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

Hadrontherapy with beams of protons and ions

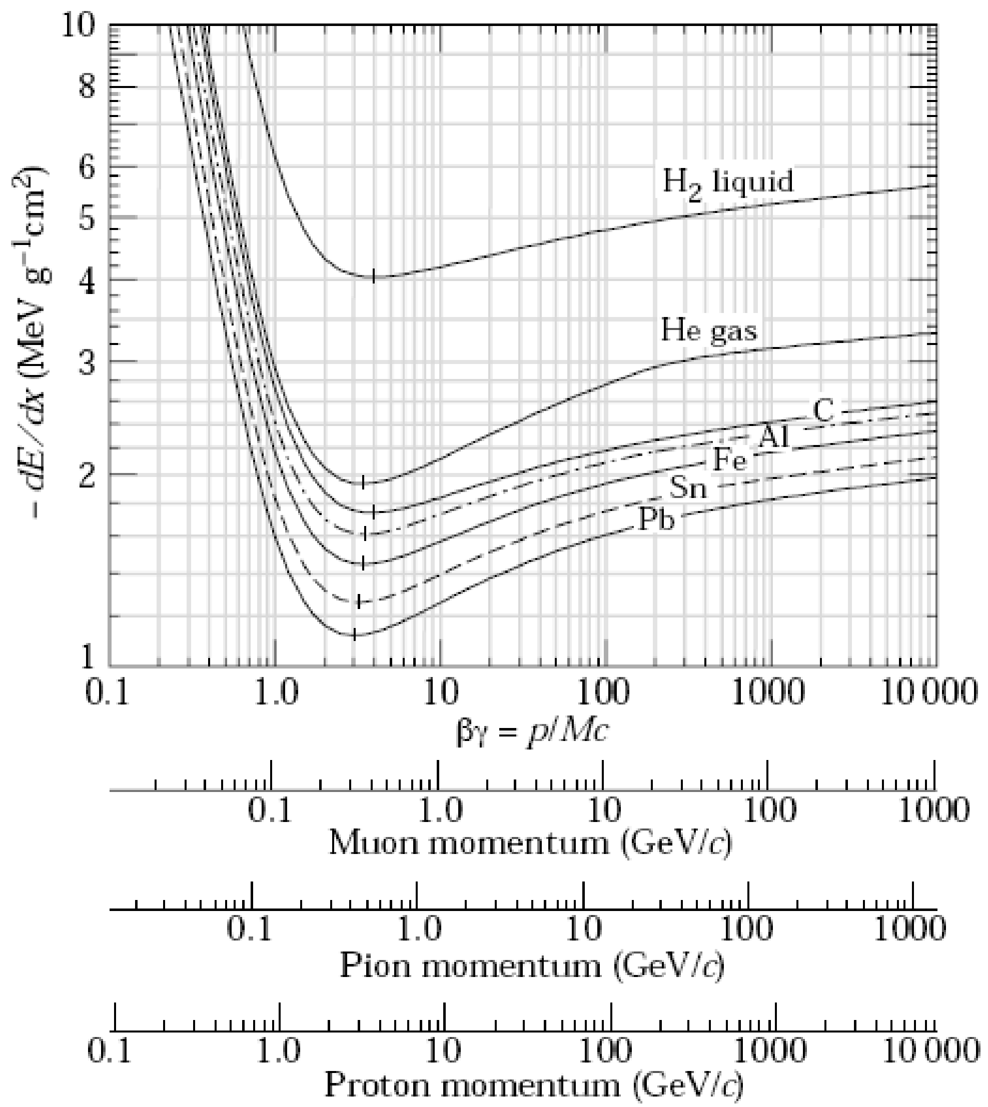
The Bethe-Bloch formula:

$$-\frac{dE}{dx} = Kz^2\frac{Z}{A}\frac{1}{\beta^2}\left[\frac{1}{2}\ln\frac{2m_ec^2\beta^2\gamma^2T_{\max}}{I^2} - \beta^2 - \frac{\delta(\beta\gamma)}{2}\right]$$

$$K = 4\pi N_A r_e^2 m_e c^2 / A$$

= 0.3071 MeV / (g/cm^2)

dx expressed in g/cm^2



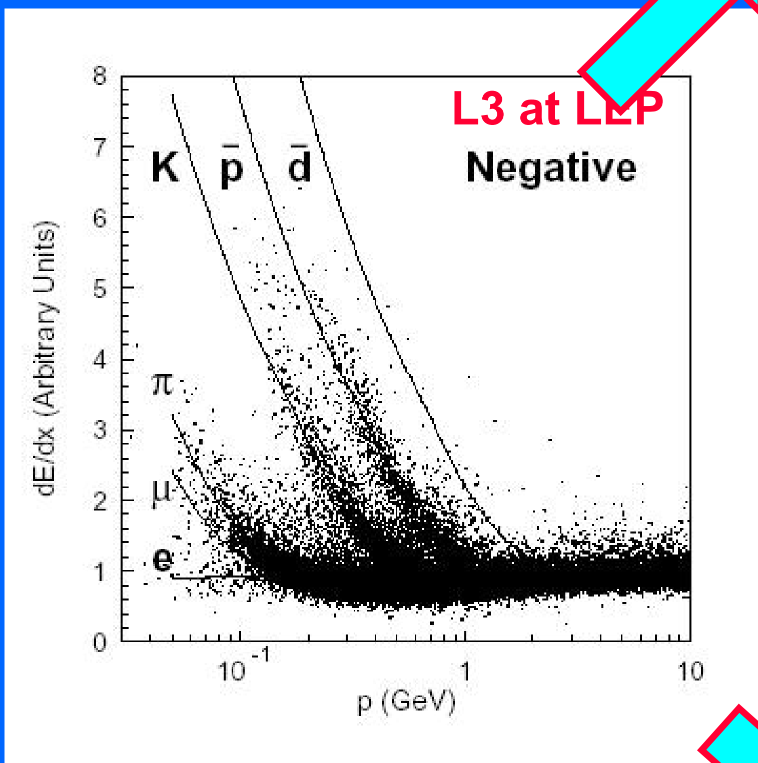
Notes:

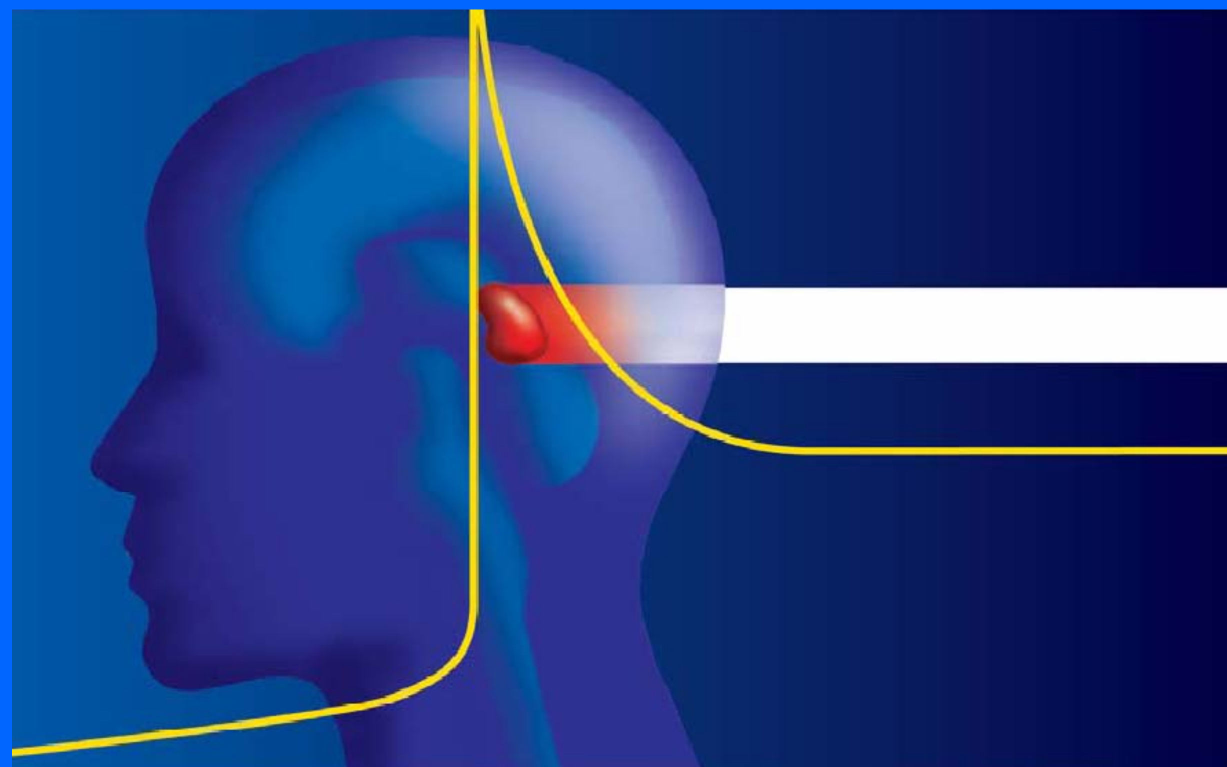
- **Ionization + eccitation**
- **MIP = Minimum Ionizing Particle**
- **MIP in water 2.0 MeV/cm → 0.2 eV/nm very low LET radiation !**

The basic concept of hadrontherapy

Fundamental physics

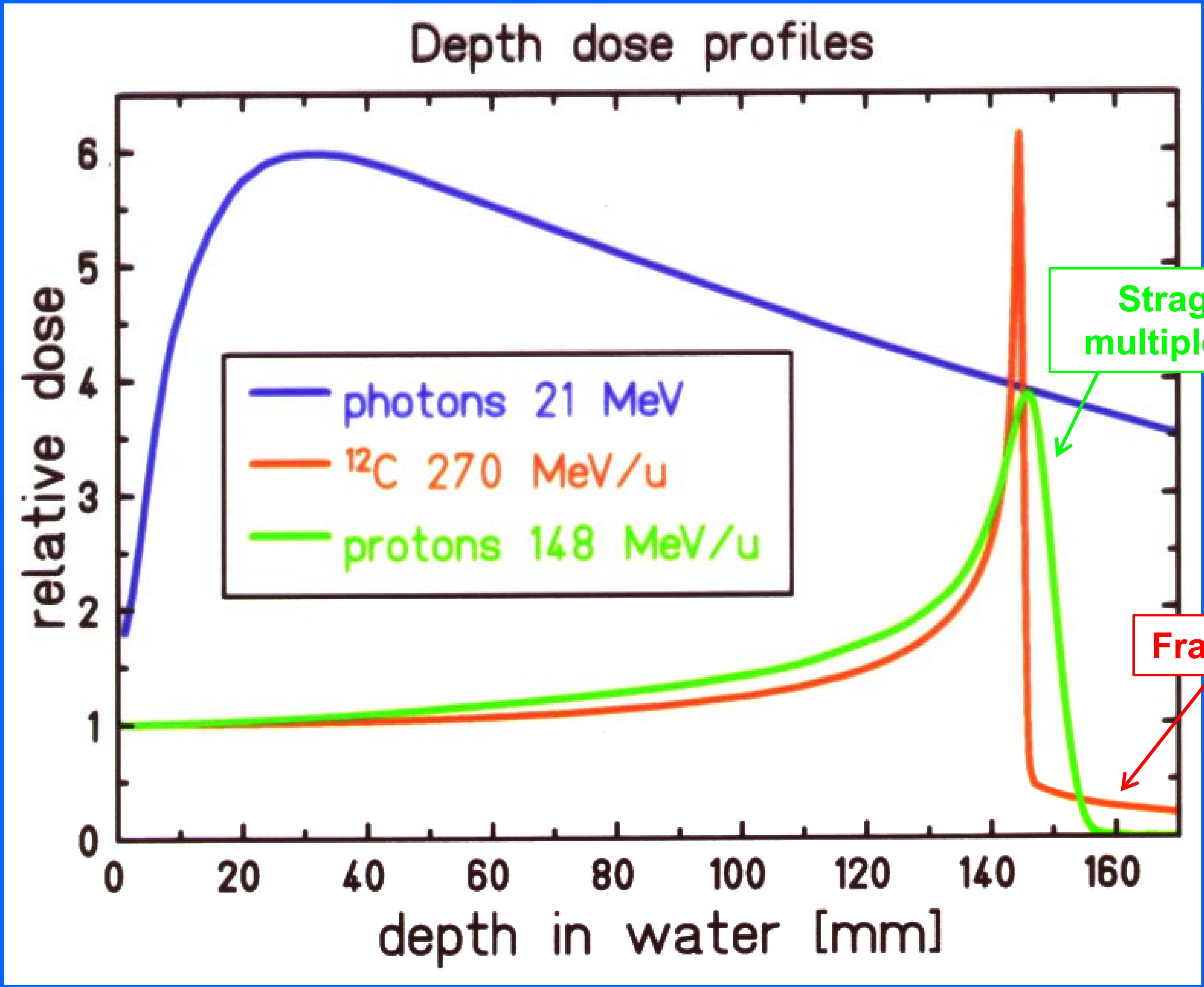
Particle identification





Medical applications

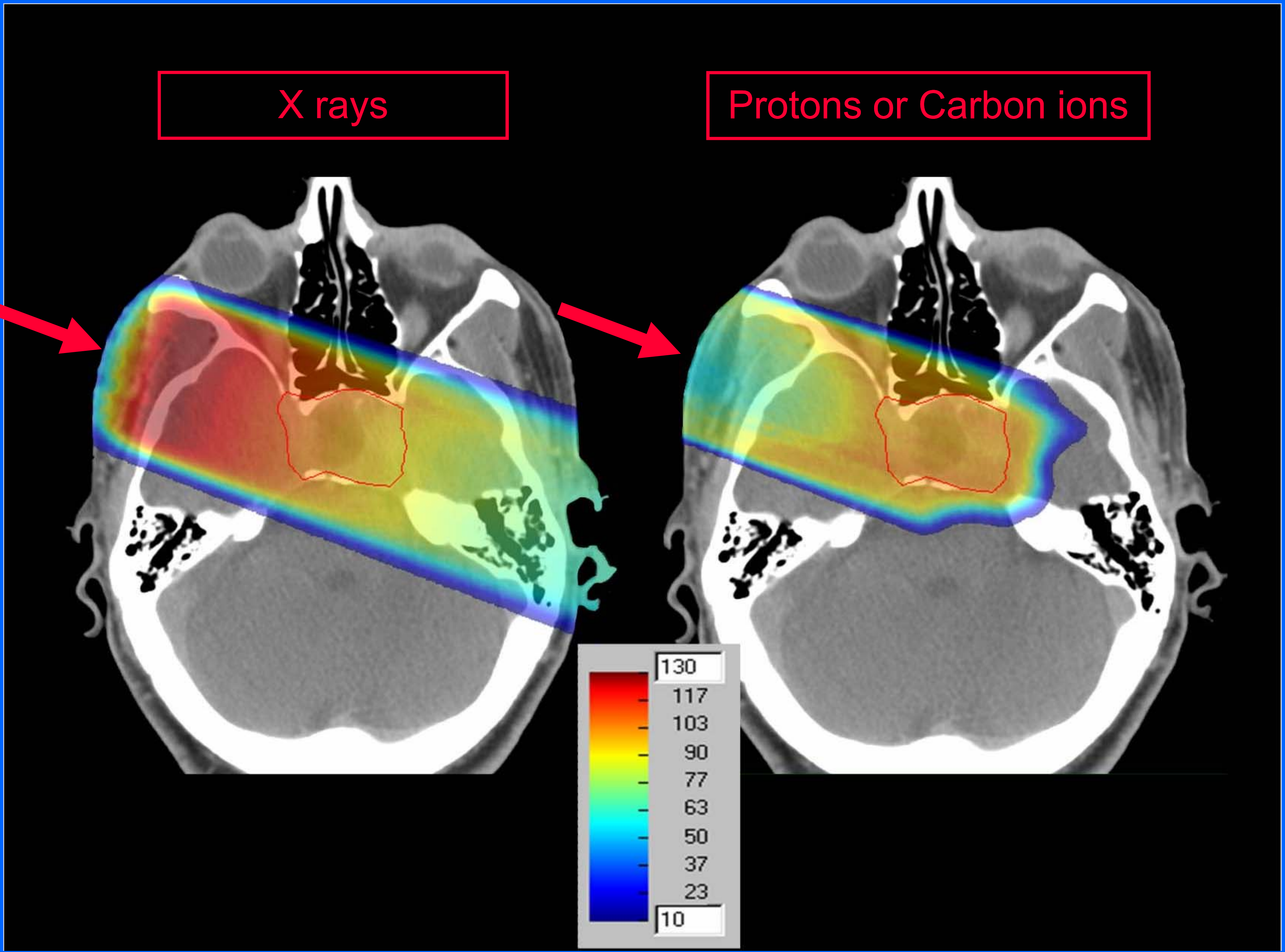
Cancer hadrontherapy



Straggling and multiple scattering

Fragmentation

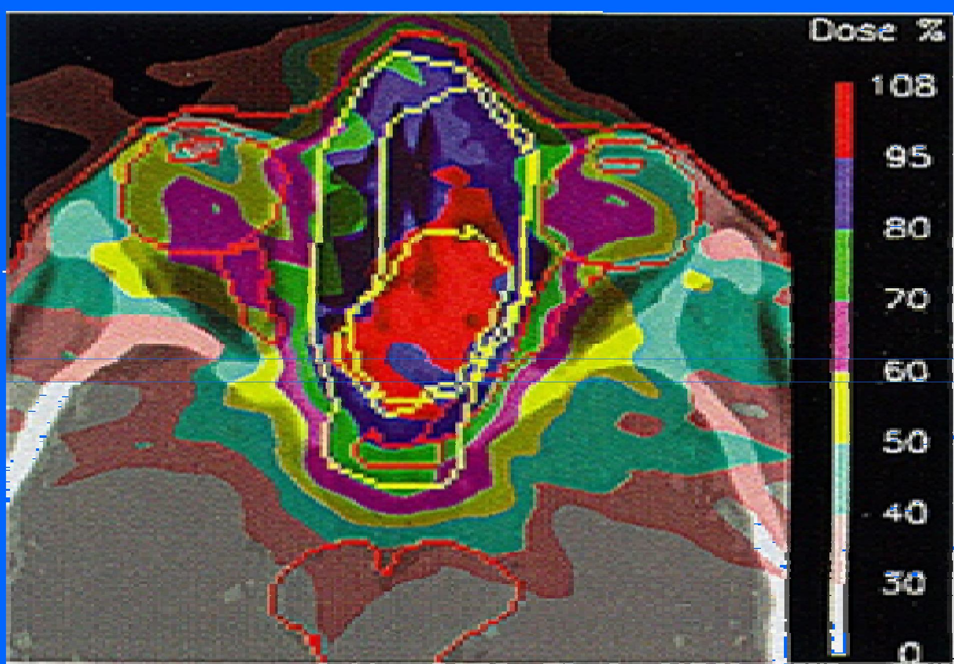
Single beam comparison



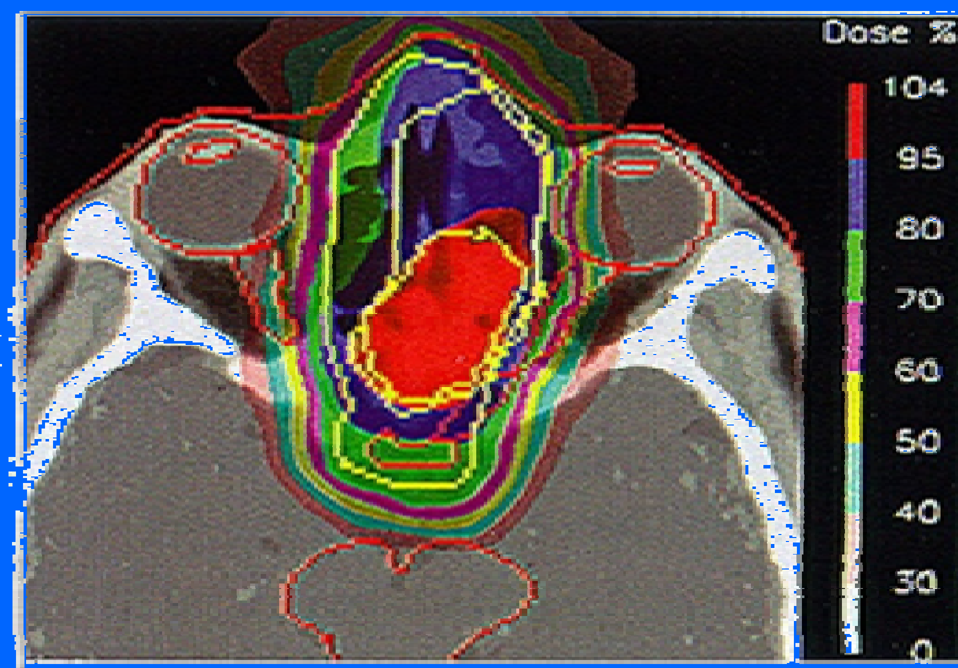
Protons and ions are more precise than X-rays

Tumour between the eyes

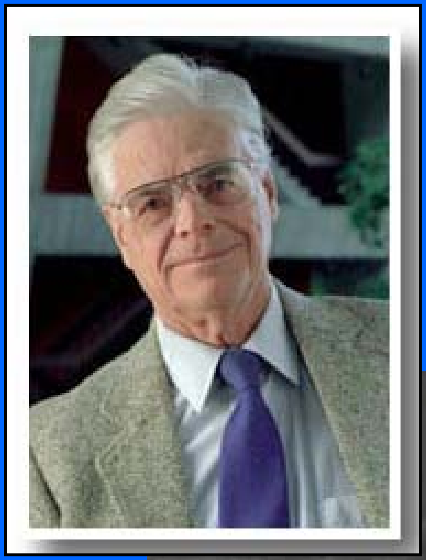
9 X ray beams



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 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

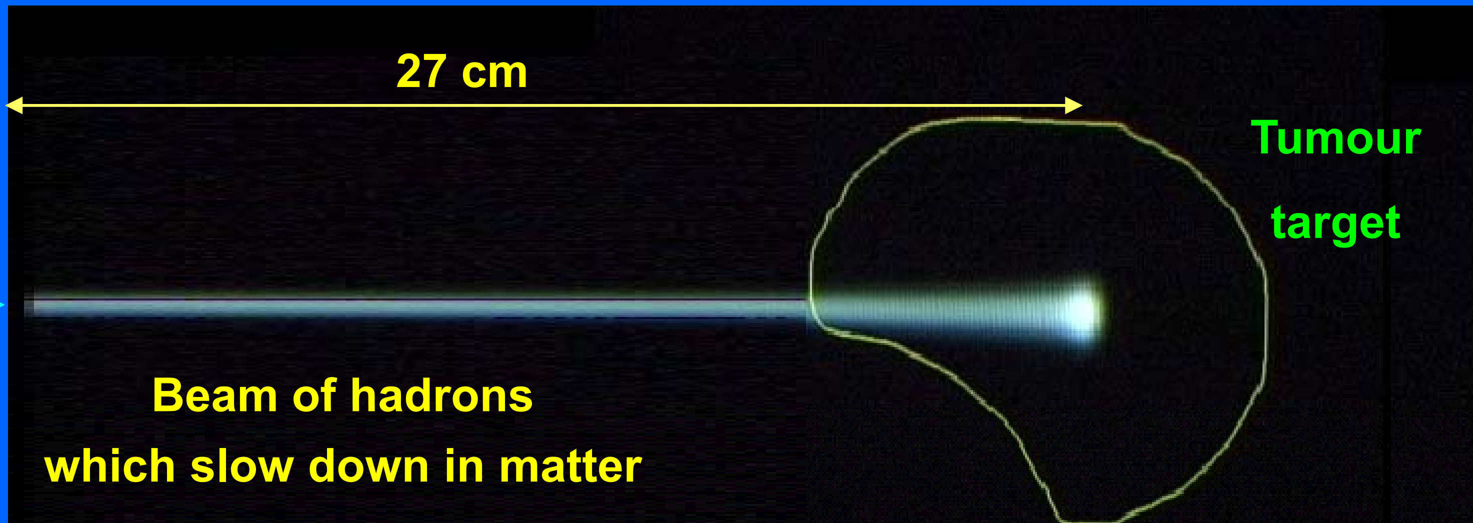
Cornelius A. Tobias

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



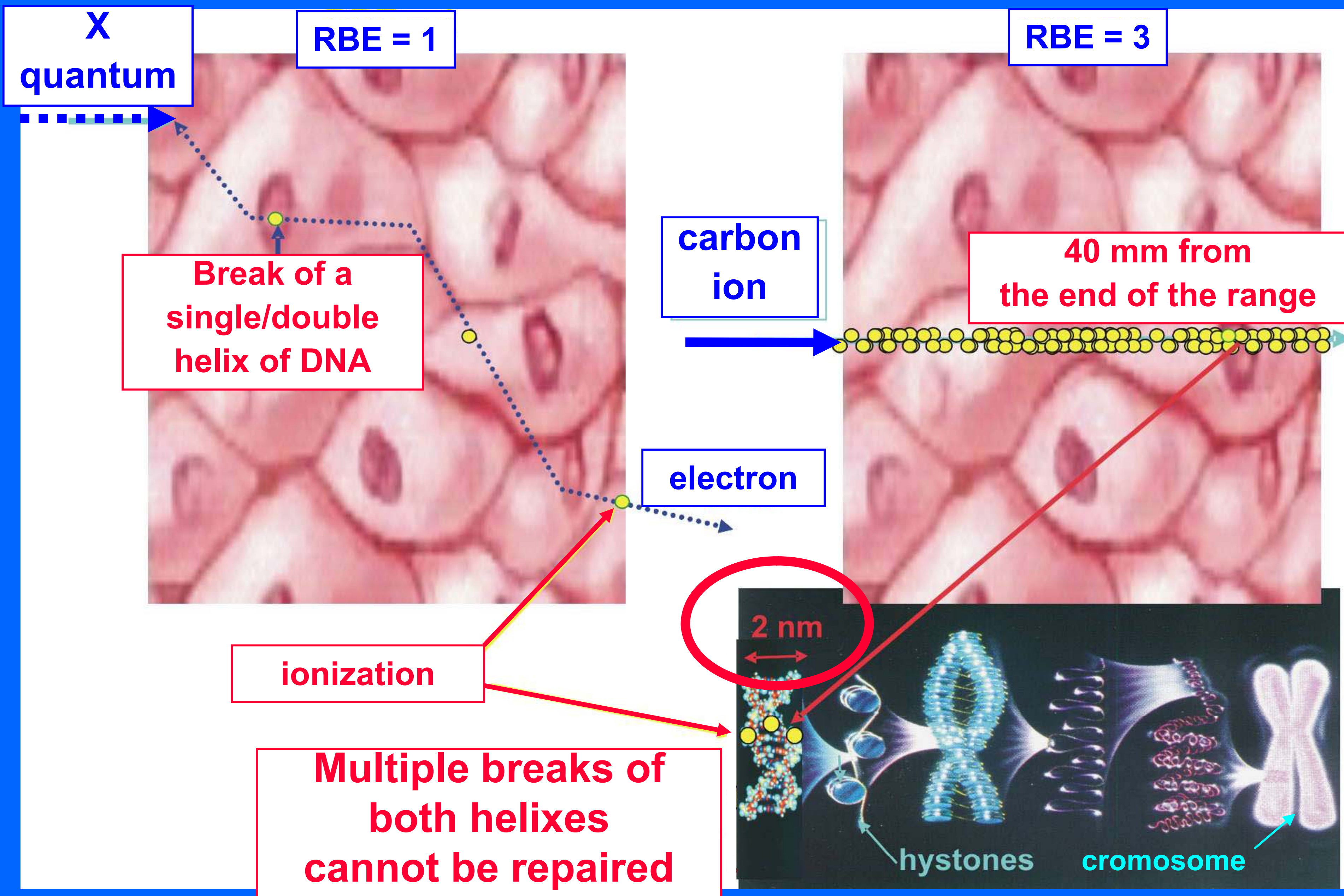
- Bragg peak
  - Better conformity of the dose to the target → healthy tissue sparing
- Hadrons are charged
  - Beam scanning for dose distribution
- Heavy ions
  - Higher biological effectiveness

Energy and current

- Why 200 MeV protons and 400 MeV/u C ions?
  - Range in water: 200 MeV p → 27 cm penetration depth
  - 4800 MeV C ions → 27 cm penetration depth

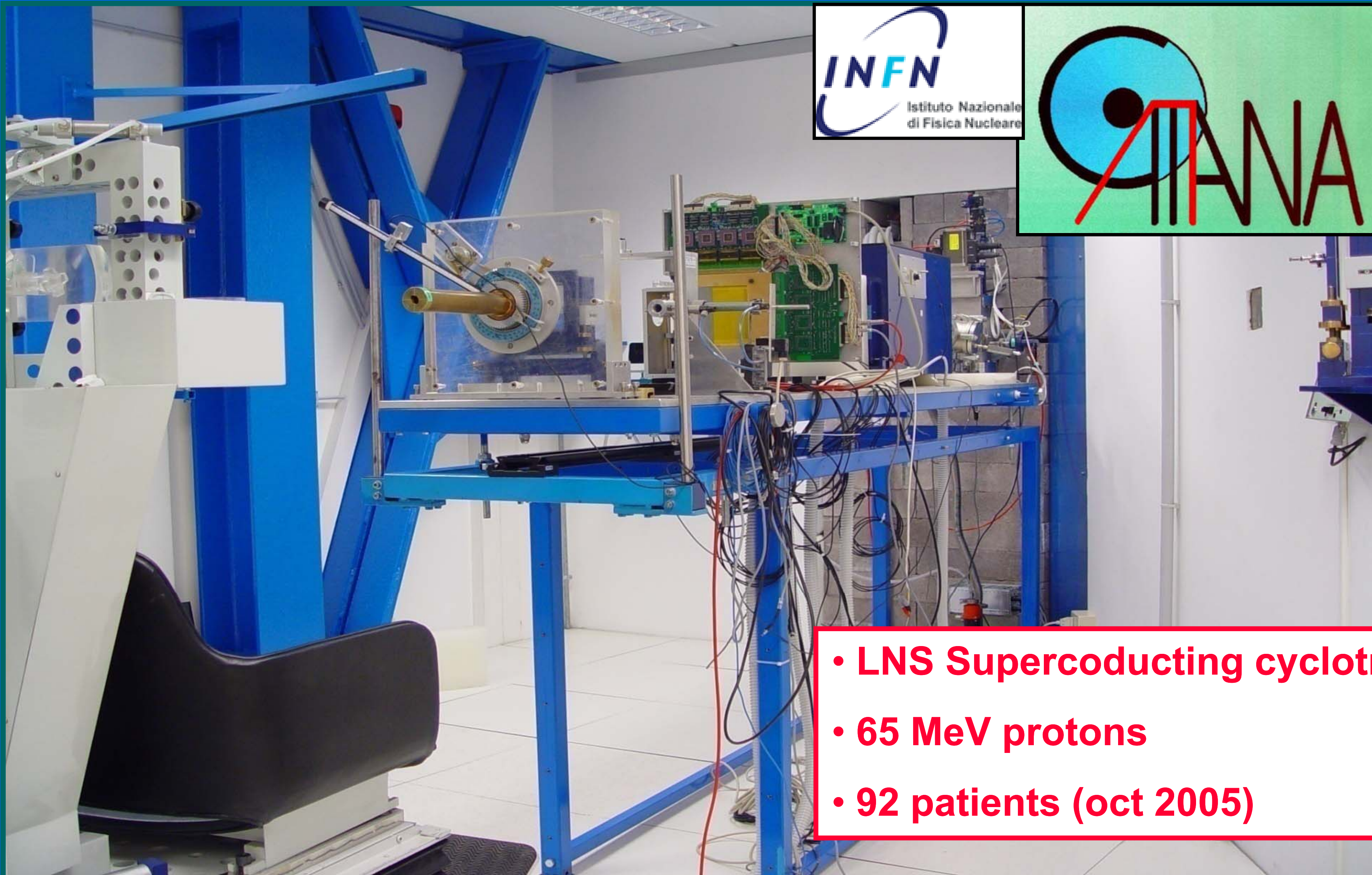
- Why 1 nA current?
  - Requirement: 2 Gy per Kg per minute
  - (2 J / 200 MeV) x (e) x (1/60 sec) ≈ 1 nA

Why ions have a large biological effectiveness?



Ions have high LET (Linear Energy Transfer)

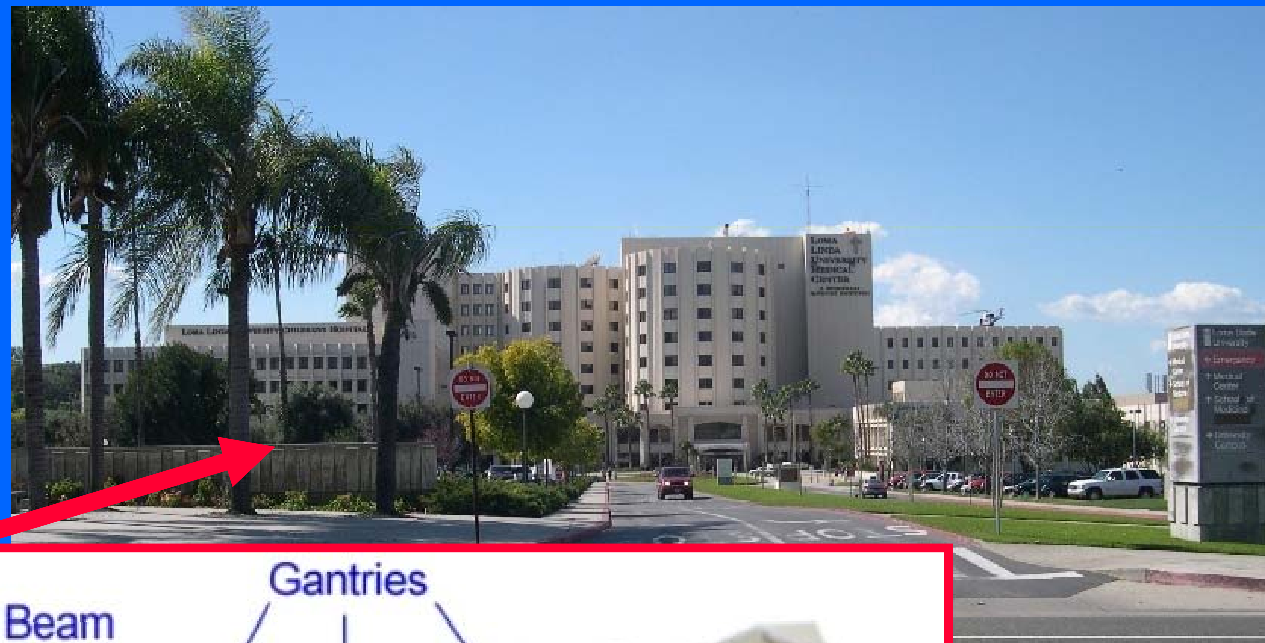
The eye melanoma treatment at INFN-LNS in Catania

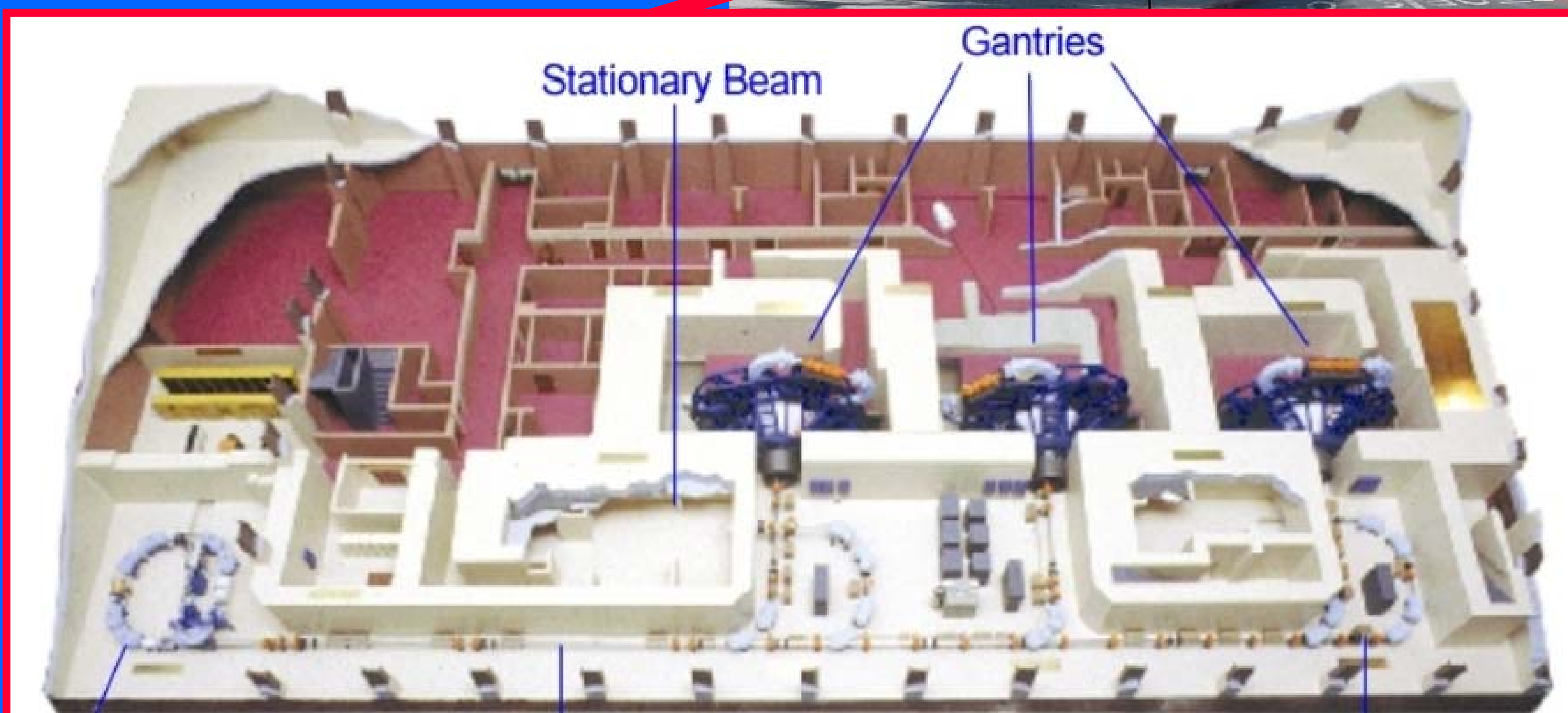


- **LNS Supercoducting cyclotron**
- **65 MeV protons**
- **92 patients (oct 2005)**

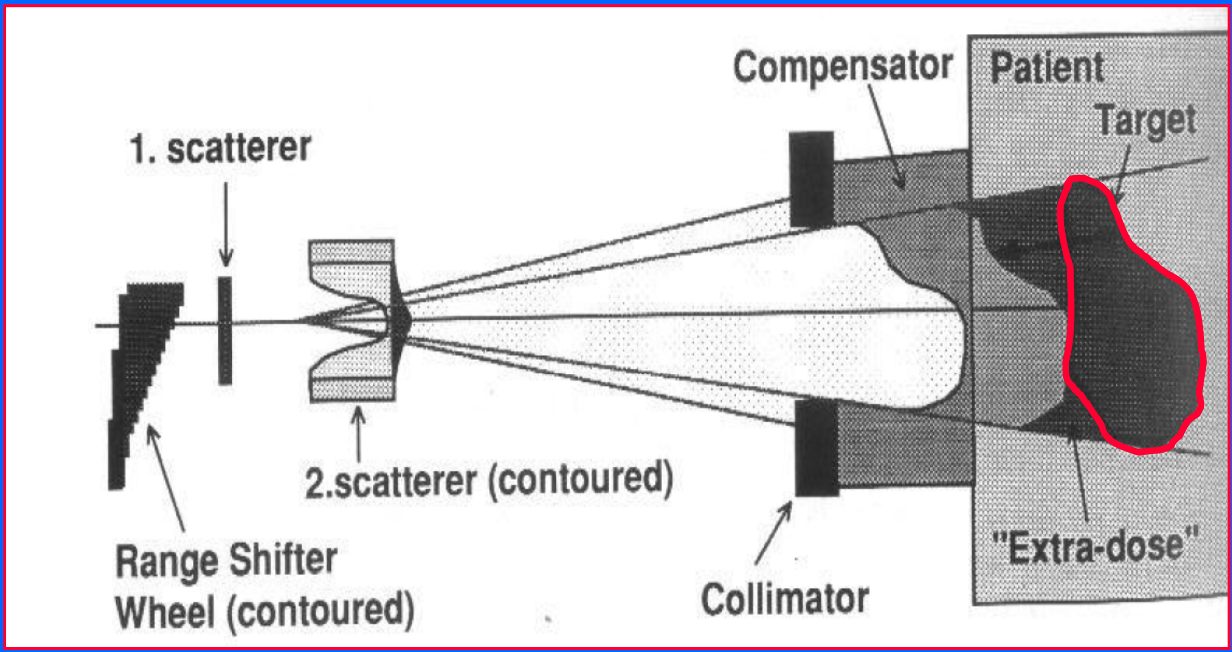
The Loma Linda University Medical Center (USA)

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

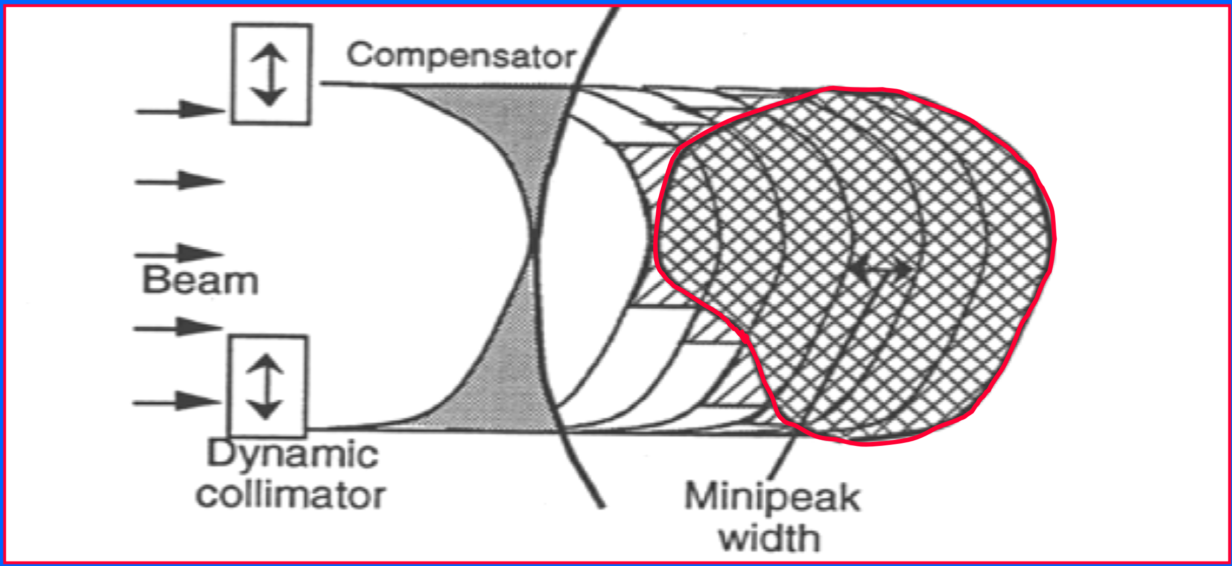




Dose distribution: passive spreading

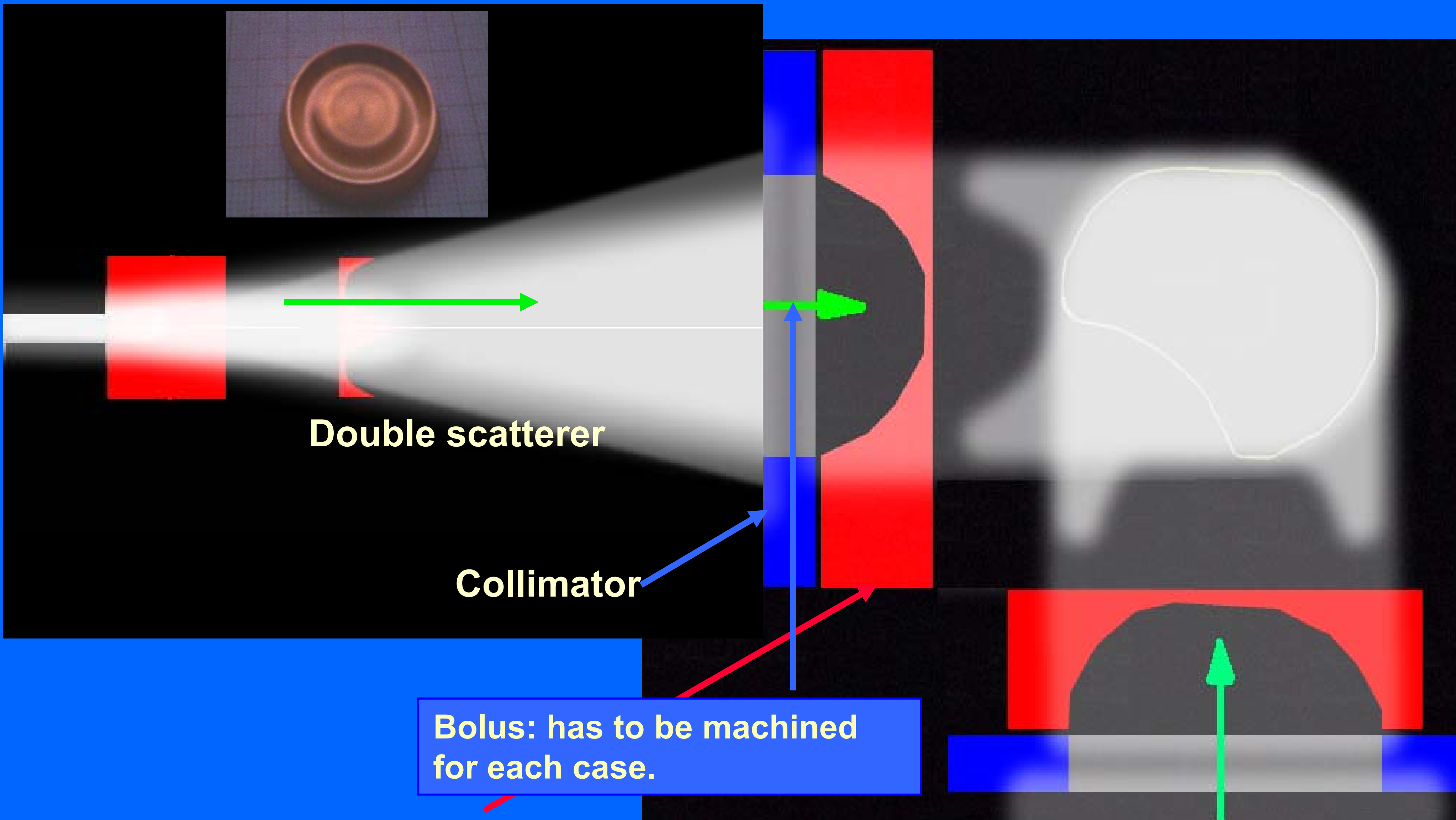


'Double scattering'

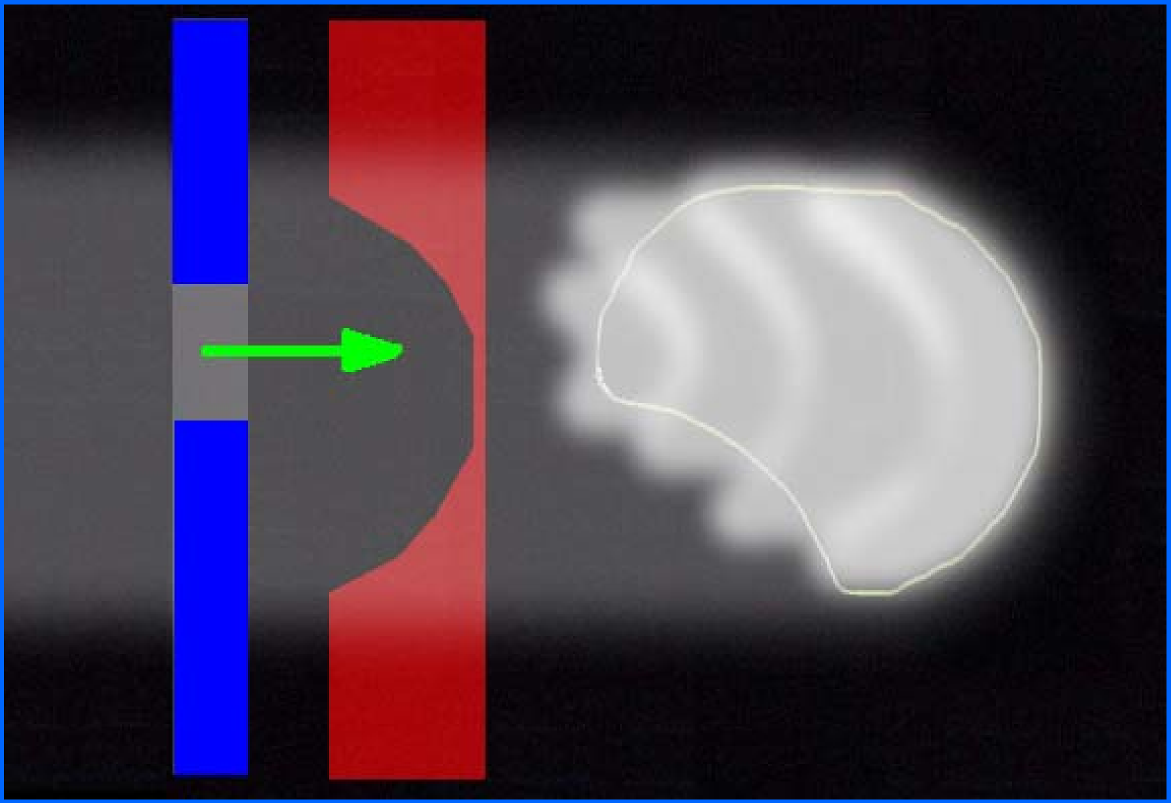


'Layer stacking'

Standard procedure: Passive beam spreading with respiratory gating

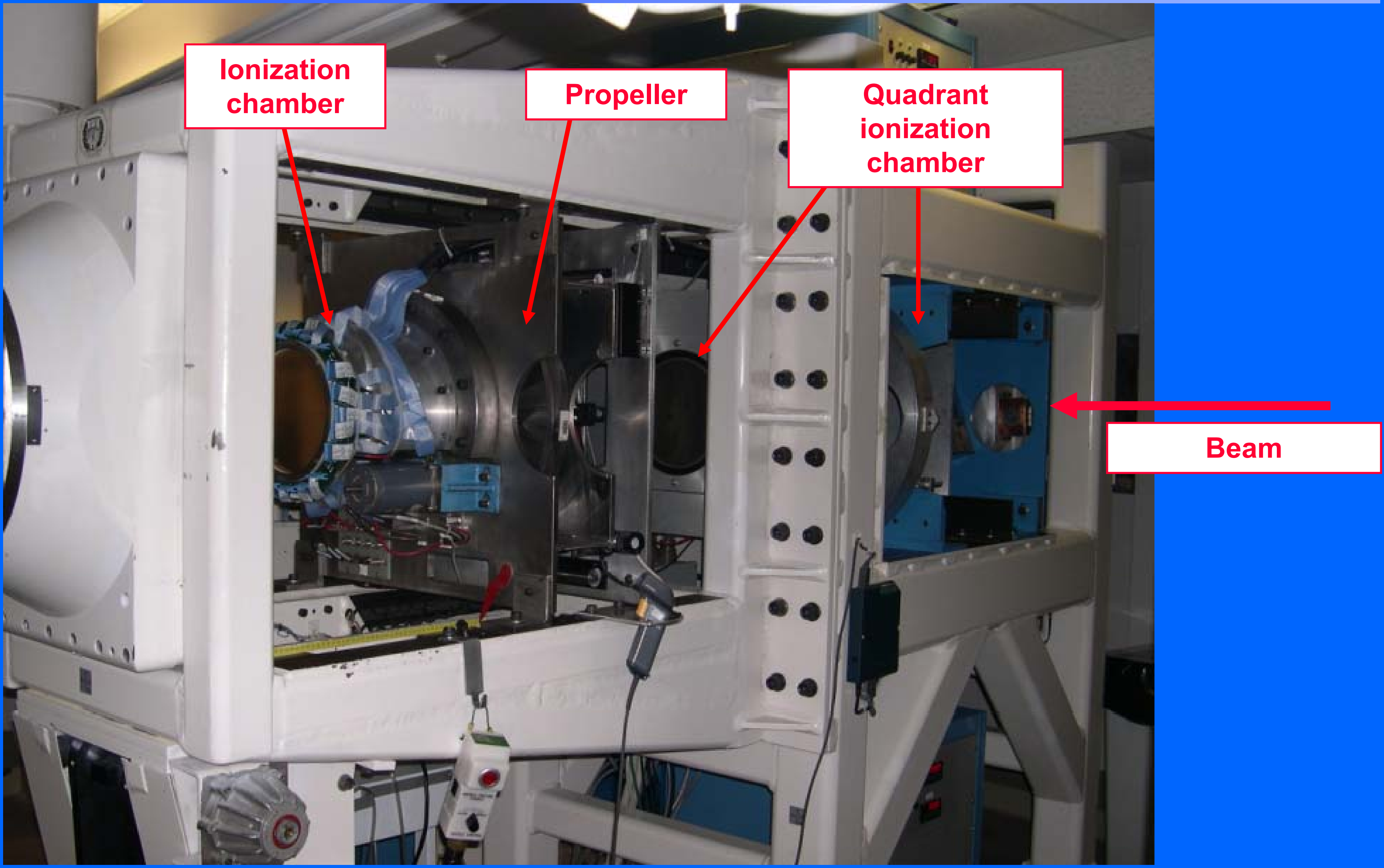


Advanced procedure: layer stacking with respiratory gating

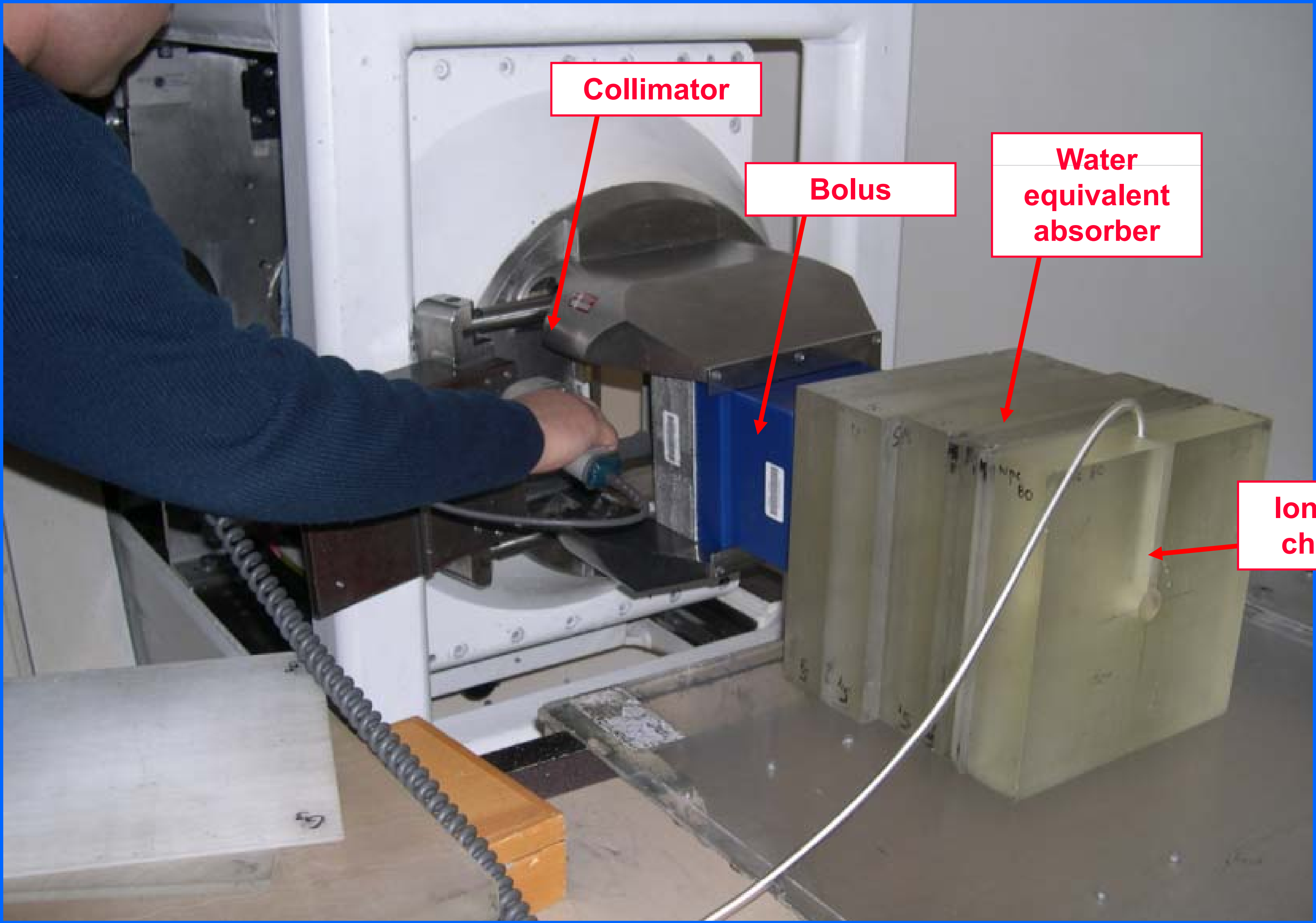


- **Collimator adapted to transverse shape of each slice.**

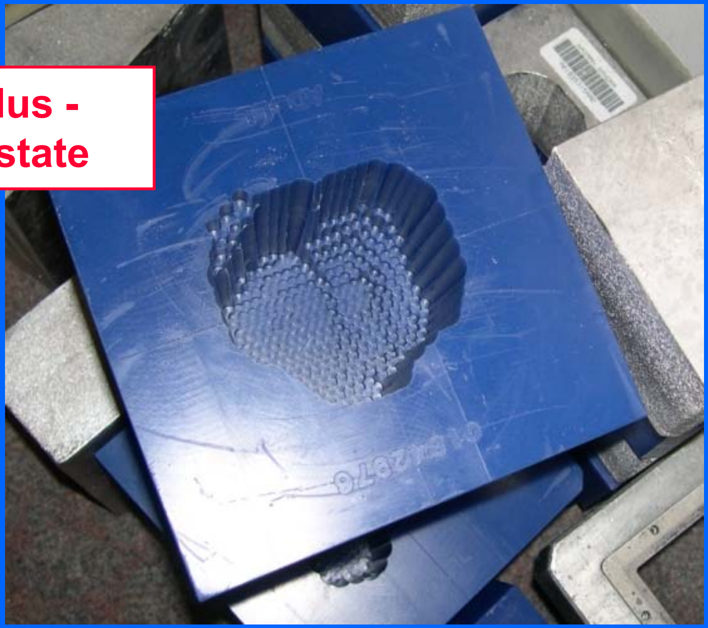
Passive spreading: the nozzle



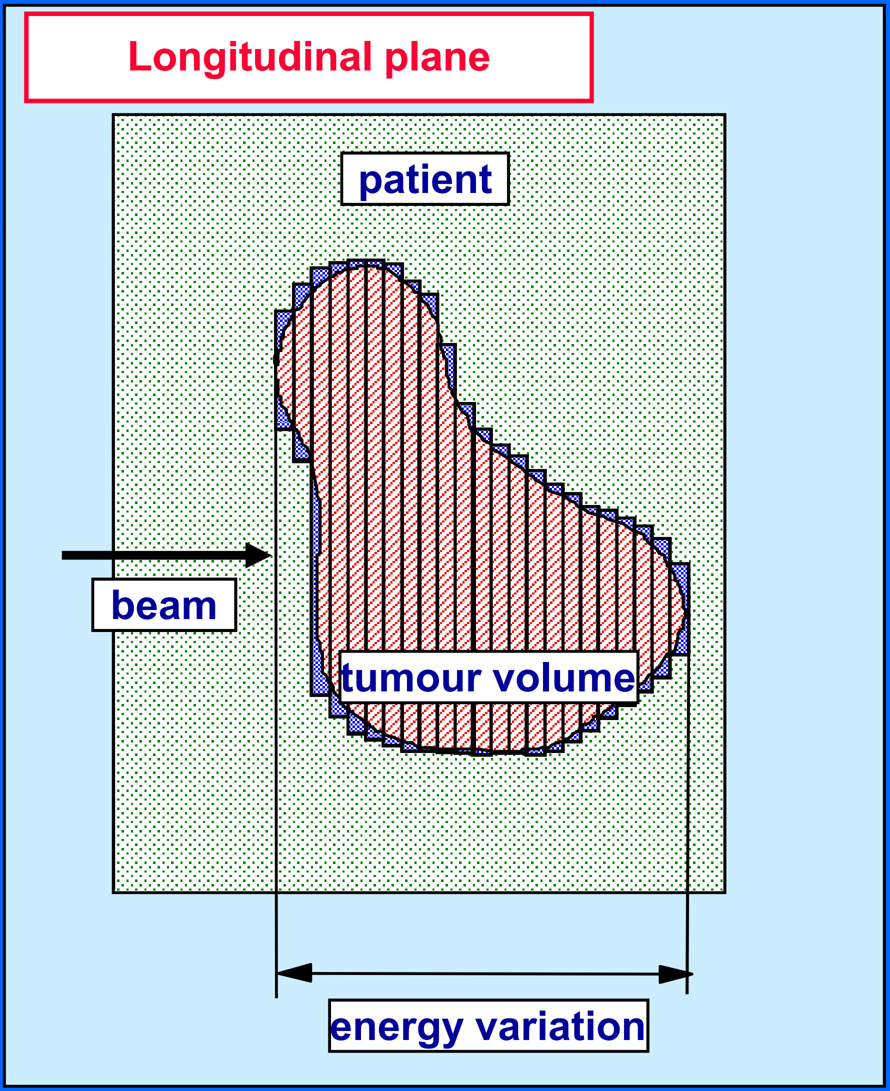
Passive spreading: calibration before treatment

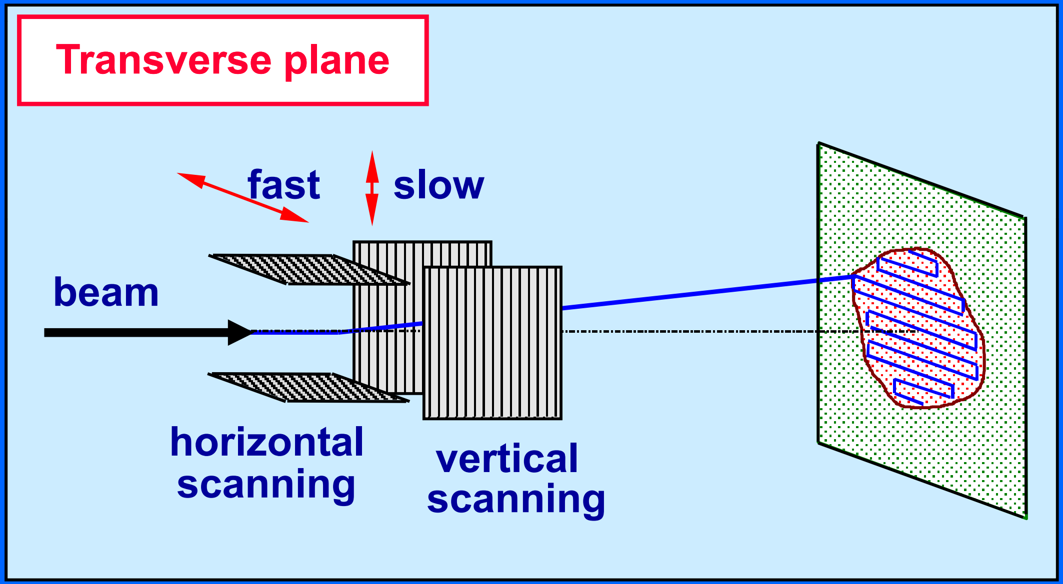


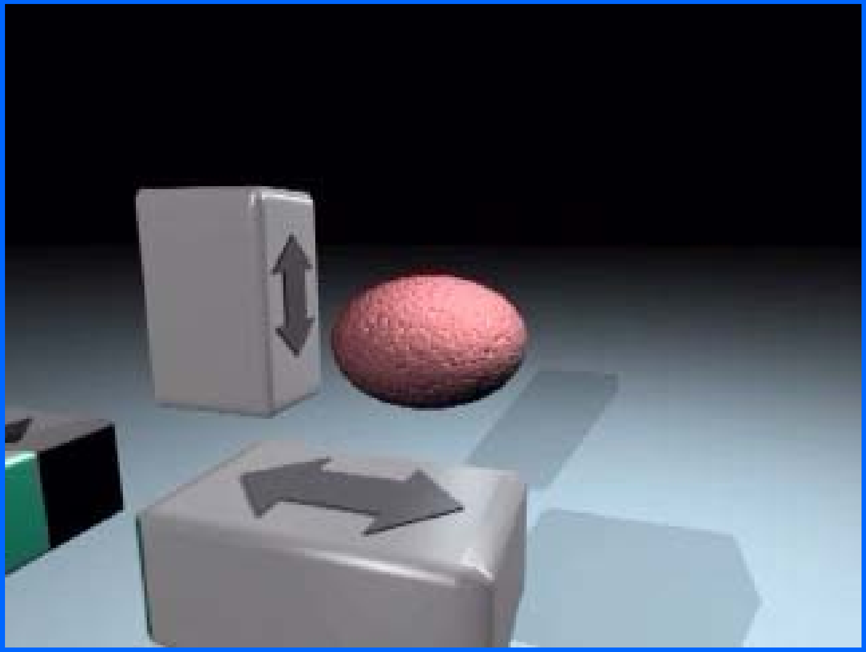
Passive spreading: personalized devices



Dose distribution: active scanning

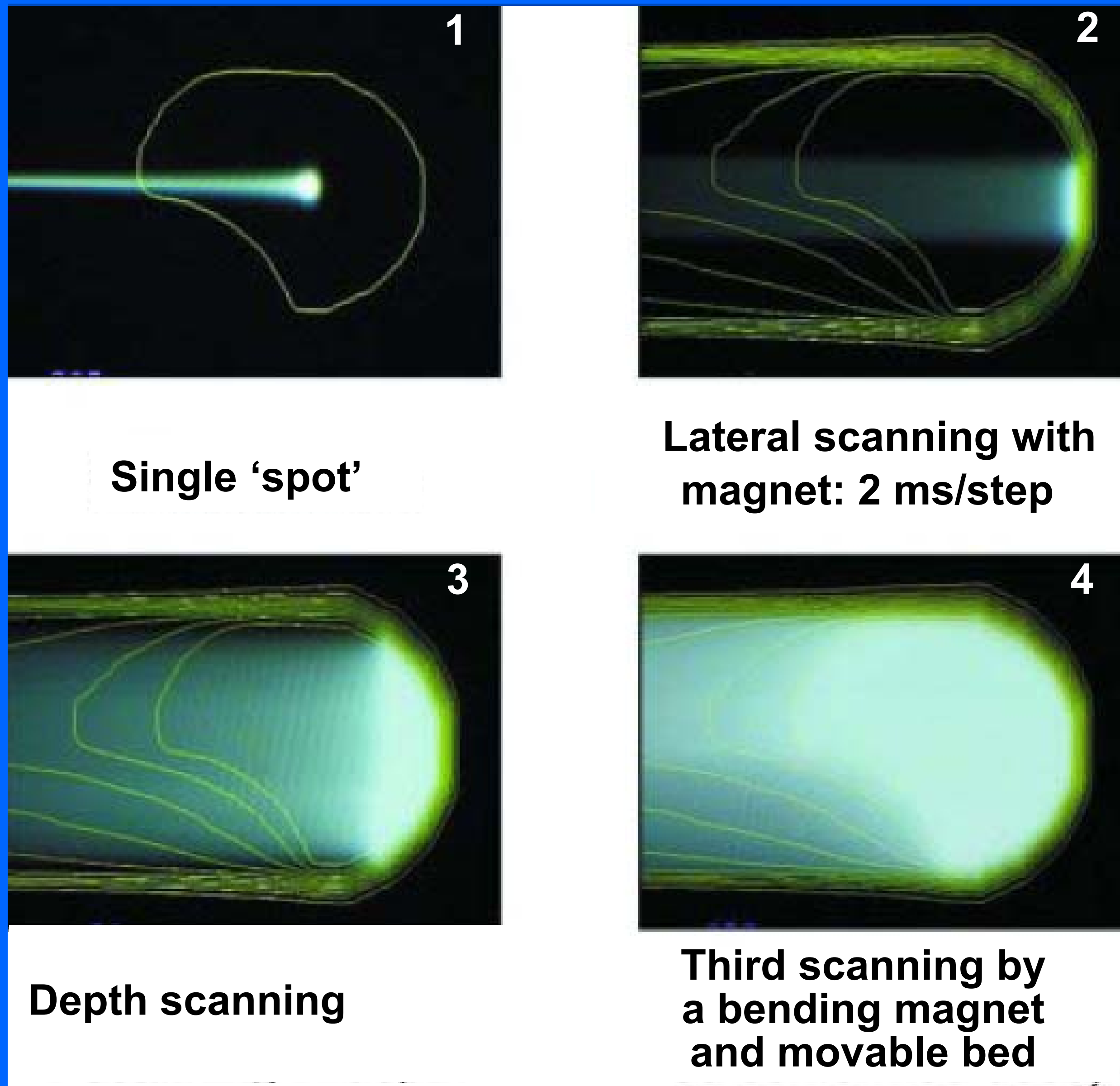


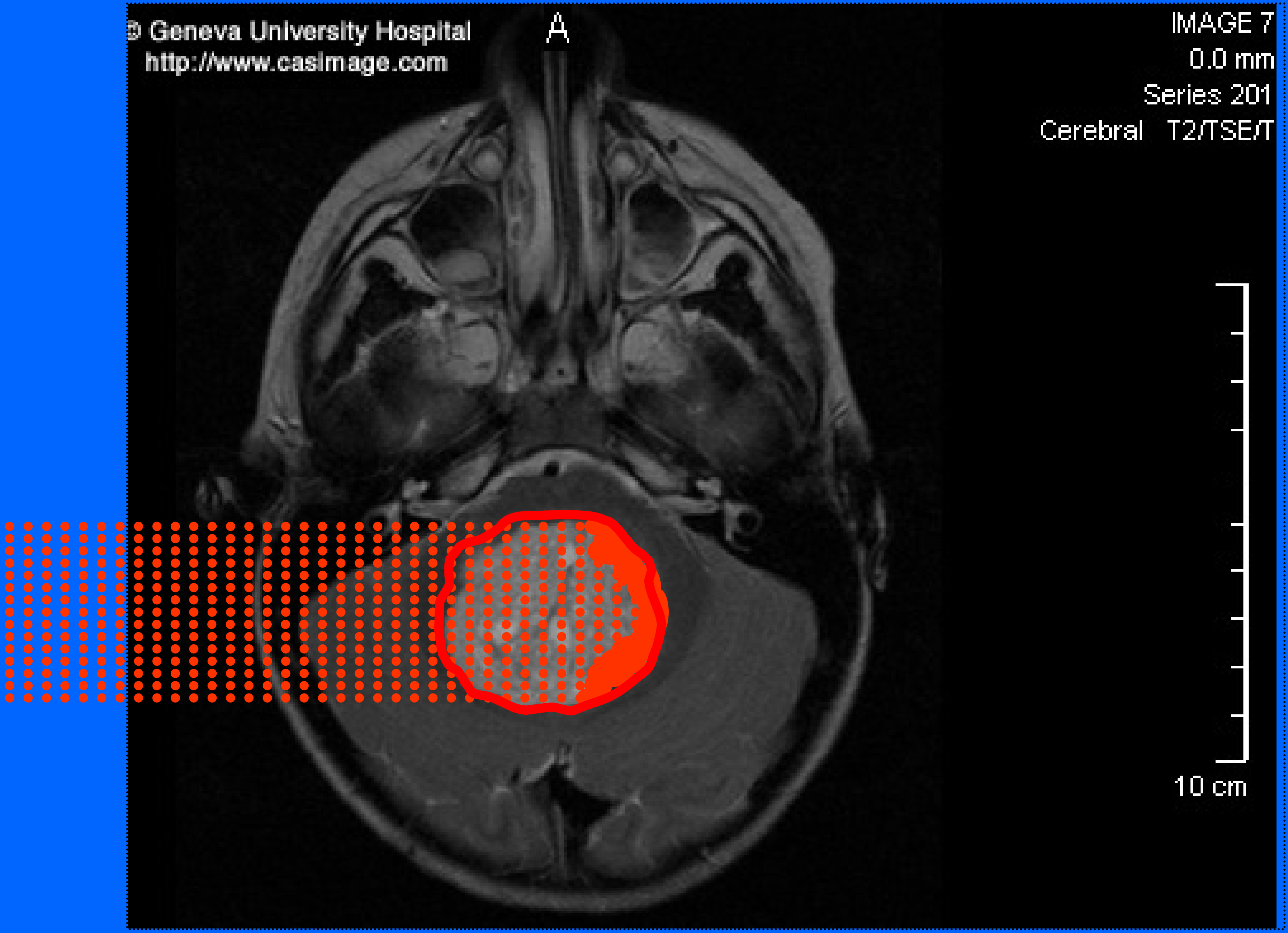




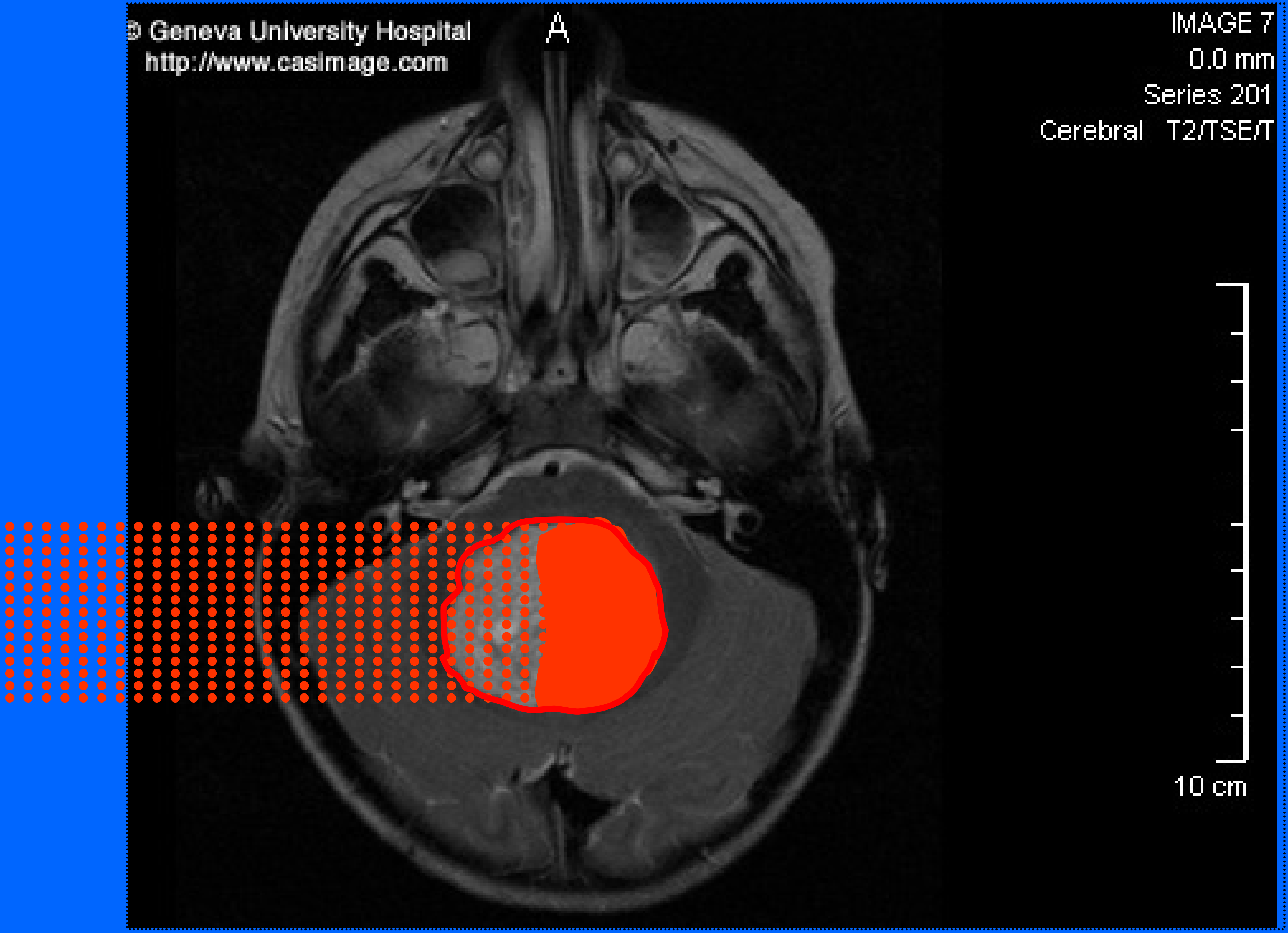
New technique developed mainly at GSI and PSI

Active “spot scanning” a la PSI

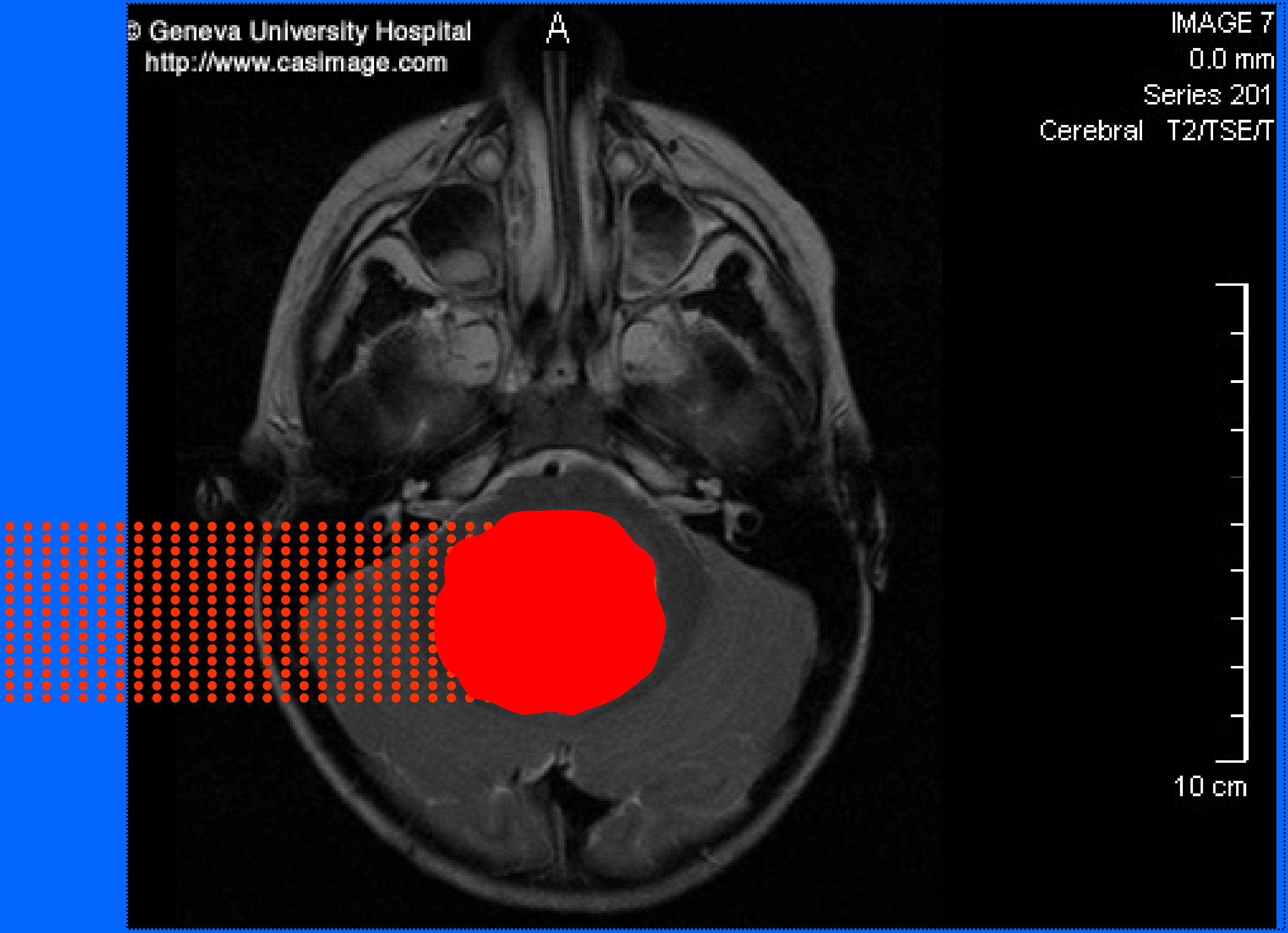




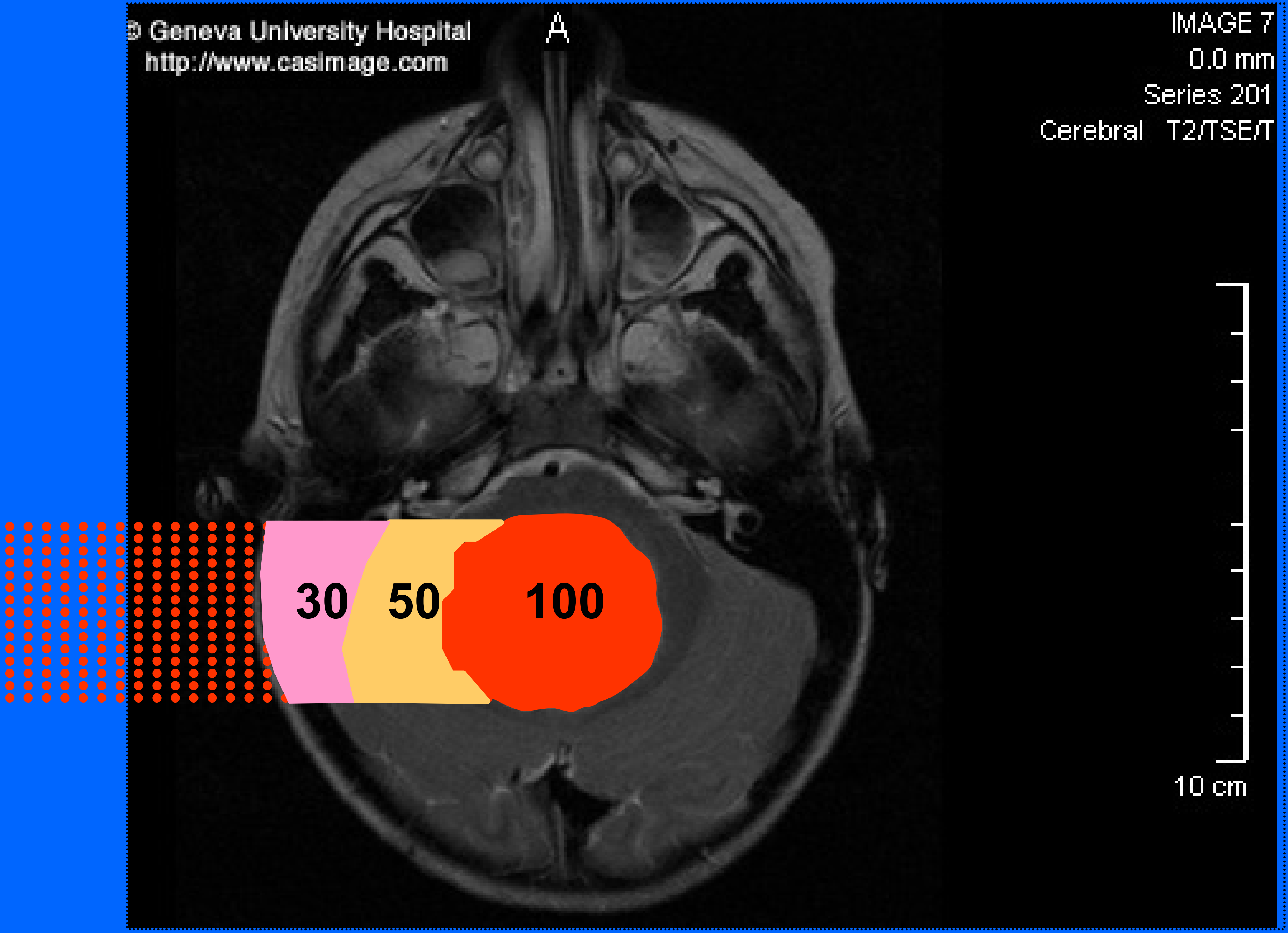
High precision RT with proton beams



High precision RT with proton beams

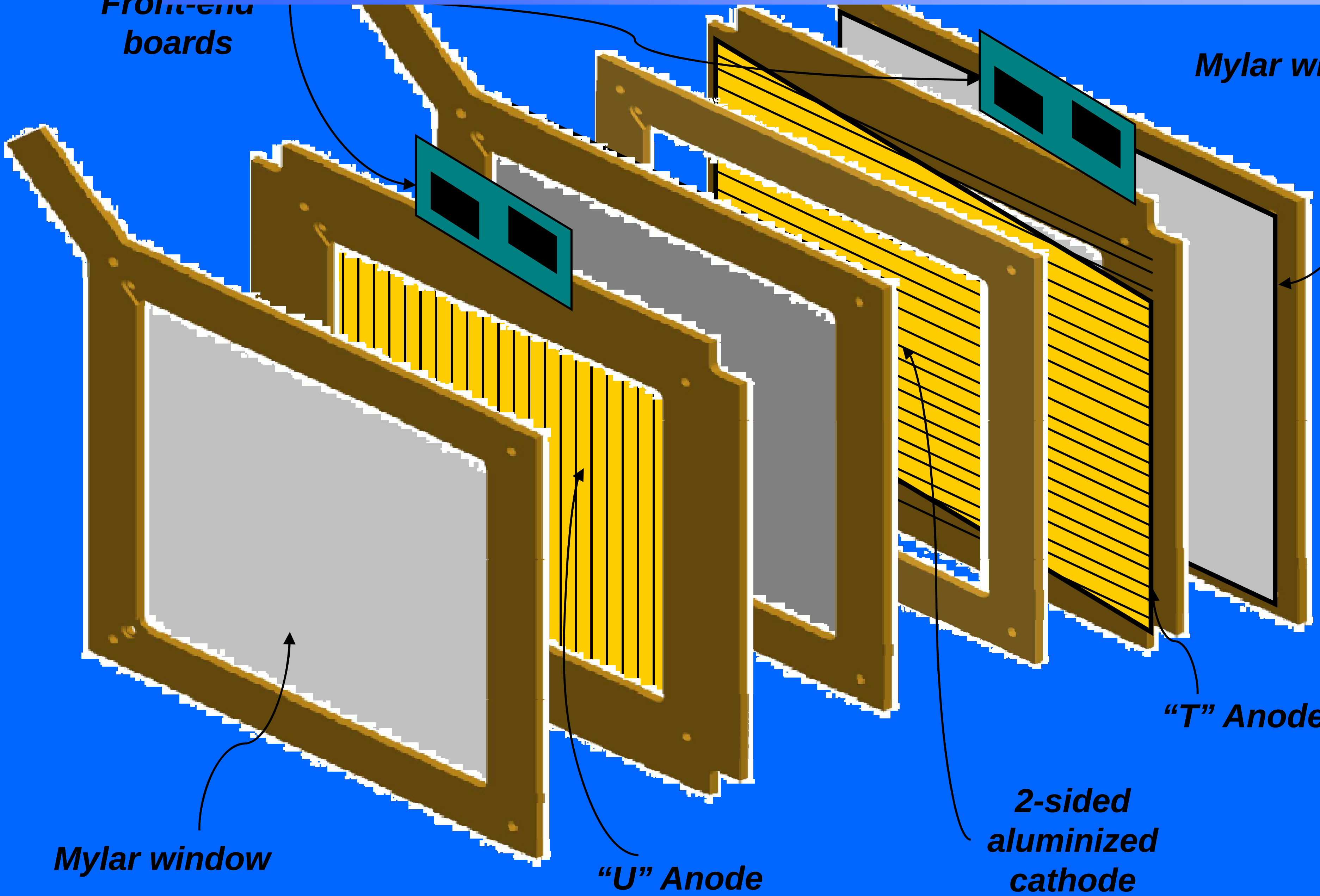


High precision RT with proton beams



High precision RT with proton beams

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

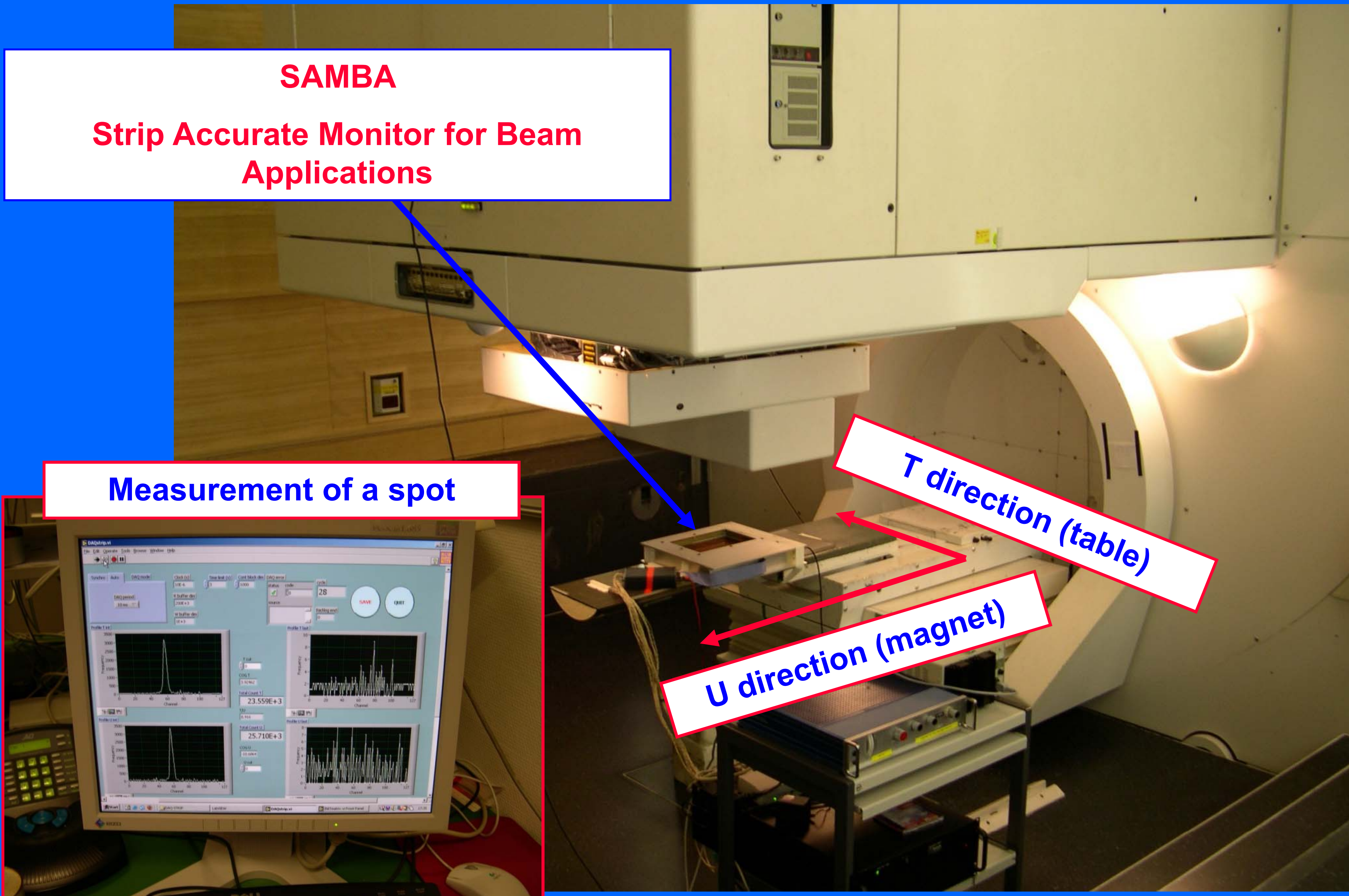


In collaboration with University and INFN Torino

Beam tests on Gantry1 at PSI

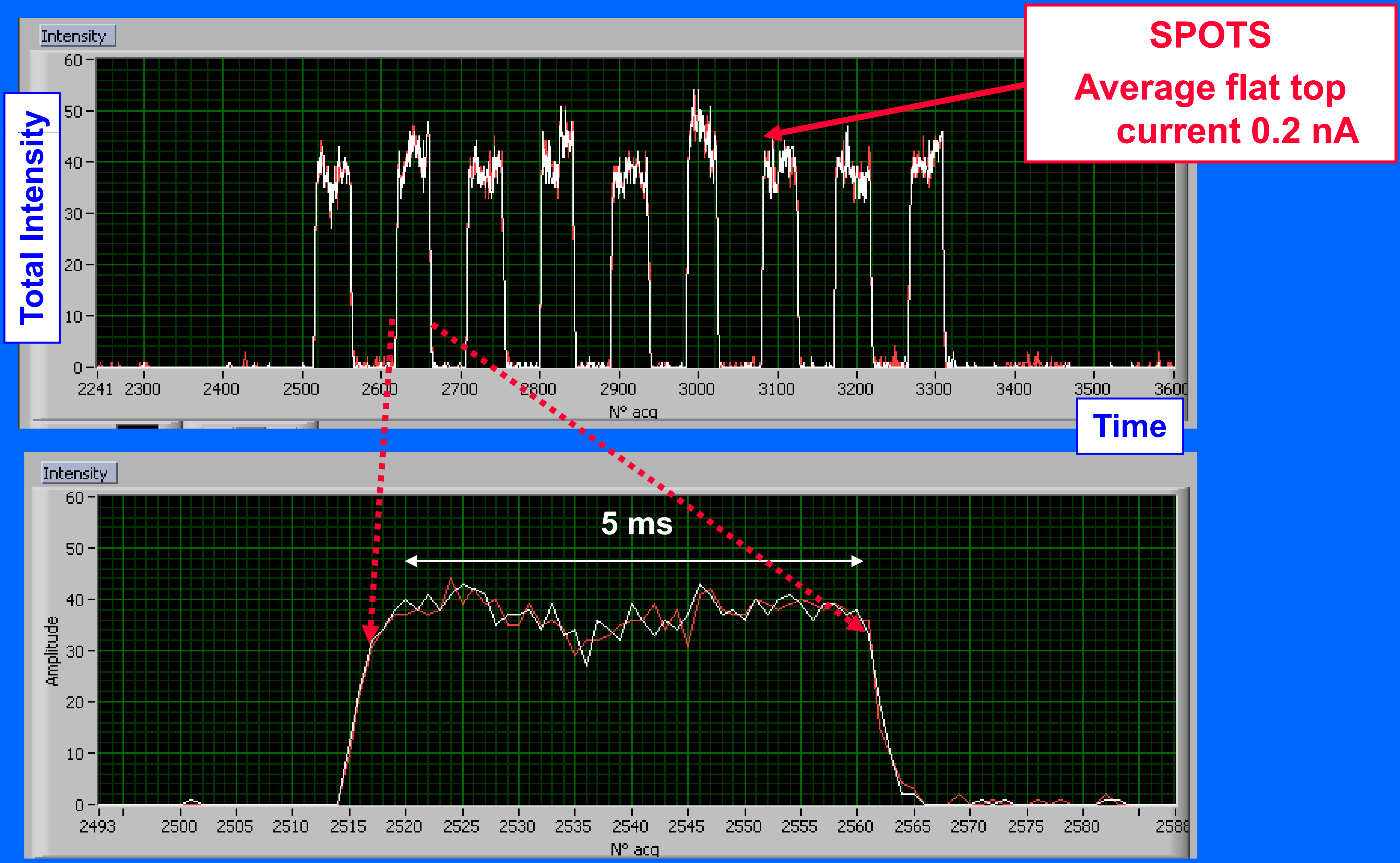
SAMBA

Strip Accurate Monitor for Beam Applications

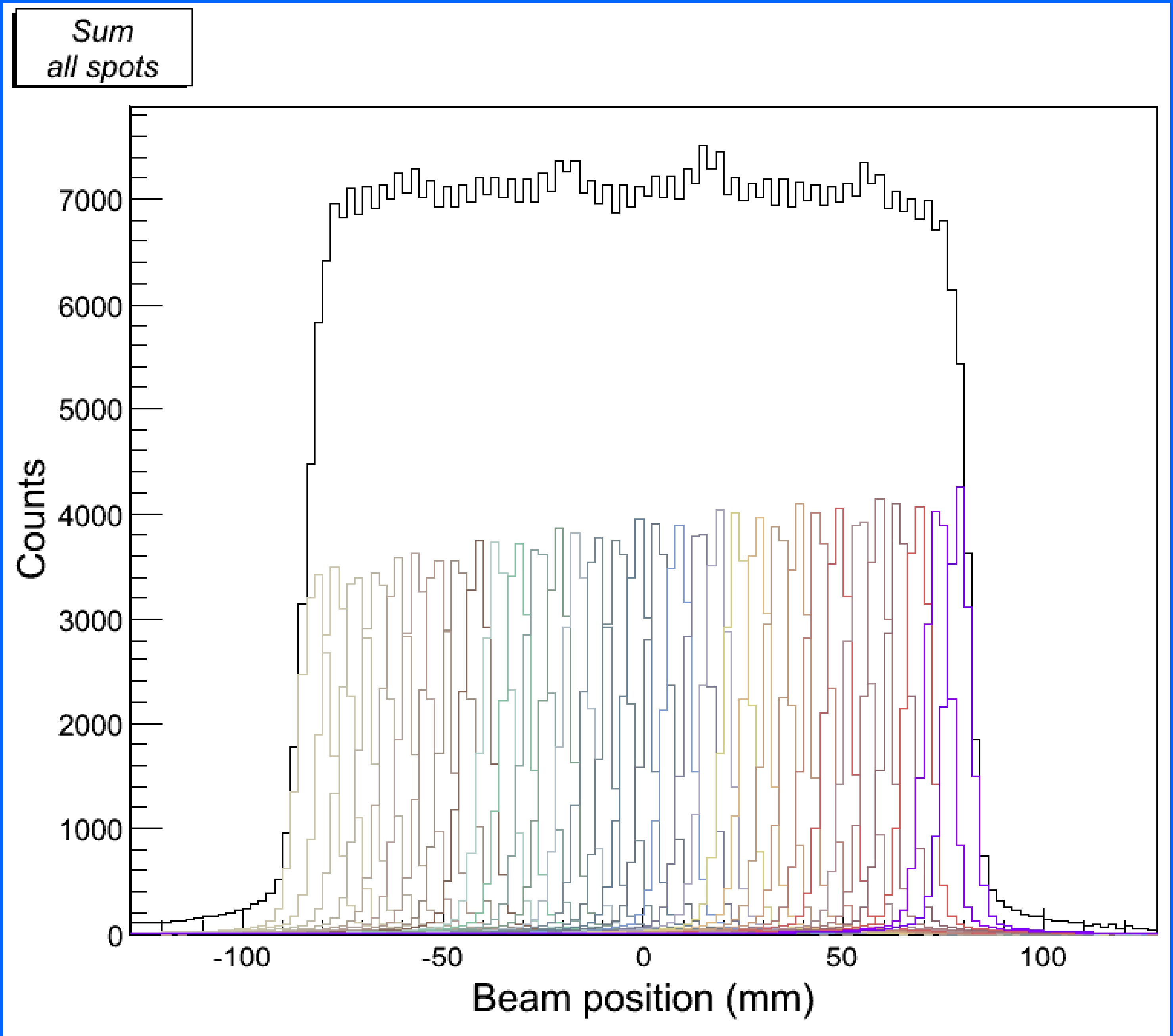


Measurement of a spot

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

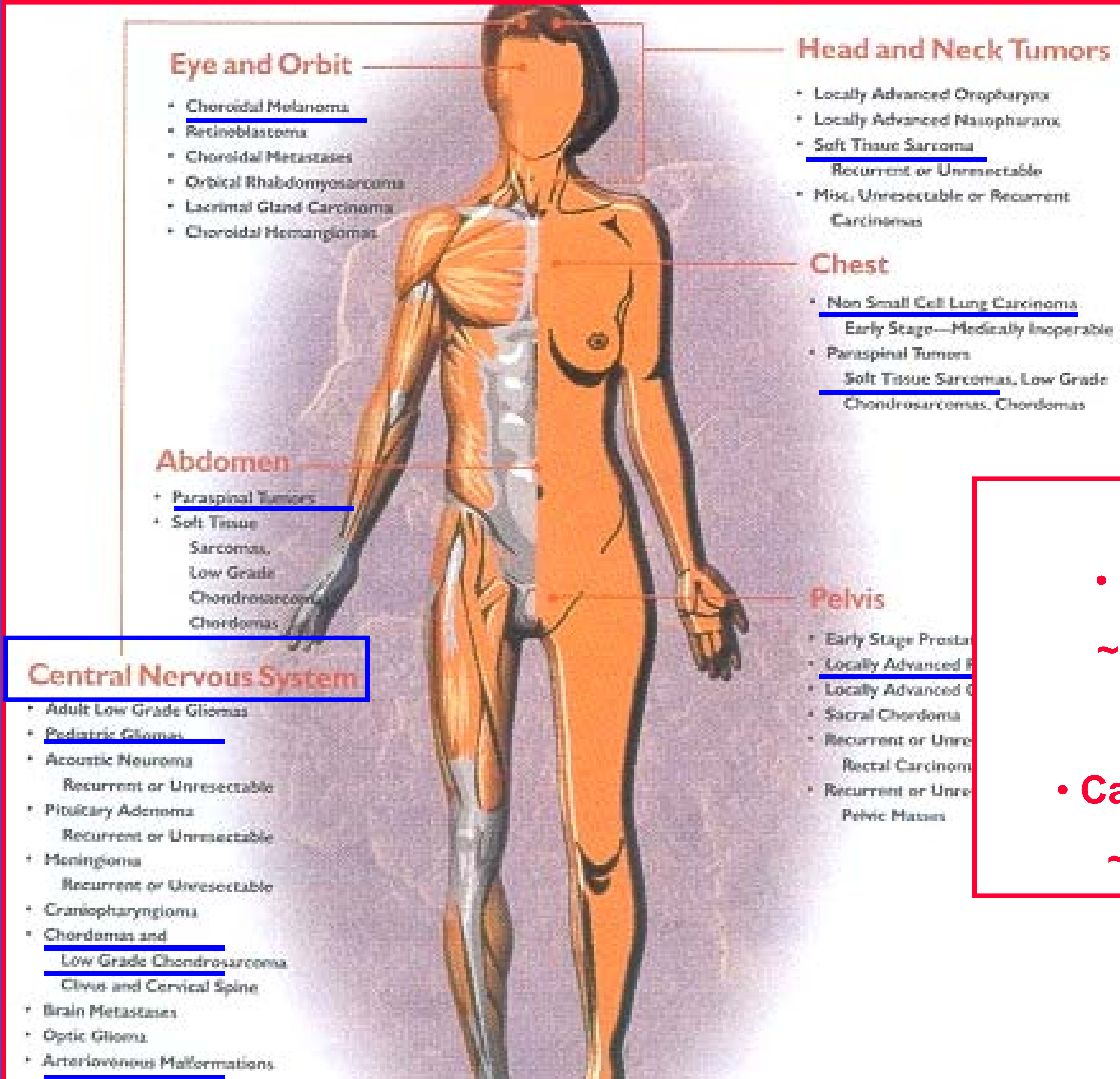
4-5 centres

- Carbon ion therapy

1 centre

TOTAL about 3'500 pts/year every 10 M

The sites



Up to present

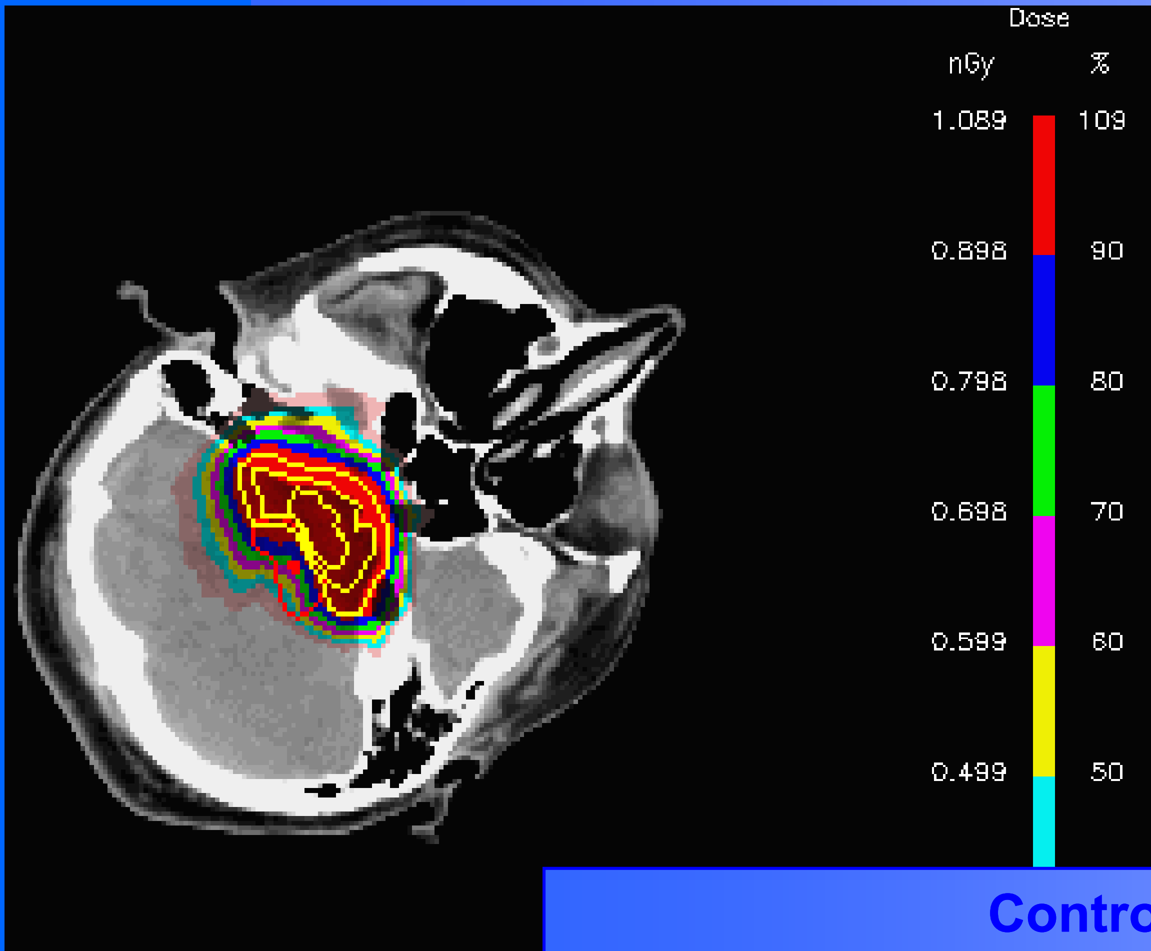
- **Proton-therapy:**

  ~ 45 000 patients

- **Carbon ion therapy:**

  ~ 2 200 patients

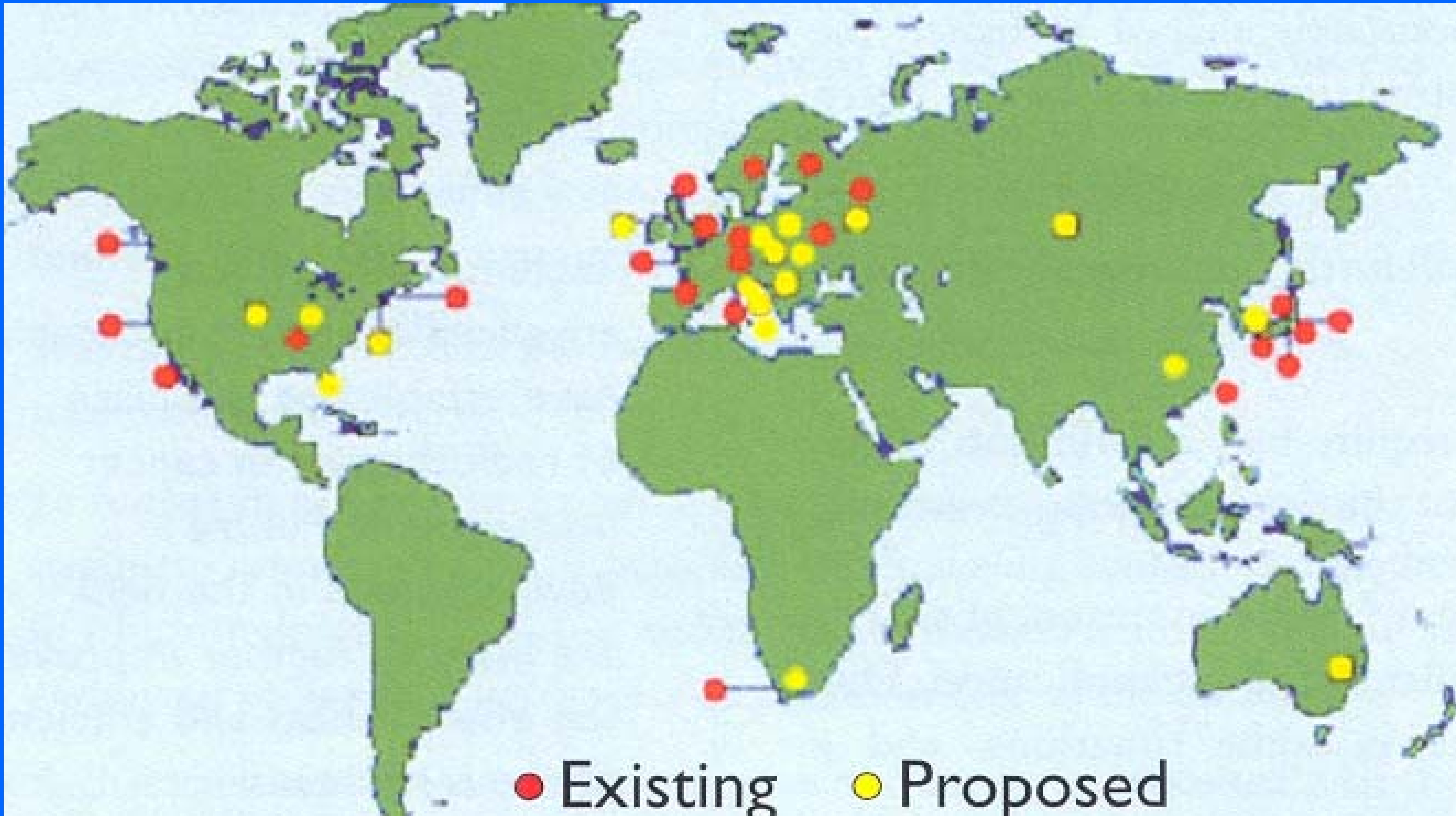
Tumours of the central nervous system



Control at 5 years

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

The map of hadrontherapy

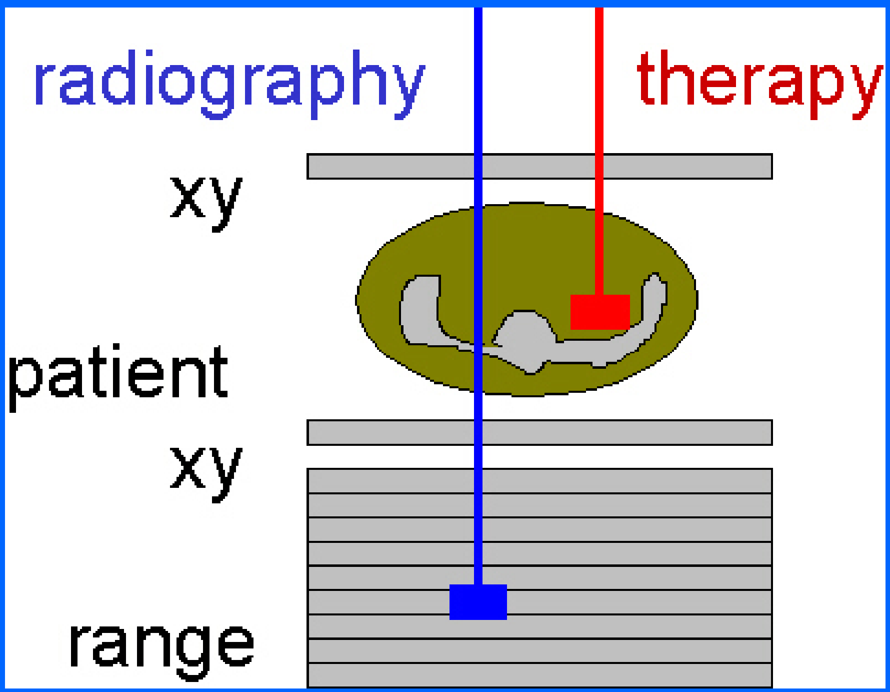


What a patient sees…

A ganrty for proton therapy

A research topic: proton radiography

- CT gives information on the density of electrons (Hounsfield numbers)
- CT is commonly used in diagnostics
- CT is commonly used in conventional radiation therapy to calculate the treatment planning
  - X and MeV gamma rays interact with the electrons
- CT is used also in proton and ion therapy to calculate the treatment planning but…
  - Protons and ions interact with matter through dE/dx -> density ρ, Z
  - Compton effect is proportional to Z but not the photoelectric effect !
  - Corrections are applied

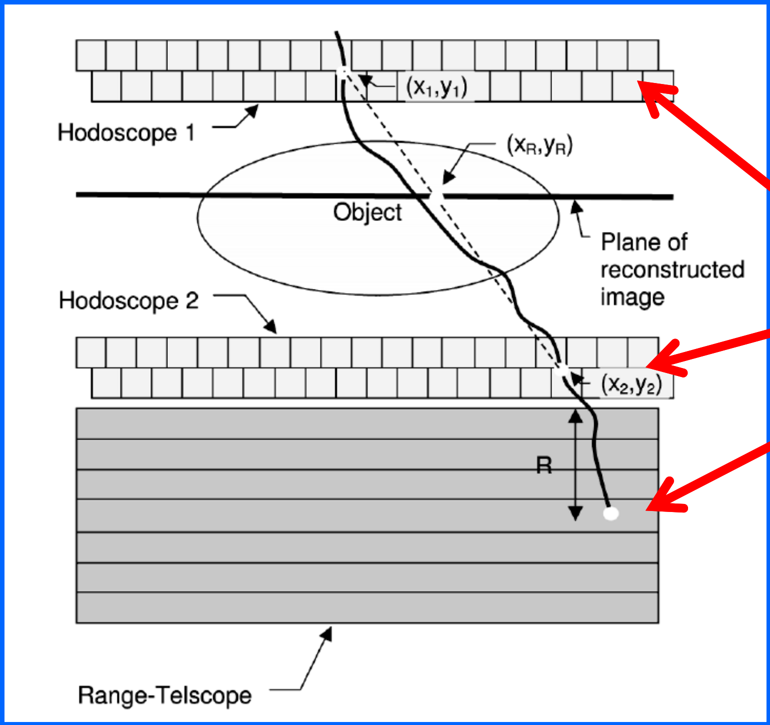


Radiography with X-rays

- **"Counts" the number of photons (attenuation coefficient)**

Proton radiography

- **Protons with enough energy to penetrate the body**
- **Residual range mesurement**



Scintillating fibers

E. Pedroni et al., PSI

Advantages

- No need for corrections like for X-ray CT
- Less dose to the patient (every proton brings information!)

Disadvantages

- Need of large accelerators usually used also for therapy (timing problem)
- For now it is a research issue (PSI)

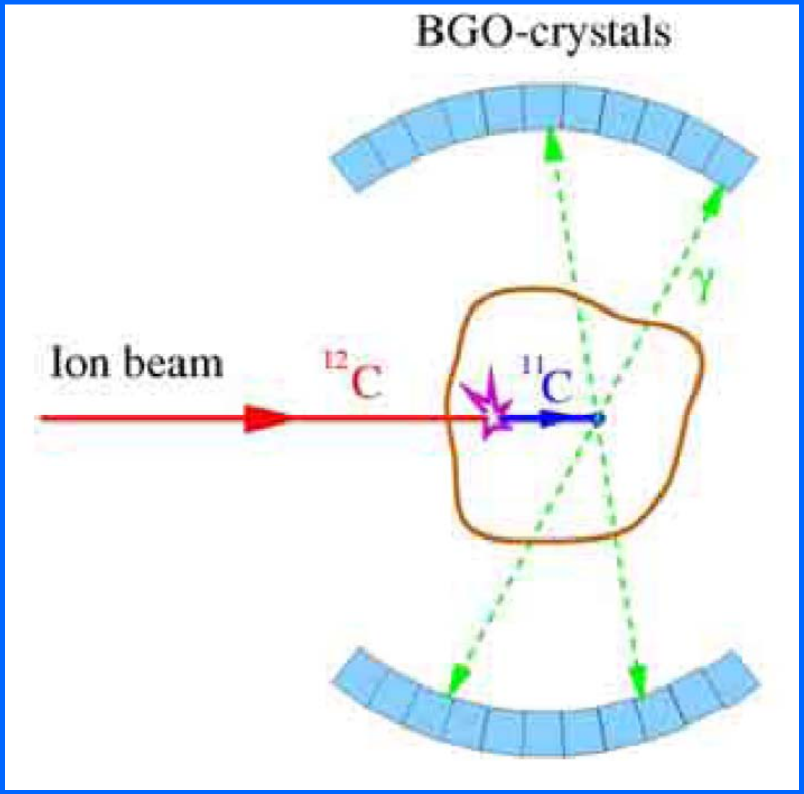
Carbon ion therapy in Europe

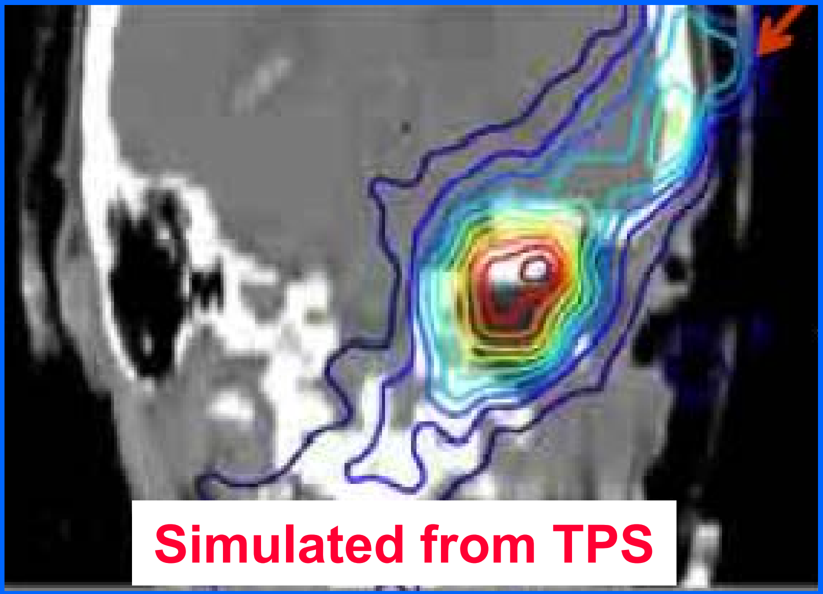
1998 - GSI pilot project (G. Kraft)

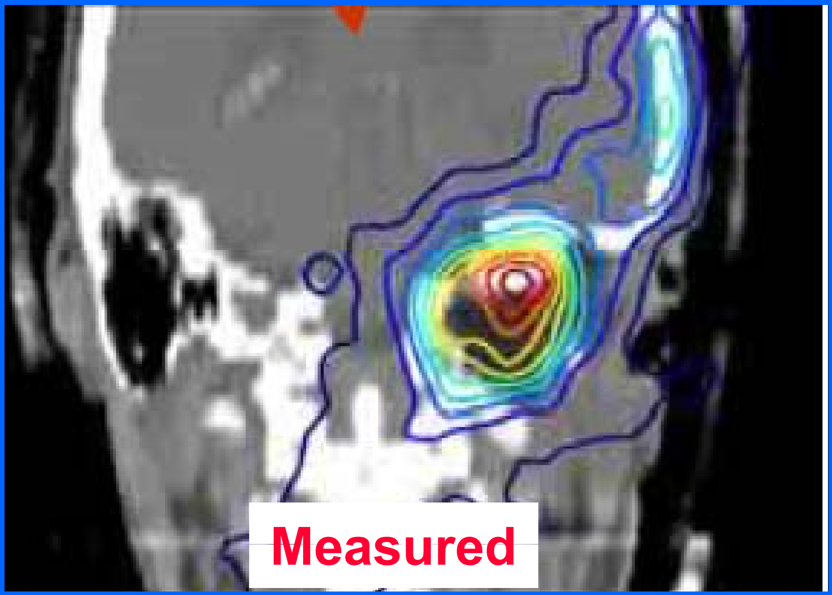
200 patients treated with carbon ions

PET on-beam

PET on-beam

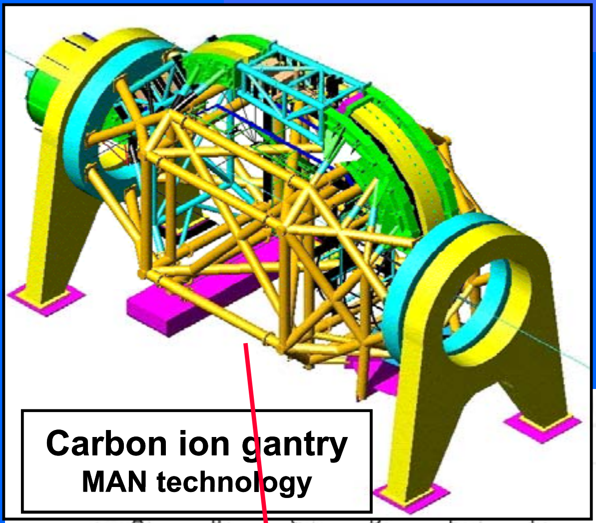


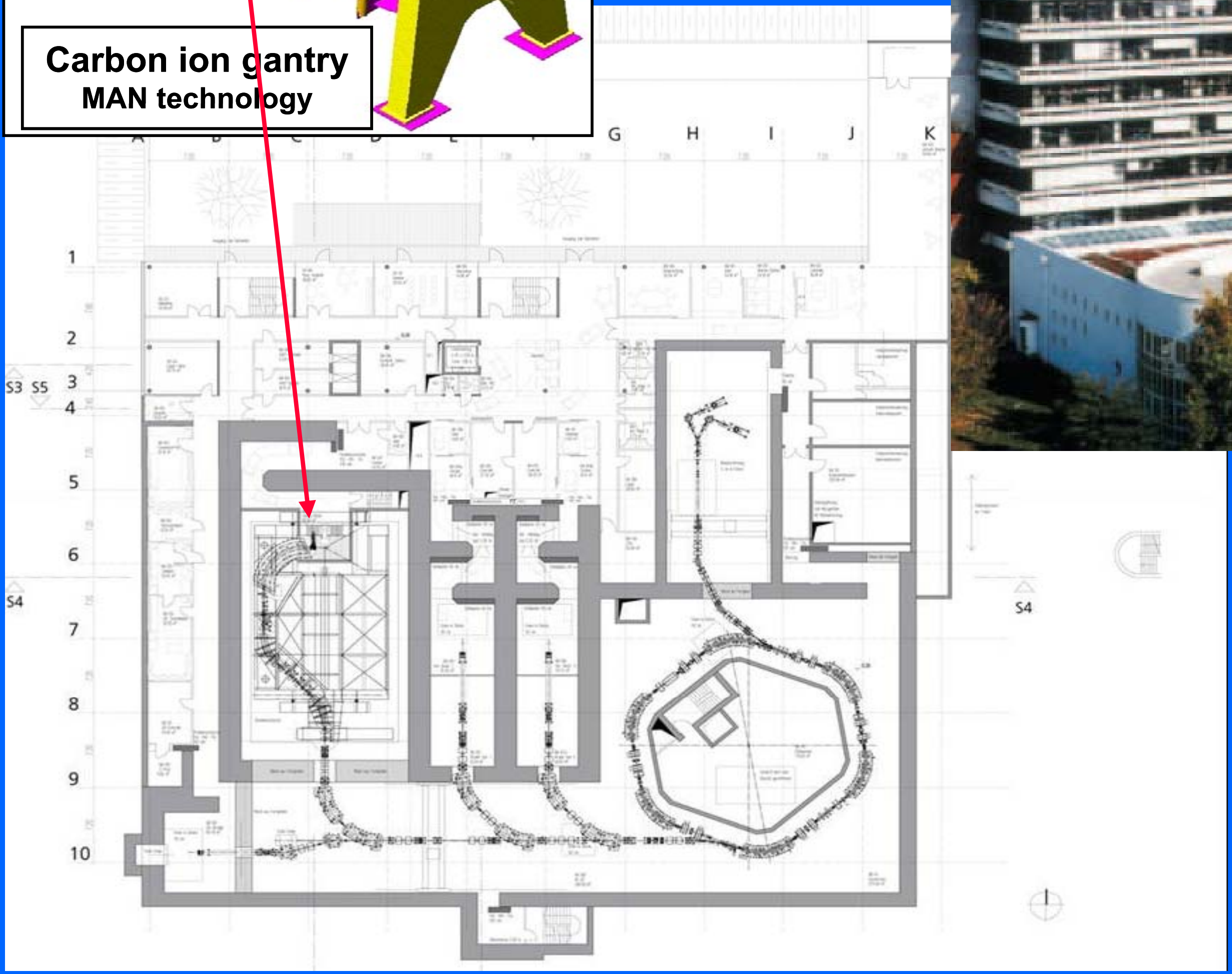




Measurement of the ”real” dose given to the patient

HIT – University of Heidelberg





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

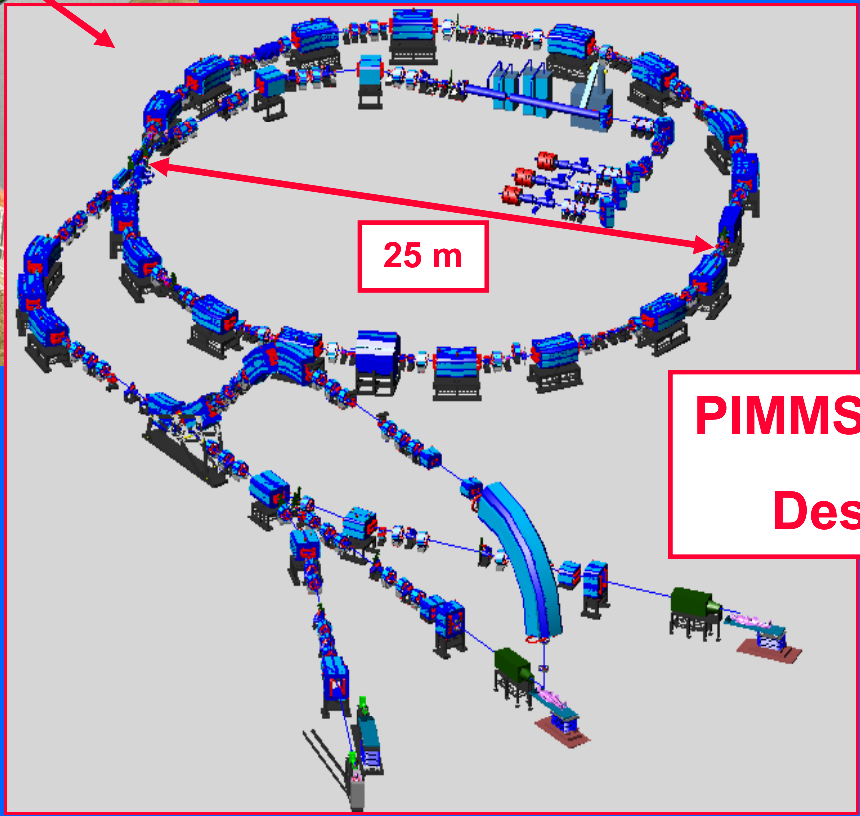
The TERA Foundation

- **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**

Ugo Amaldi

CNAO on the Pavia site

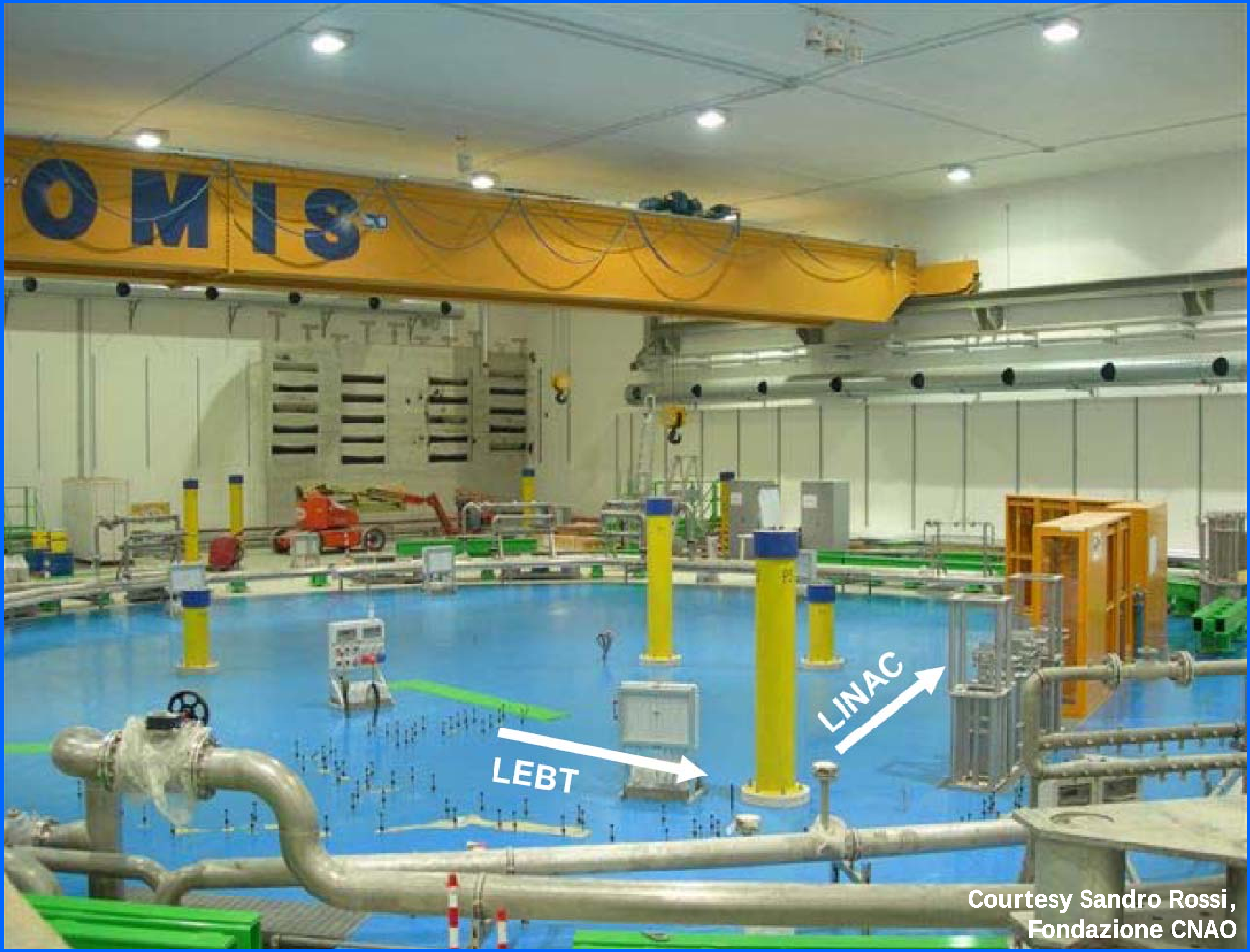
- Main source of funds:
Italian Health Ministry
- Ground breaking: March 2005



PIMMS/TERA Design

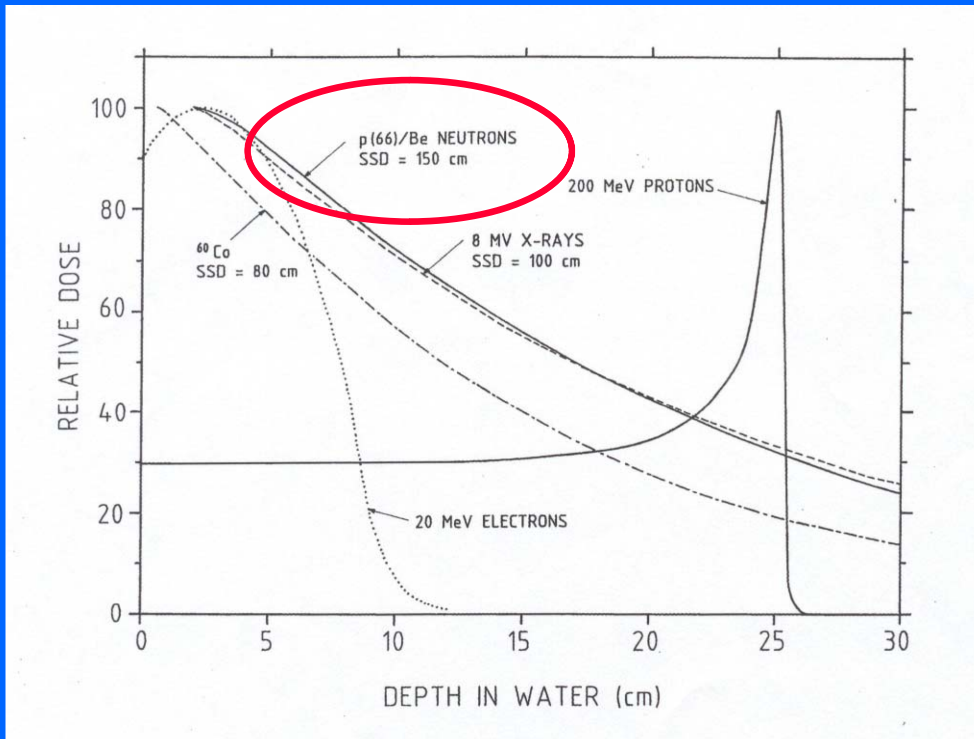
- Hospital based centre
- Protons and carbon ions

CNAO synchrotron hall in March 2007



Neutrons in cancer therapy

Hadrontherapy with fast neutrons



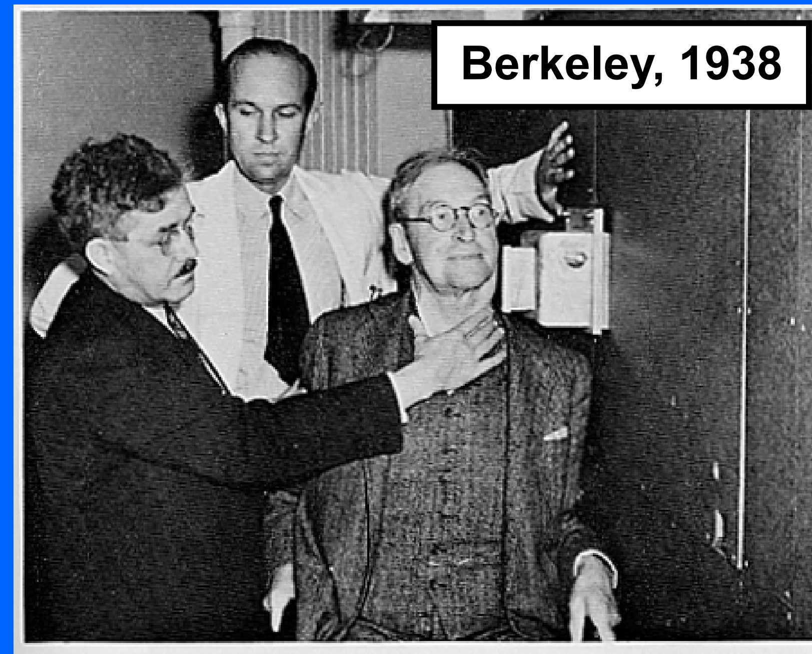
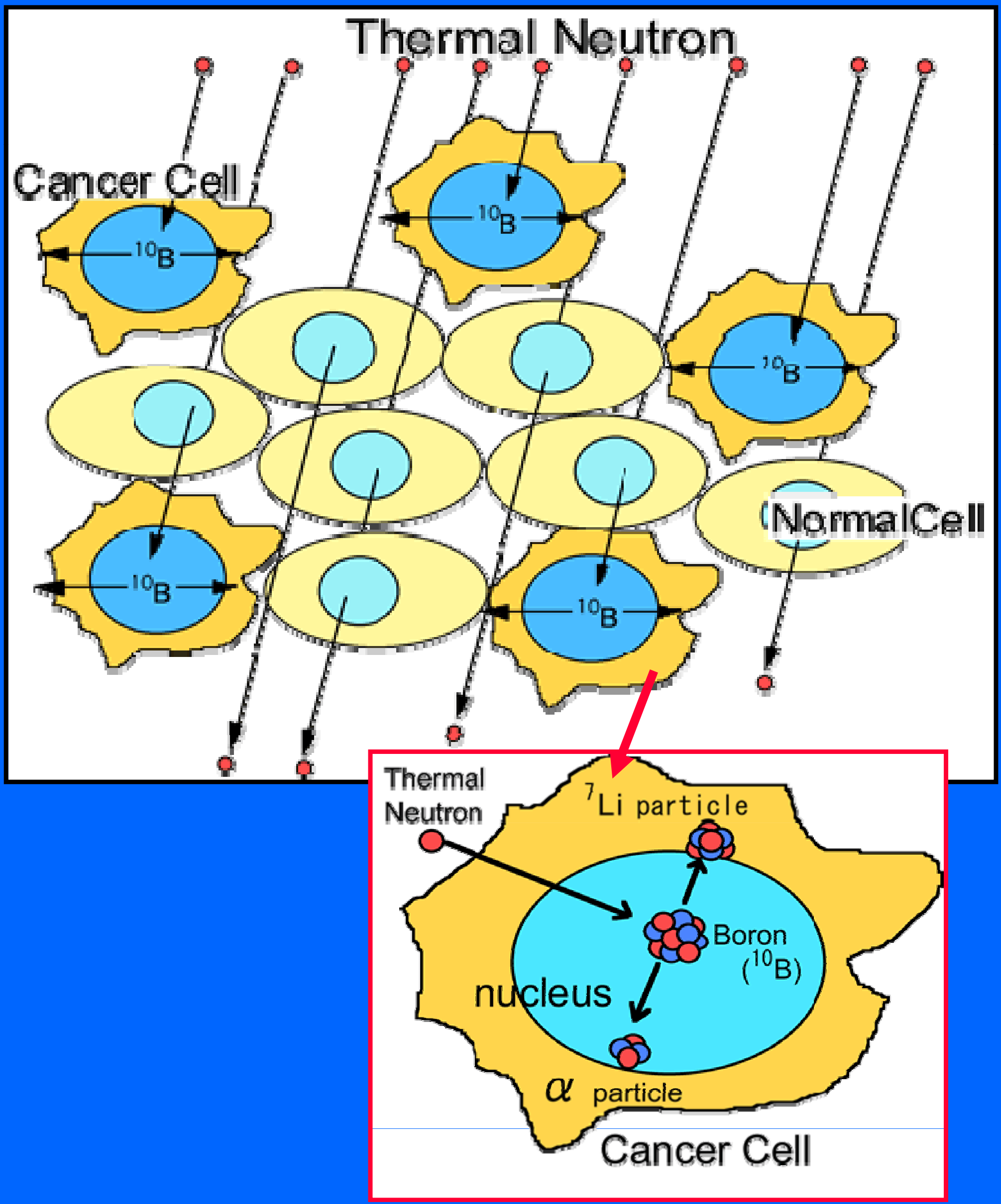


PLATE 8.4 Robert Stone and John Lawrence treating Robert Penney at the 60-inch neutron port. LBL.

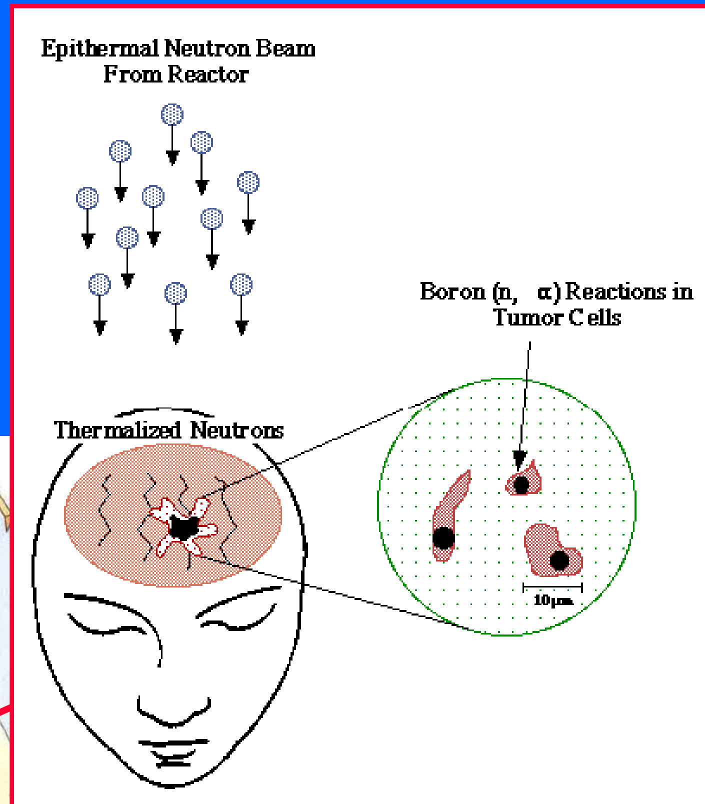
- Neutrons are neutral → no Bragg peak
- MeV neutrons are produced with cyclotrons (p + Be reaction)
- MeV neutrons produce nuclear interactions → high LET radiation
- Used for radio resistant tumours (ex. salivary glands, tongue, brain)
- About 9 centers in the world [ex. Orleans (France), Fermilab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

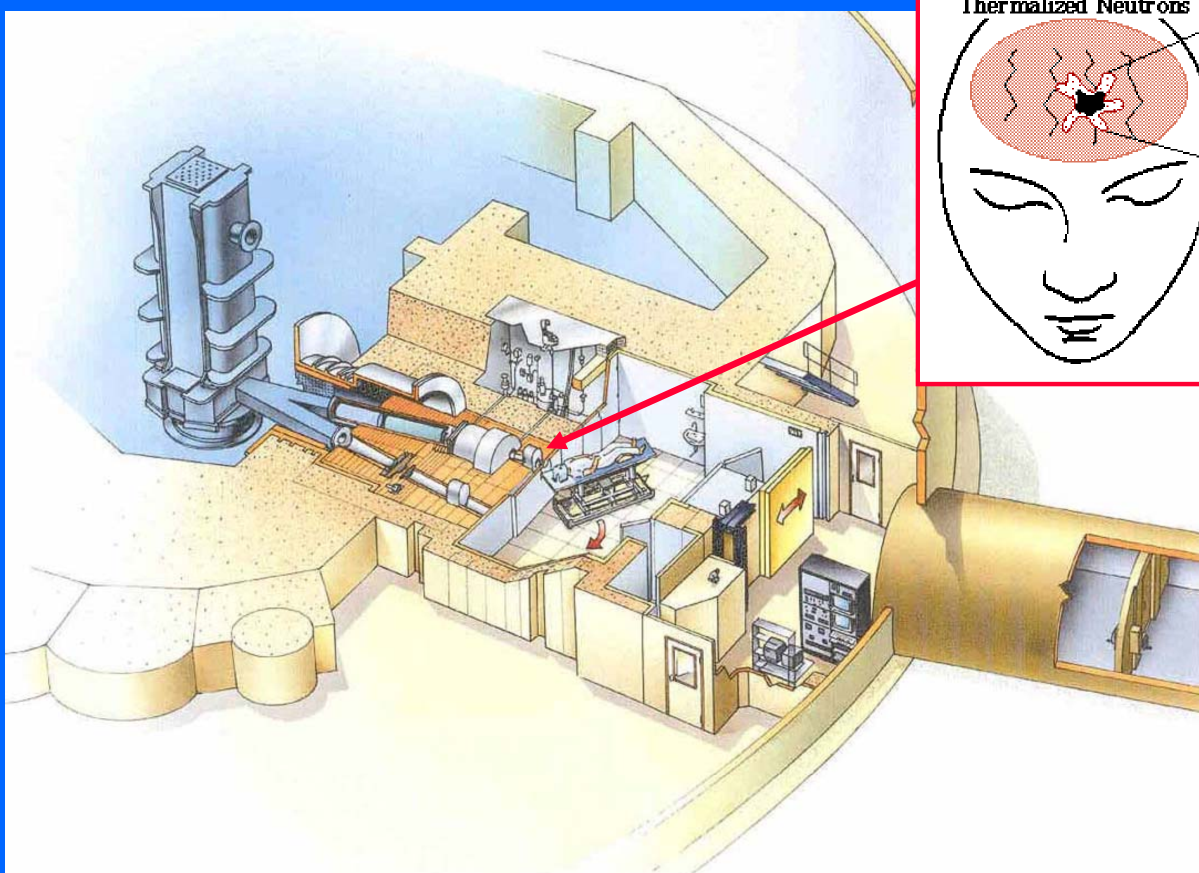
Boron Neutron Capture Therapy (BNCT)



- 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

- 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 !

End of part V