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

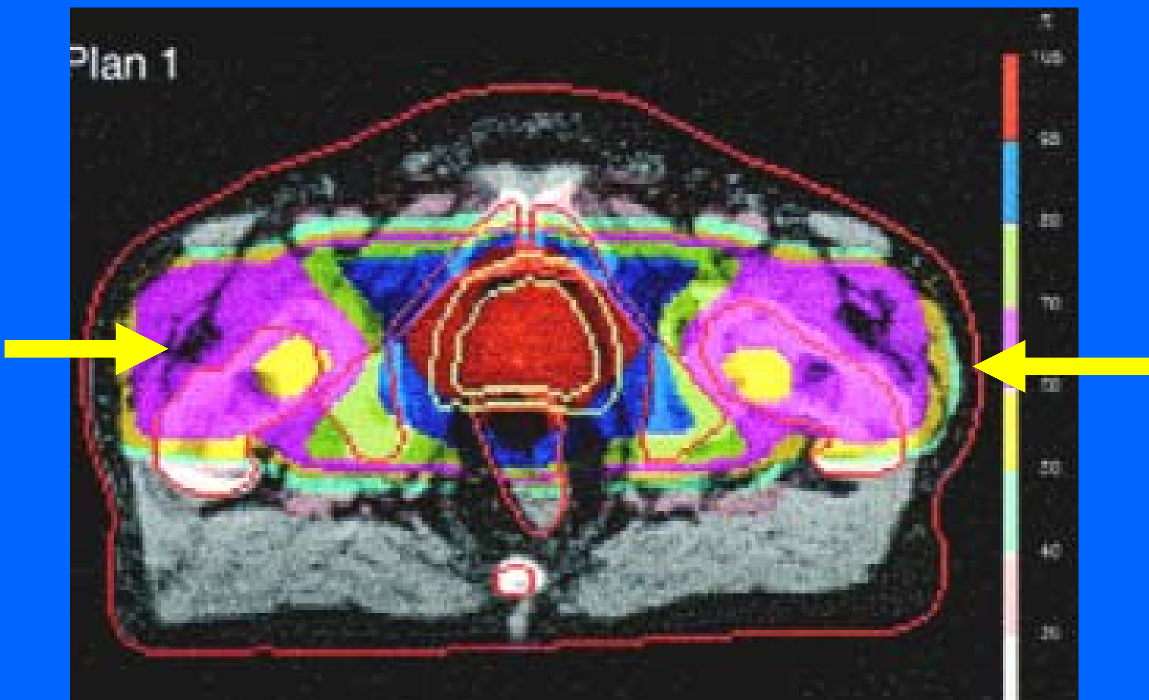
II

Hadronthetapy

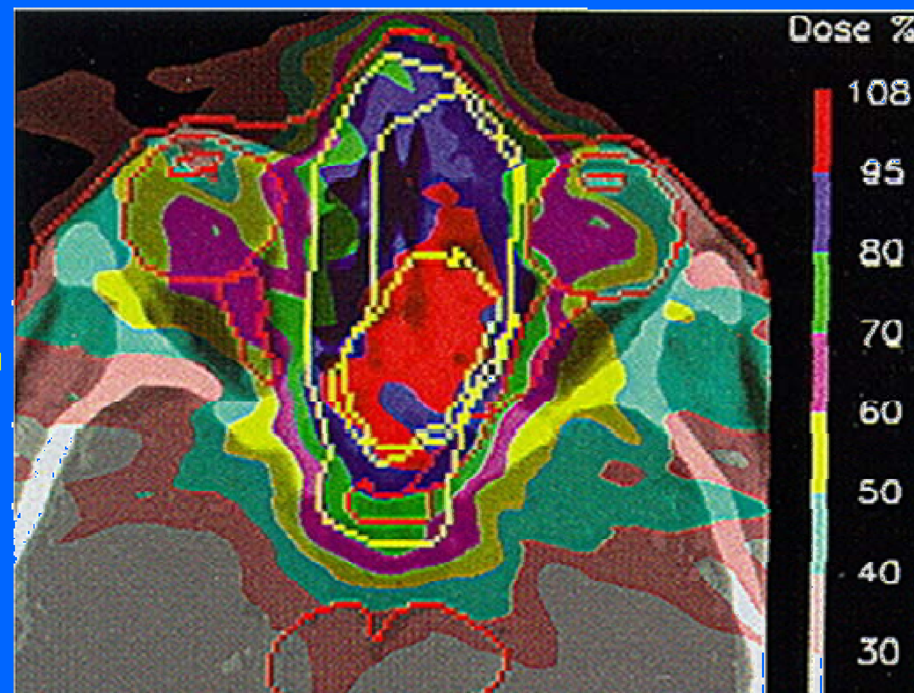
The frontier of cancer radiation therapy

Can we do better than conventional radiotherapy ?

2 X ray beams



9 X ray beams (IMRT)



A question for a particle physicist

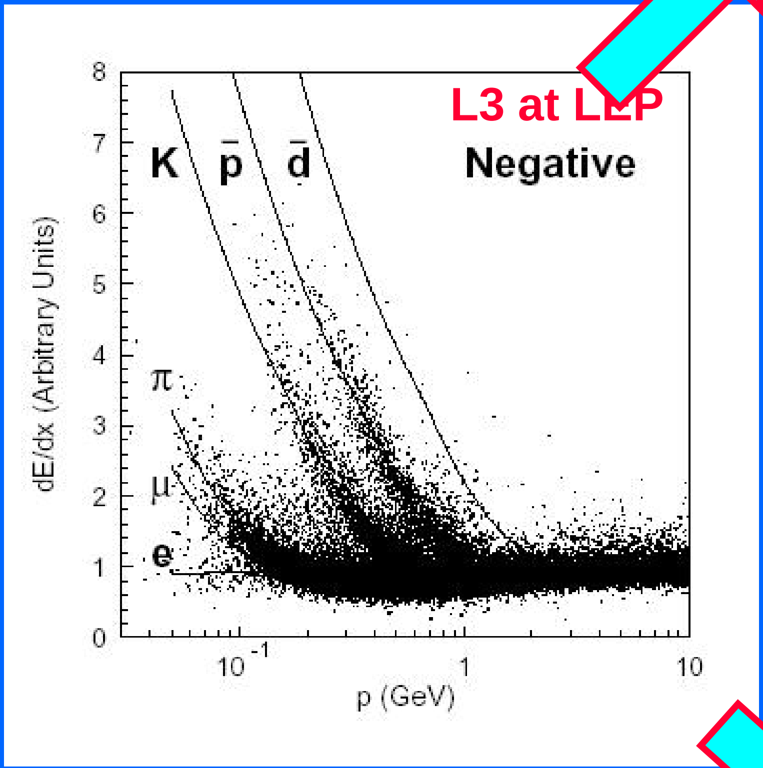
Are there better radiations to attack the tumour and spare at best the healthy tissues?

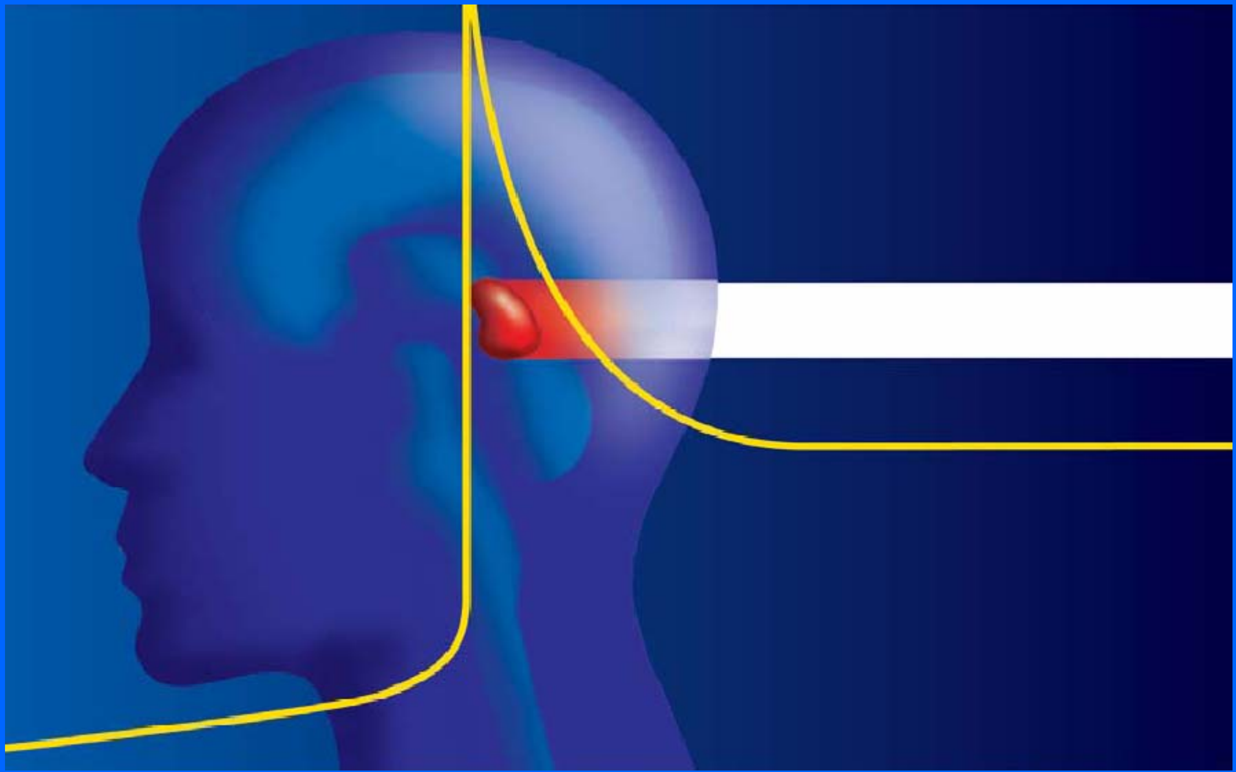
Answer : BEAMS OF CHARGED HADRONS

Let's go back to physics...

Fundamental physics

Particle identification

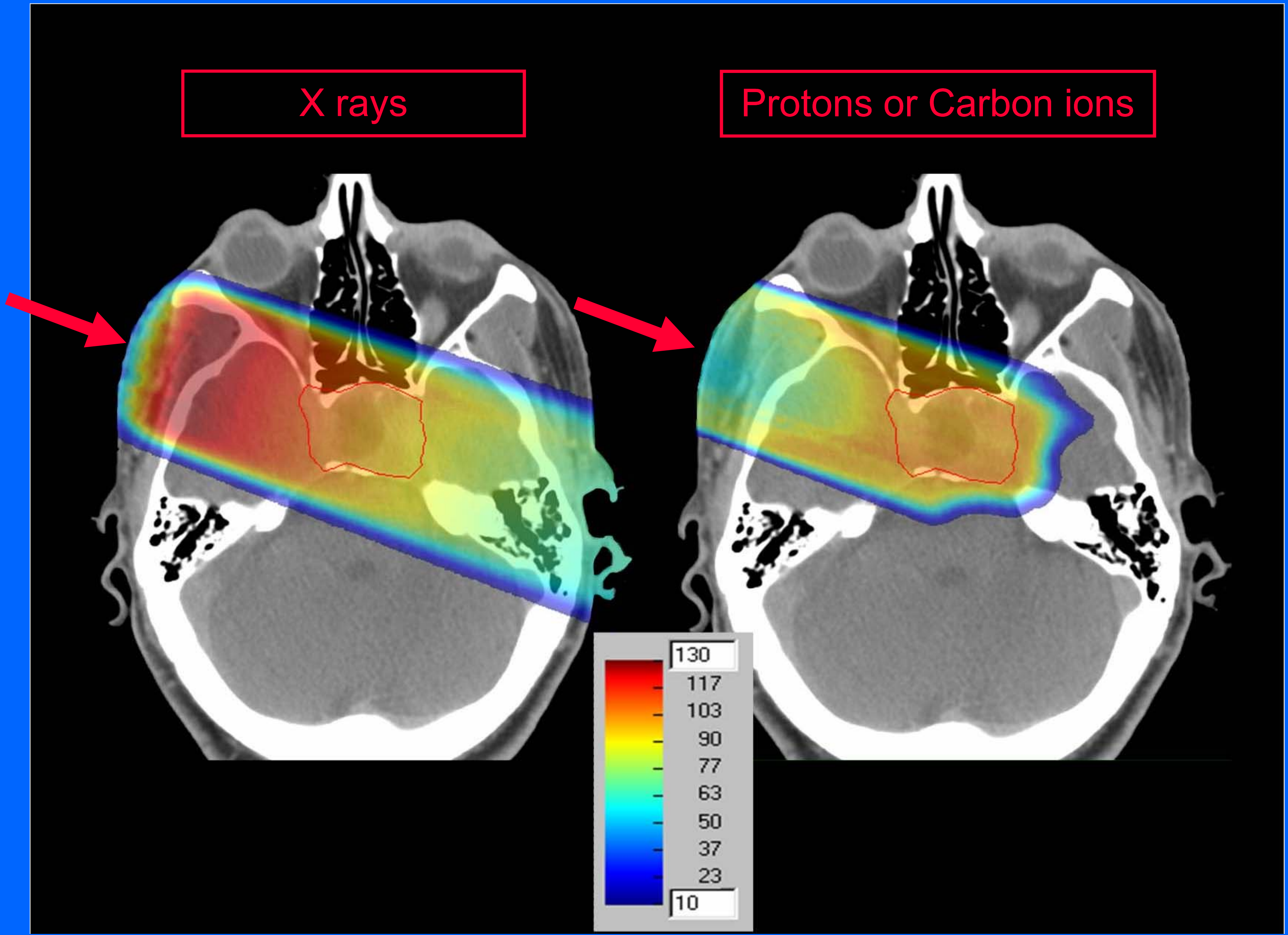




Medical applications

Cancer hadrontherapy

Single beam comparison



What are the hadrons?

- Hadrons are not elementary particles
- They are made of quarks and antiquarks…

Quark

Antiquark

What can we do with hadrons?

Proton : u u d

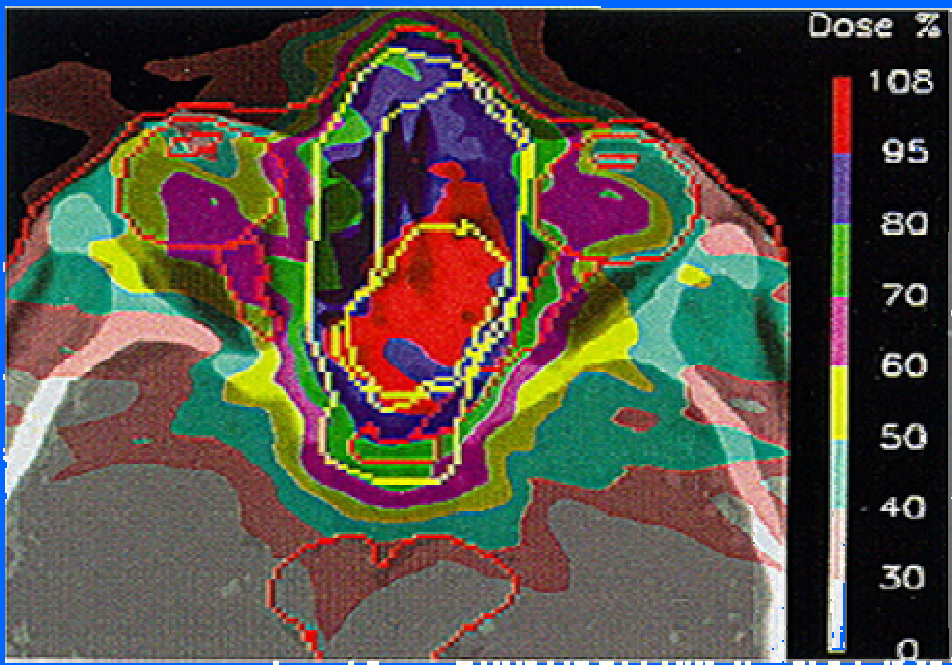
- **All nuclei**
- **Proton and ion beams for cancer hadrontherapy**

Neutron : u d d

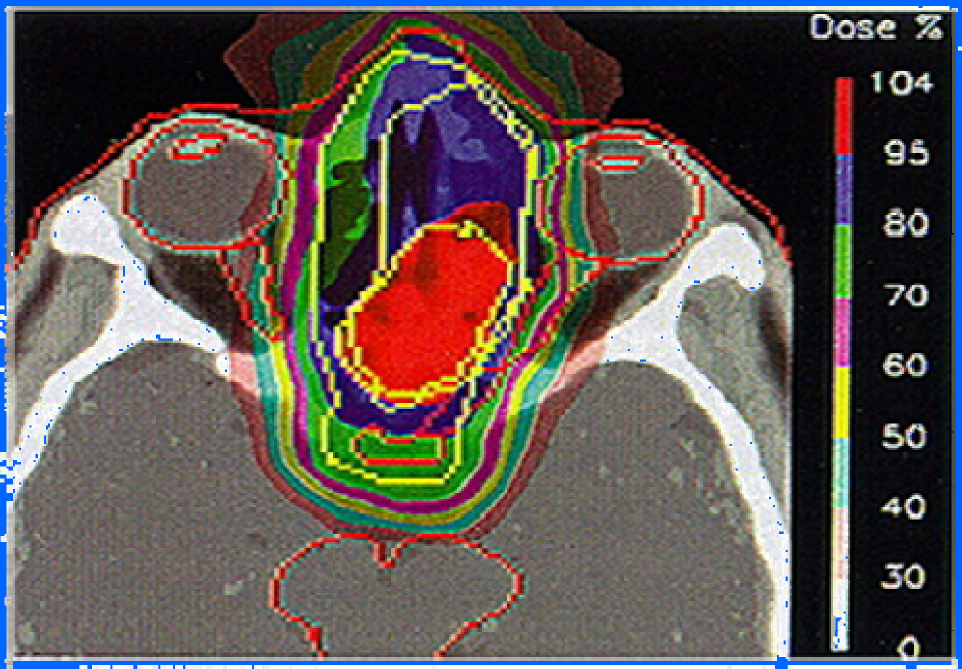
Protons and ions are more precise than X-rays

Tumour between the eyes

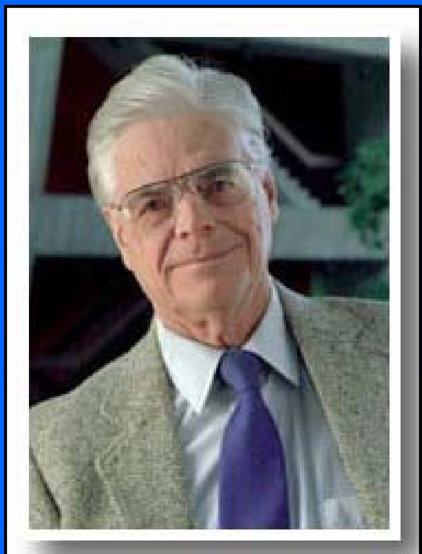
9 X ray beams

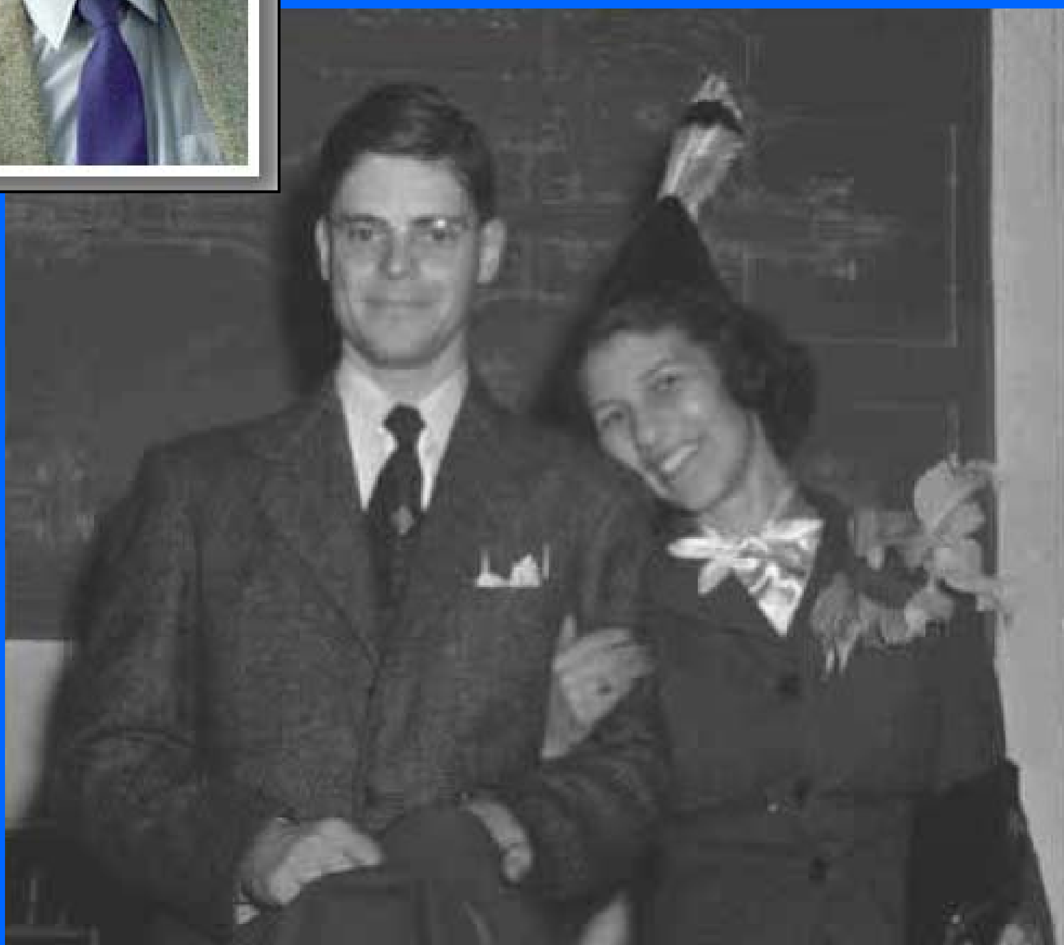


1 proton beam



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 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

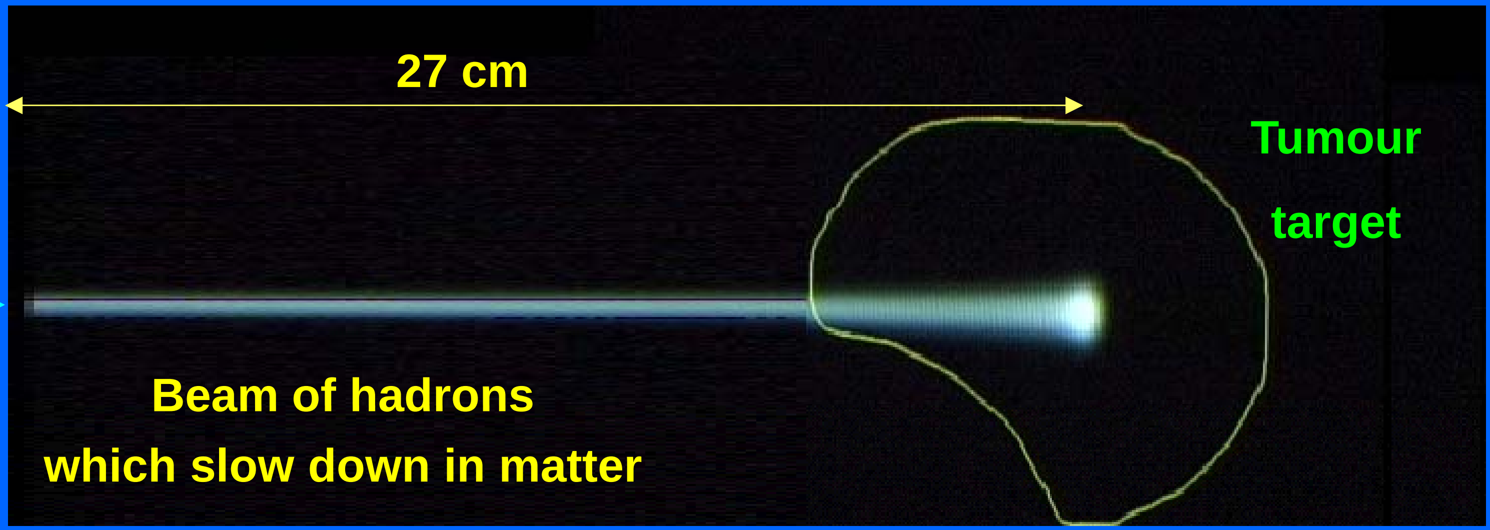
Cornelius A. Tobias

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

The basic principles of hadrontherapy

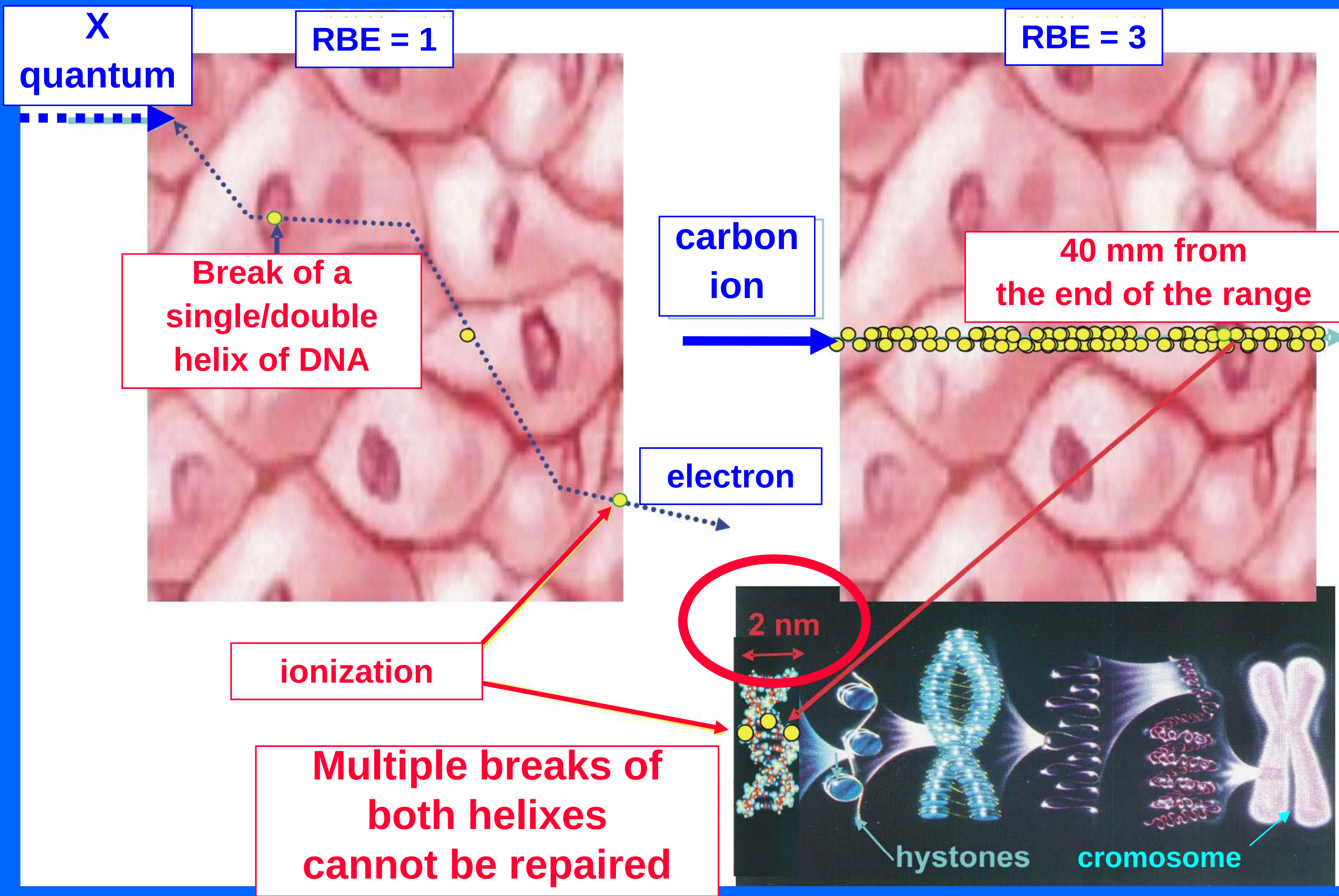
Protons
200 MeV
1 nA

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

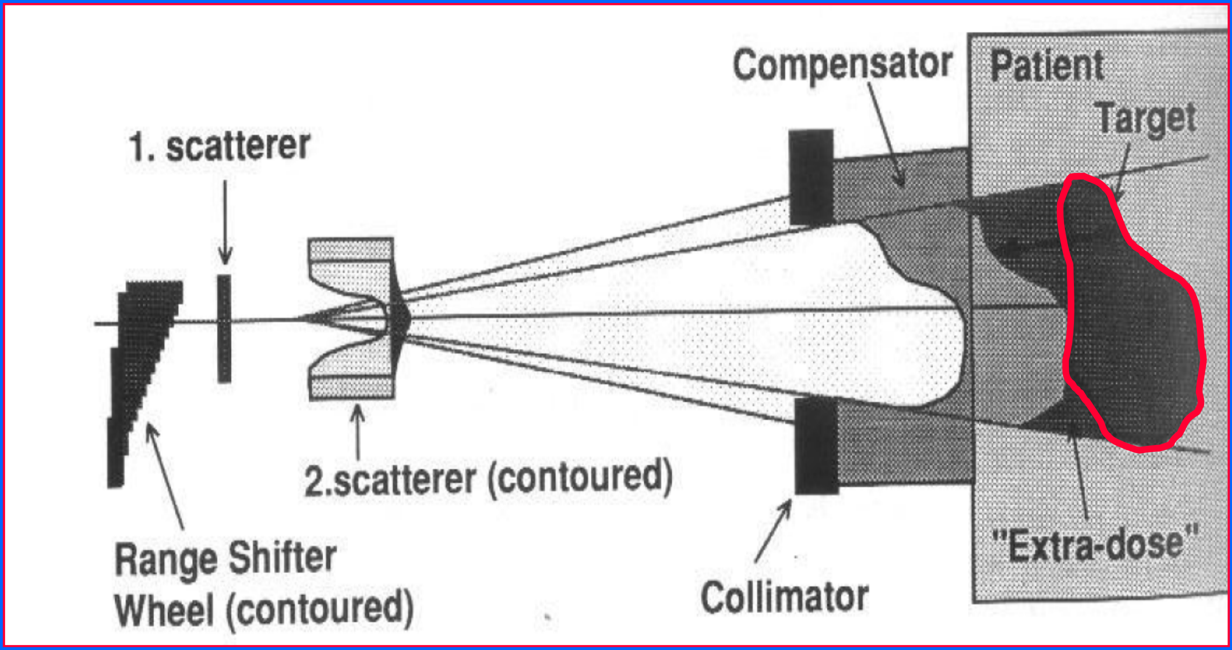
Why ions have a large biological effectiveness?



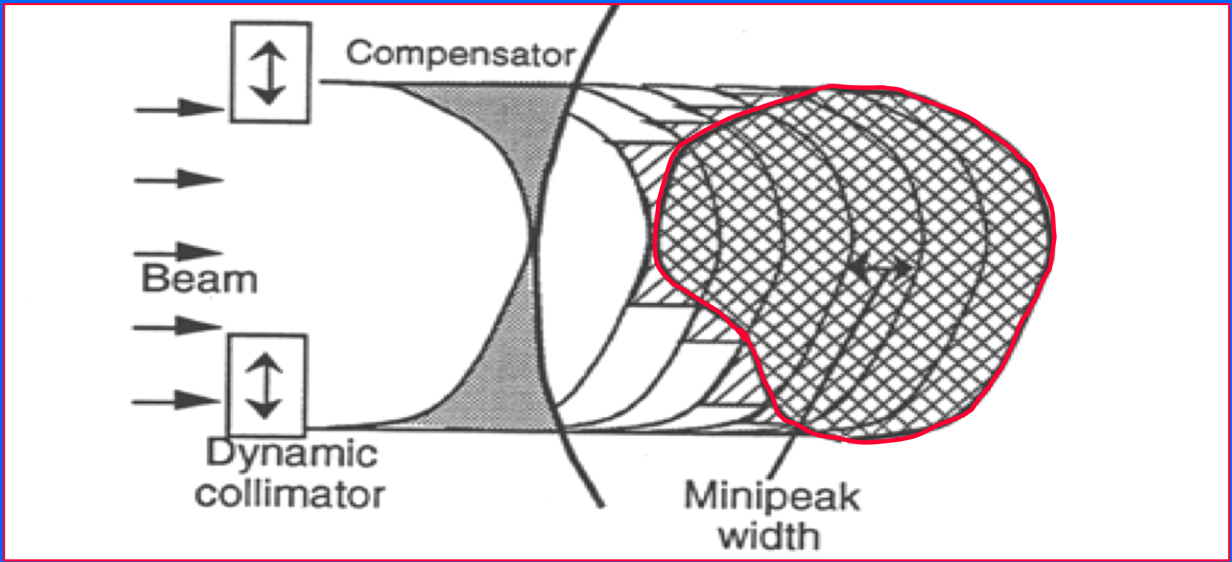
Ions have high LET (Linear Energy Transfer)

A gantry for proton therapy

Dose distribution: passive spreading

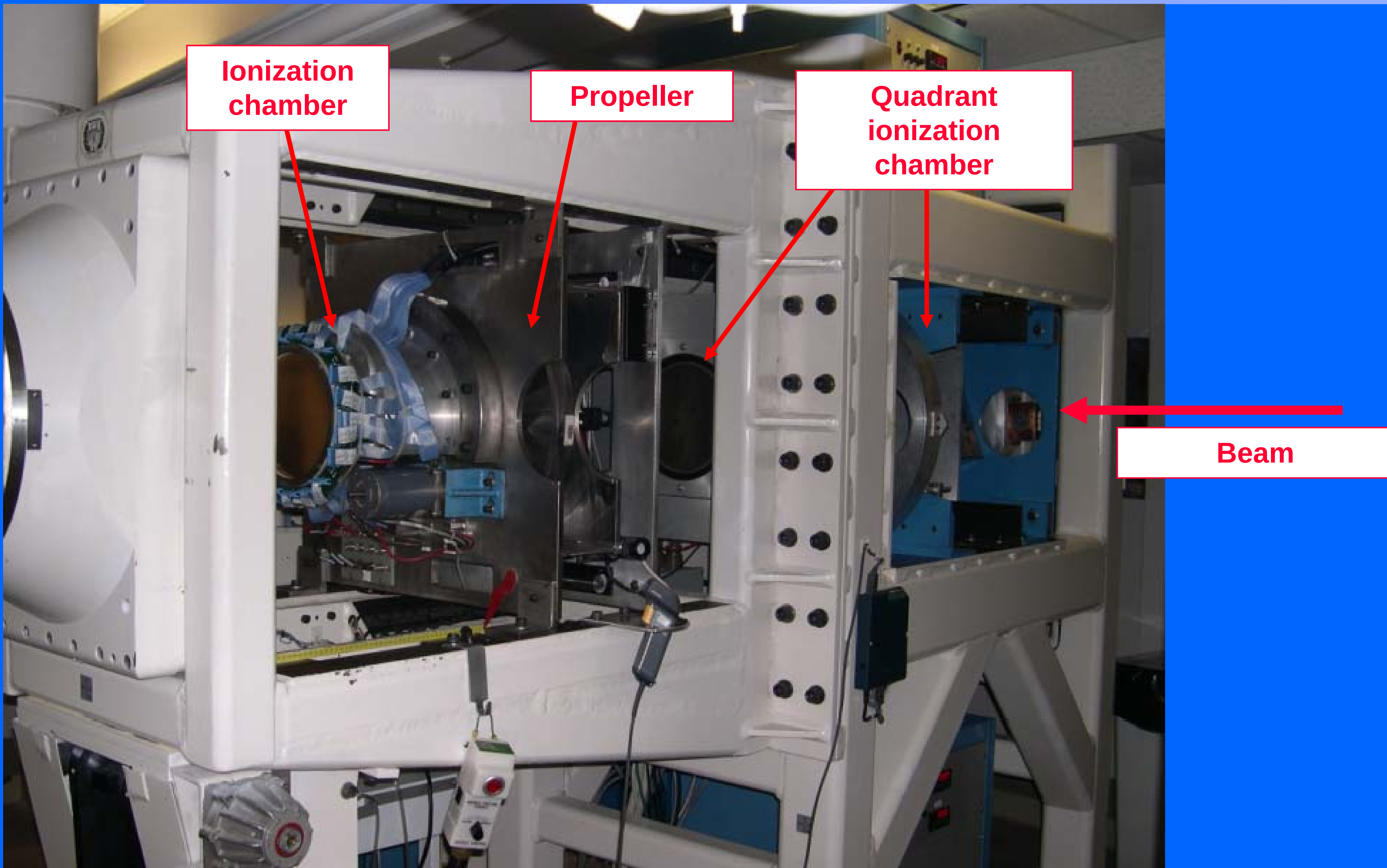


'Double scattering'

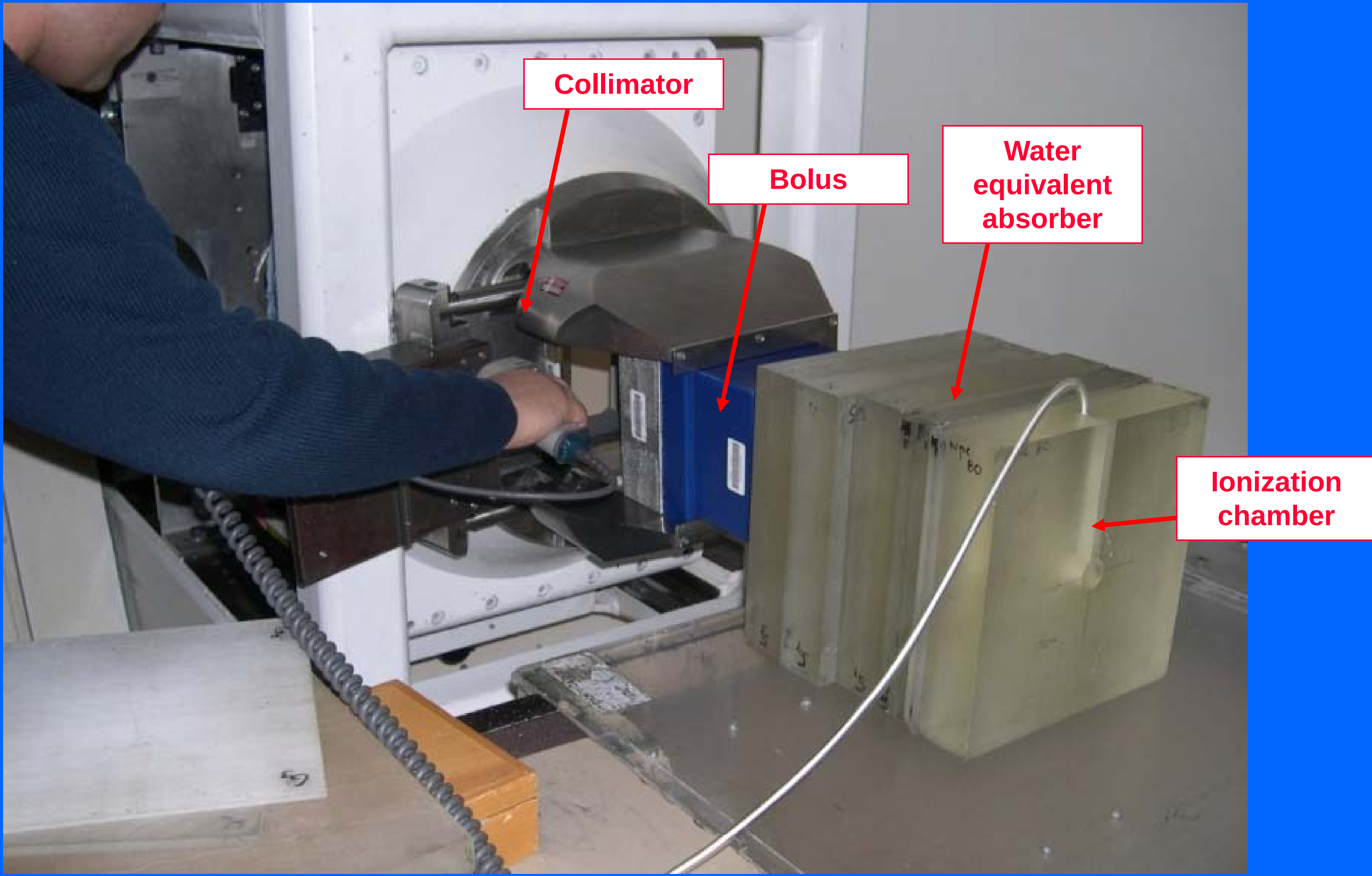


'Layer stacking'

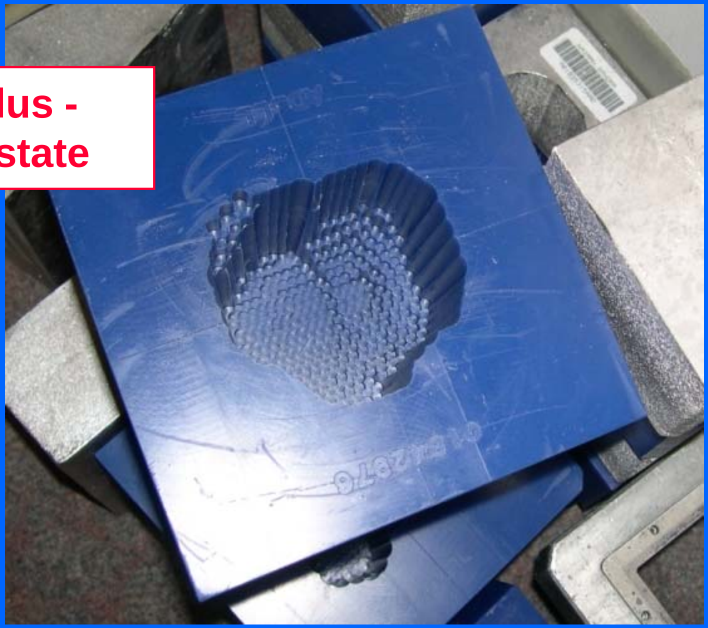
Passive spreading: the nozzle



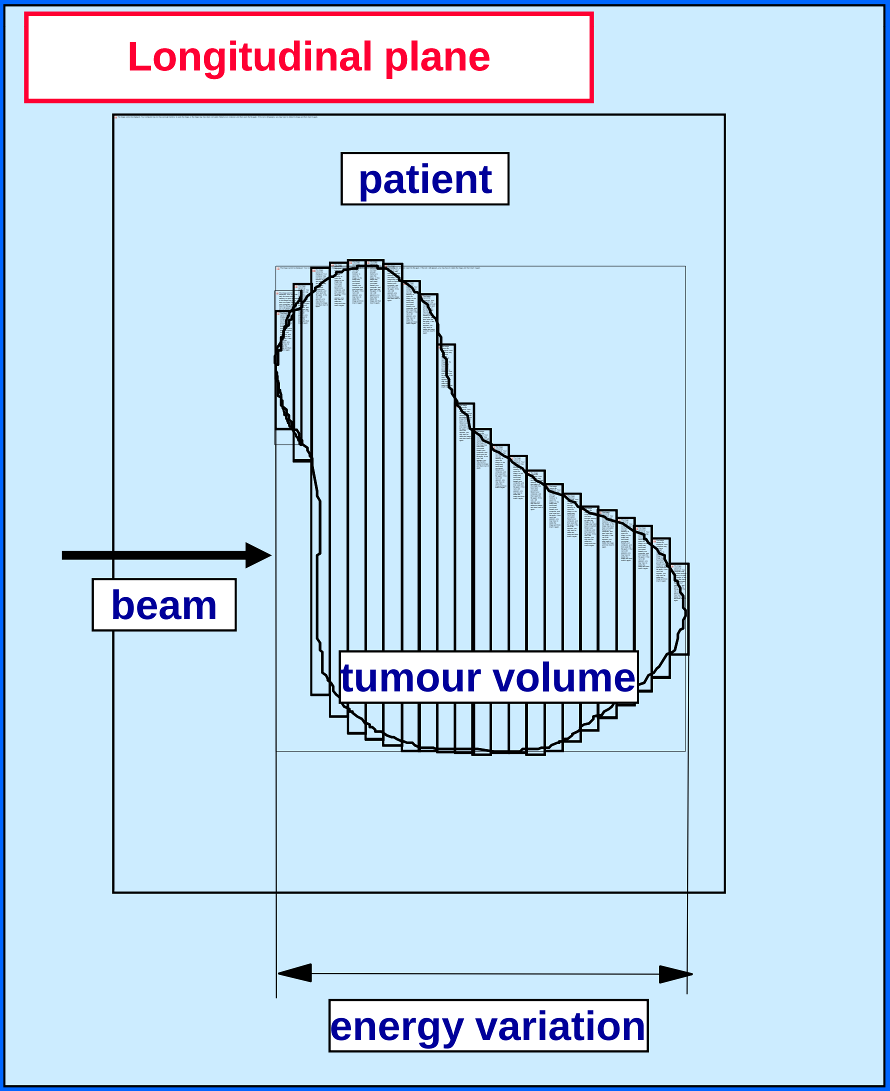
Passive spreading: calibration before treatment

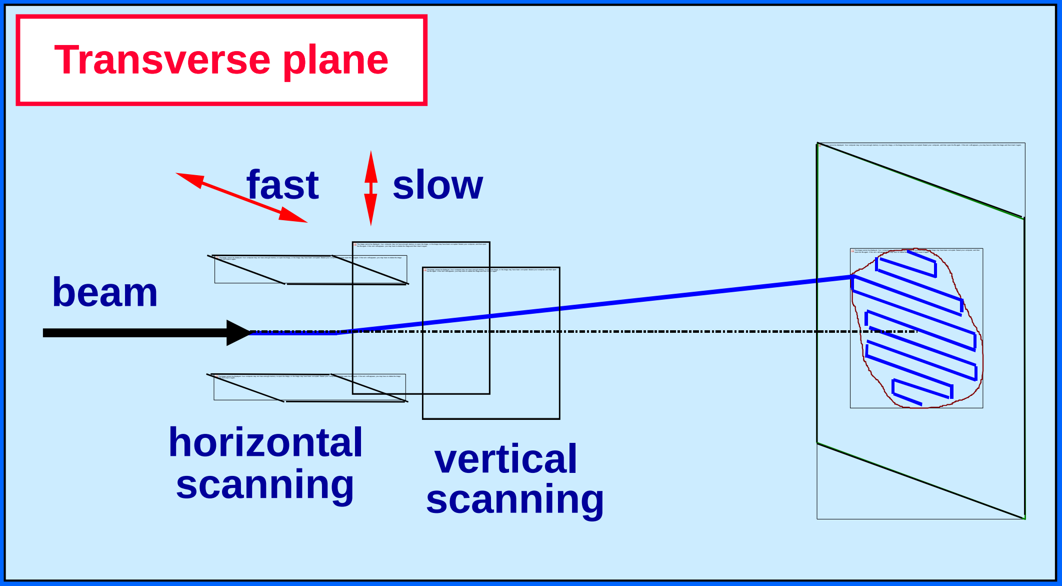


Passive spreading: personalized devices



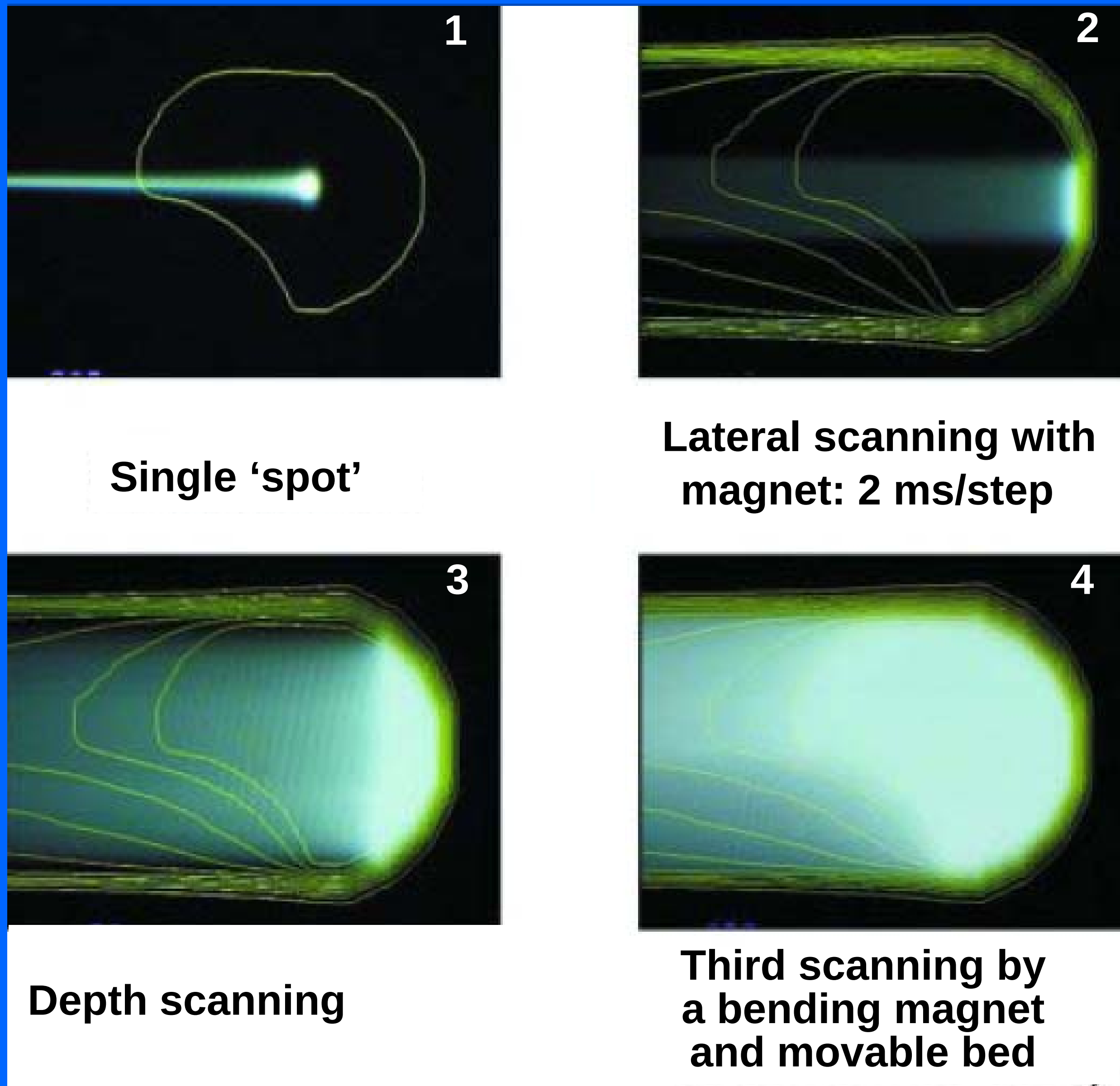
Dose distribution: active scanning





New technique developed mainly at GSI and PSI

Active “spot scanning” a la PSI



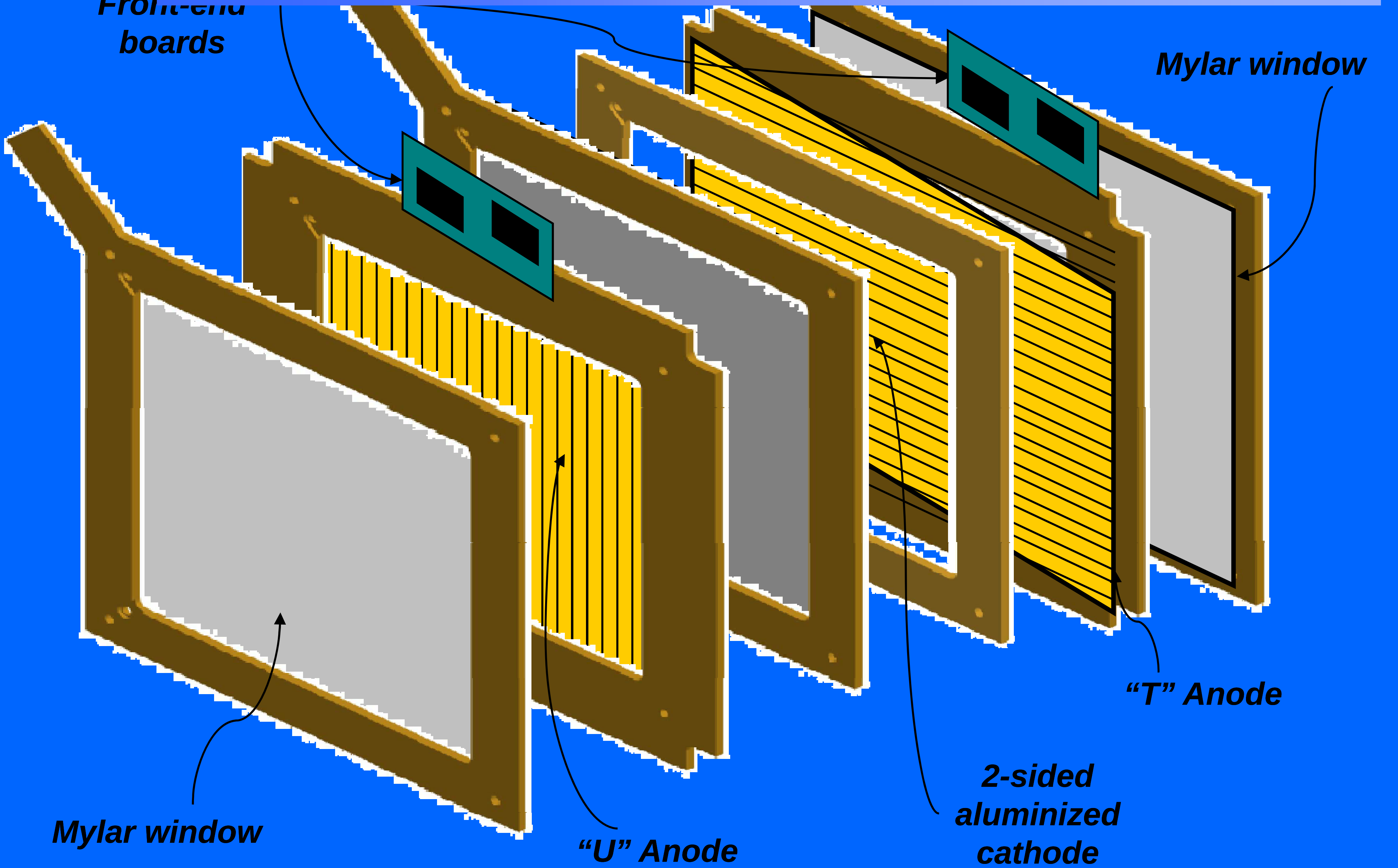
Single ‘spot’

Lateral scanning with magnet: 2 ms/step

Depth scanning

Third scanning by a bending magnet and movable bed

A detector for spot scanning:
The strip chamber developed by TERA for PSI

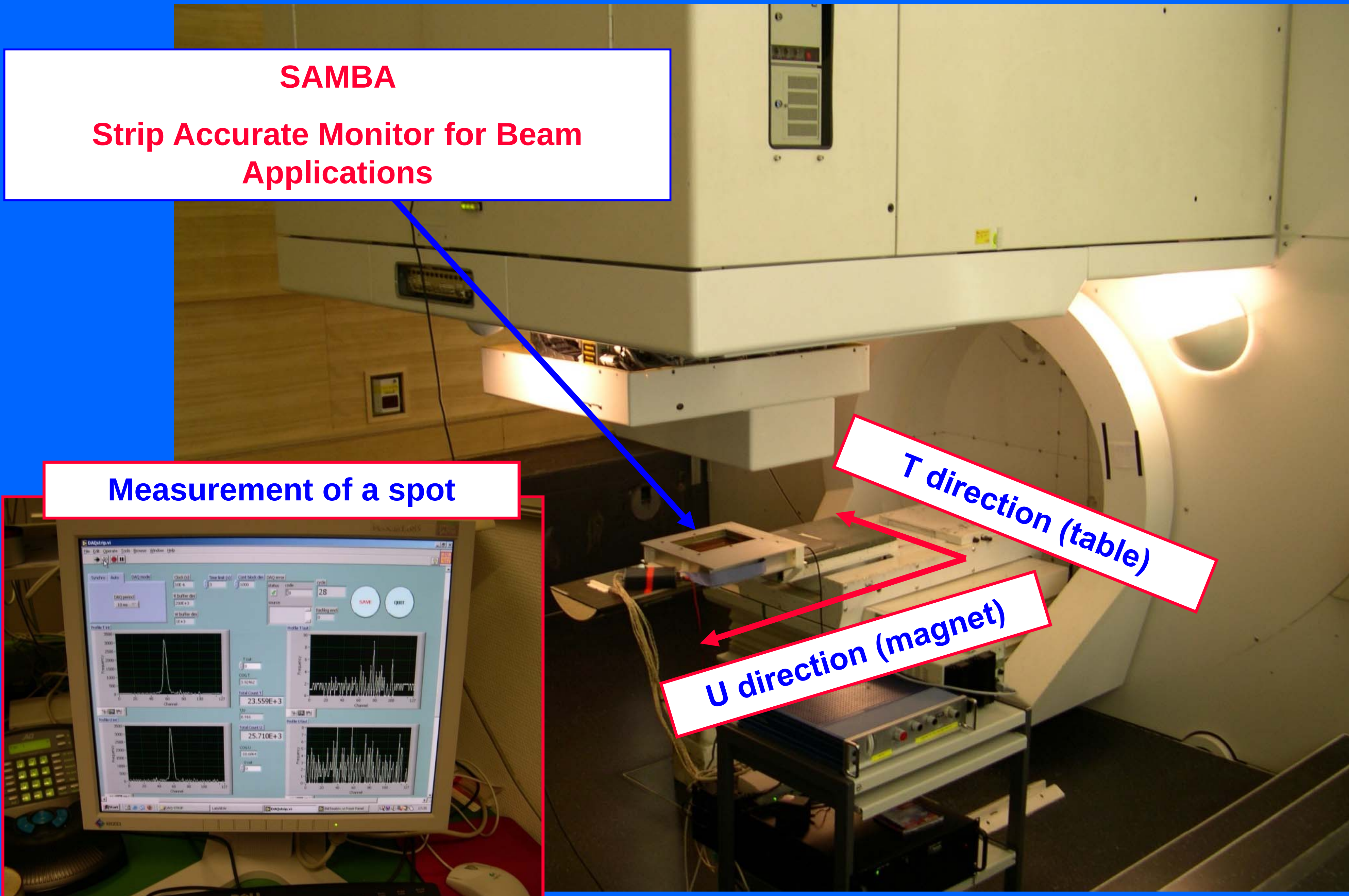


In collaboration with University and INFN Torino

Beam tests on Gantry1 at PSI

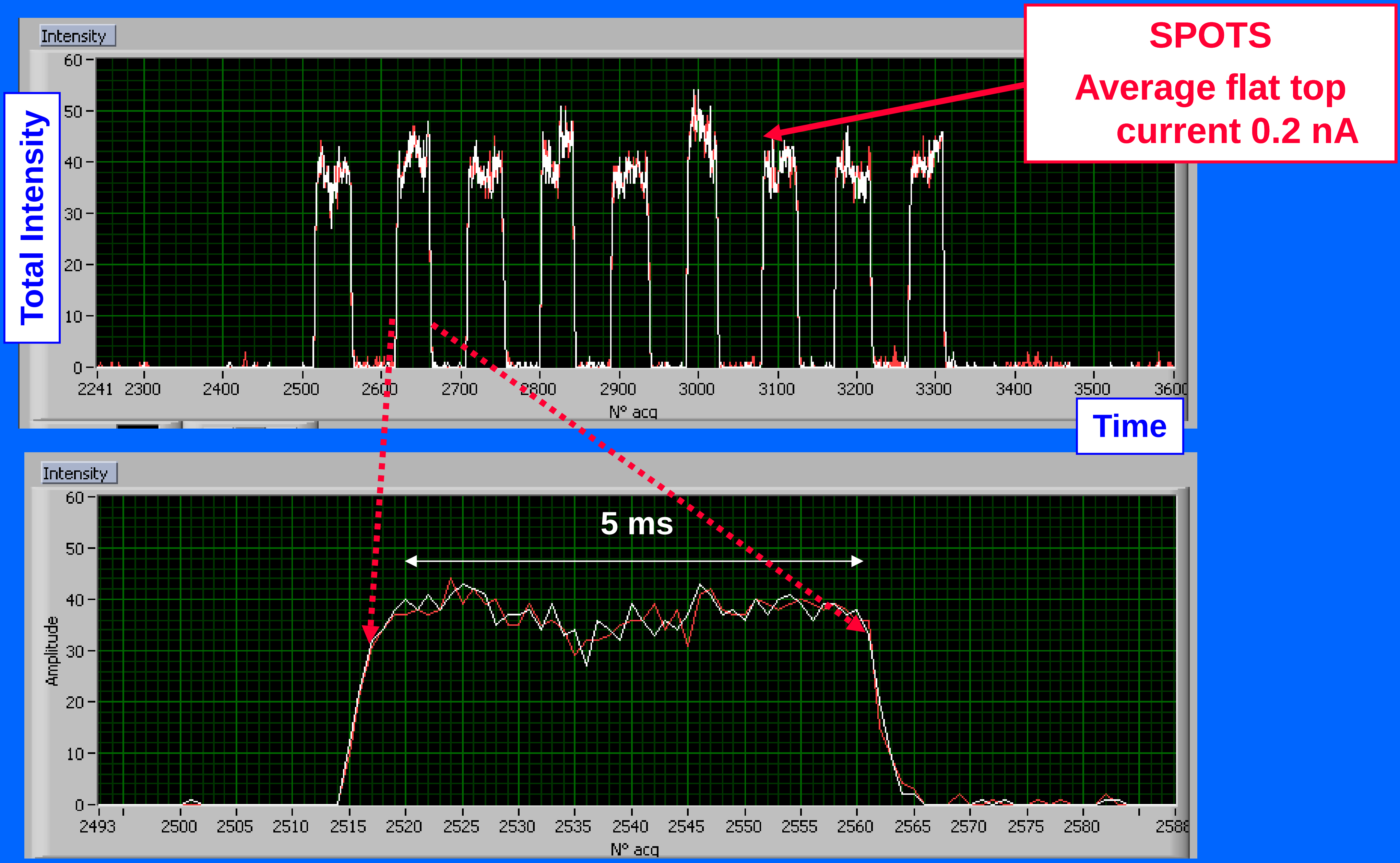
SAMBA

Strip Accurate Monitor for Beam Applications

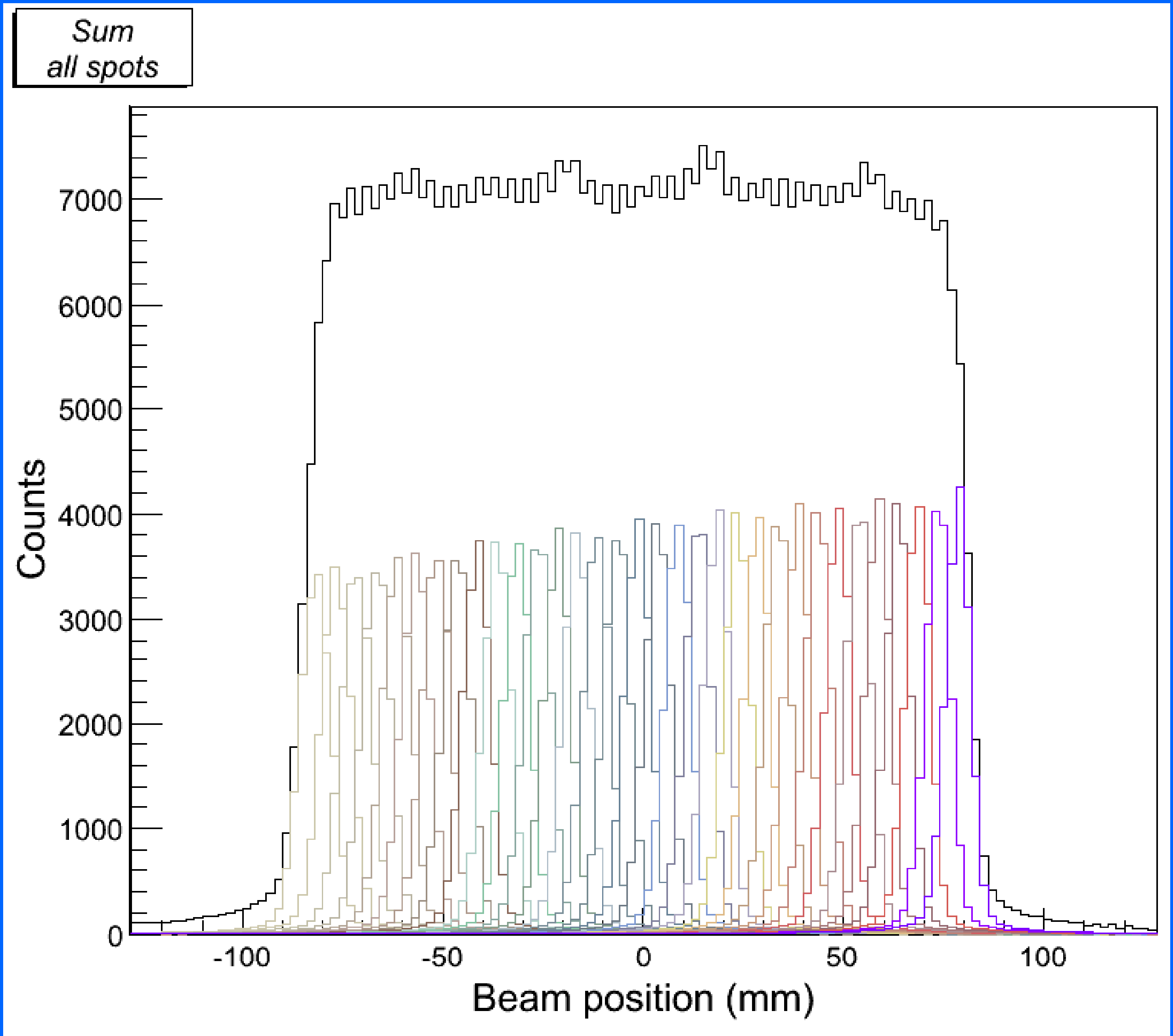


Measurement of a spot

Time profile of the clinical beams



A line of dose made of spots



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

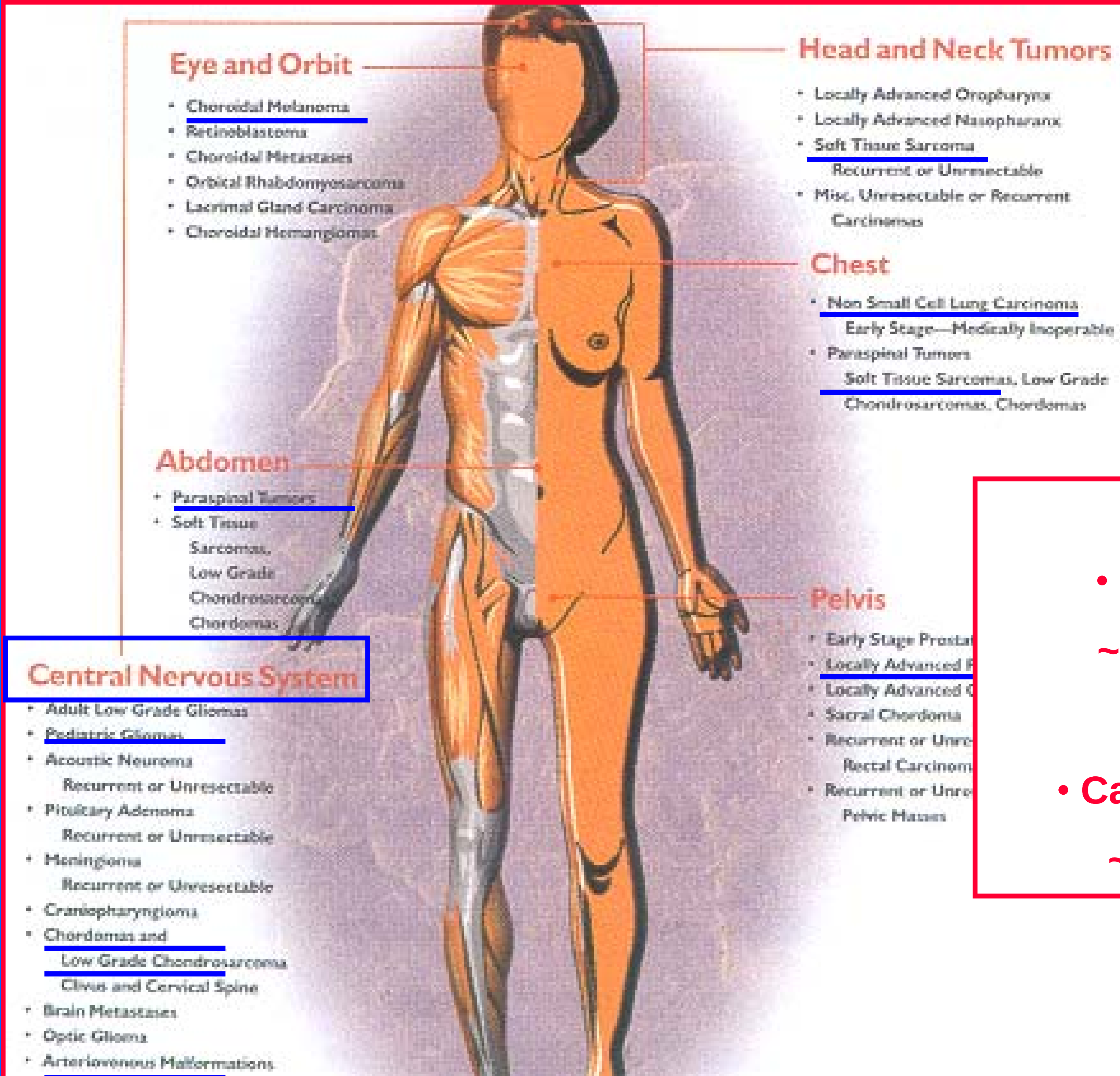
- **Carbon ion therapy**

1 centre

TOTAL about 3‘500 pts/year

every 10 M

The sites



Up to present

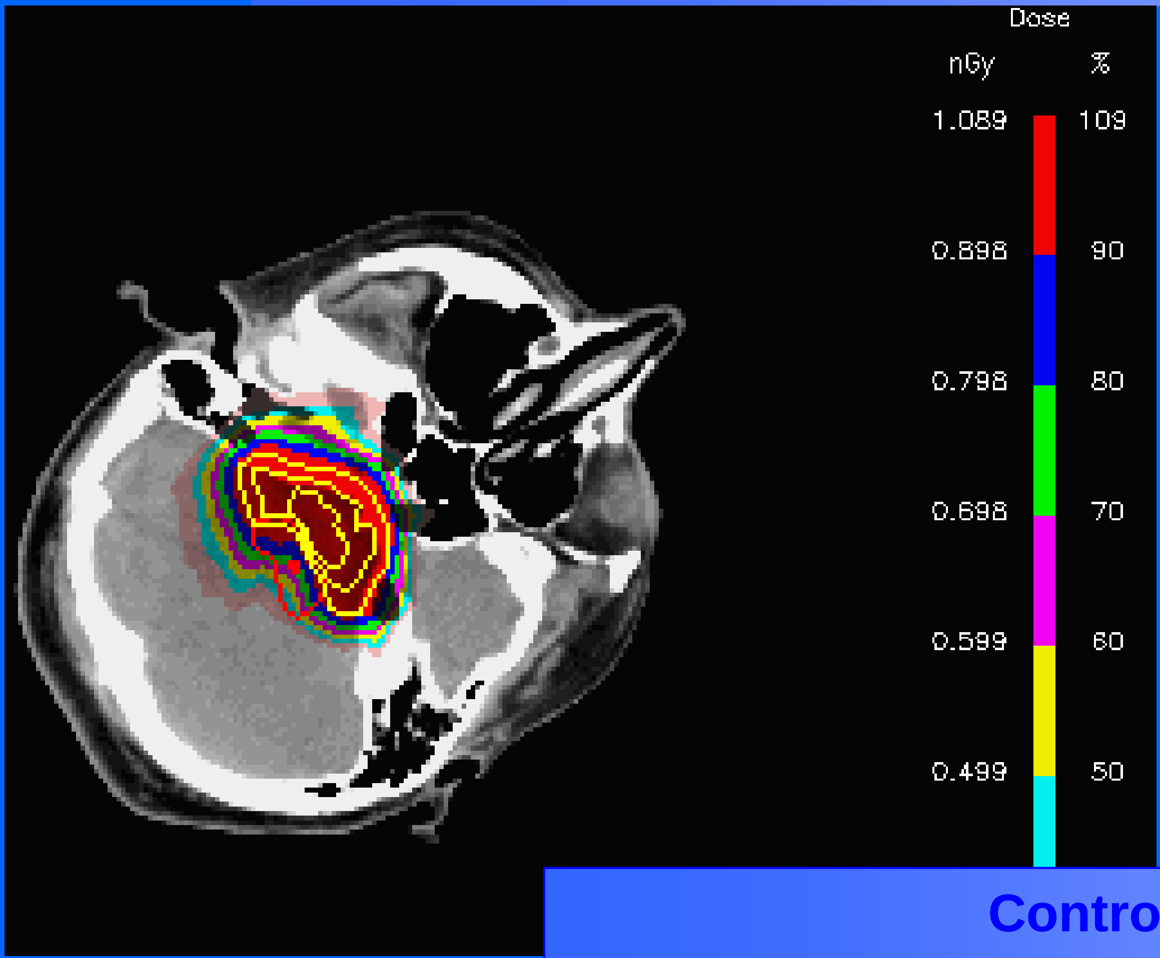
- **Proton-therapy:**

  ~ 50 000 patients

- **Carbon ion therapy:**

  ~ 2 500 patients

Tumours of the central nervous system



Control at 5 years

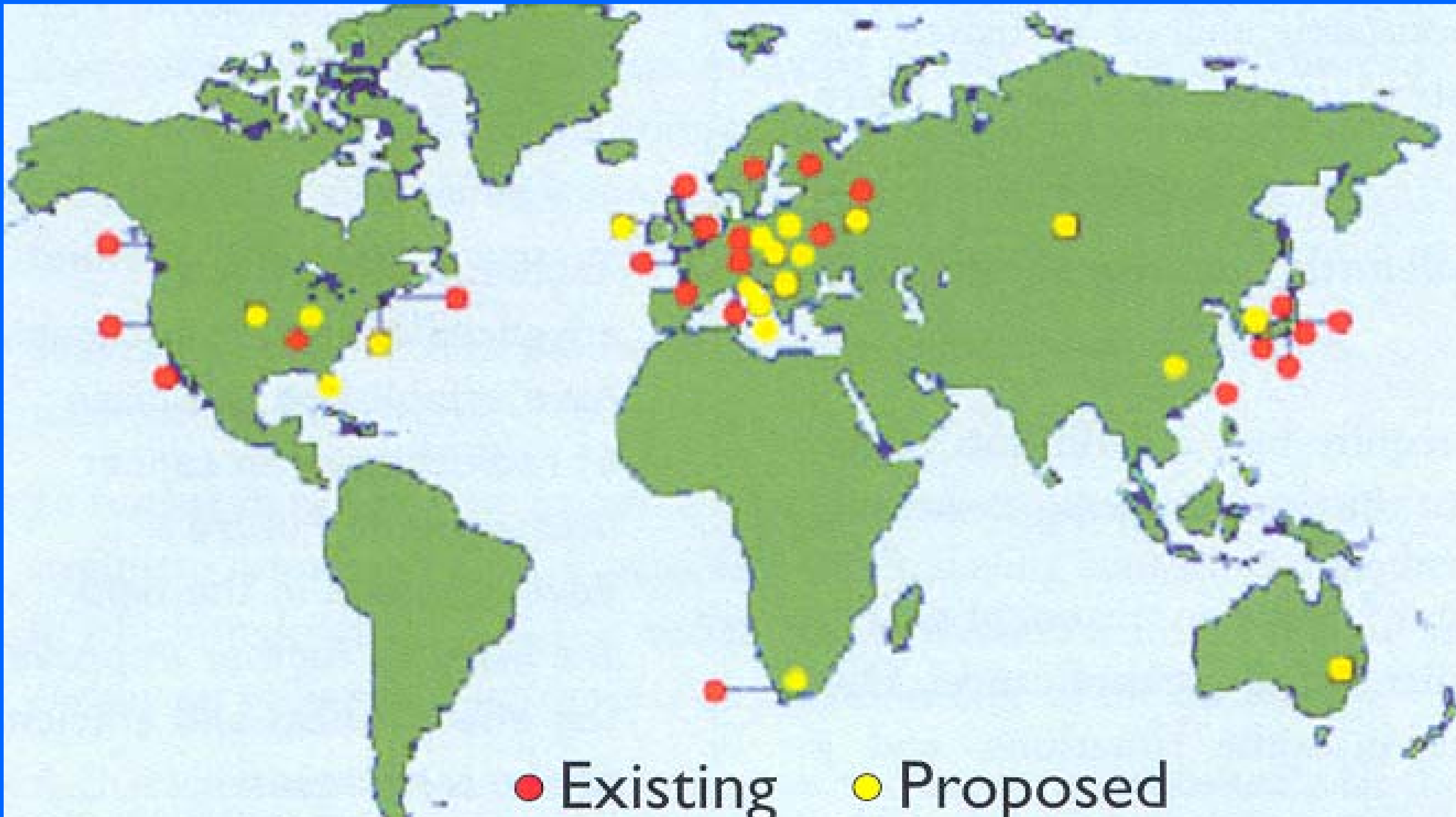
	RT	Protons
Chordomas	**17-50%**	**73-83%**
Chondrosarcomas	**50-60%**	**90-98%**

Present and “near” future of hadrontherapy

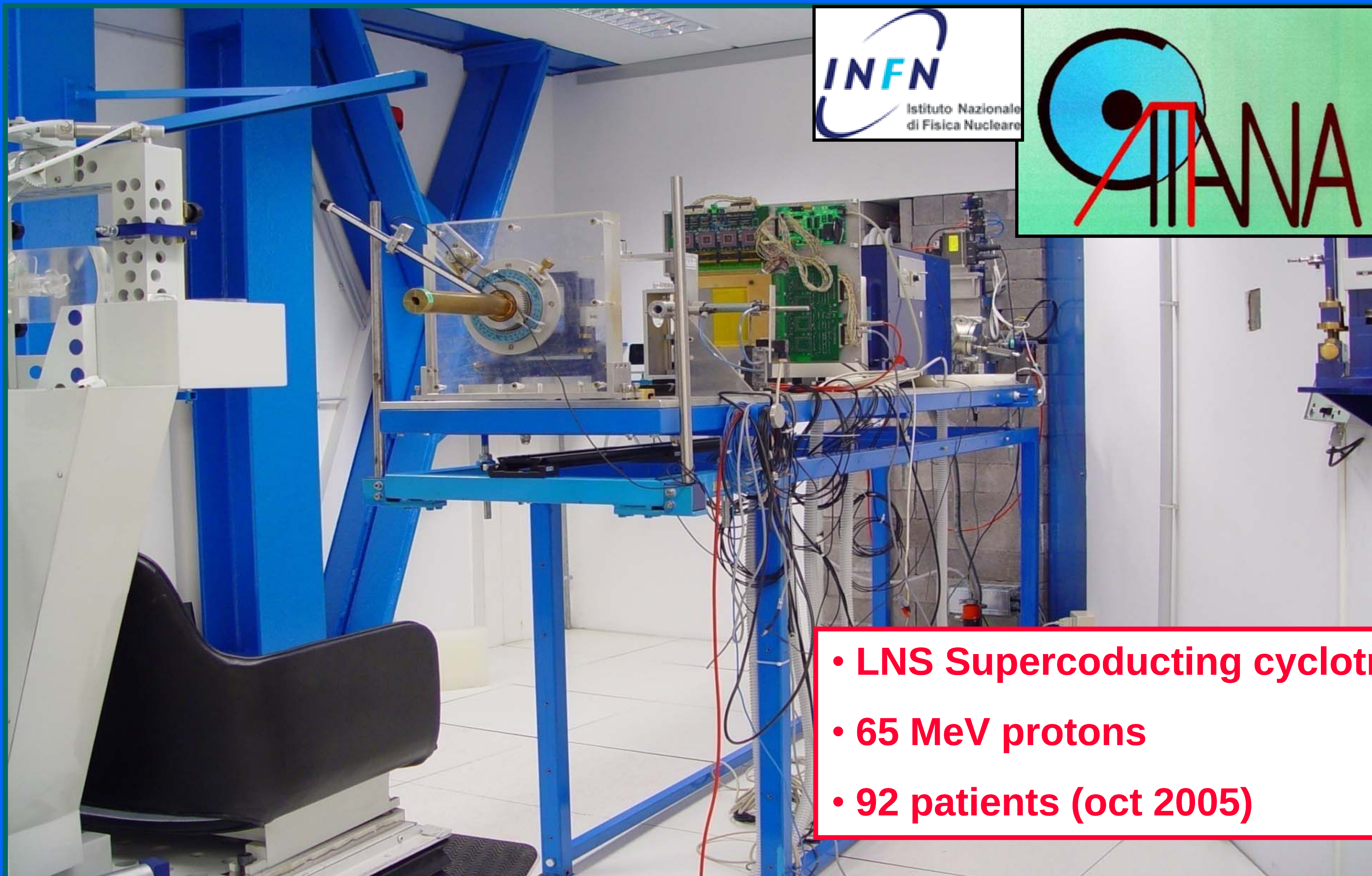
- **Proton-therapy is “booming”!** *(for more information see PTCOG, www.ptcog.com)*
  - **Laboratory based centres: Orsay, PSI, INFN-Catania, …**
  - **Hospital based centres: 3 in USA, 4 in Japan and many under construction (USA, Japan, Germany, China, Korea, Italy, …)**
  - **Companies offer “turn-key”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

A (not up to date) map of hadrontherapy

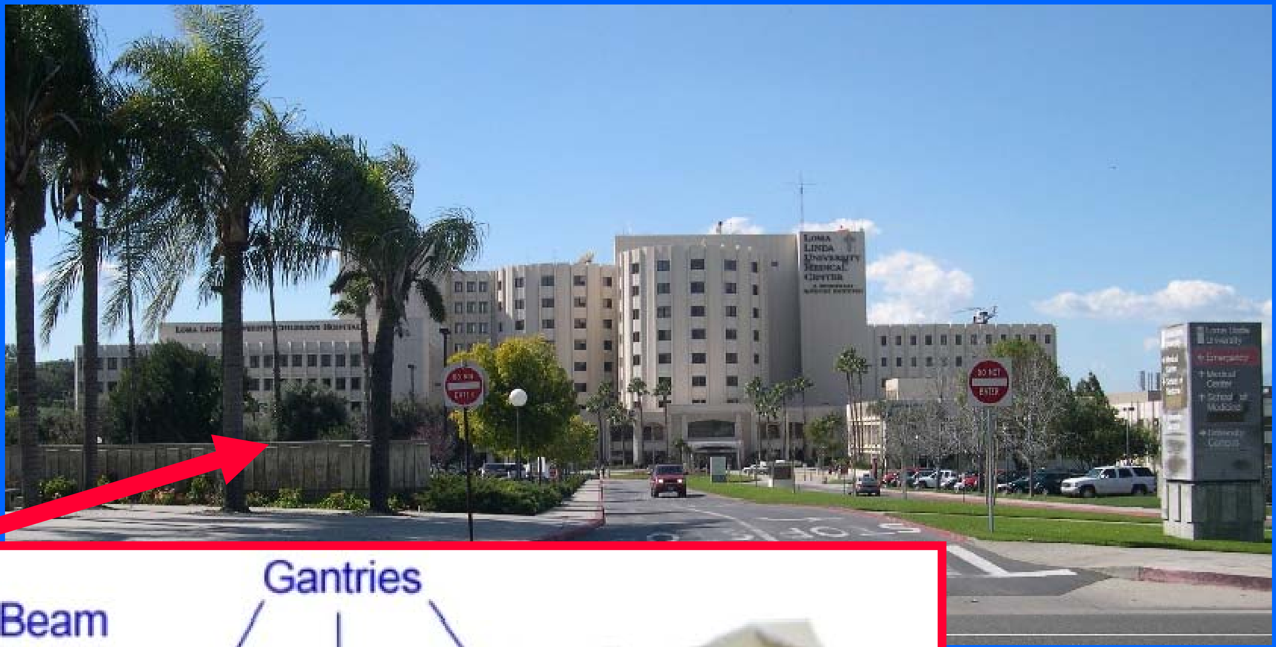


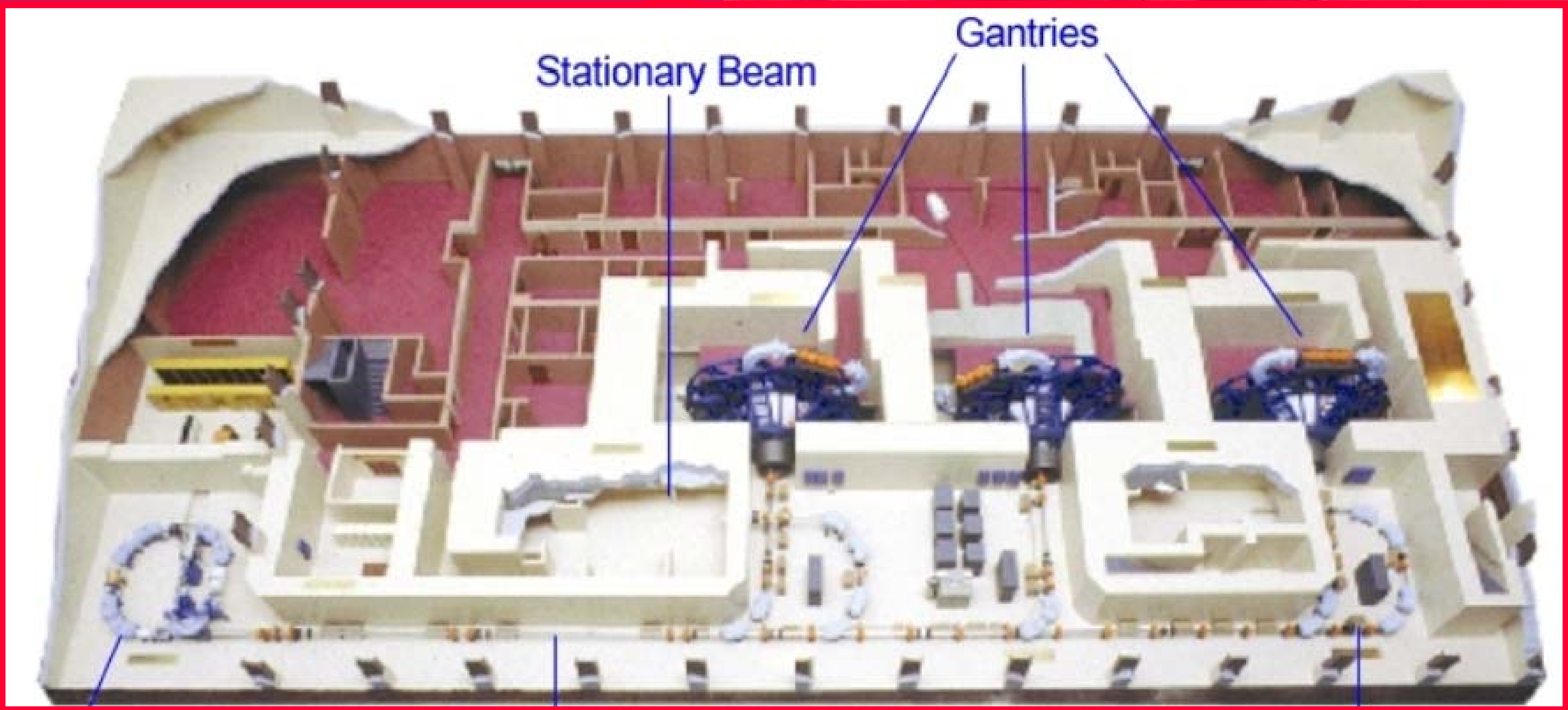
The eye melanoma treatment at INFN-LNS in Catania



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

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



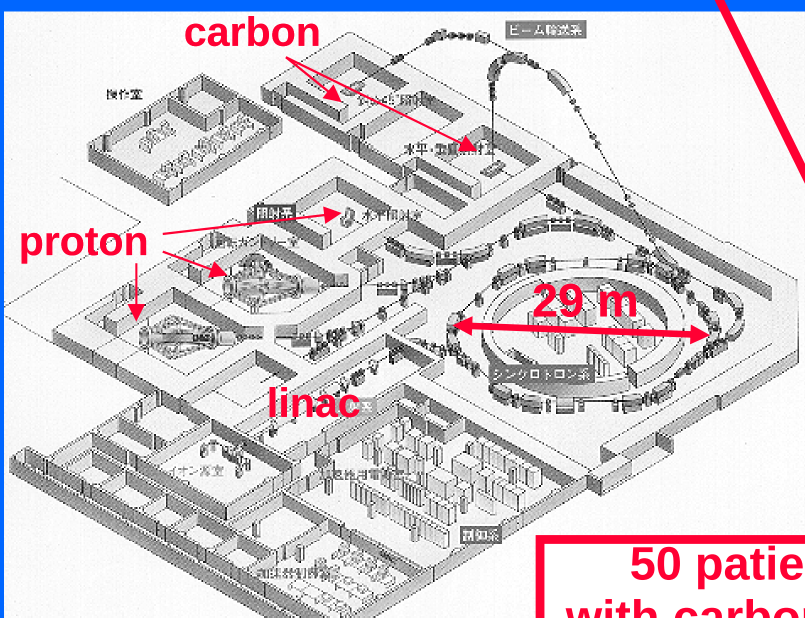


What a patient sees…

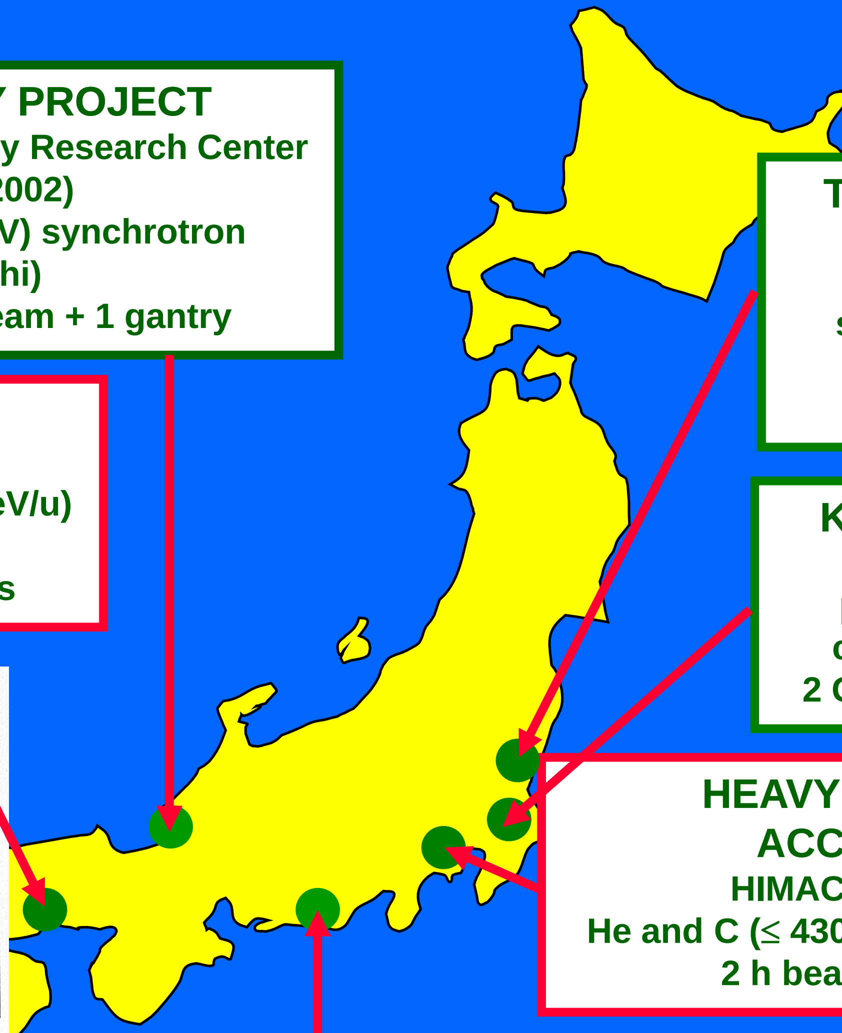
Japan: 4 proton and 2 carbon ion therapy centres

WAKASA BAY PROJECT
by Wakasa-Bay Energy Research Center
Fukui (2002)
protons (≤ 200 MeV) synchrotron
(Hitachi)
1 h beam + 1 v beam + 1 gantry

HYOGO MED CENTRE
Hyogo (2001)
protons (≤ 230 MeV) - He and C ions (≤ 320 MeV/u)
Mitsubishi synchrotron
2 p gantries + 2 fixed p beam + 2 ion rooms



50 patients with carbon ions



TSUKUBA CENTRE
Ibaraki (2001)
protons (≤ 270 MeV)
synchrotron (Hitachi)
2 gantries
2 beam for research

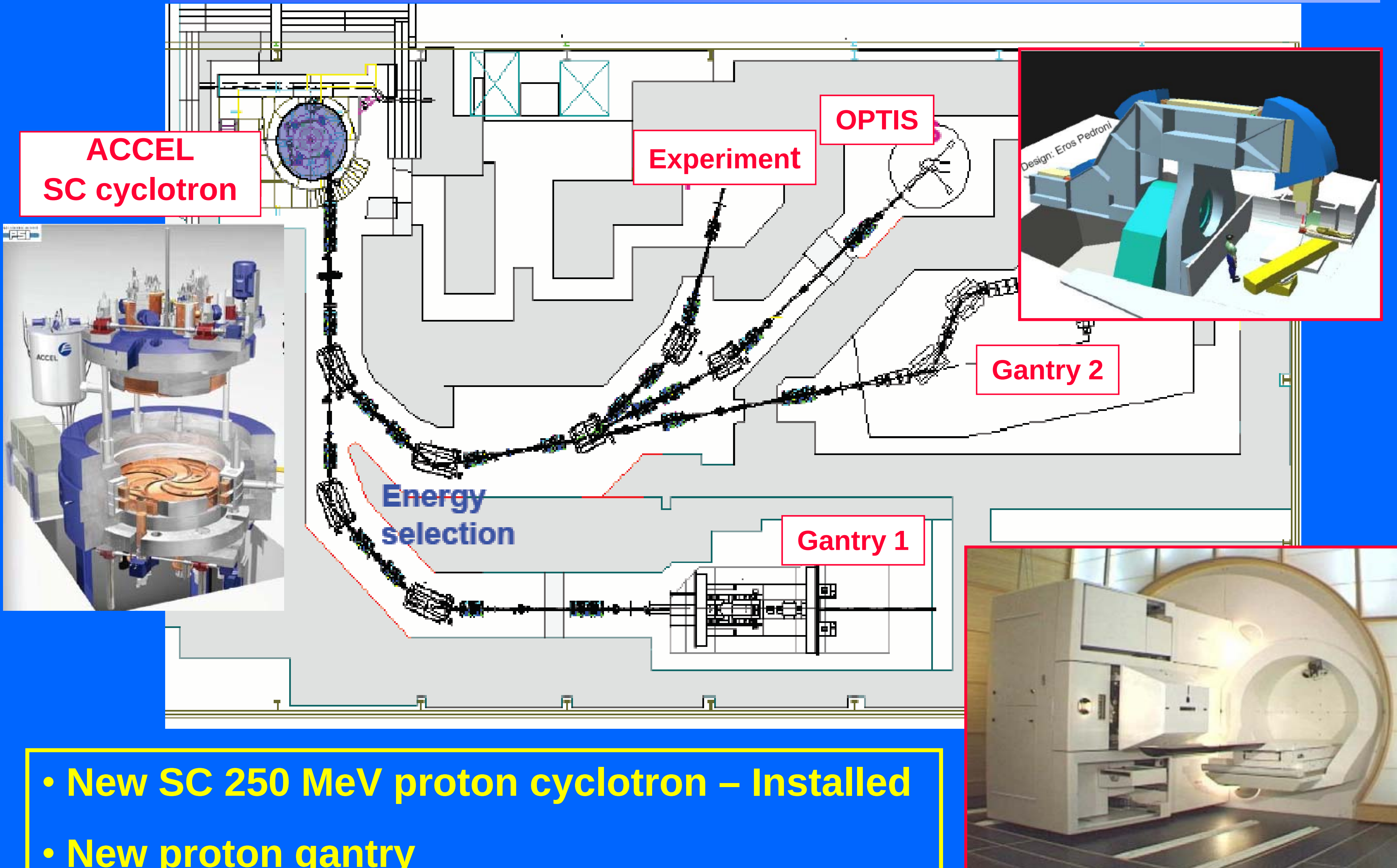
KASHIWA CENTER
Chiba (1998)
protons (≤ 235 MeV)
cyclotron (IBA – SHI)
2 Gantries + 1 hor. beam

HEAVY ION MEDICAL ACCELERATOR
HIMAC of NIRS (1995)
He and C (≤ 430 MeV/u) 2 synchrotrons
2 h beams + 2 v beams

2000 patients with carbon ions

SHIZUOKA FACILITY
Shizuoka (2002)
Proton synchrotron
2 gantries + 1 h beam

PROSCAN project at PSI



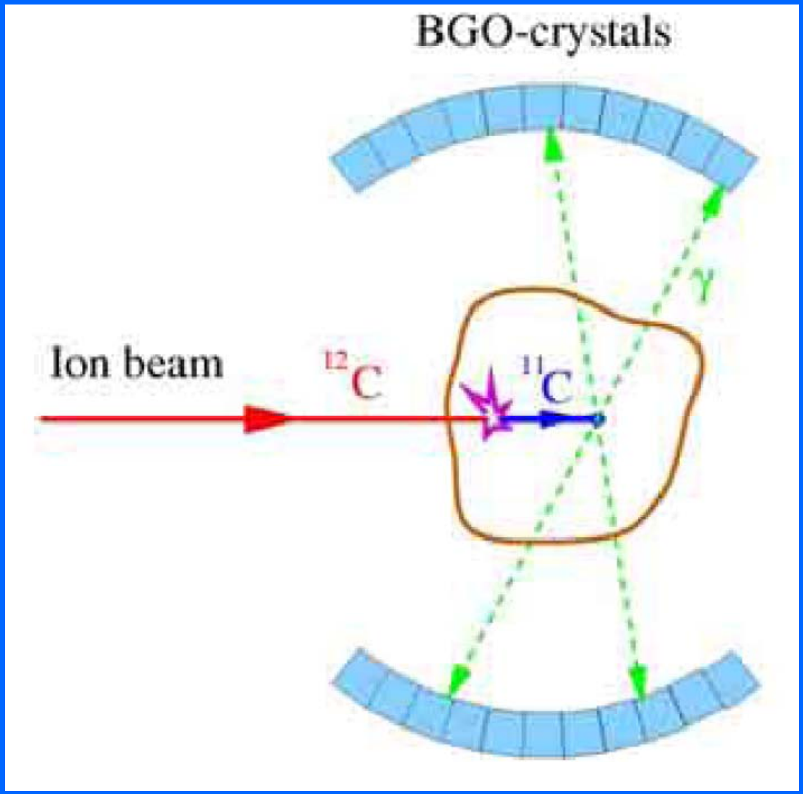
- **New SC 250 MeV proton cyclotron – Installed**
- **New proton gantry**

1998 - GSI pilot project (G. Kraft)

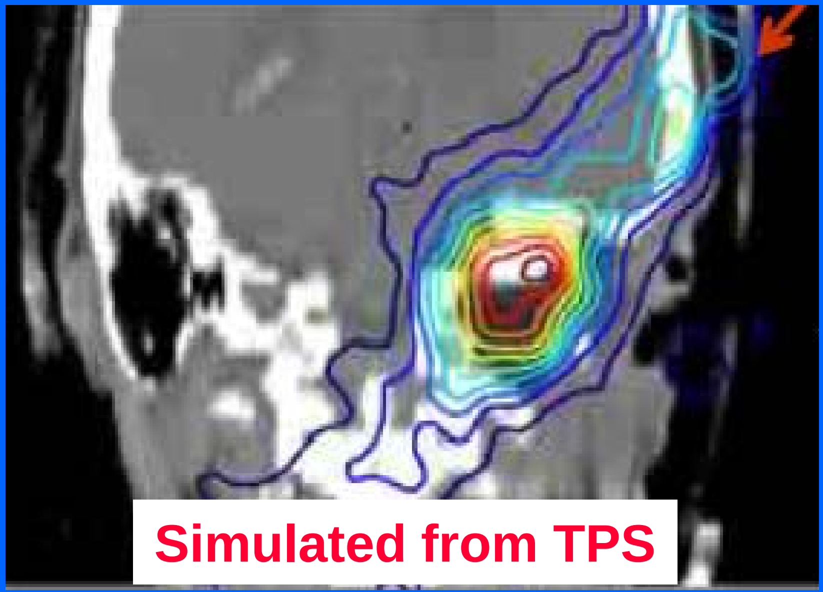
200 patients treated with carbon ions

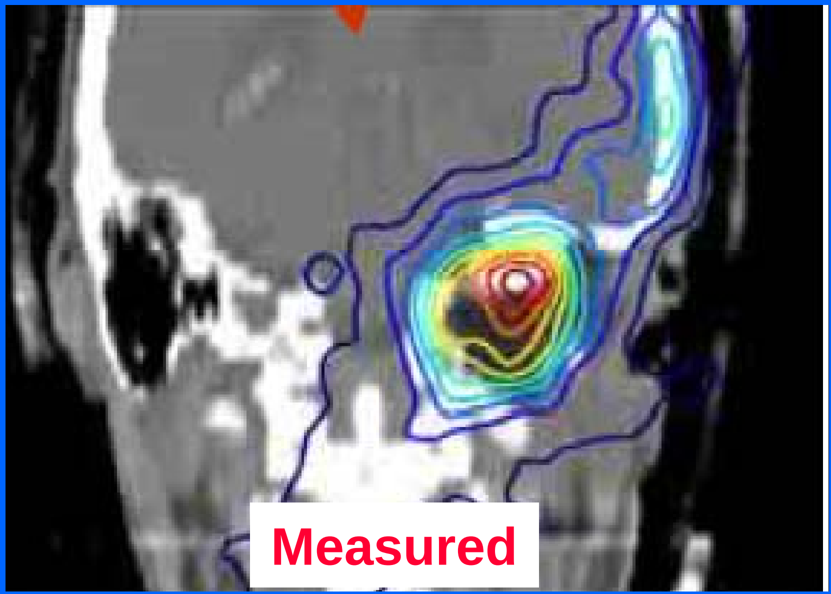
PET on-beam

PET on-beam

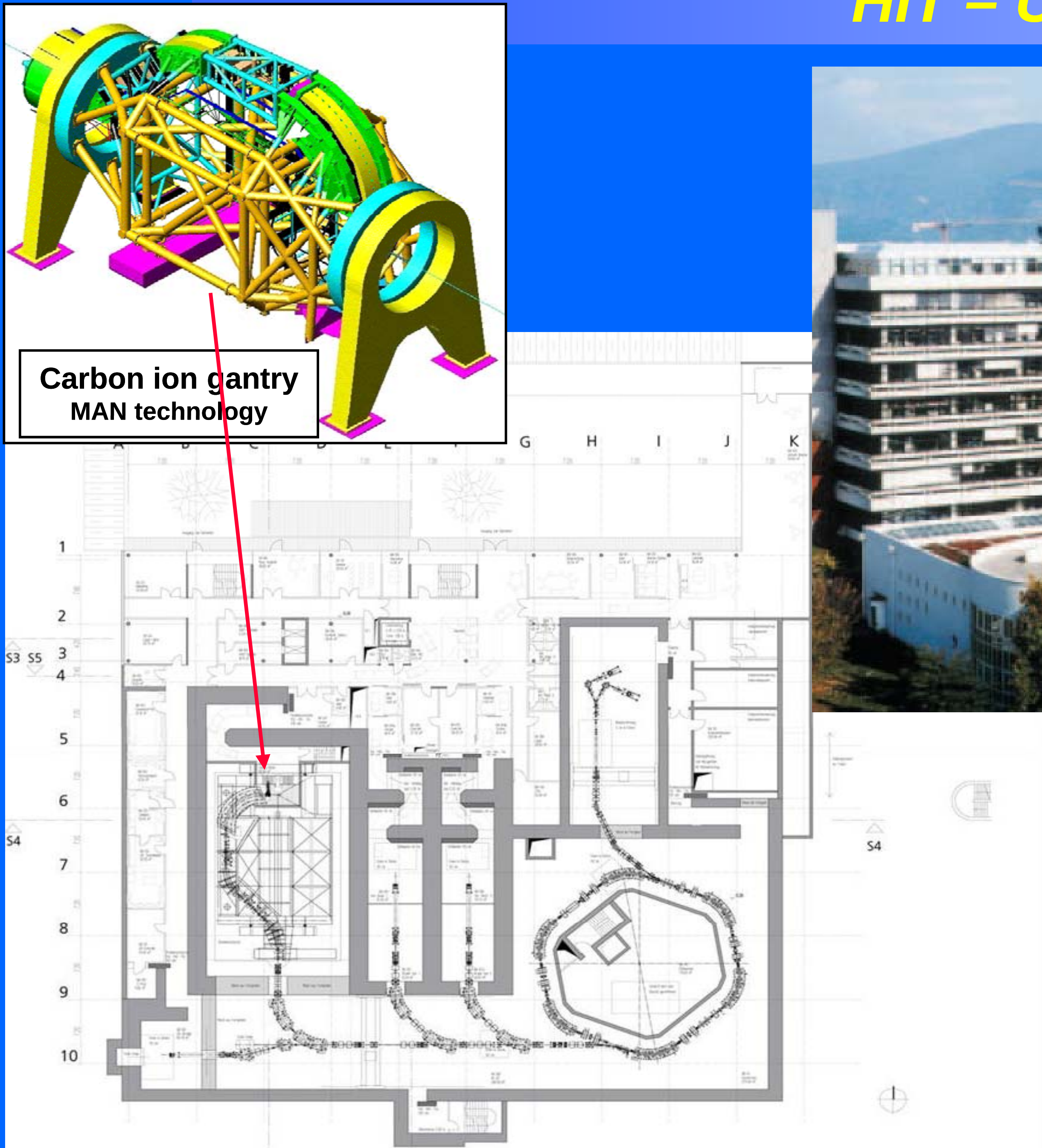


Measurement of the "real" dose given to the patient





HIT – University of Heidelberg



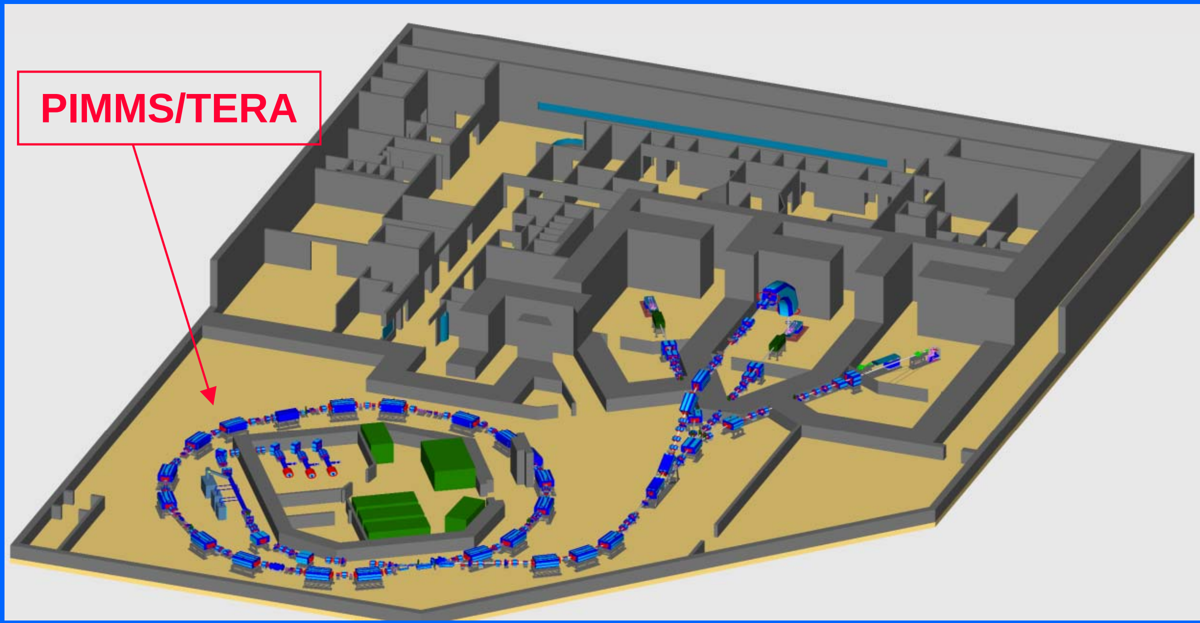
- **Hospital based centre**
- **Project started in 2001**
- **First patient treatment foreseen in 2007**

Hadron-therapy in Italy and 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**

Status of CNAO – May 2009

New accelerators for the future?

Medium term

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

Long term

- Laser plasma accelerators

A “dual” accelerator

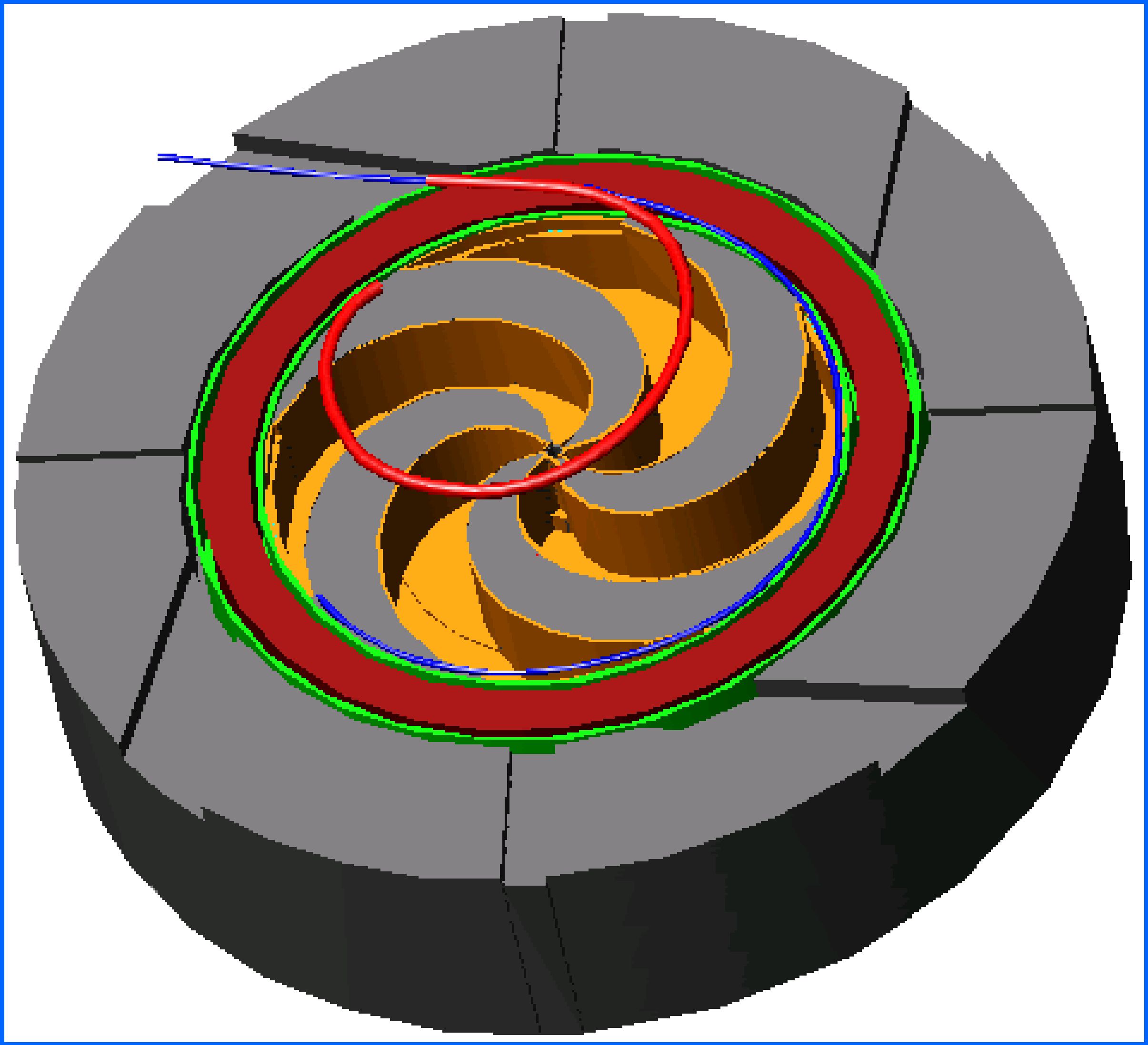
250 MeV/u SC cyclotron

- H_2^+ molecules

  250 MeV proton beam for deep seated cancer treatment

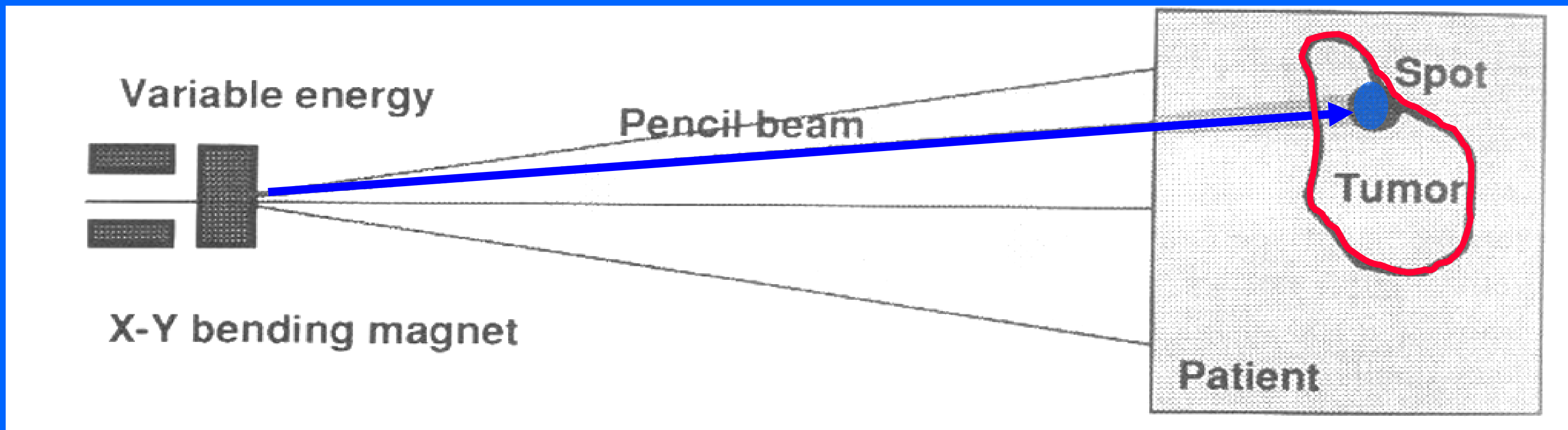
- 250 MeV/u fully stripped C ions

  maximum penetration of 12 cm in water

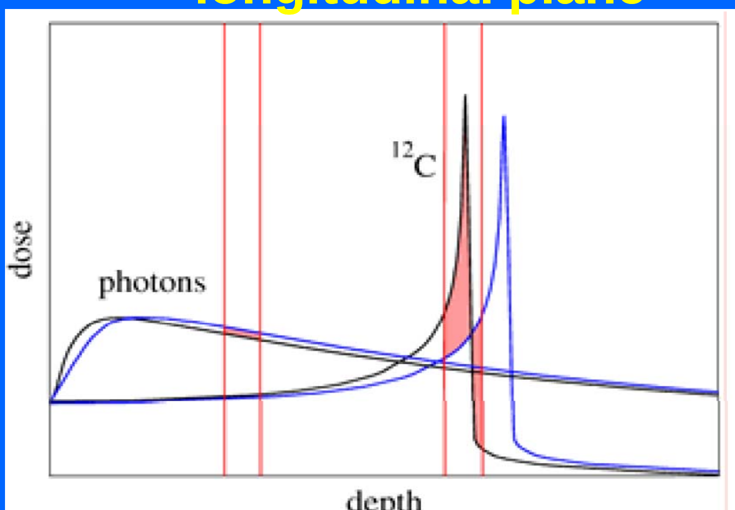


Project of INFN LNS

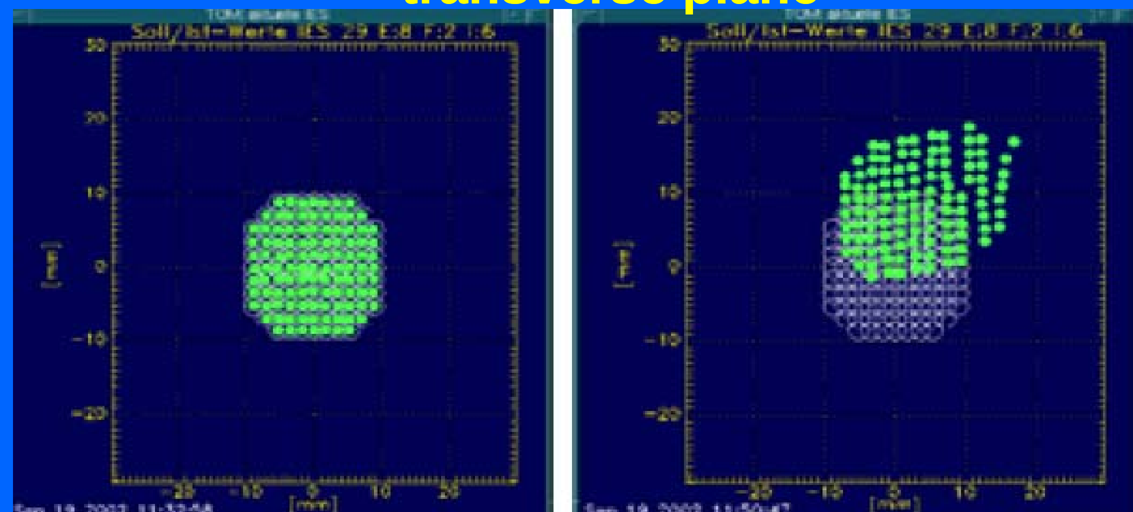
"Spot scanning" is sensitive to movements



longitudinal plane



transverse plane



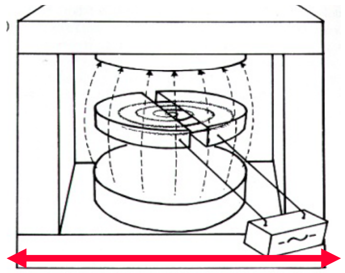
Two approaches can be combined:

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

The accelerators used today in protontherapy

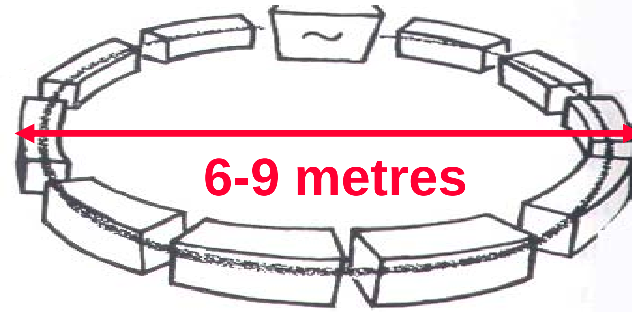
- **200-250 MeV protons**

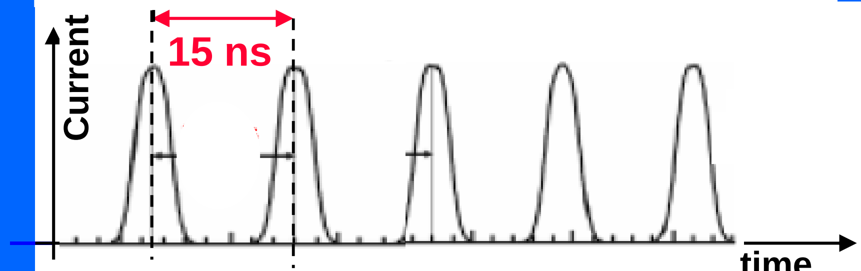
CYCLOTRONS (Normal or SC)

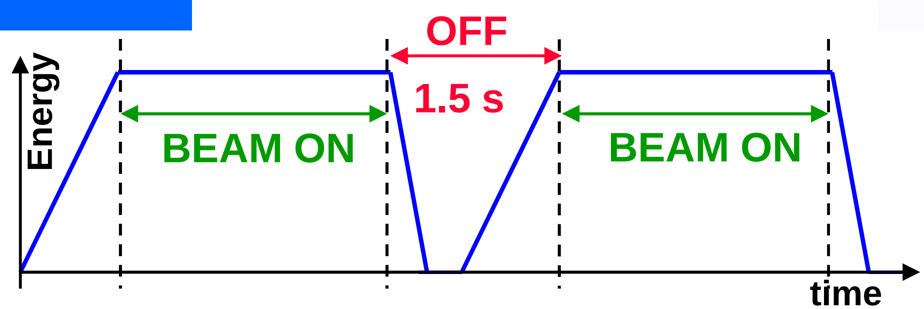


OR

SYNCHROTRONS







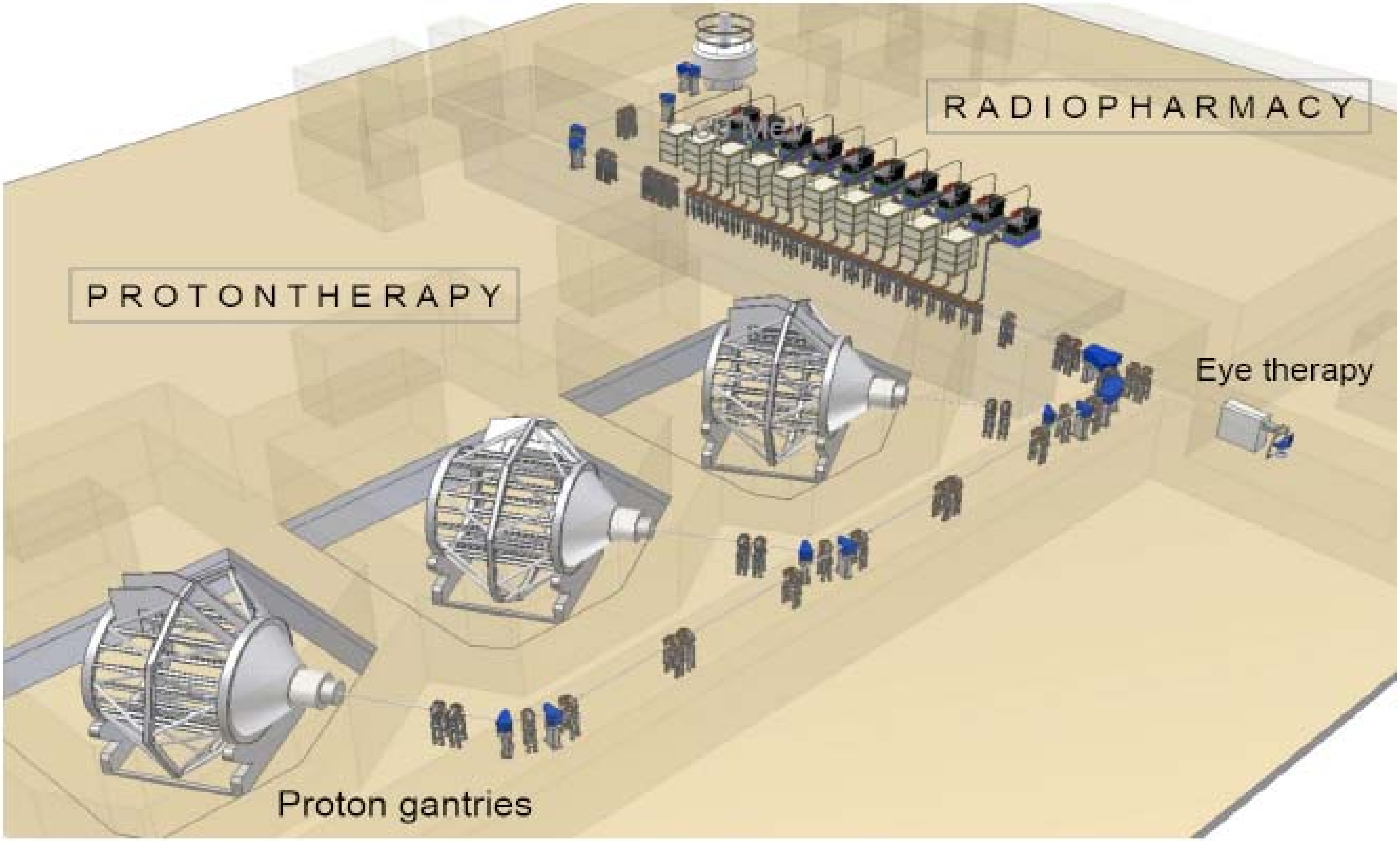
CYCLOTRONS

- **Almost continuous beam**
- **Fixed energy**

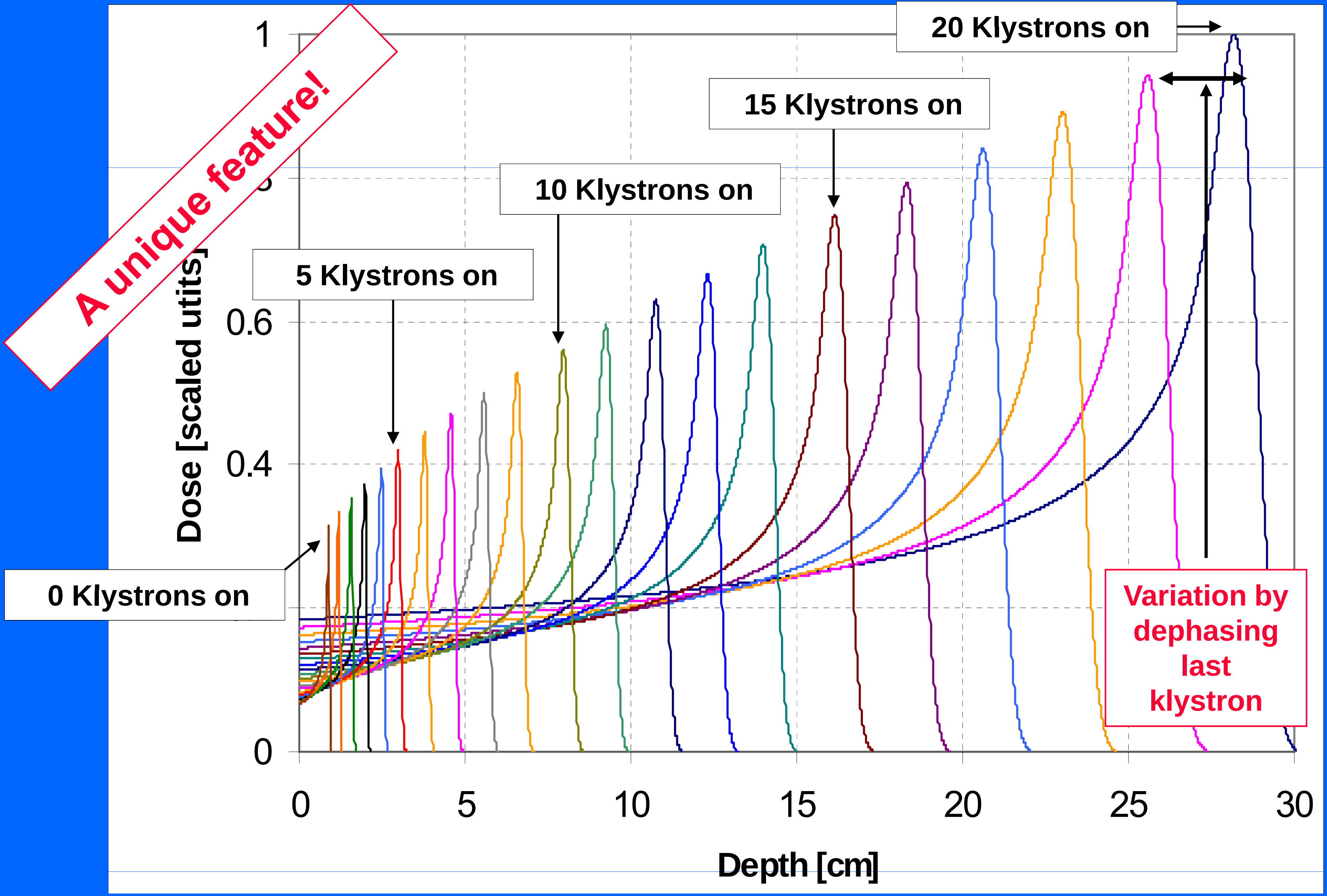
SYNCHROTRONS

- **Beam ON and OFF**
- **Continuous energy**

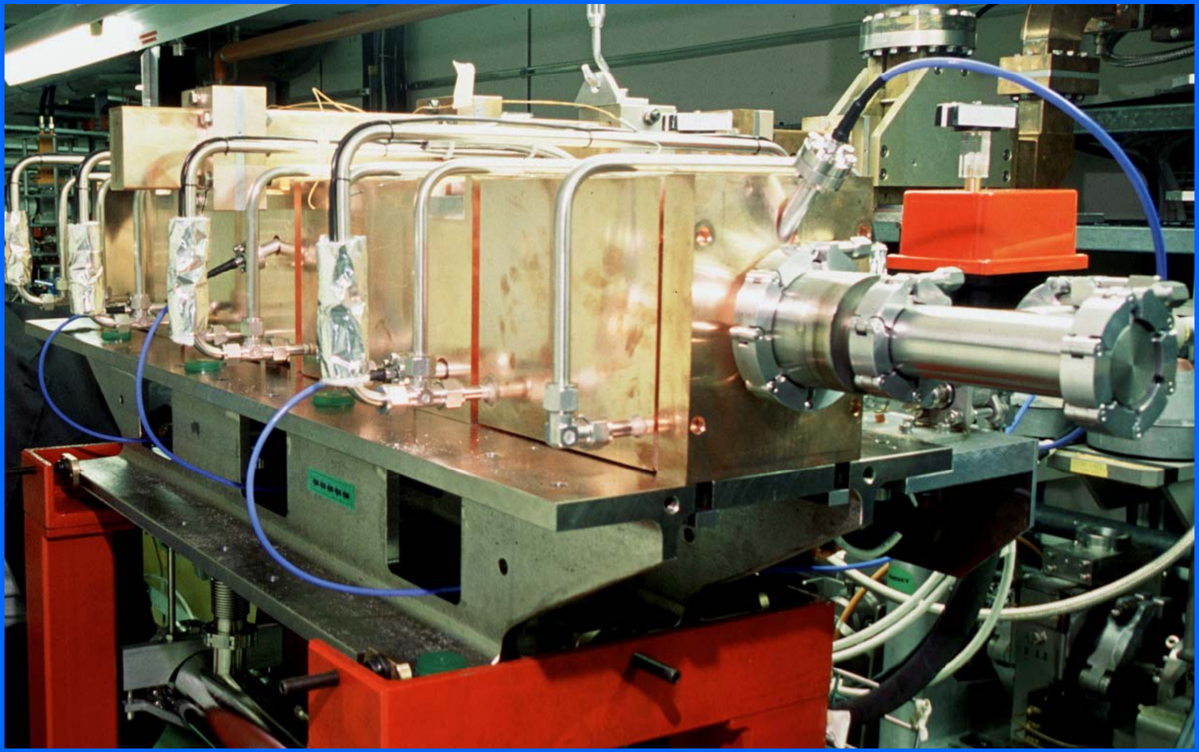
IDRA

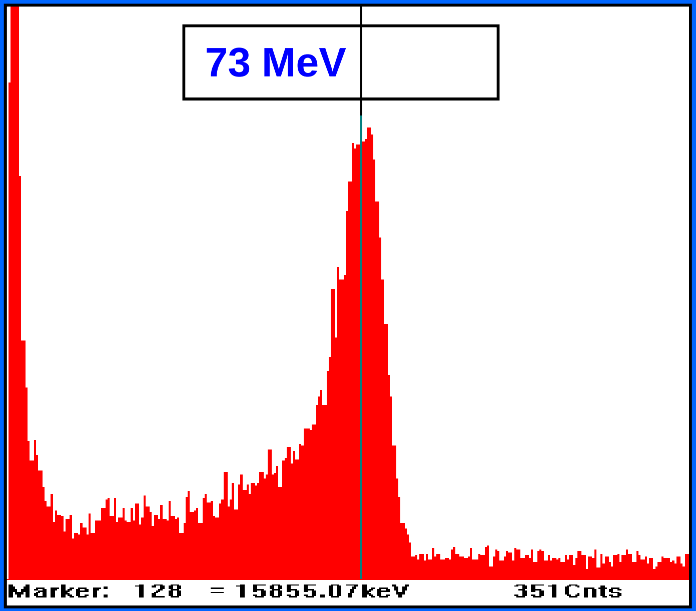

RADIOPHARMACY
PROTONTHERAPY
Eye therapy
Proton gantries

Bragg curves obtained by switching off klystrons



Prototype of LIBO (on display at CERN TERA stand)





Collaboration INFN-CERN-TERA 1999-2002

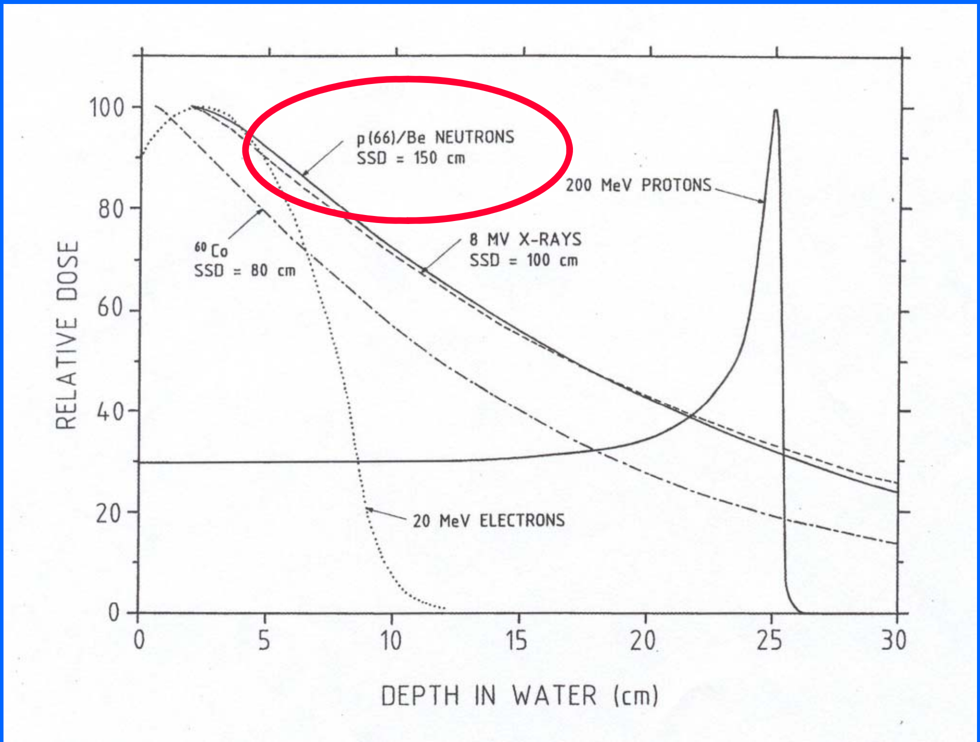
Module tested at LNS of INFN, Catania

NIM A 521 (2004) 512

Accelerated beam from the 60 MeV cyclotron of LNS

Neutrons in cancer therapy

Hadrontherapy with fast neutrons



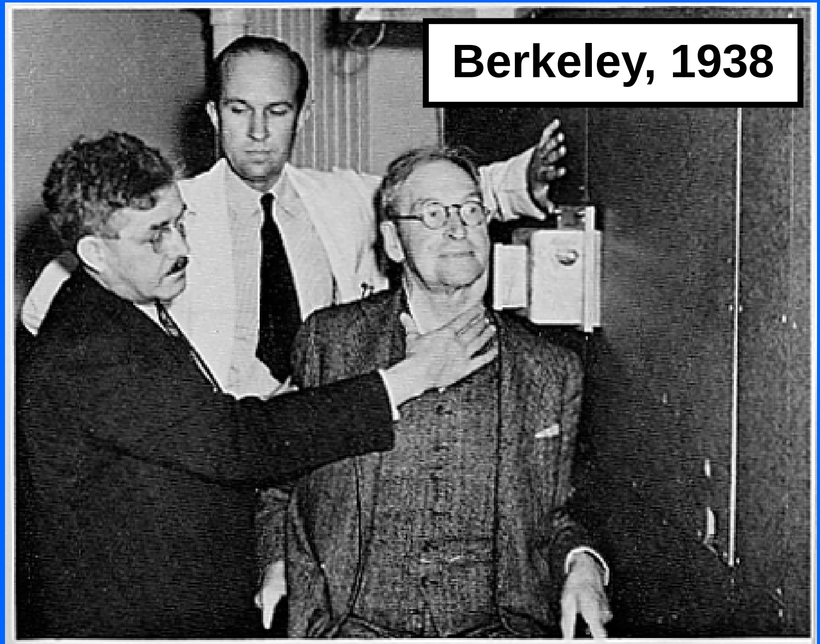
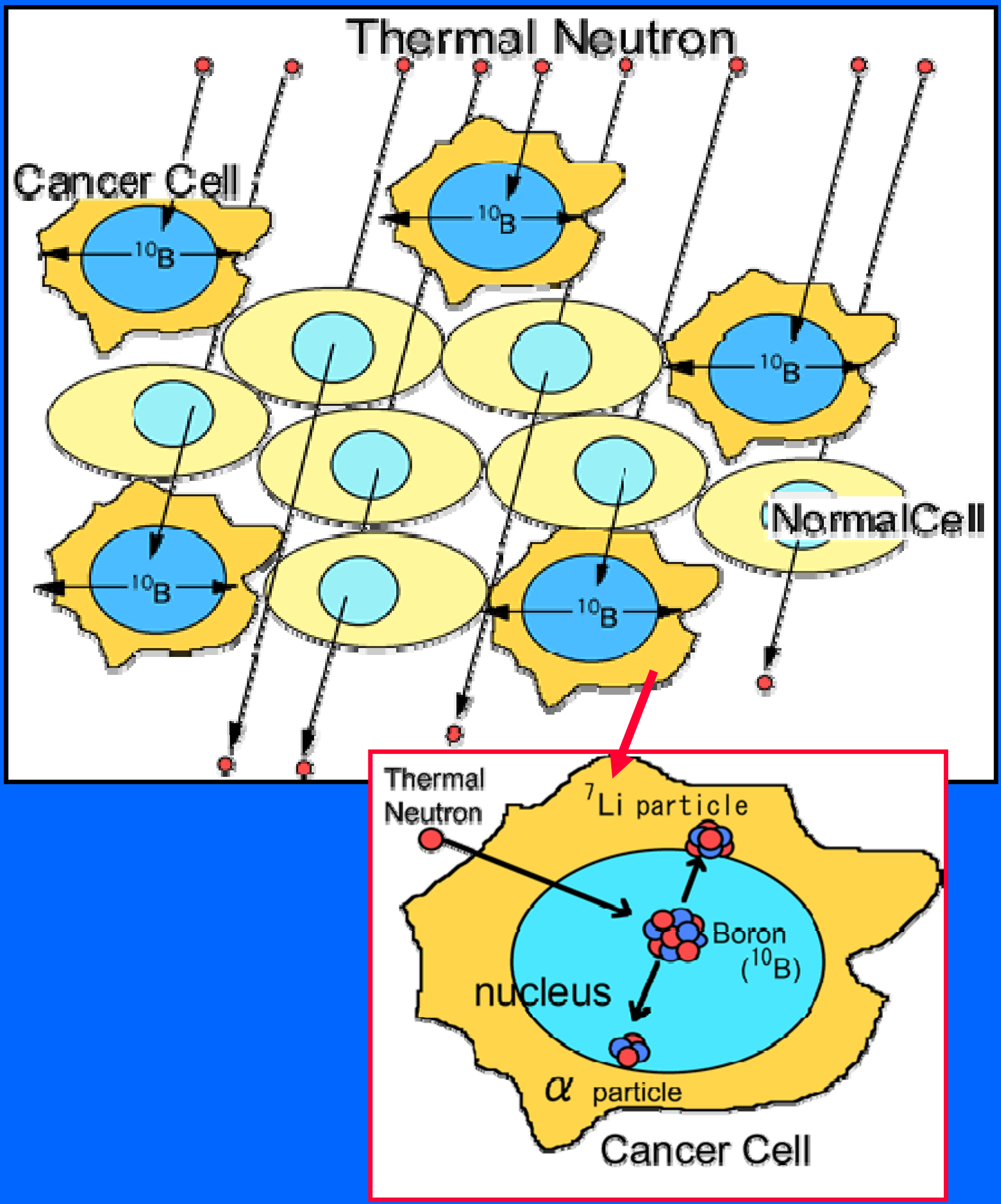


PLATE 8.4 Robert Stone and John Lawrence treating Robert Penney at the 60-inch neutron port. LBL.

- Neutrons are neutral → no Bragg peak
- MeV neutrons are produced with cyclotrons (p + Be reaction)
- MeV neutrons produce nuclear interactions → high LET radiation
- Used for radio resistant tumours (ex. salivary glands, tongue, brain)
- About 9 centers in the world [ex. Orleans (France), Fermilab (USA)]

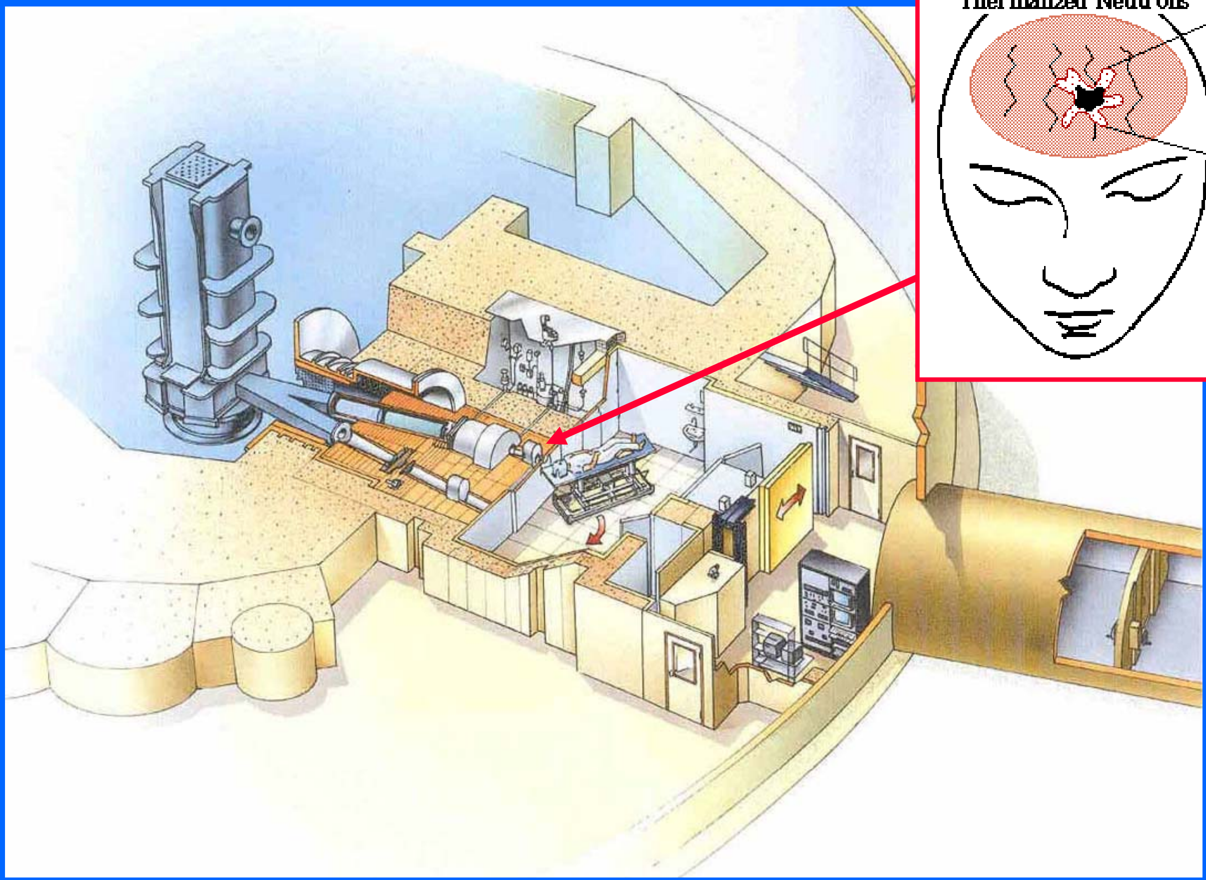
Boron Neutron Capture Therapy (BNCT)

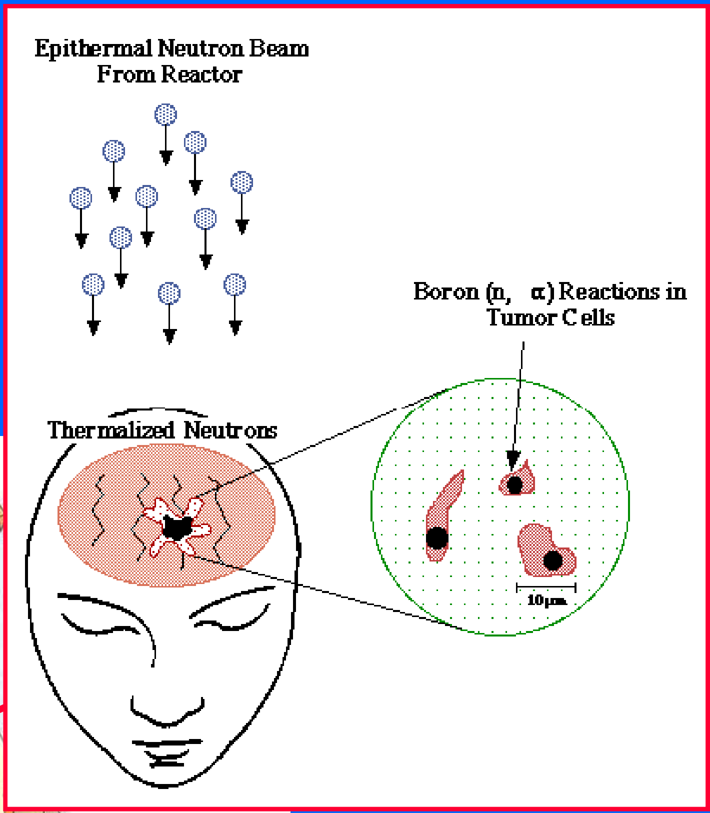


- Concept proposed in 1936 by G.L. Locher (only 4 years after the discovery of the neutron!)
- Bring into cancer cells a nuclide that captures neutrons and disintegrates into high LET fragments
- ^{10}B is used
  - Available (20% of natural B)
  - Fragments of high LET and path lengths approximately one cell diameter (about 12 microns)
  - Well known chemistry

BNCT facilities

- Nuclear reactors or accelarators are used as sources of epithermal neutrons
- Many centers in the world, mostly for clinical trials





Limitation

Difficult to achieve selective localization in the tumour !

The challenge of medical sciences

Three fundamental questions to detect and cure the disease:

Where ?

When ?

How ?

As Precisely As Possible

As Soon As Possible

As Effectively As Possible

One answer :

Multidisciplinary approach

Some examples :

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

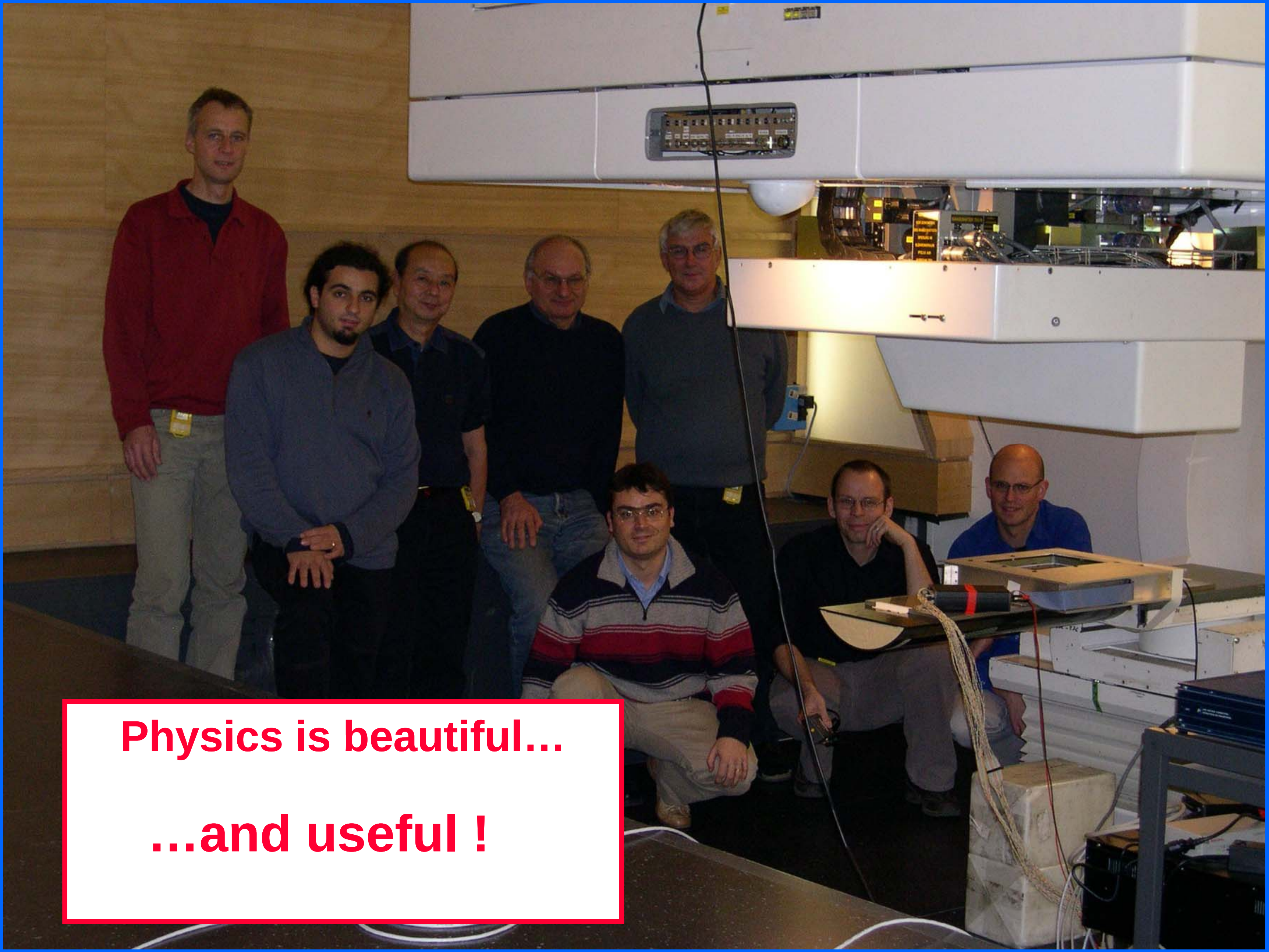
Conclusions and Outlook

- 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 !