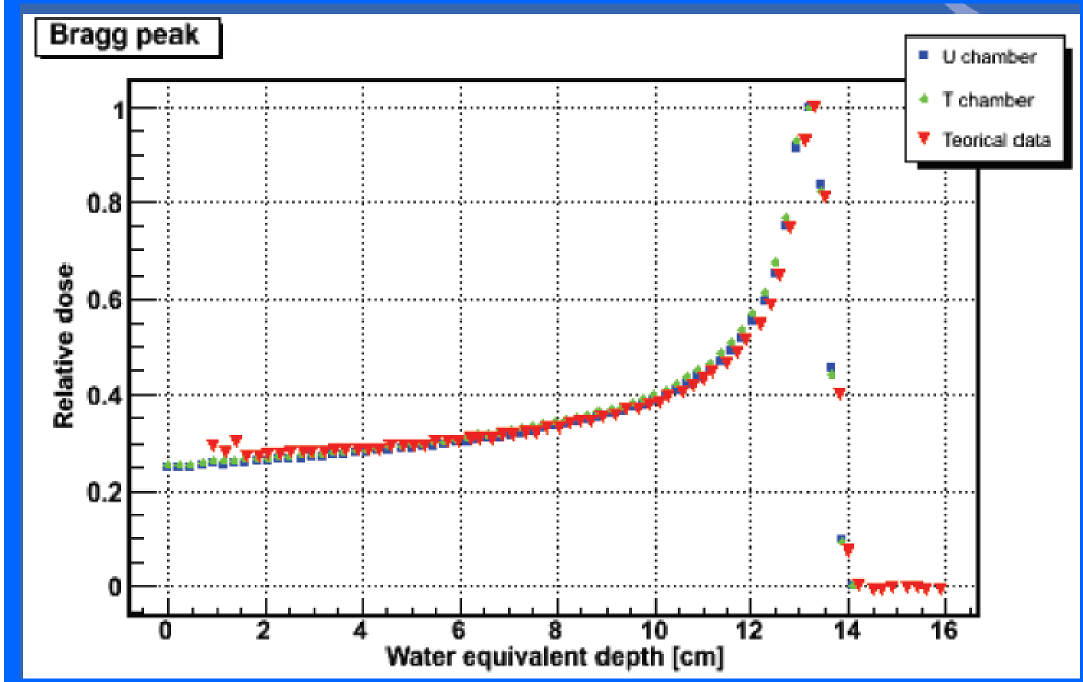
Strip Accurate Monitor for Beam Applications



A single “spot” of dose

SAMBA: an innovative detector for on-line monitoring





- Red points: PSI daily check data
- On line QA of the beam!

- Square of dose: 21 x 21 spots spaced 5 mm
- Precision 0.1 mm !

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

14.5% of X-ray patients = 2'900 pts/year

Therapy with Carbon ions for radio-resistant tumours

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

Every 50 M inhabitants

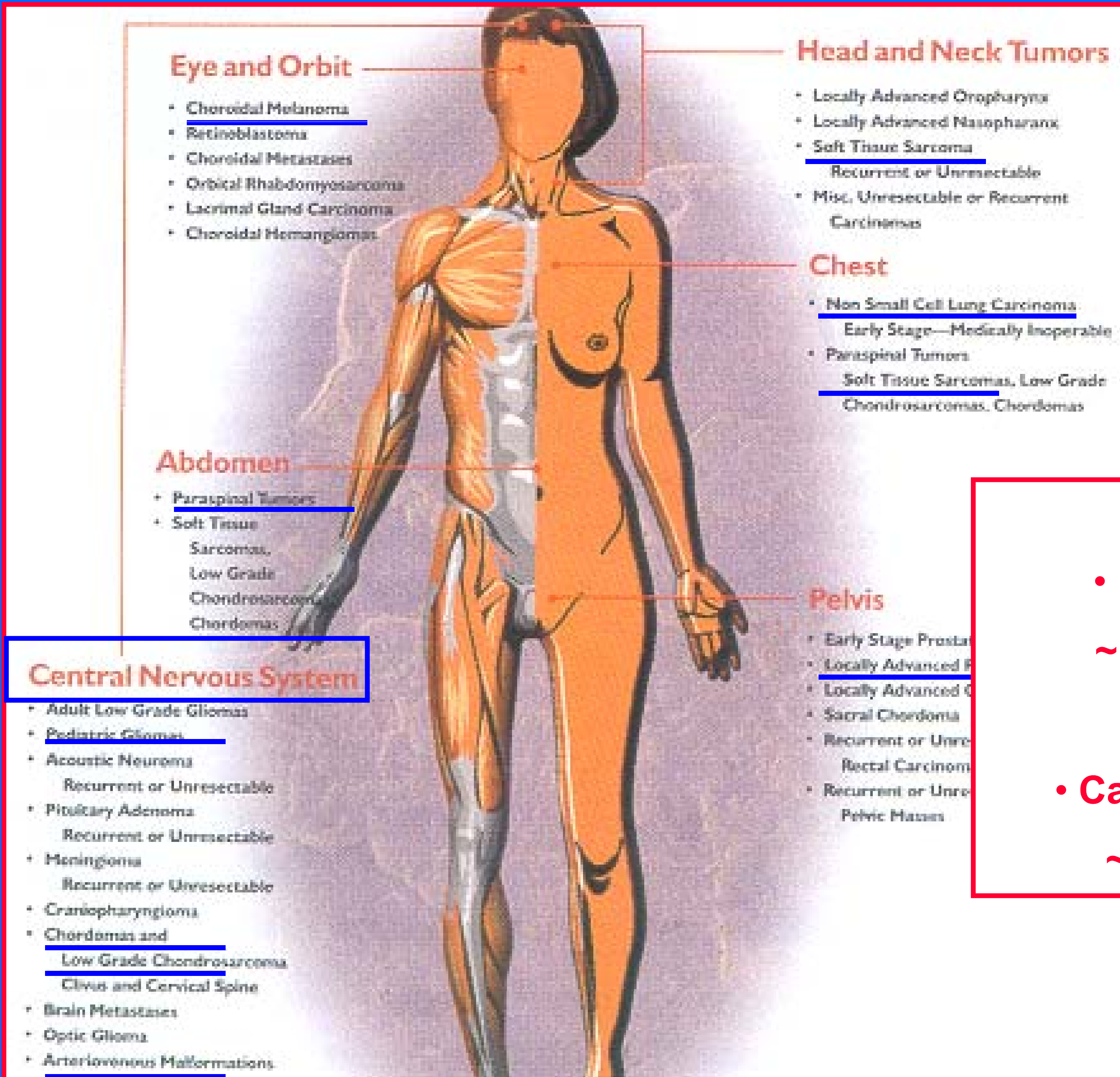
- **Proton-therapy**

4-5 centres

- **Carbon ion therapy**

1 centre

TOTAL about 3'500 pts/year
every 10 M



Up to present

• **Proton-therapy:**

~ 45 000 patients

• **Carbon ion therapy:**

~ 2 200 patients

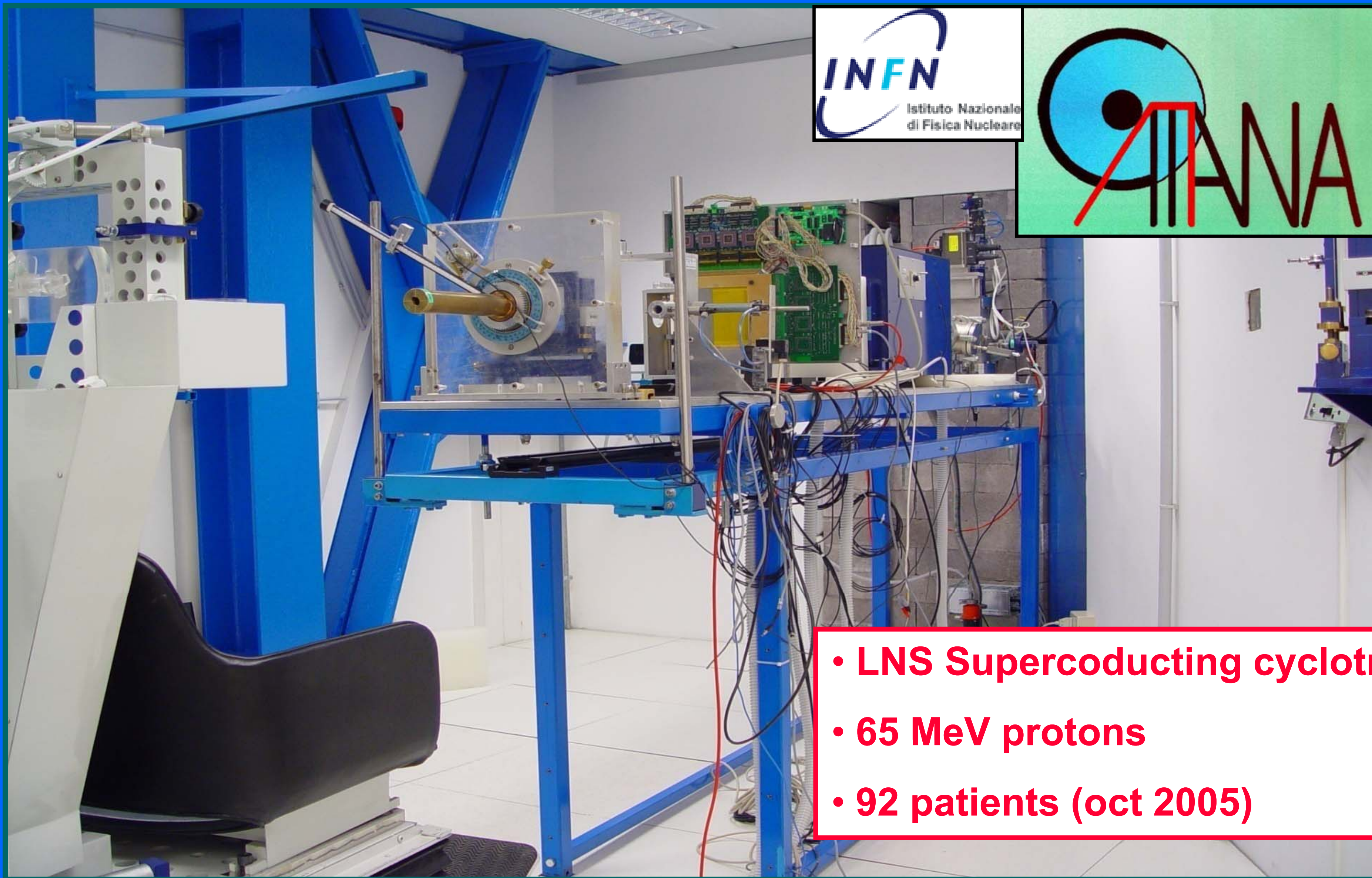
Present and "near" future of hadrontherapy

- **Proton-therapy is "booming"!** *(for information see PTCOG, ptcog.web.psi.ch)*
  - **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 almost approved (France and Austria)**
  - **European network ENLIGHT**

The map of hadrontherapy

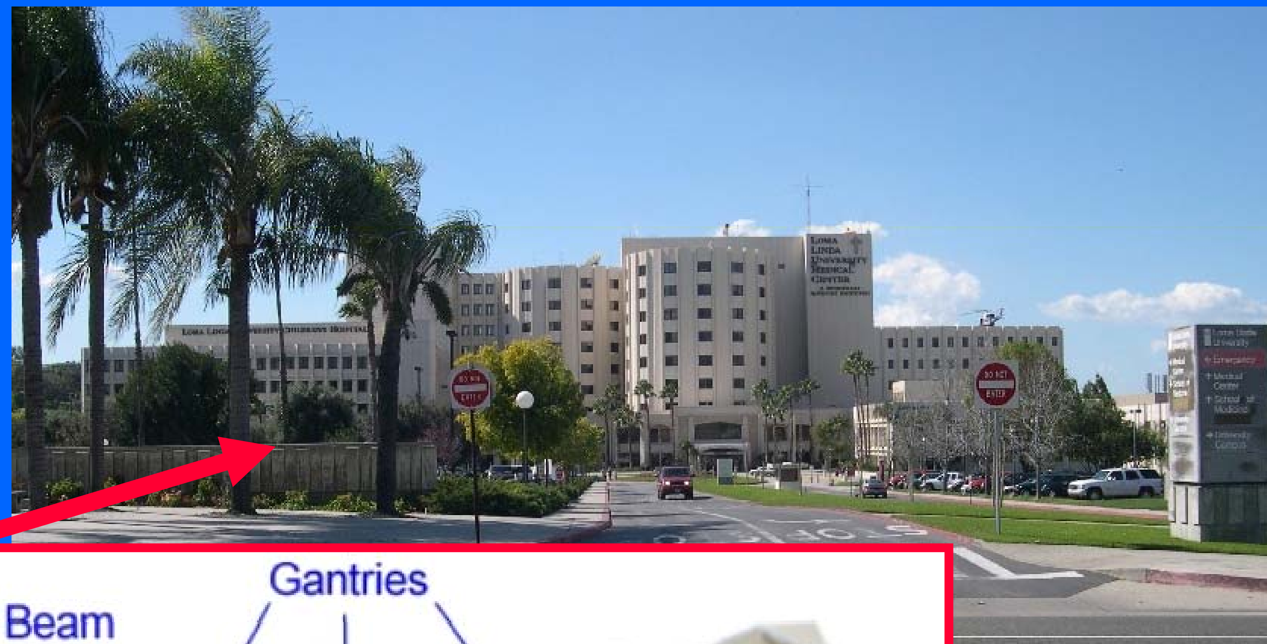
The eye melanoma treatment at INFN-LNS in Catania

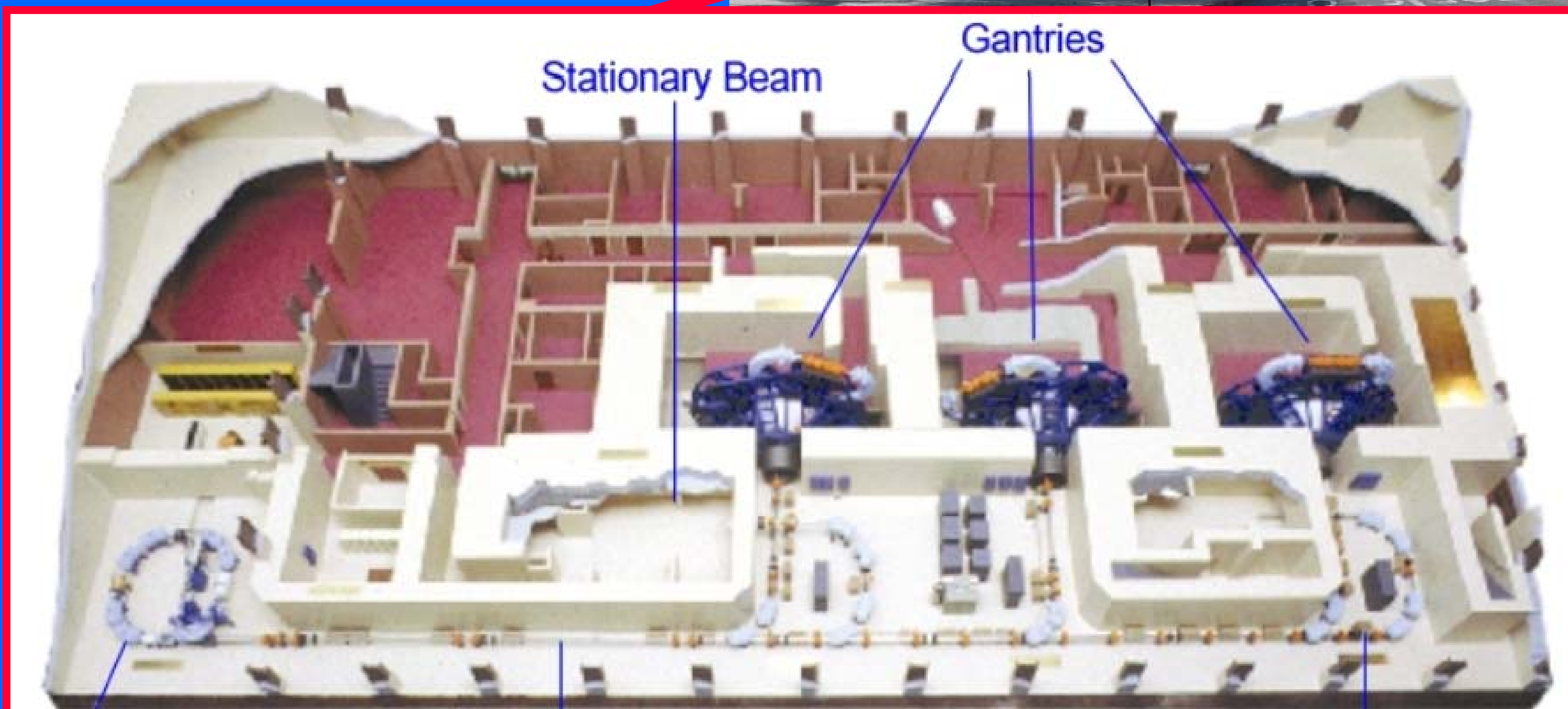


- **LNS Supercoducting cyclotron**
- **65 MeV protons**
- **92 patients (oct 2005)**

The Loma Linda University Medical Center (USA)

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

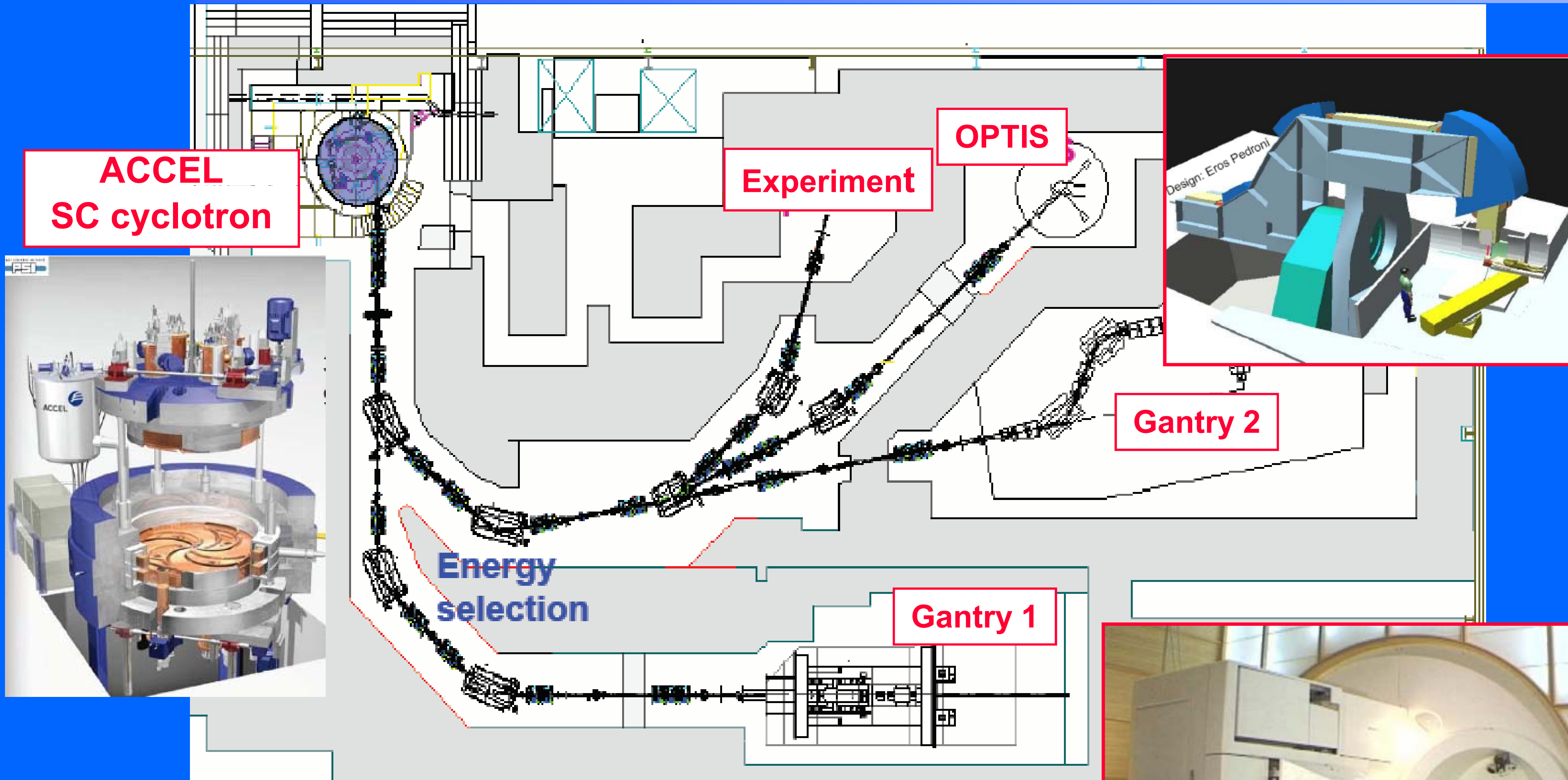




What does a patient see of all that?

The best care for the patient is our objective!

PROSCAN project at PSI



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

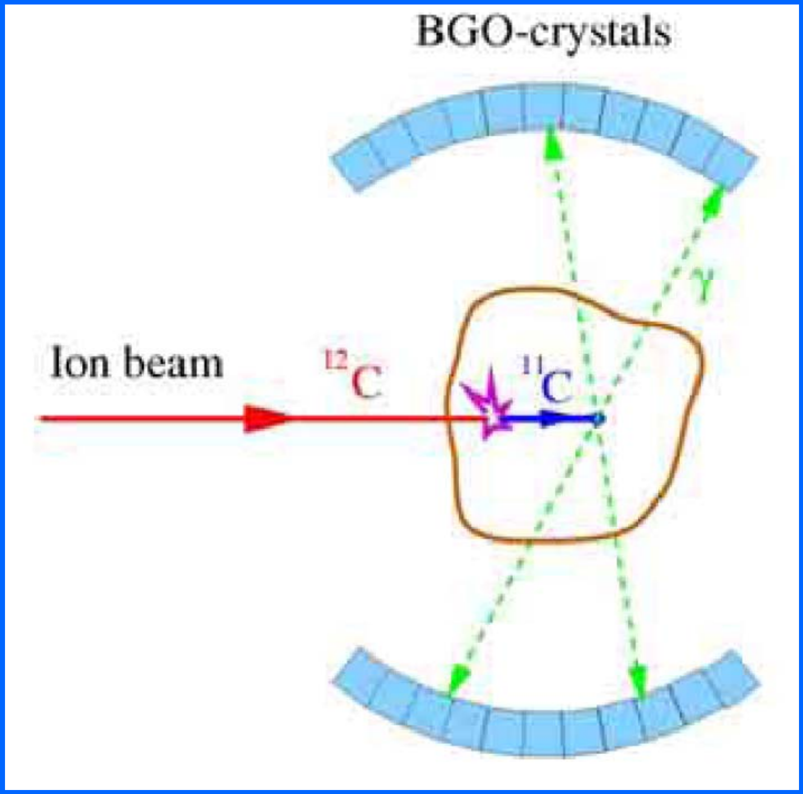
Carbon ion therapy in Europe

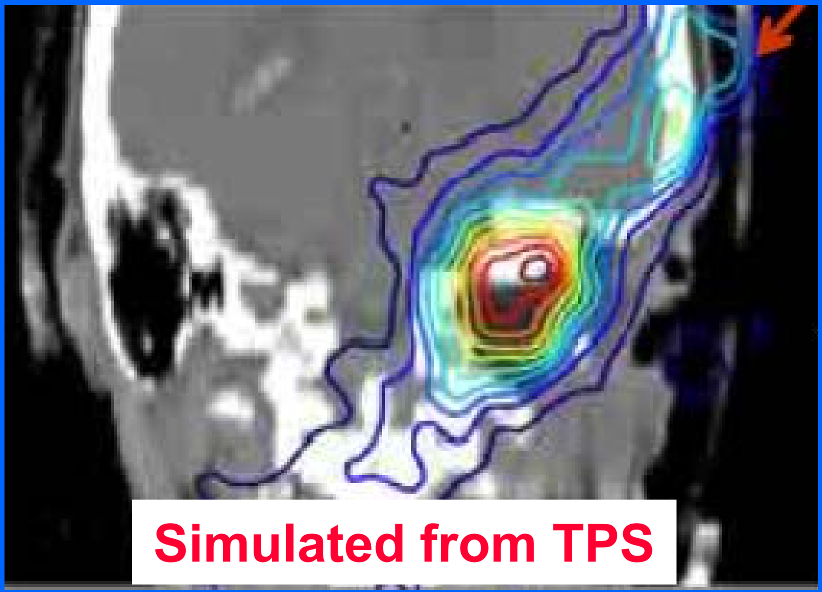
1998 - GSI pilot project (G. Kraft)

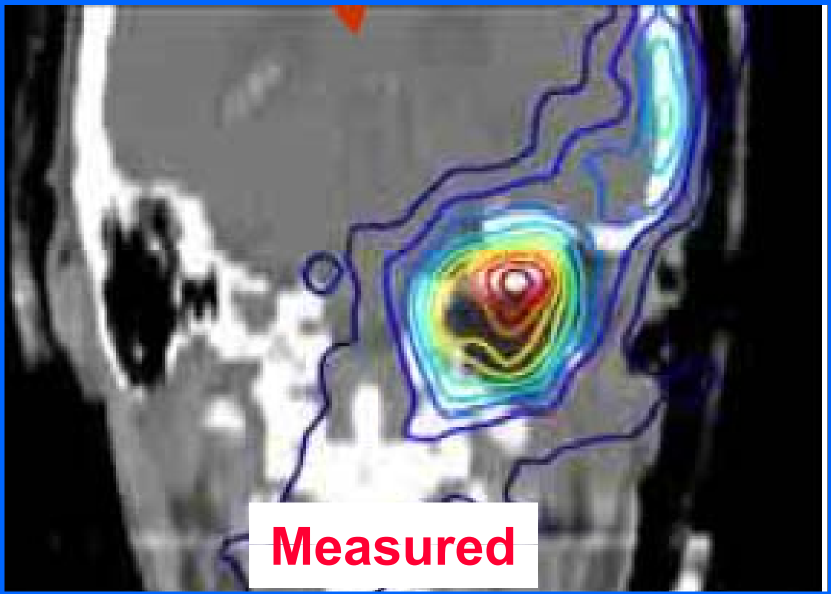
200 patients treated with carbon ions

PET on-line

PET on-beam







Measurement of the "real" 3D dose distribution given to the patient

New ideas for 2D measurement of the dose

- PET on-beam with:
  - RPC (INFN Frascati)
  - GEM (TERA/CERN)
- More sensitive area, cheaper than crystals

- PET on beam with protons
  - Some PET isotopes are formed along the path (ex ^{11}C)
  - No Bragg peak but one can see where protons stop!

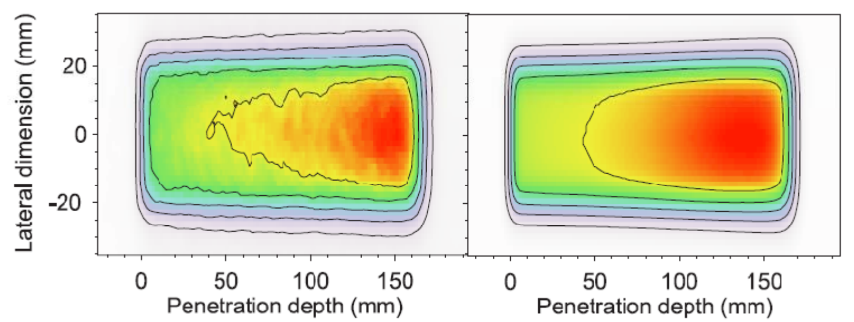
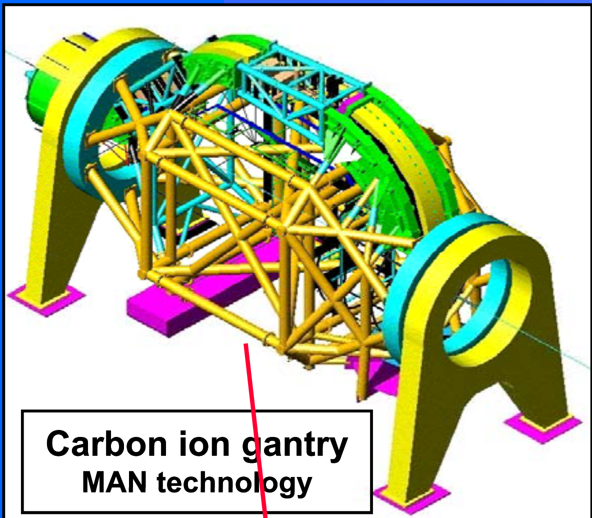
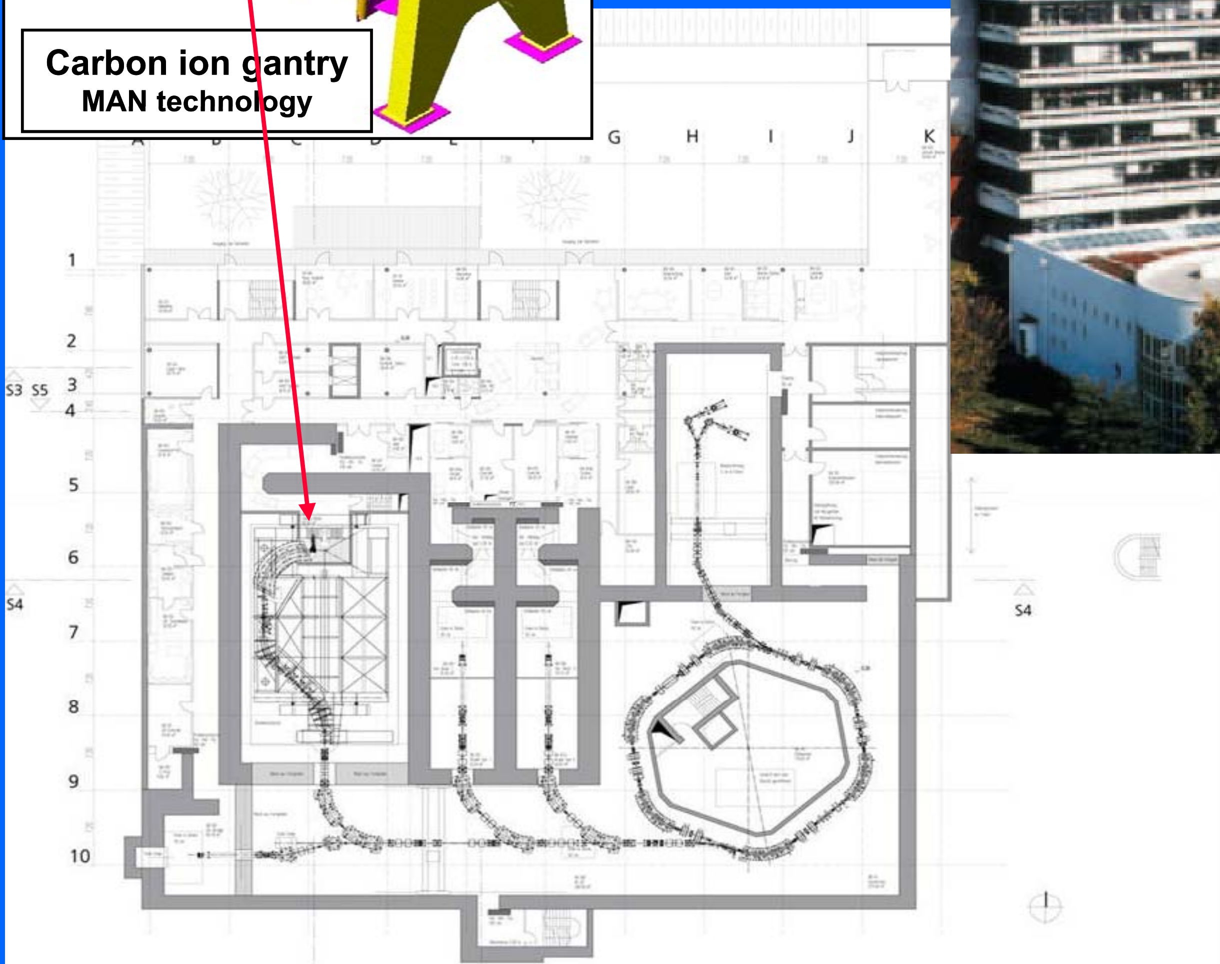


Fig. 4. Measured (left) and predicted (right) β^+-activity distributions for a scanned mono-energetic irradiation at 171.62 MeV energy.

- PET "off-beam" after proton irradiation (MGH Boston)
  - Use of a normal PET camera located nearby
  - Blood flow → distortions of the image!

HIT – University of Heidelberg

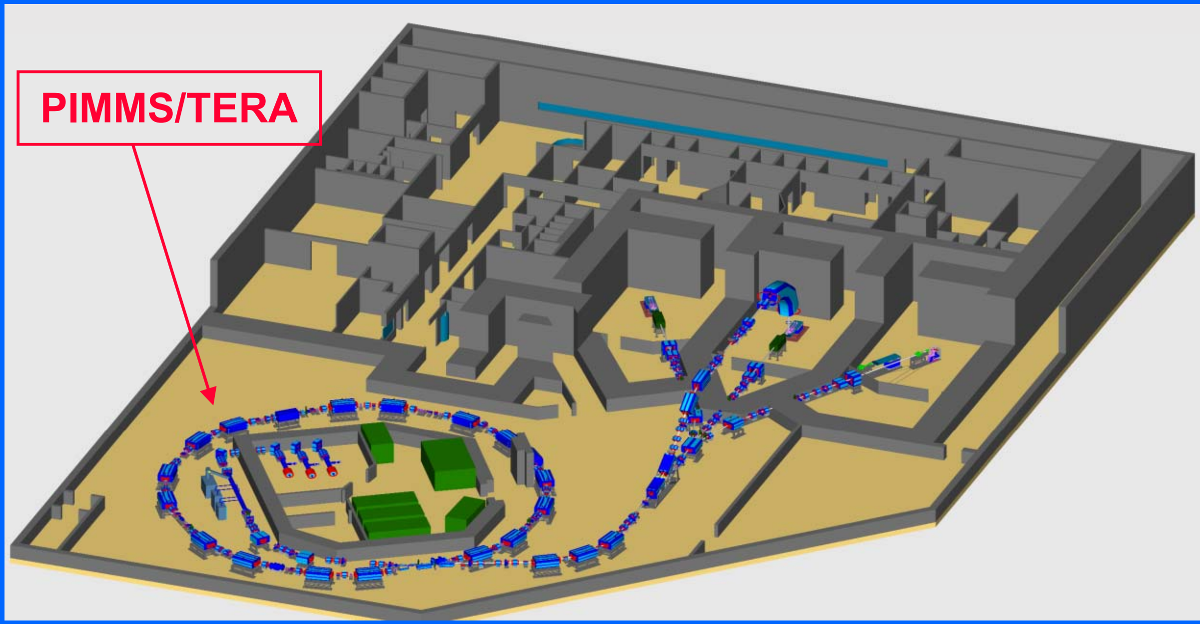




- **Hospital based centre**
- **Project started in 2001**
- **First patient treatment foreseen in 2007**

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



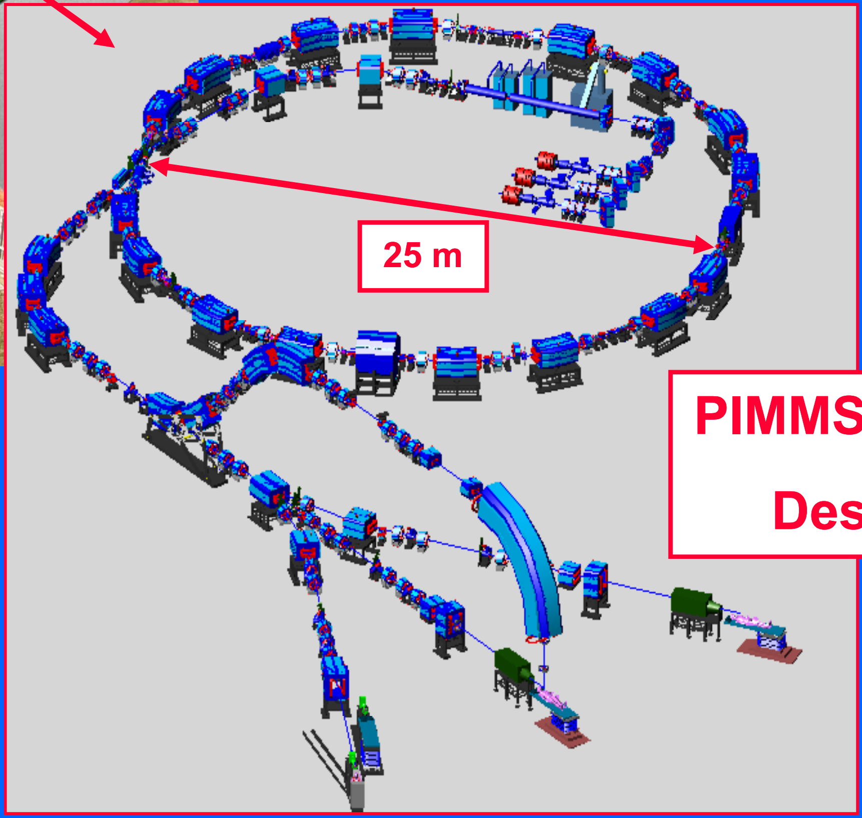
- Collaborations with many research institutes and universities
  - in particular CERN, INFN, PSI, GSI, JRC, Universities of Milan, Turin and Piemonte Orientale

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 2008



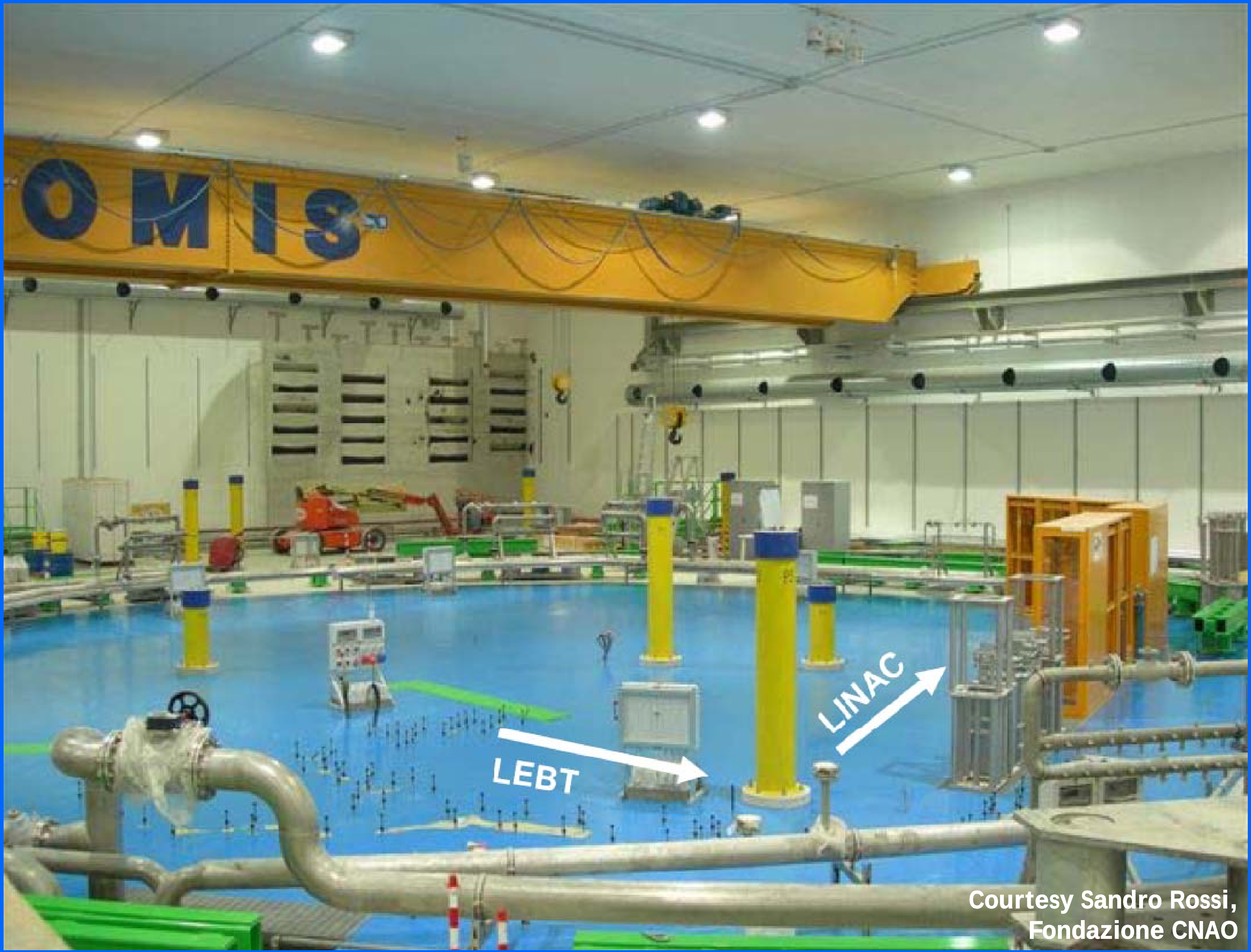
PIMMS/TERA

Design

- Hospital based centre
- Protons and carbon ions

The hospital building in March 2007

CNAO synchrotron hall in March 2007



Medium term

- "Dual" cyclotrons for protons and carbon ions
- Very compact SC proton synchrocyclotrons
- CYCLINAC = Cyclotron + LINAC

Long term

- Laser plasma accelerators

250 MeV/u SC cyclotron

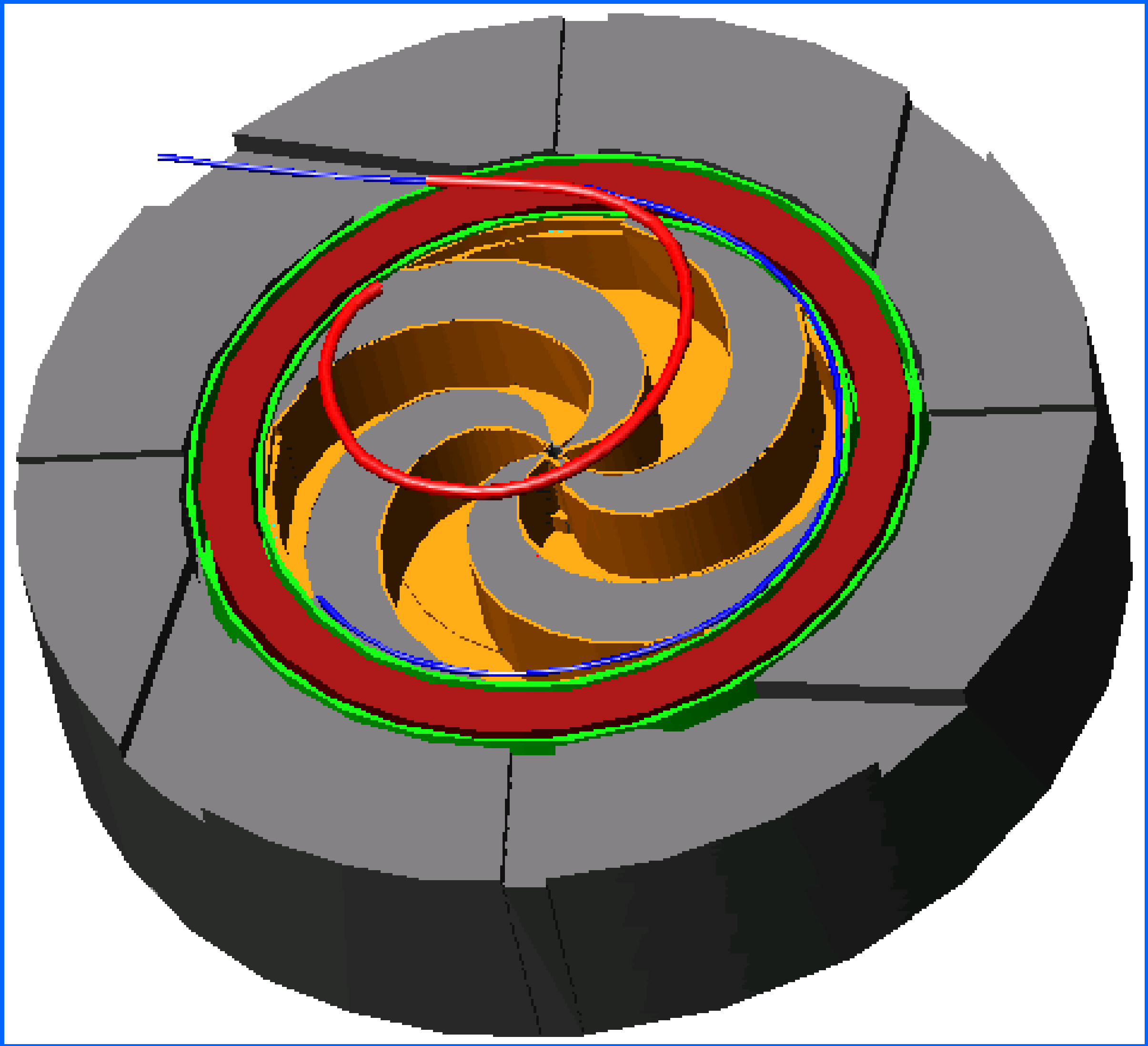
- H_2^+ molecules

  250 MeV proton beam for deep seated cancer treatment

- 250 MeV/u fully stripped C ions

  maximum penetration of 12 cm in water

400 MeV/u SC cyclotron is proposed by IBA



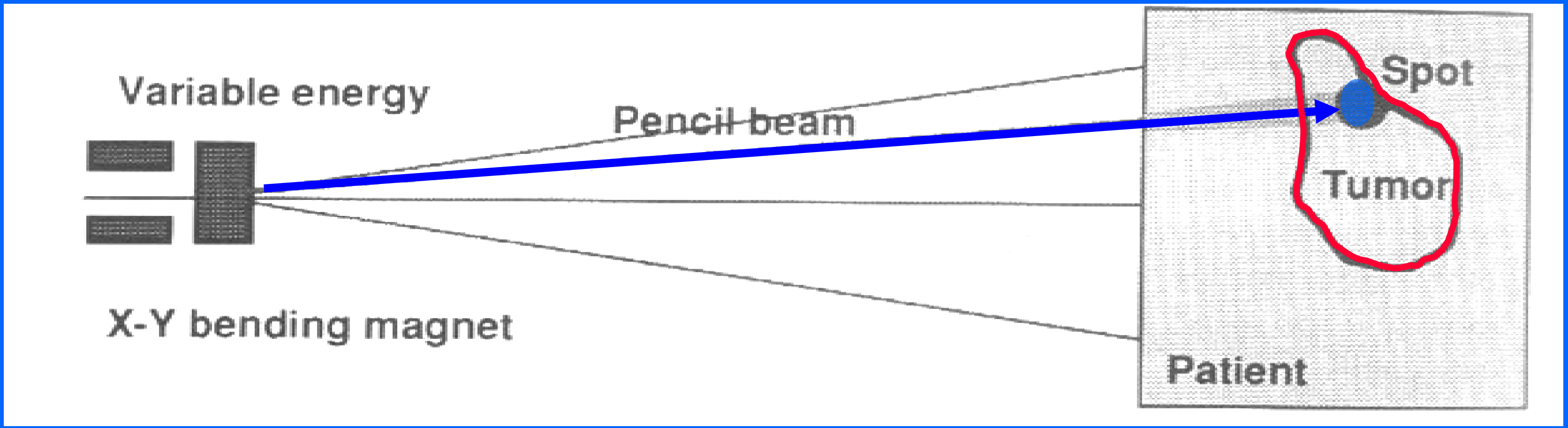
250 MeV/u proposed by INFN – IBA

Very compact SC synchrocyclotrons

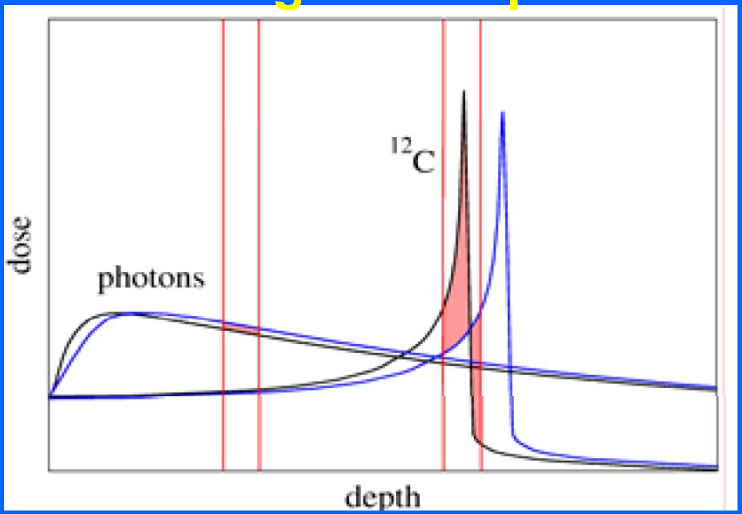
- 9.5 T SC magnet → ~50 cm diameter for 250 MeV protons
- Innovative double scattering spreading technique based on scatterers made of “low Z” and “high Z” liquid materials
- Project MIT and Still River Systems

- Goal: “One gantry-One room” apparatus
- Very difficult project that could lead to a “change of scale”!

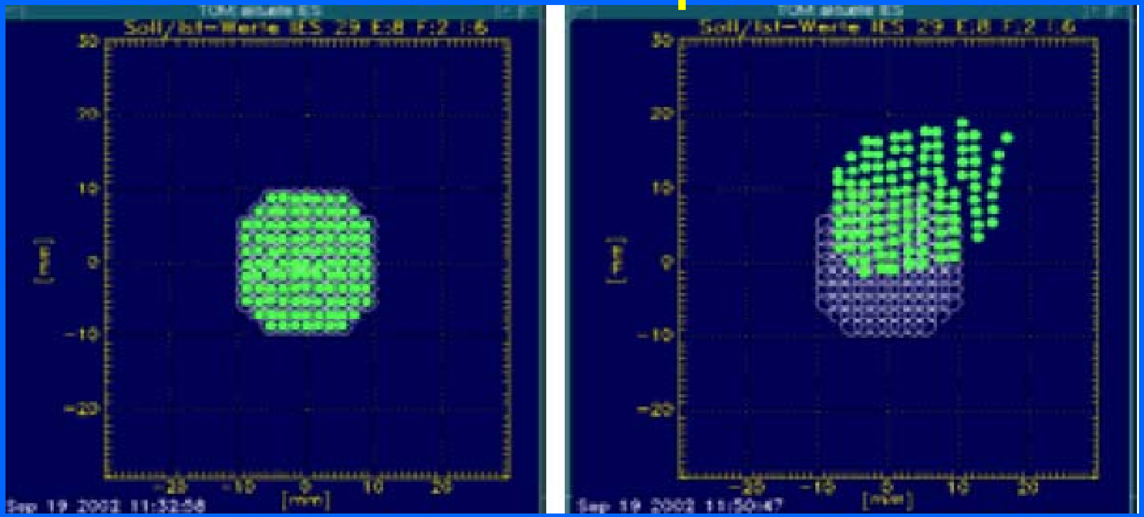
"Spot scanning" is sensitive to movements



longitudinal plane



transverse plane



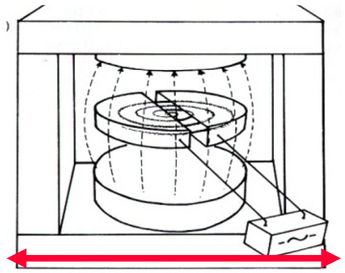
Two approaches can be combined:

1. **multiple 'repainting, of the tumour target**
2. **feedbacks in the tranverse and energy dimensions**

The accelerators used today in protontherapy

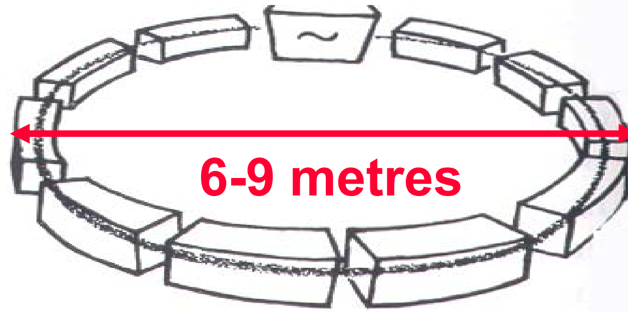
- 200-250 MeV protons

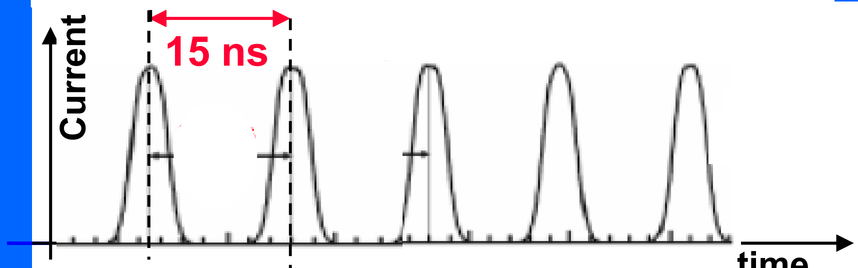
CYCLOTRONS (Normal or SC)

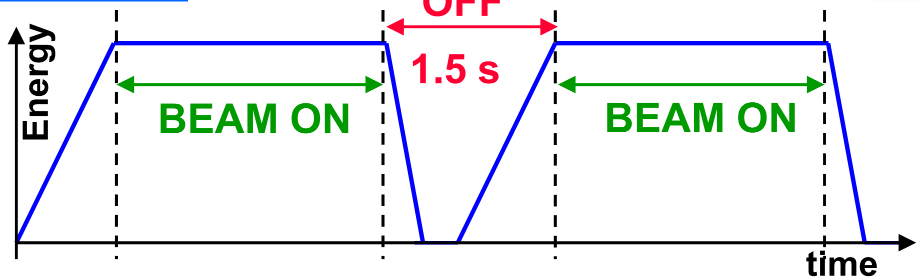


OR

SYNCHROTRONS







CYCLOTRONS

- Almost continuous beam
- Fixed energy

SYNCHROTRONS

- Beam ON and OFF
- Continuous energy

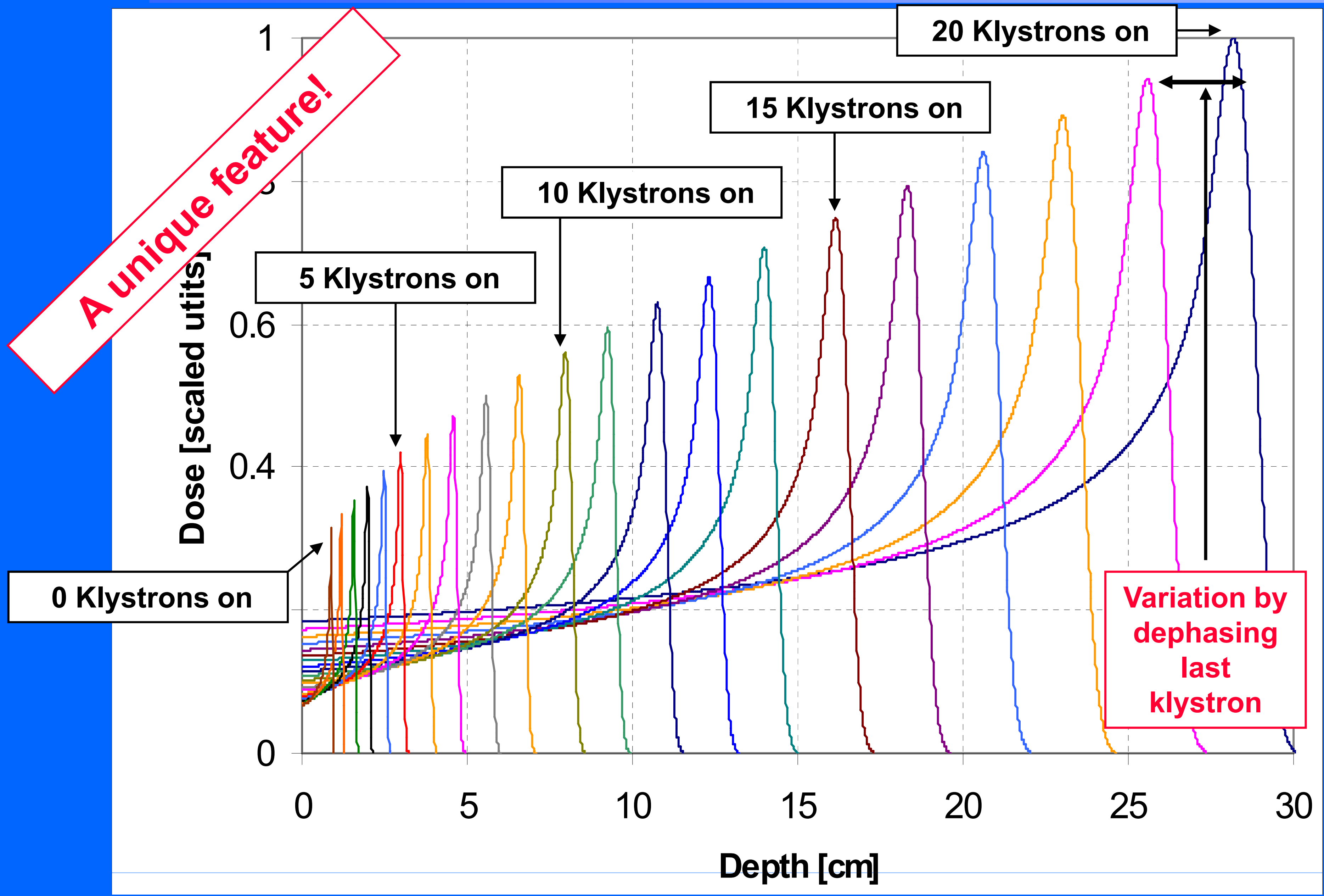
The CYCLINAC: the new project of TERA

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

Two main functions

DIAGNOSTICS + THERAPY

Bragg curves obtained by switching off klystrons



The challenge of medical sciences

Three fundamental questions to detect and cure the disease:

When ? → **As Soon As Possible**

Where ? → **As Precisely As Possible**

How ? → **As Effectively As Possible**

<u>One answer :</u>

Multidisciplinary approach

Some examples :

- **Non-invasive screening (molecular markers, imaging, …)**
- **High precision diagnostics (MRI, TC, PET, SPECT, …)**
- **High precision non-invasive therapy (hadrontherapy, …)**

Conclusions and Outlook

- **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 !