Particle therapy Critical issues and Challenges

P. Le Dû

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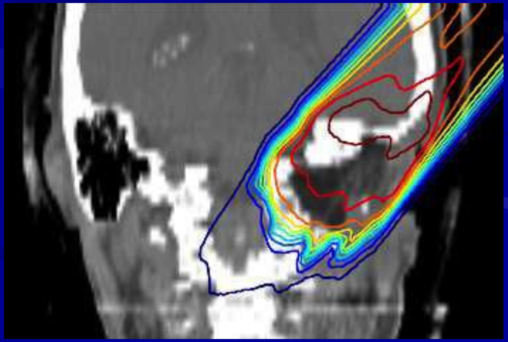
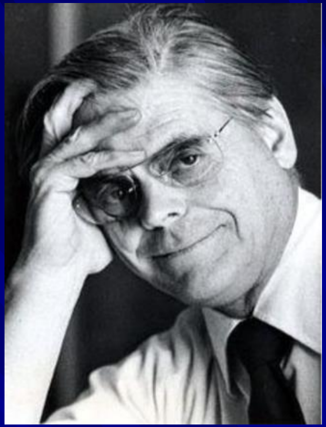
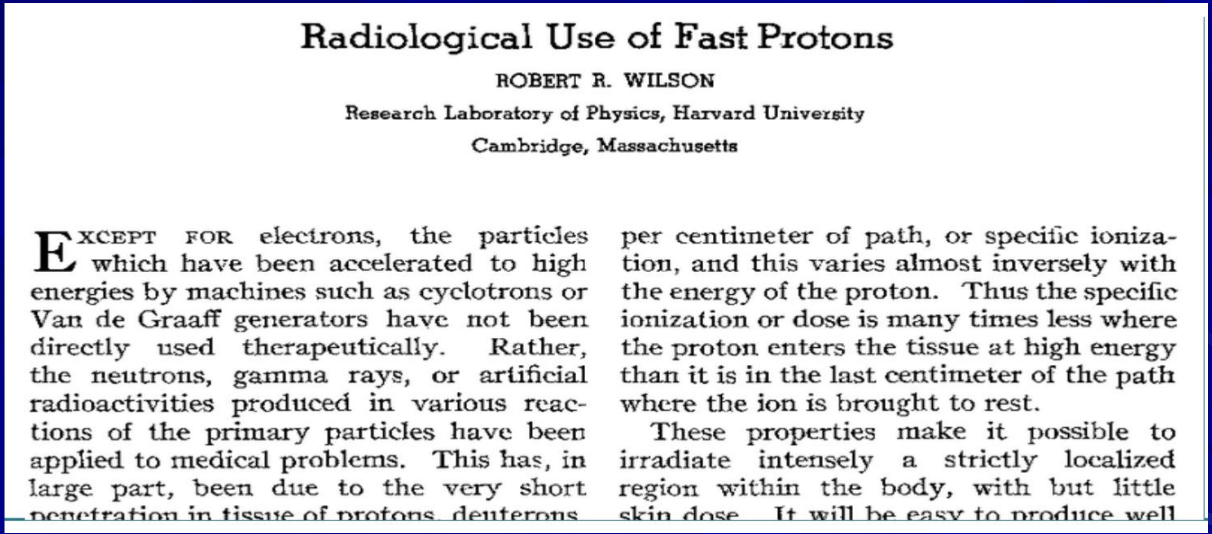


History of Hadrontherapy

- 1946: R. Wilson first proposed a possible therapeutic application of proton and ion beams
- 1954: first patient treated with deuteron and helium beams at Lawrence Berkeley Laboratory (LBL)





Radiological Use of Fast Protons

ROBERT R. WILSON

Research Laboratory of Physics, Harvard University

Cambridge, Massachusetts

EXCEPT FOR electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reactions of the primary particles have been applied to medical problems. This has, in large part, been due to the very short penetration in tissue of protons, deuterons

per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

These properties make it possible to irradiate intensely a strictly localized region within the body, with but little skin dose. It will be easy to produce well

R. Radiologial use of fast protons, Radiology 47, 487-491, 1946

Treating Cancer

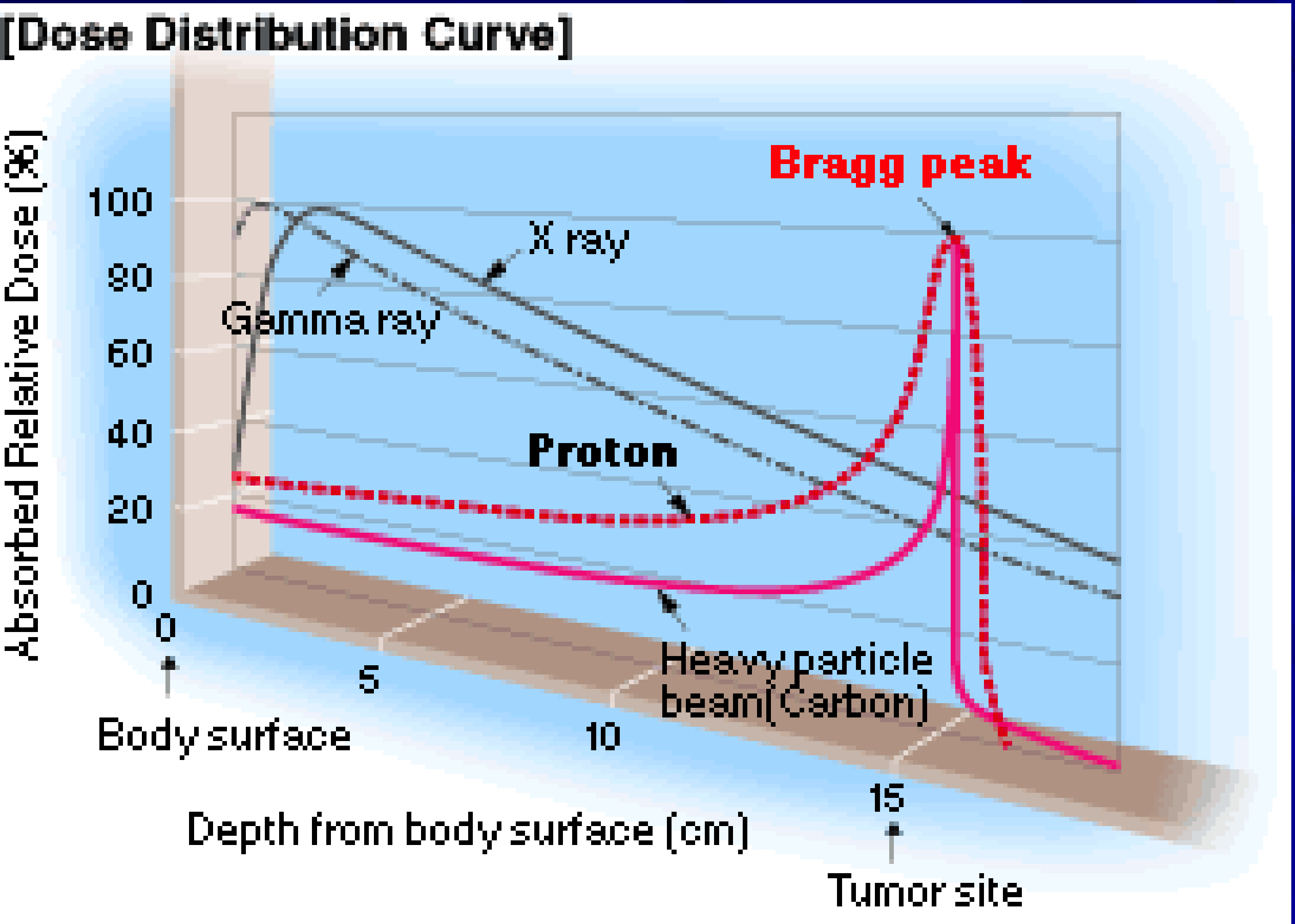
- Radiotherapy X
  - Local irradiation → 100 Gy = 90 % of sterilization
  - Frequent treatment (2/3 of cases).
  - Allow good quality of life and tolerance
  - non invasive, itinerant and without important physical effects.
  - Cheap (< 10%) of the cancer budget (France)
  - Essentially X rays (Linear accelerators) & photons (curietherapy)
  - **Efficient treatment but ….**

Particle therapy: The Context

- *Why Radiotherapy X is NOT 100 % efficient?*
  - Complication < 5 %
  - Tolerance of saine tissue is the limiting factor
    - Close to Organ at Risk
  - Failures due to radioresistant tumors!
  - Second cancer 30 years after Radio Therapy (from recent statistics)
    - Adult : 1.1
    - Chidren : 6

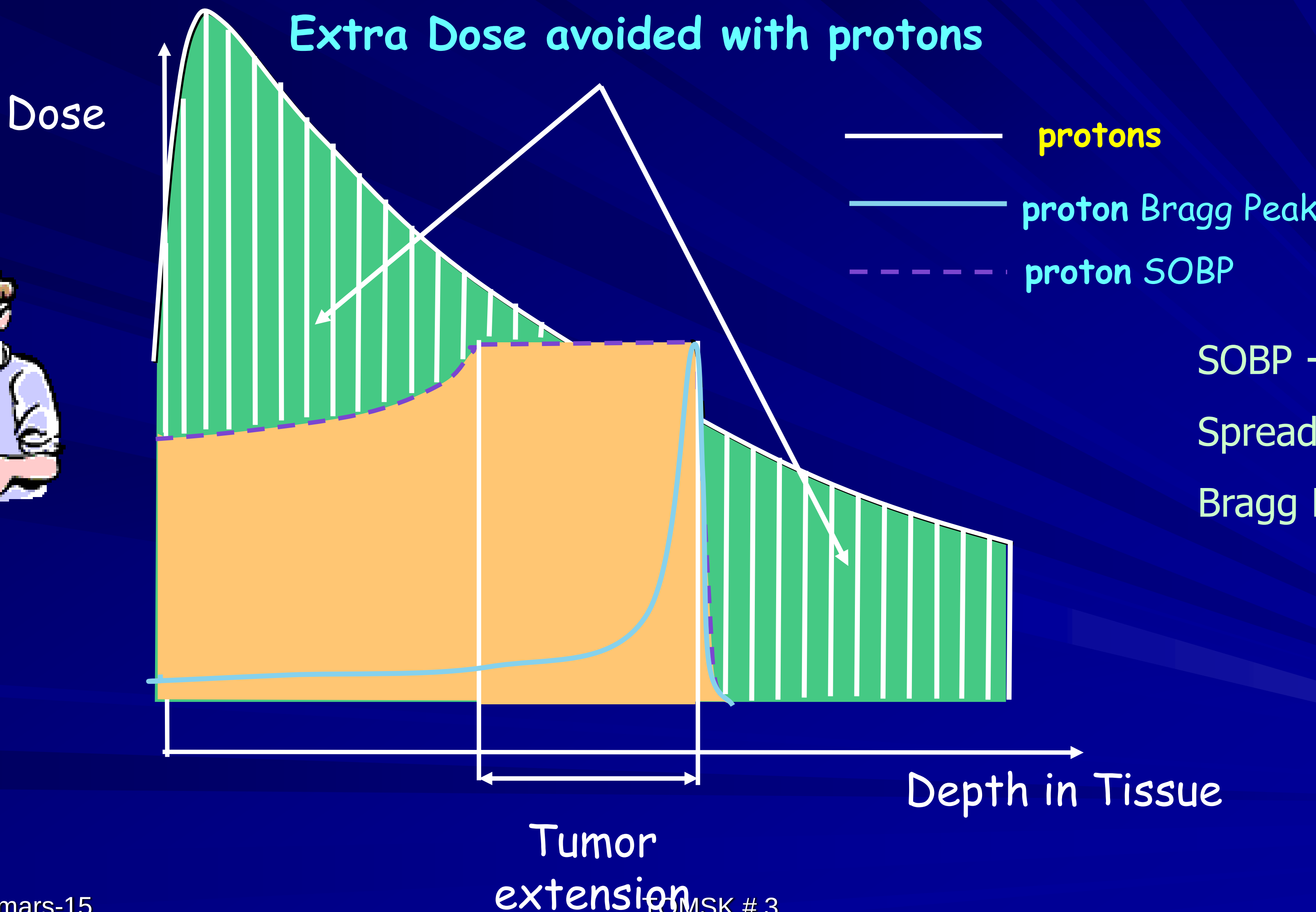
→Particle therapy around 15%of the cases

Why use Hadrons for Therapy?



- Most dose is deposited in the sharp "Bragg Peak", with no dose beyond
- Escalate the dose in the tumor
- Reduction of dose in surrounding normal tissue

The advantage of Protons

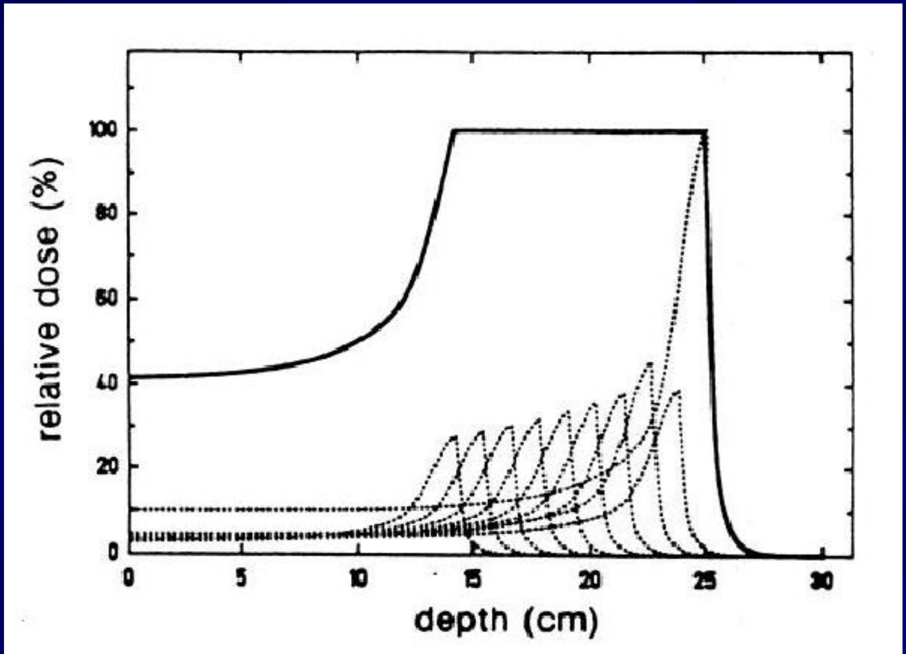


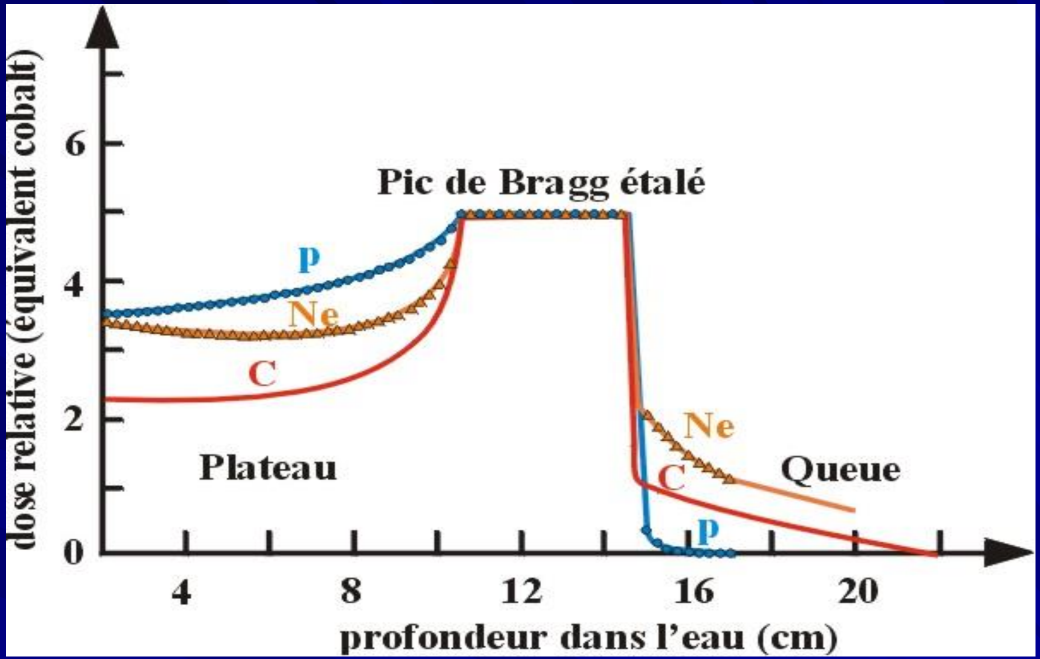
SOBP →

Spread Out

Bragg Peak

How to irradiate the tumor ?



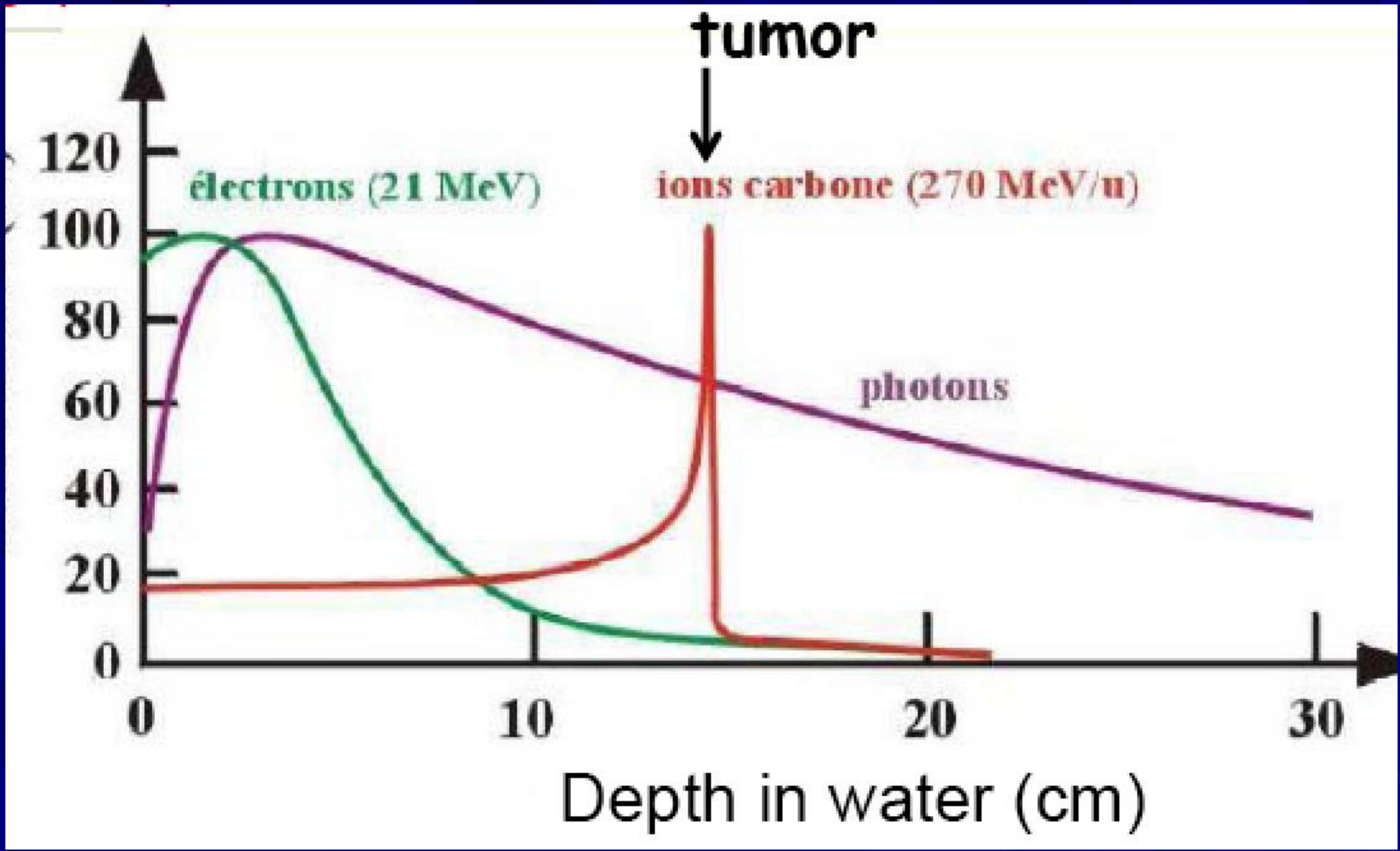


Spread Bragg peak

- Treatment in depth → combine
  - Energy modulation → Scan the energy to make a Spread Out Bragg Peak (SOBP) that spans the tumor
  - Intensity modulation

Hadrontherapy principle (C ion)

Absorbed dose



Electron : most of the energy released in first cm

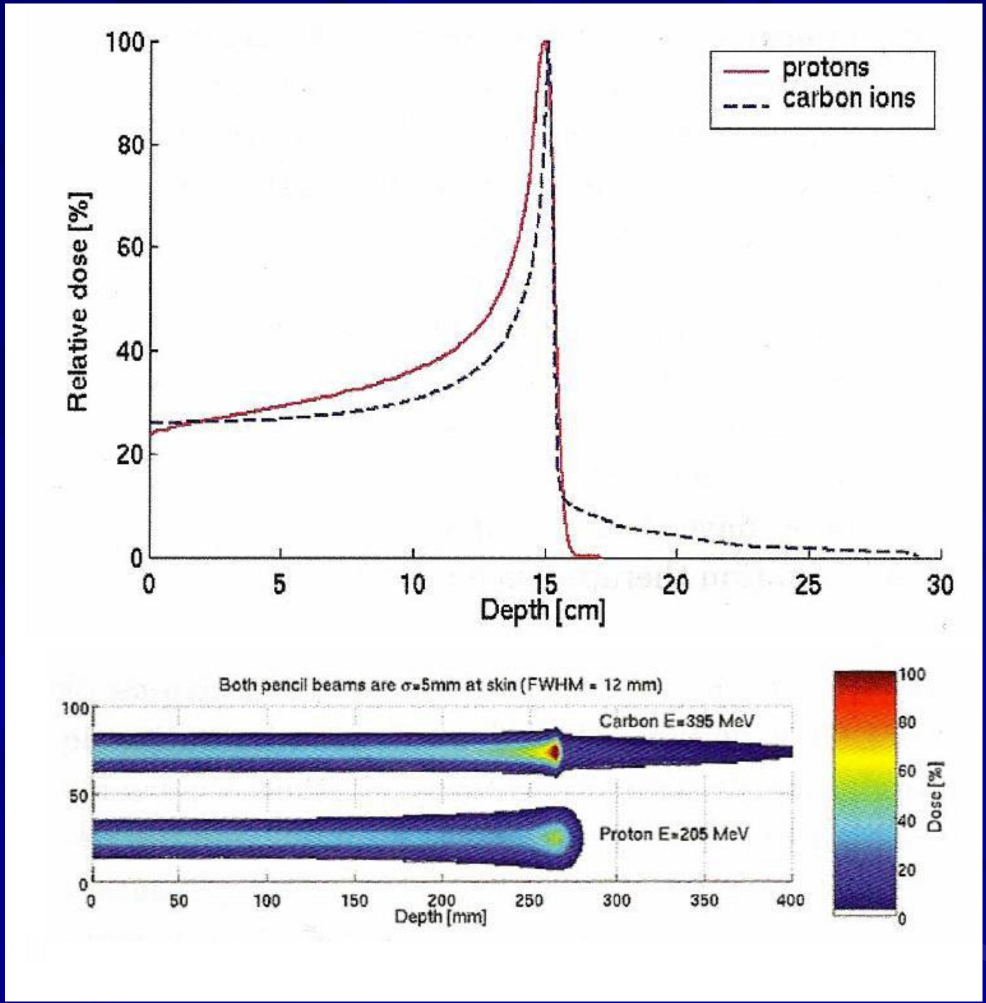
Photon : Large energy loss all over the path (X rays therapy)

C ions : heavy charged particle : most of the energy lost at the end of path (Braggs peak)

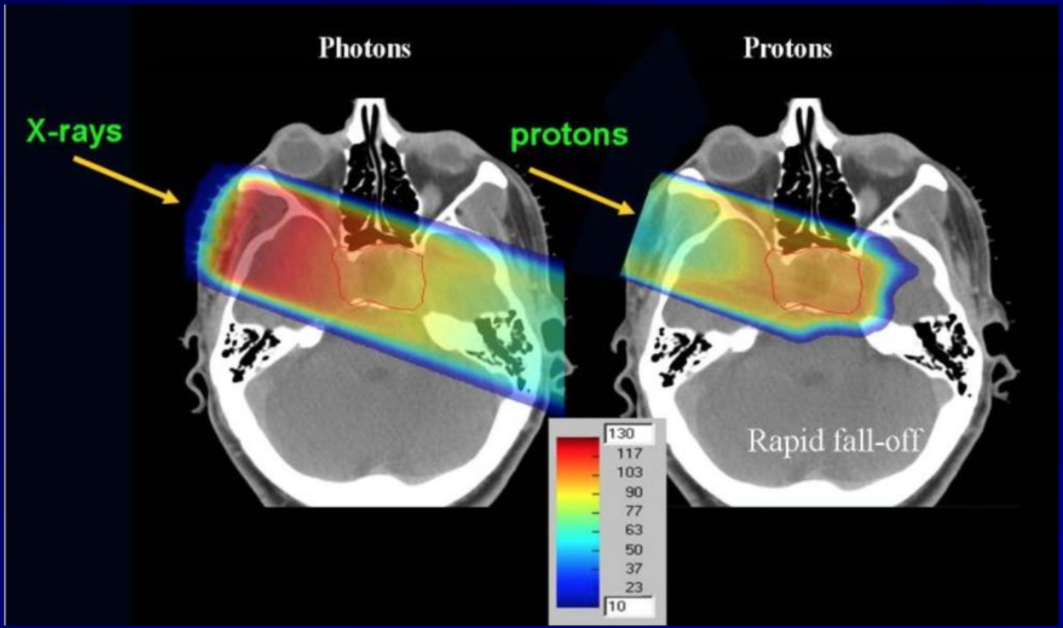
Protons and Carbon in Comparison

- Compared to the lighter protons,carbon ions produce pencil beams with a sharper peak and less penumbra

- Carbons have, however, a dose tail due to fragmentation



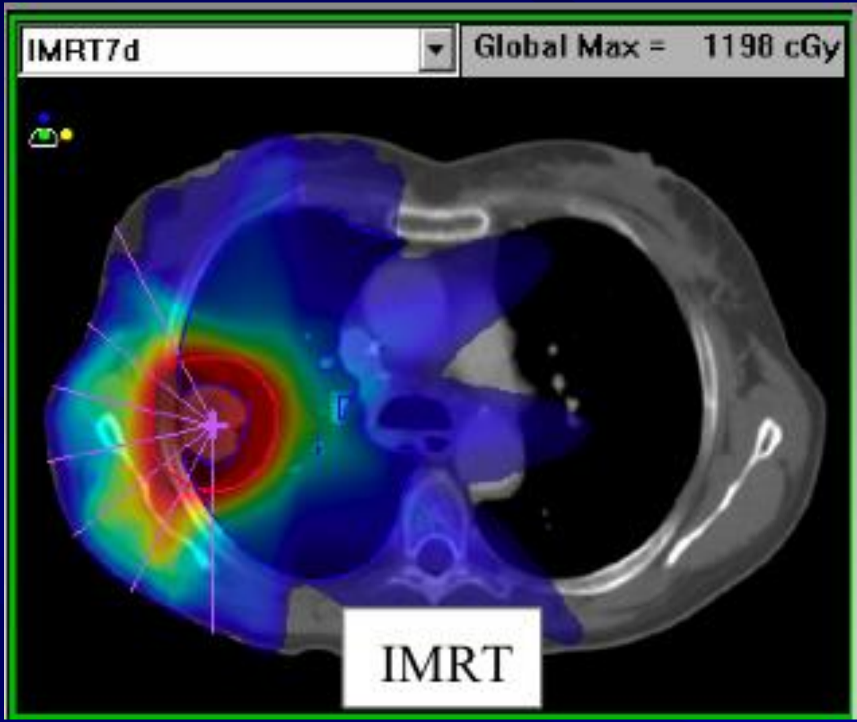
Summary :BIOLOGICAL BASICS
Protons vs photons

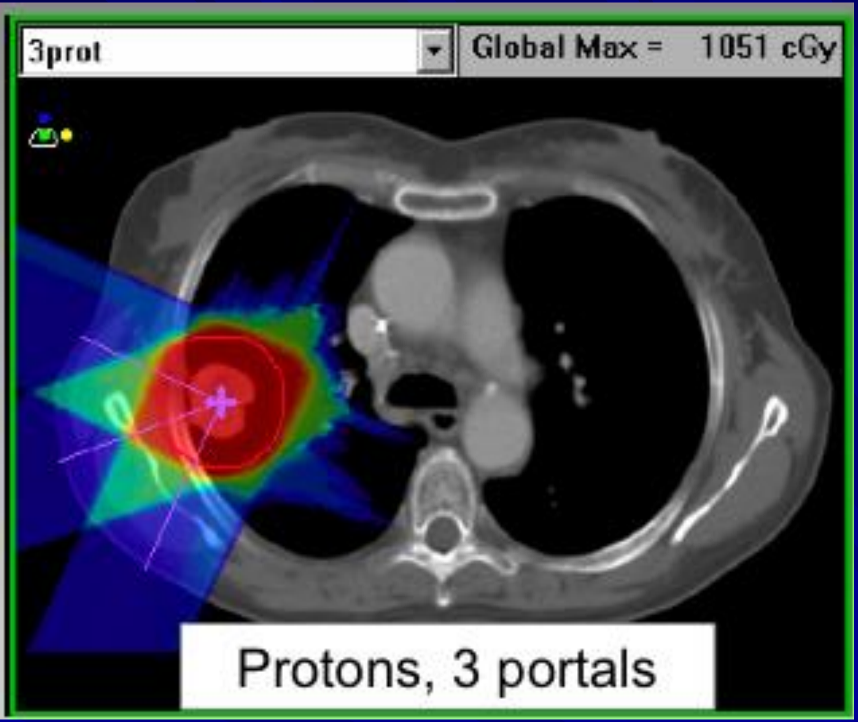


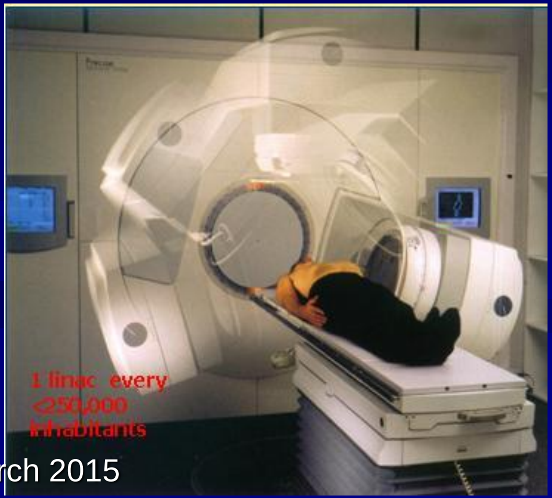
TC image: dose distribution calculated for proton beams and X-rays.

- *Clinical advantages :*
- *✓ treatment of deep-seated, irregular shaped and radioresistant tumors;*
- *✓ small probability of side effects in normal tissue (critical structrure);*
- *✓ proton therapy suitable for pediatric diseases (reduced toxicity).*

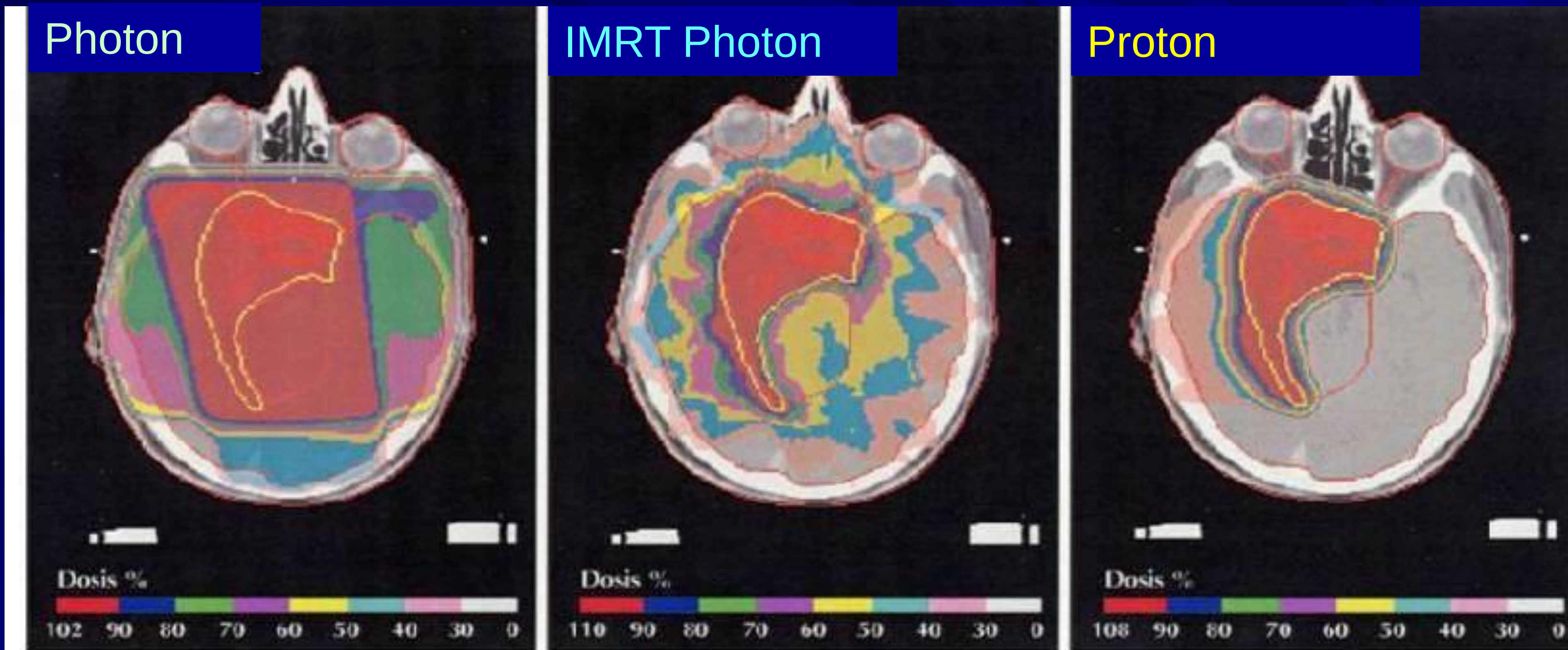
Comparison IMRT-Protons







Comparing Proton and conventional RT



Conventional Radiotherapy:
Important dose outside the tumor

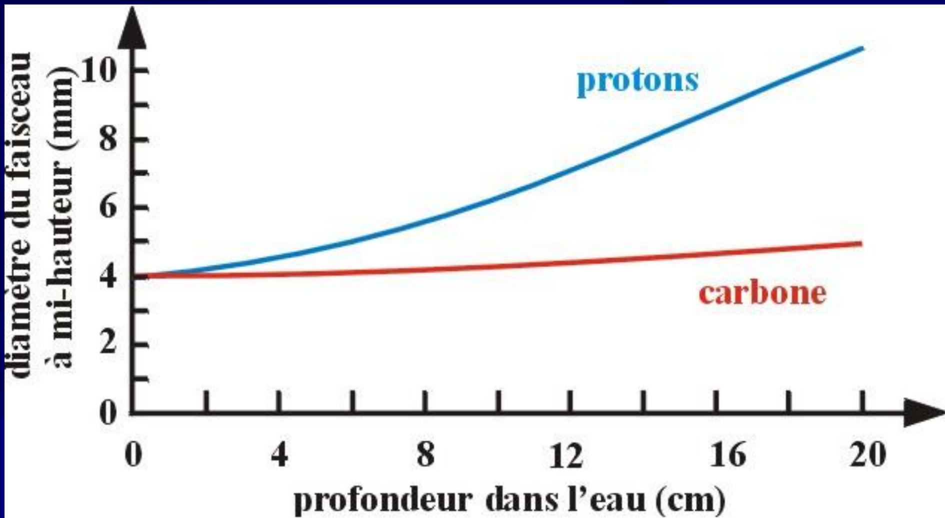
IMRT = Intensity Modulated Radio Therapy:
still non negligable dose outside the tumor

Scattering technique :
Low dose outside

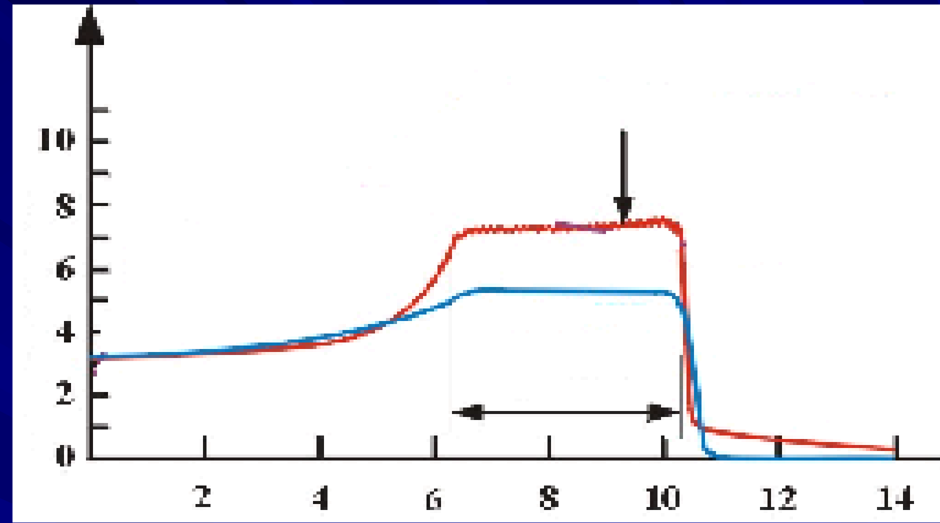
Estimated absolute yearly rate (%) of 2nd cancer after radiotherapy

Tumor site	X-rays	IMXT	Protons
Oesoph. & stomach	0.15	0.11	0.00
Colon	0.15	0.07	0.00
Breast	0.00	0.00	0.00
Lung	0.07	0.07	0.01
Thyroid	0.18	0.06	0.00
Bone & soft tissue	0.03	0.02	0.01
Leukemia	0.07	0.05	0.03
All	0.75	0.43	0.05
Compared to X-rays	1	0.6	0.07

Proton vs light ion



Multiple scattering



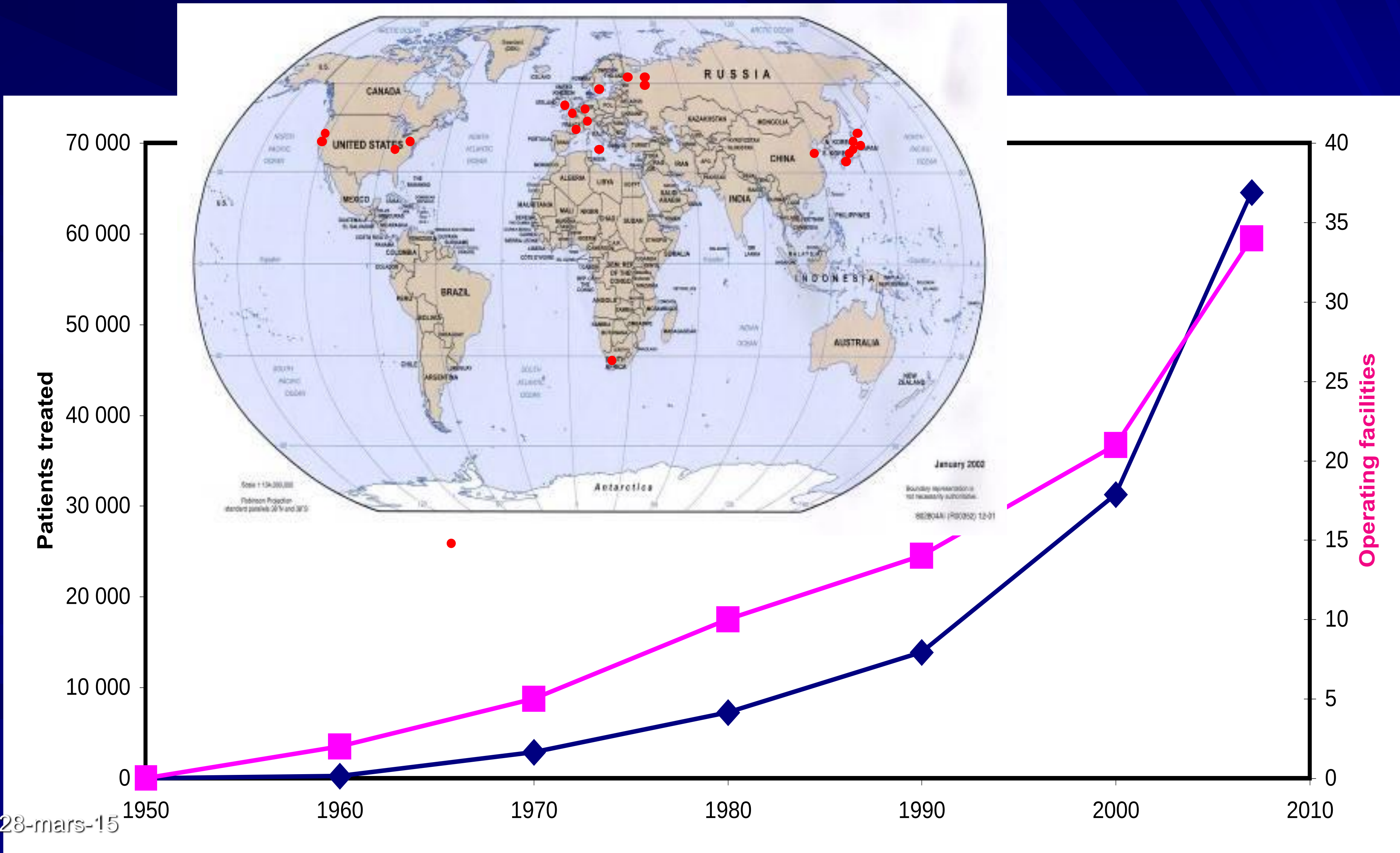
Depth in water (cm)

- Biologic →High Biological Effectiveness (RBE)
  - - Oxygen effect = OER = 1
  - - EBR relative 1 to 2
- Physics → Lower lateral diffusion
  - C12 > P 4 mm at the entrance
  - after 16 cm 4,5 mm vs 8 mm

- Good depth dose distribution

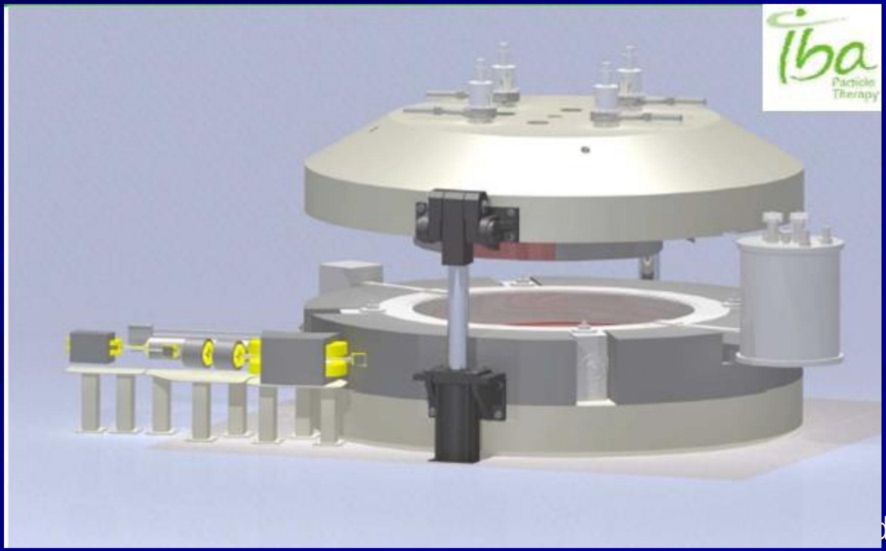
Carbon looks the best but ? ..

Proton Therapy is growing rapidly!



Iontherapy around the world

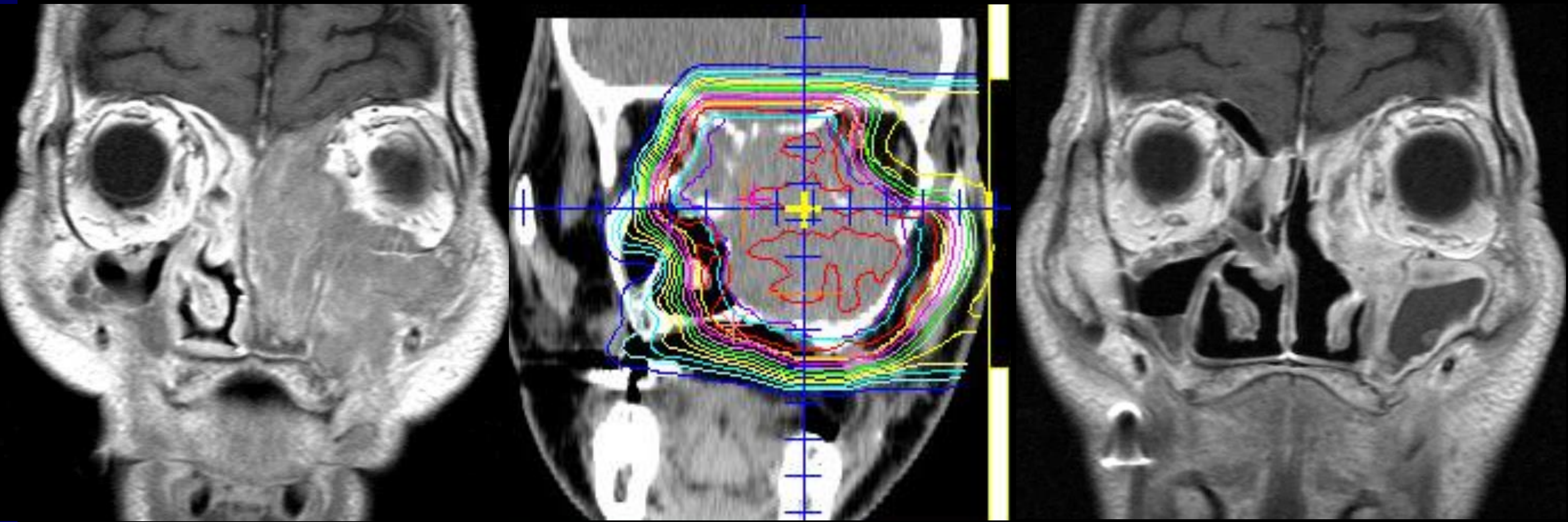
- Need a bigger Accelerator → : Synchrotron (70-300 Mev/nucleon) → more complex and expensive (x5?)
  - Initiator: Berkeley (1954-1993) - 2500 patients
  - Experimental : GSI (Germany- 120 patients
  - Routine : Chiba (Japan) → 1000 patients/year
  - New facilities: HIT (Heidelberg), Pavia (TERA)
  - Vienna (MED- AUSTRON), Caen-Ganil (F)



The IBA C400 Medical Ion Cyclotron Prototype for ARCADE (Caen, France)

Efficacity of ion therapy

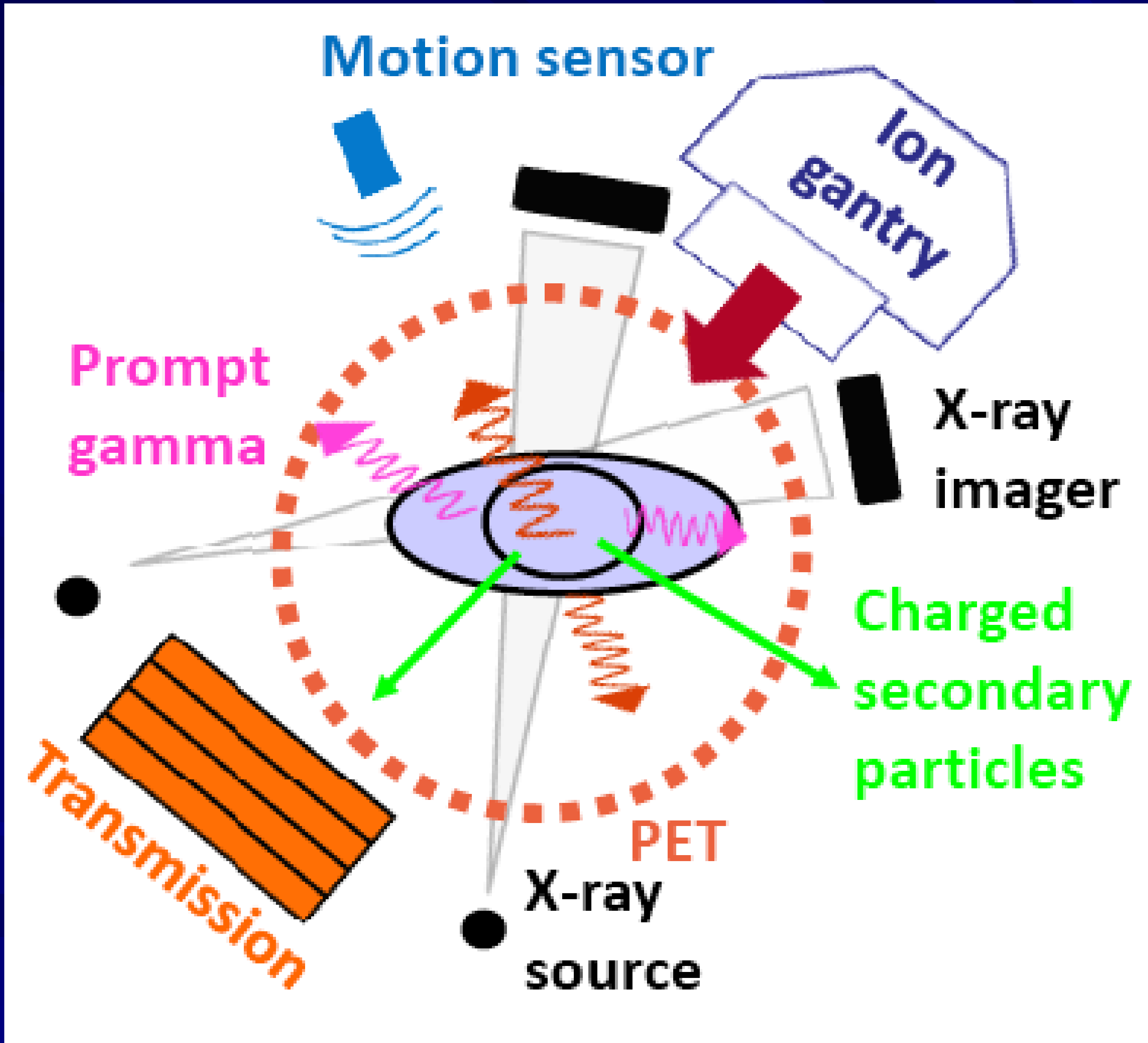
73M Lt. Nasal Cavity Malignant Melanoma T4N0M0 57.6GyE/16fr/4w



Before **2 months after RT**

GSI- W. Enghardt courtesy

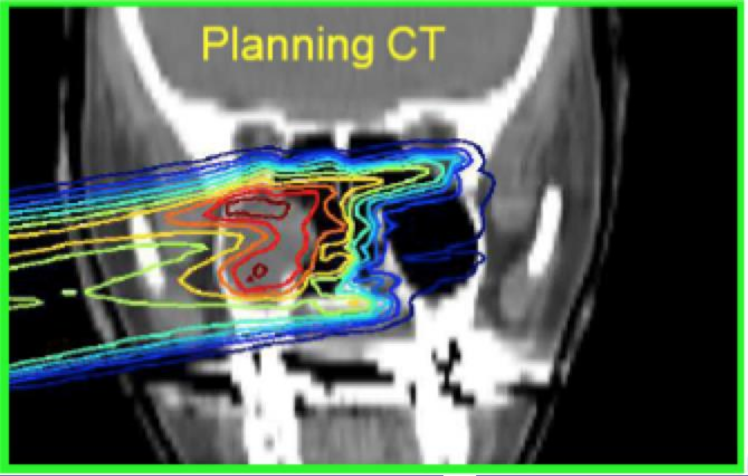
Particle therapy environment



- Machine
- Beam delivery
- Photon detectors
- CT imaging
- Motion sensor

Courtesy Katia Parodi

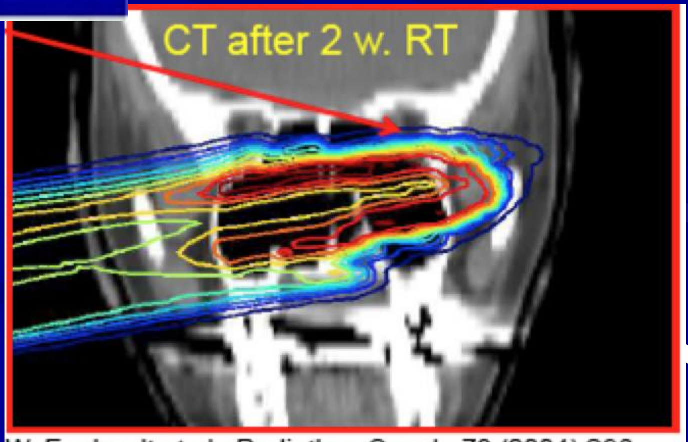
Treatment



Particle therapy workflow

- Step 1 → Treatment planning after CT scan
  - Dose to be distributed
  - MC simulation
  - Give information to the machine

Step 2 → Treatment
- 10-20 fractions (tumour irradiation)



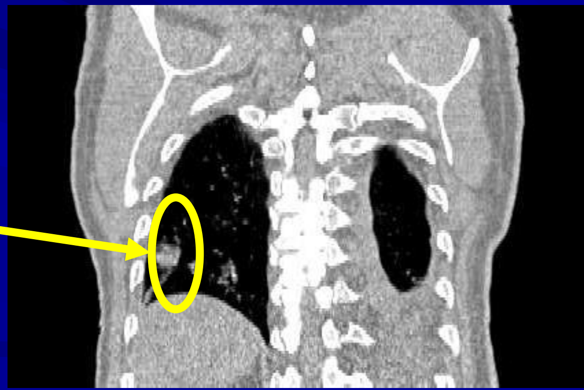
W. Enghardt et al.: Radiother. Oncol 73 (2004) S96

- *Step 3 → verification using CT scan*

Overdosage in normal tissue

What are the critical issues & challenges?

- This is NOT a 'simple target' but a human body
  - Treatment and quality assurance techniques of conventional radiotherapy not adequat for particle therapy
    - A complex procedure for the 'treatment planning'
- How to be sure that the dose is delivered at the right place (tumour) ?
  - Particle beam are error sensitive
    - Displaced organ & overdose
    - Moving organ in some case



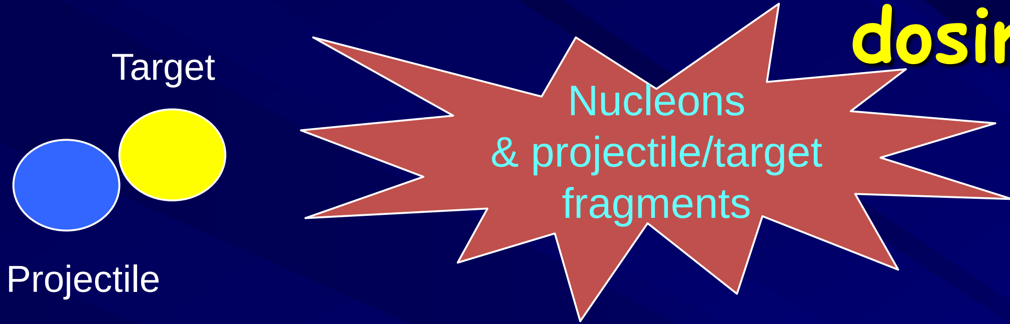
What is the dose deposited ?
How to verify the treatment?

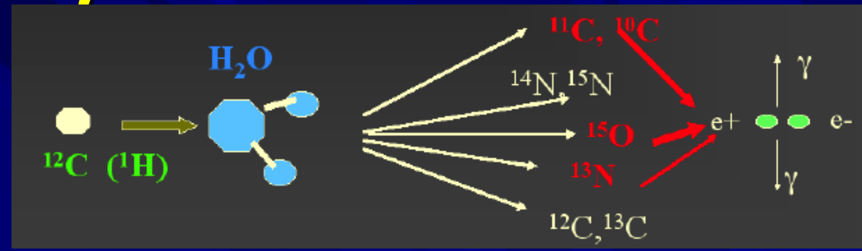
The two 'simultaneous' challenges

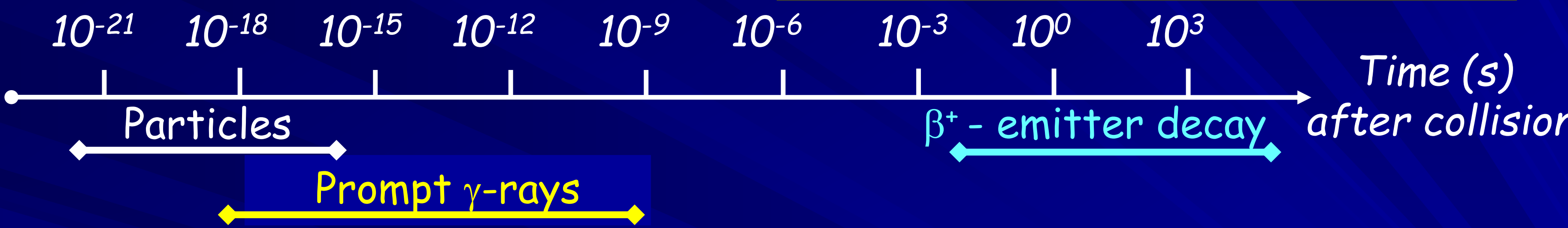
- Reducing error means → Real Time imaging
  - 3D in vivo dosimetry and tomography
    - *Use fragments of beam projectile reactions in the biological matter emerging from the tumor target volume*
- Verification using Computed Tomography/Radiography:
  - CT imaging in charged Particle therapy is needed for:
    - Target volume definition (anatomical boundaries with additional information from multimodality imaging (CT/MRI/PET studies)
    - Dose and range calculation
    - Patient alignment verification

But today these process are made at different moment and place

In-beam nuclear method principle for 'in vivo' dosimetry

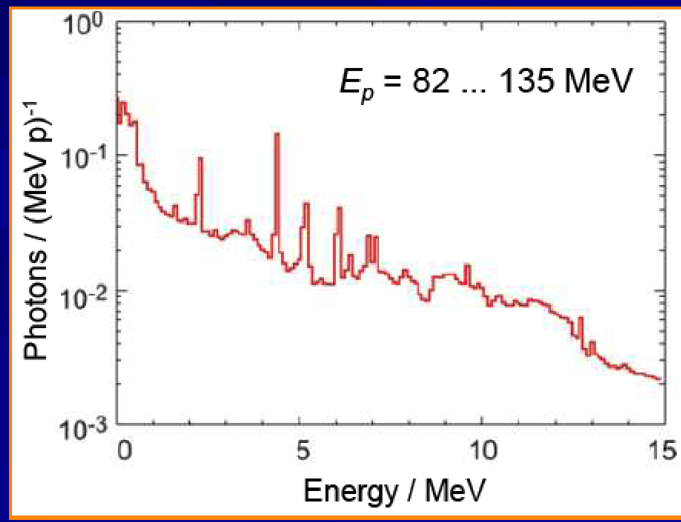


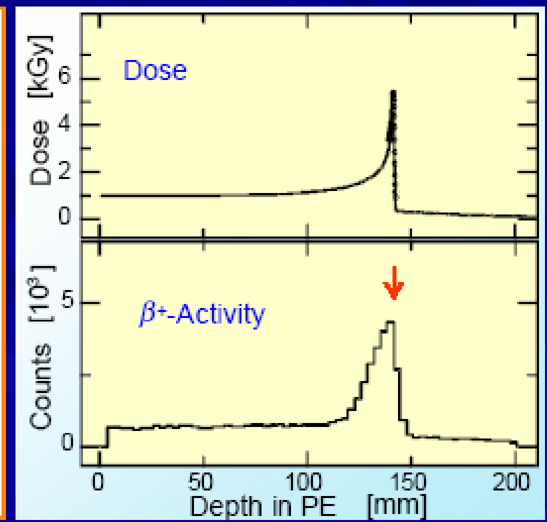




Balance of promptly emitted particles outside the target:

Incident protons:	1.0	($\sim 10^{10}$)
γ-rays:	0.3	($3 \cdot 10^{9}$)
Neutrons:	0.09	($9 \cdot 10^{8}$)
Protons:	0.001	($1 \cdot 10^{7}$)
a-particles:	$2 \cdot 10^{-5}$	($2 \cdot 10^{5}$)



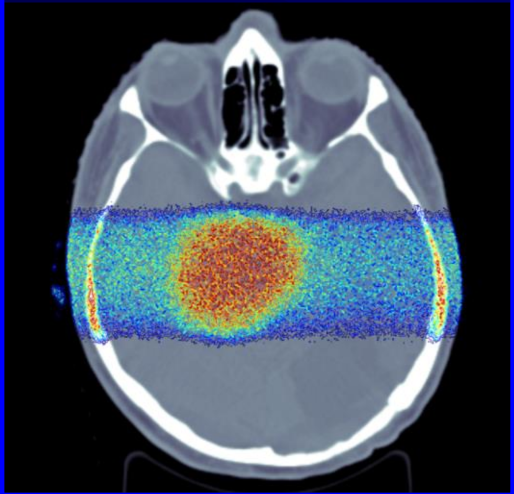


Relation between dose and β+ activities

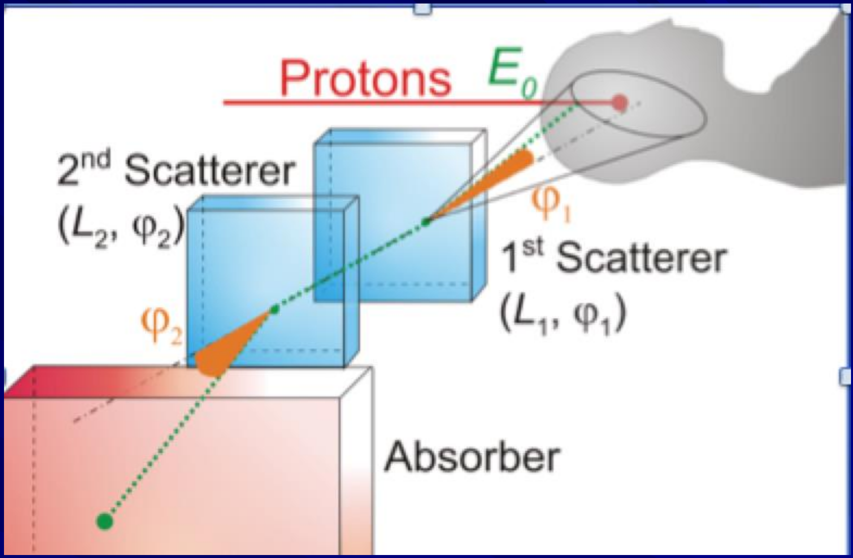
- However the photon energy different from standard medical (Anger) SPECT camera

Single photon: in vivo Compton Camera

γ-rays MC simulation

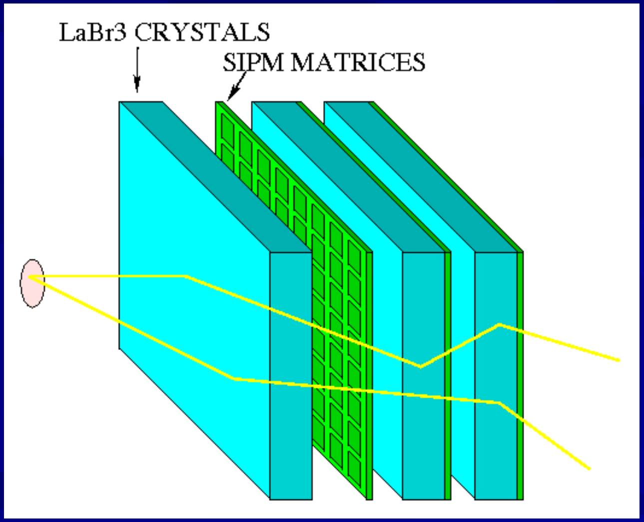


(A.Muller,TU Dresden)

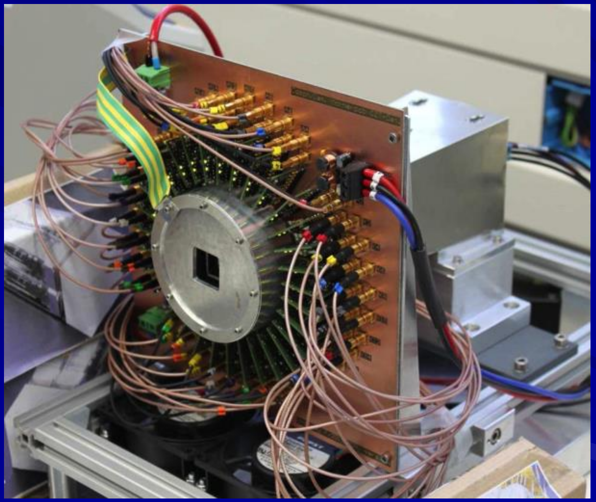


- Required devices:
  - Hodoscope (x,y,t)
  - Scatterer (x,y,E)
  - Absorber (x,y,z,E,t)

Scintillating-fibre Hodoscope + MA PMT
Ray et al. IPN Lyon

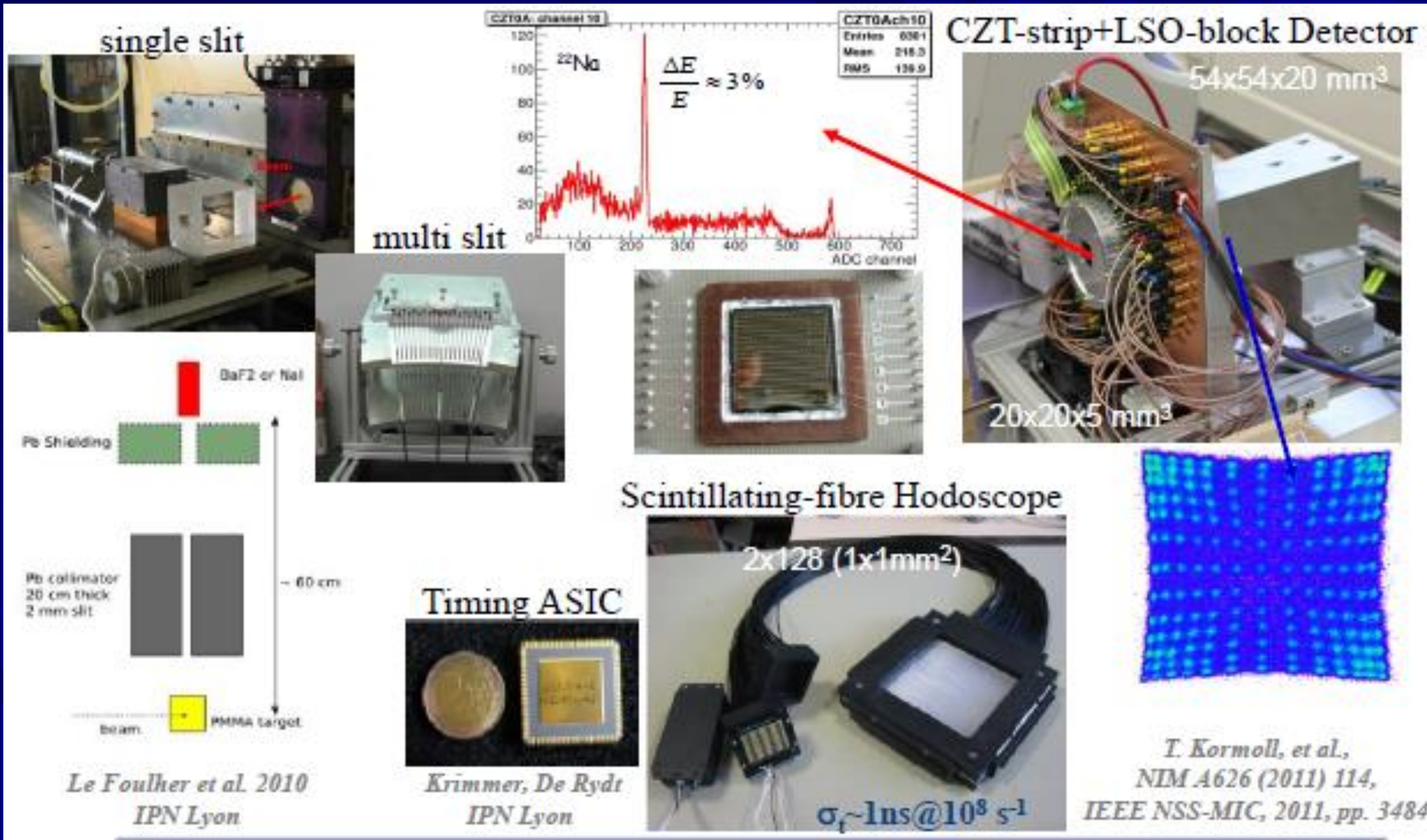


C.Llosa, IFIC



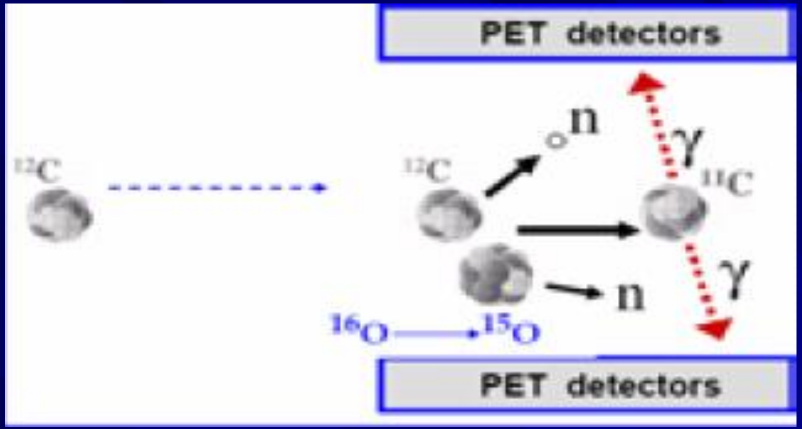
CZT-strip+LYSO-block Detector
F.Fiedler et al. Dresden

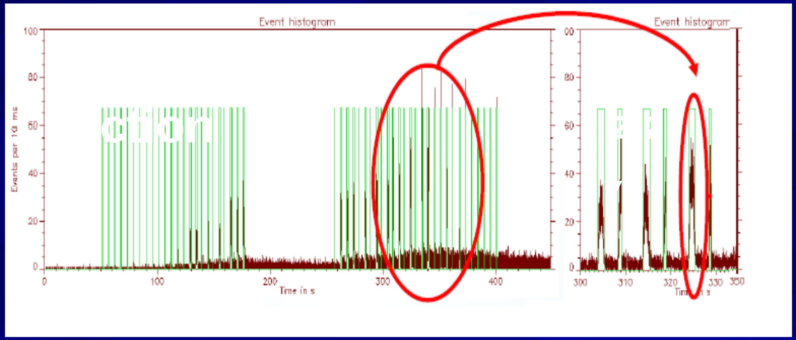
Exemple of Single photon: in vivo SPECT

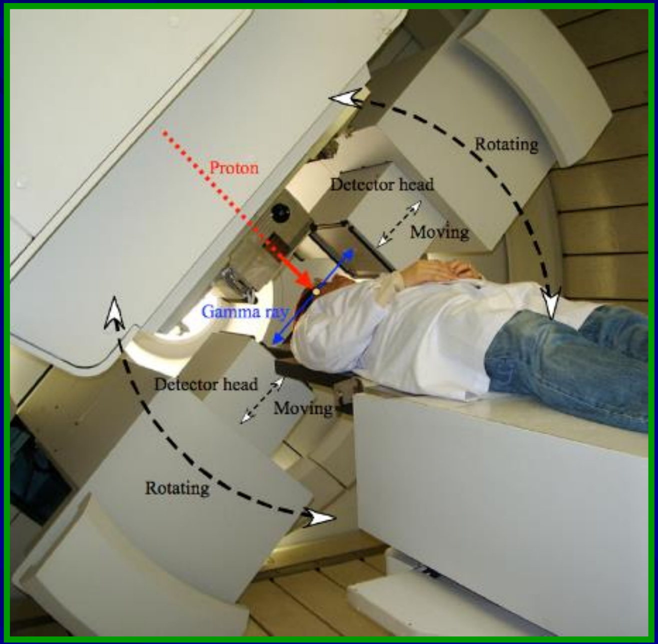


Present examples: in beam PET

In-beam PET scanner at ^{12}C-therapy unit at GSI





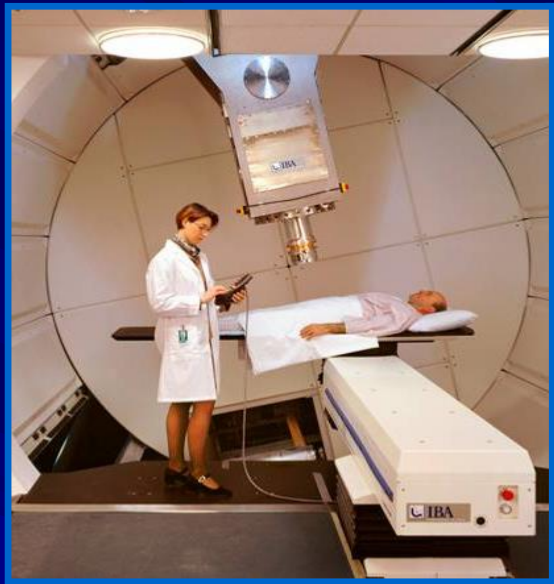


^{1}H-therapy at the National Cancer Center, Kashiwa, Japan

- Large beam background
- No Real time capability
- Low signal to noise ratio

Positron Emission Tomograph …some Hardware

In-beam: GSI Darmstadt *Off-line: MGH Boston, HIT Heidelberg*



more…

- *HIMAC, Chiba*
- *NCC, Kashiwa*
- *HIBMC, Hyogo*
- *MDACC, Houston*
- *Univ. of Florida*

☺ *In-vivo range measurements*

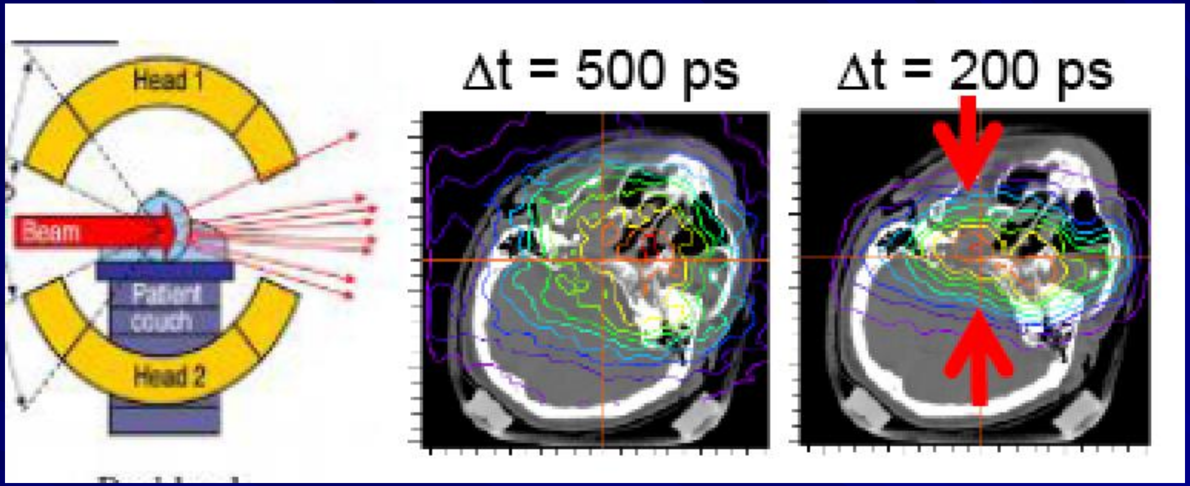
☹ *In-vivo dosimetry & real-time image guidance*

- *Ongoing developments (TOF-PET, PET+CT)*
  reduce unfavorable in-beam random coincidences/background (by 20-30%)

Mature technology

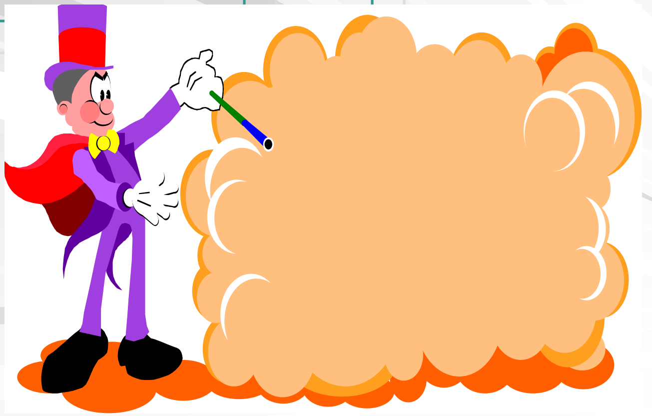
Courtesy W. Enghardt / OncoRay

In vivo PET recent developments



MGH

A long termdream
The Proton CT



X ray & CT after each fraction ?

- X ray is agressive --> see table below about estimated absolute rate of (%) of 2nd cancer
  - 30-50 mGy/scan
  - 30 fraction daily --> Total : 0,6 -3 Gy

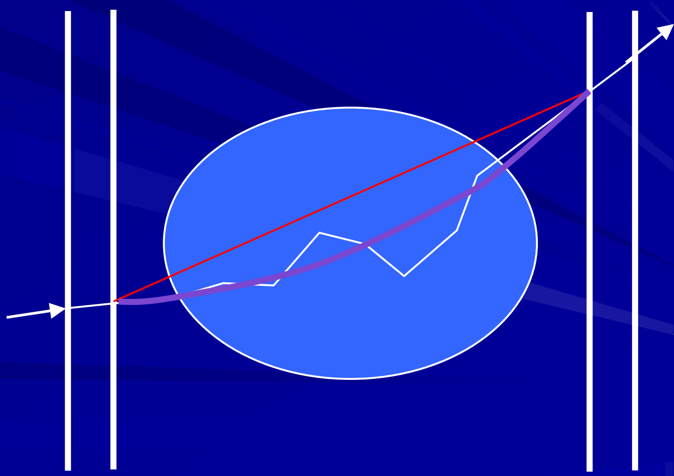
Tumor site	X-rays	IMXT	Protons
Oesoph. & stomach	0.15	0.11	0.00
Colon	0.15	0.07	0.00
Breast	0.00	0.00	0.00
Lung	0.07	0.07	0.01
Thyroid	0.18	0.06	0.00
Bone & soft tissue	0.03	0.02	0.01
Leukemia	0.07	0.05	0.03
All	0.75	0.43	0.05
Compared to X-rays	1	0.6	0.07

Basics of particle imaging

- *The particle (proton/ion) go through the patient at high energy*
- *Advantages:*
  - *Decrease the uncertainties → better dose accuracy*
  - *Reduce the dose delivered to the patient*
- *Challenge → the data reconstruction*
  - *correctly reconstruct the path of the proton*

Radiograph of a phantom
Uwe Schneider PhD thesis
(1978,PSI)

Proton CT:
1) replaces X-ray absorption with proton energy loss
2) reconstruct mass density distribution instead of electron distribution



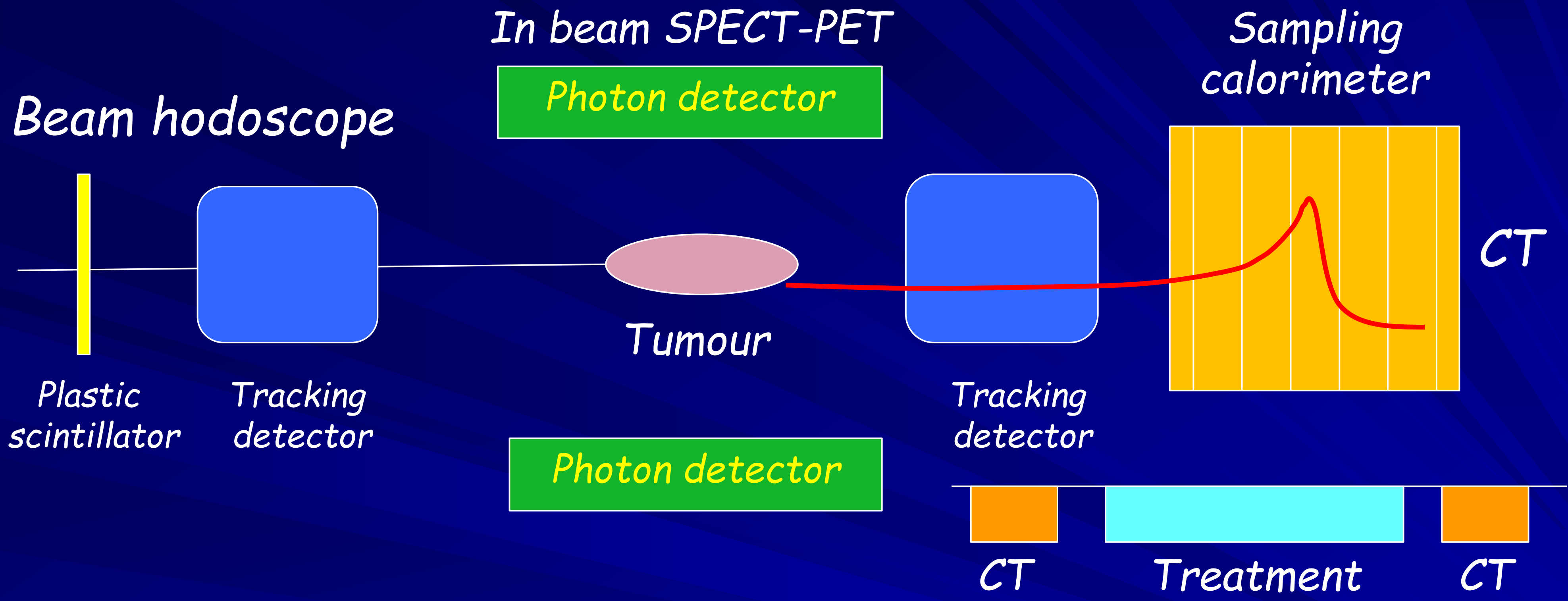
A tribute to G.Charpak

The Basics Ingredients

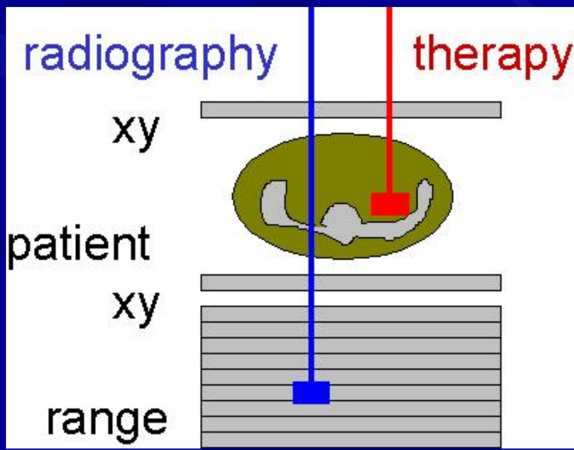
- Beam
  - Measurement (position and direction) particle per particle
- Photon detectors
  - In beam selection of
    - single photon → compton camera (SPECT)
    - two photons → in Beam TOF-PET
- Proton (ion) CT
  - Measure the energy (position, energy and time) of the diffracted particle in an imaging calorimeter
- The Global aspect!
  - Event by event selection particle like in a nuclear & HEP physics experiment.
  - Deatimeless electronics
  - Real time acquisition and reconstruction

Need all HEP modern instrumentation tools & technique

Schematic block diagram of an integrated concept of radiography / therapy system



- Identify tracks and energy deposition of individual protons
- Scintillators for trigger to read-out detectors
- Tracking detectors for 3D tracks
- Sampling Calorimeter for energy determination
- High rate integrated DAQ



Present examples : PCT

- Different prototypes are proposed based on the same "philosophy" (Reinhard Schulte et Al.)
  - BNL, Santa Cruz, Loma Linda, Stony Brook layout (2003)

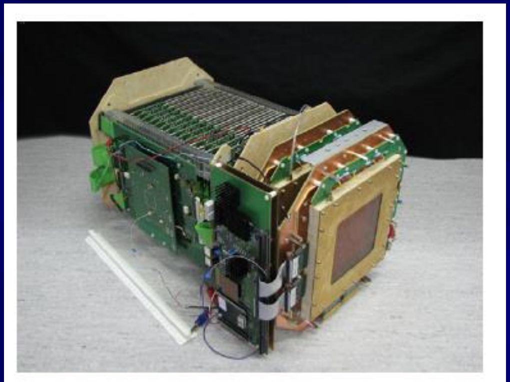
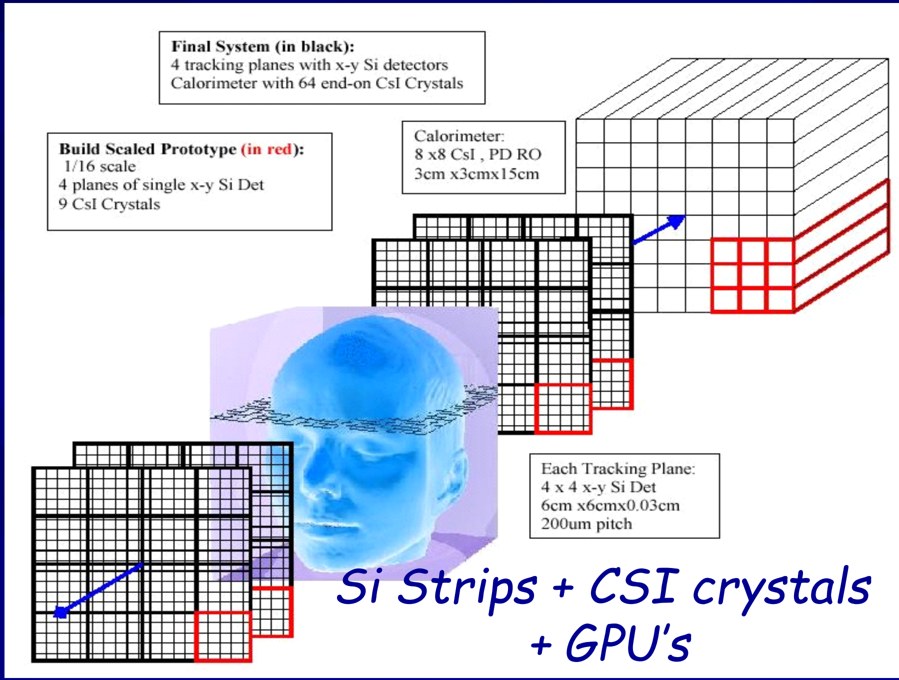
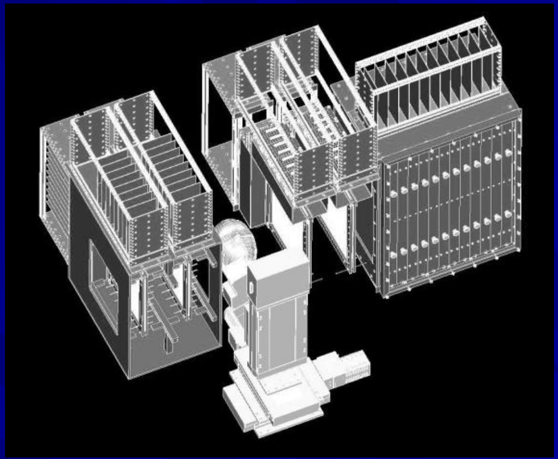


Fig. 1. The Proton Range Radiography setup.

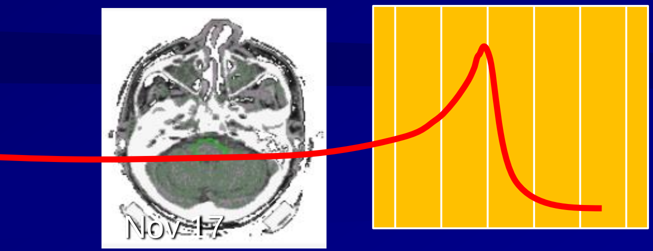
AQUA-CNAO
Scint/MPPC/GEM



Si Strips + CSI crystals + GPU's

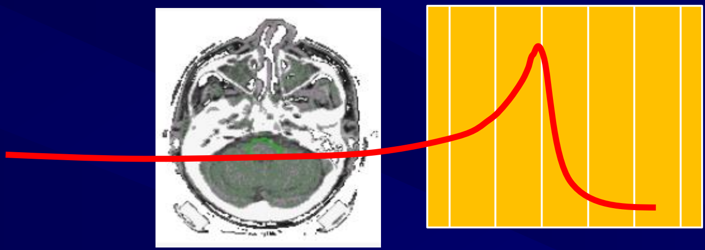


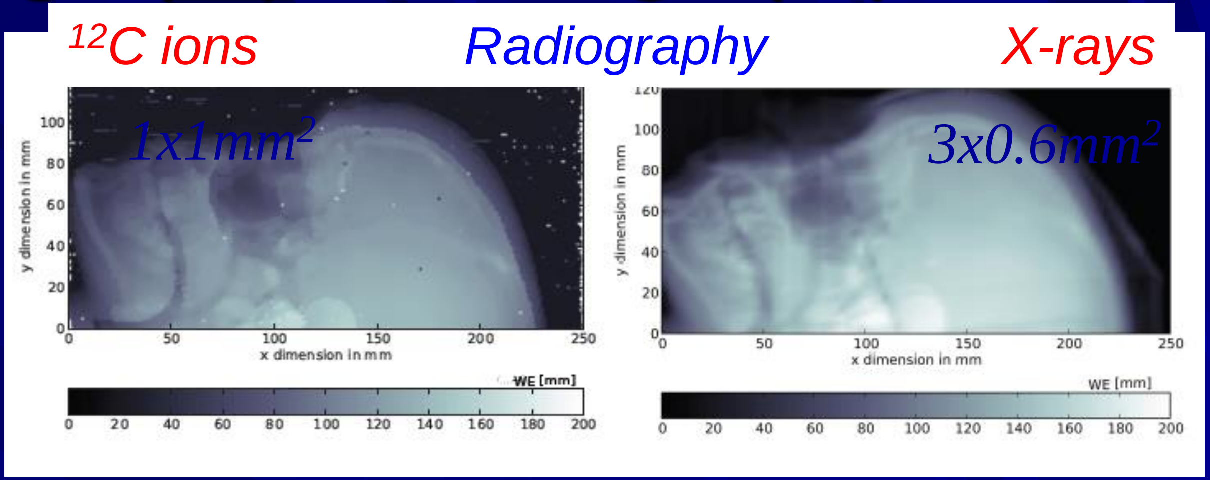
NIU/FNAL
Scint/WLS+SiPM
GPU farm



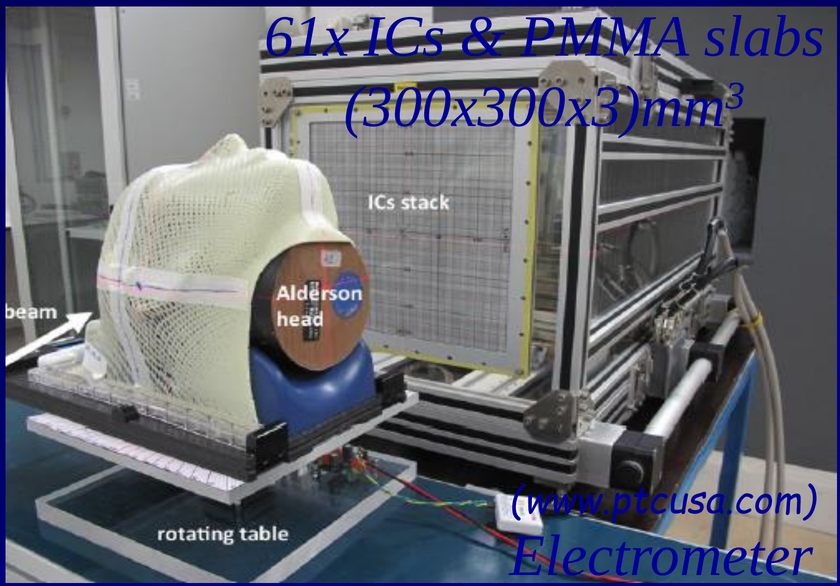
- *Ion Transmission Imaging*
  - *→ See talk from B.Voss*

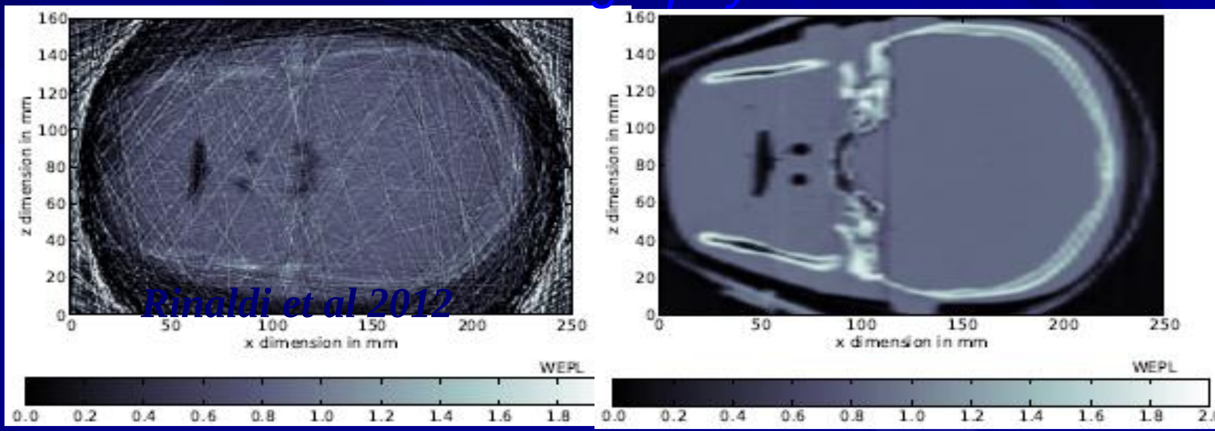
Primary-Ion Radiography / Tomography





Water equivalent thickness





Water equivalent path length

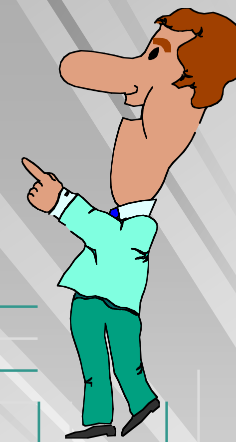
Transmission ion imaging prior to or in-between RT is feasible

Conclusion from a pioner
Prof. W. Enghardt Oncoray, Dresden

Particle thearapy units should be equipped with the most advanced imaging and motion tracking devices available

And Not with the **technology** of the last century

Final Conclusions



There is a lot to do
Particularly
for students

References
Proceedings
of NSS-MIC
conferences
Transaction on Nuclear Sciences (TNS)
http://www.nss-mic.org/2016/NSSMain.asp

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- W. Enghardt (Dresden)
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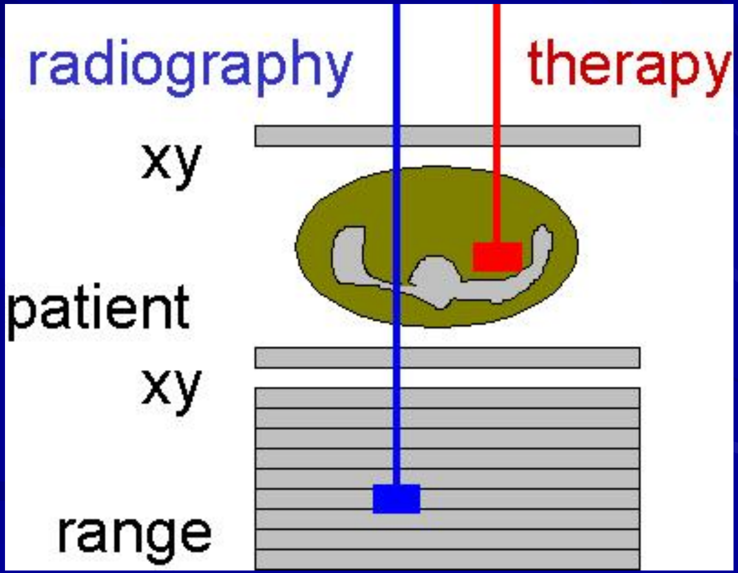
- Etoile Collaboration Lyon)
- R. Schulte (Loma Linda)
- and many others

Thank you
for your attention

Why particle CT ?

- *The role of CT imaging in charged Particle therapy is needed for:*
  - *Target volume definition (anatomical boundaries with additional information from fused MRI and PET studies*
  - *Dose and range calculation*
  - *Patient alignment verification*



The protons go through the patient
Higher energy, small dose