IFMP WORKSHOP IN IONIAN UNIVERSITY, CORFU, GREECE
Friday 10/11/2017 8:30

PARTICLE THERAPY CRITICAL ISSUES AND CHALLENGES

Patrick Ledu, PhD

INP Lyon and IEEE

This talk will illustrate this comment from Prof. Wolfgang Enghardt, one of the pioneer in particle therapy:

"Particle therapy units should be equipped with the most advanced imaging and motion tracking devices available and Not with the technologies of the last century"

. The topics presented are:

- Machine and beam production
- Patient monitoring in real time
- Proton and ion CT developments

Particle therapy
Critical issues and Challenges

P. Le Dû

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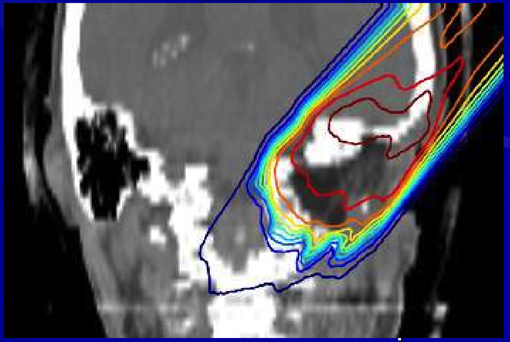
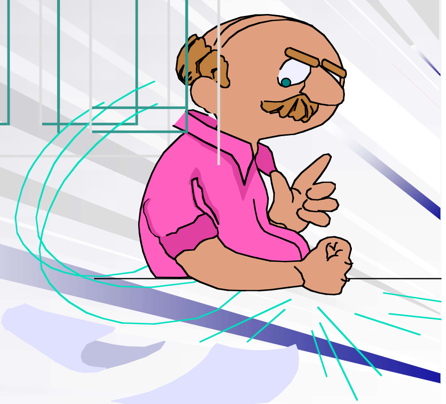


Conclusion from a pioner
Prof. W. Enghardt Oncoray, Dresden

Strongly Approve

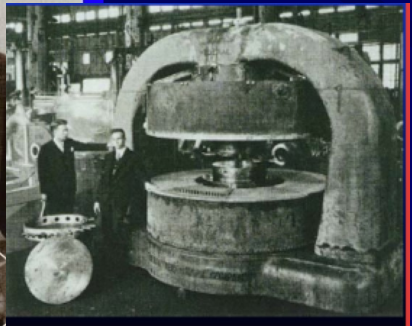
Particle thearapy units should be equipped with the most advanced imaging and motion tracking devices available

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



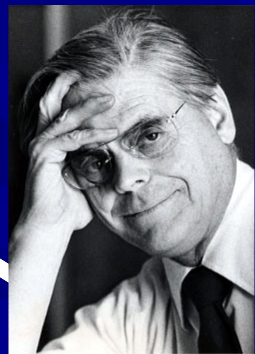
How physics discoveries impact our life (2)

1932 - The Invention of the cyclotron
Production of radioisotopes



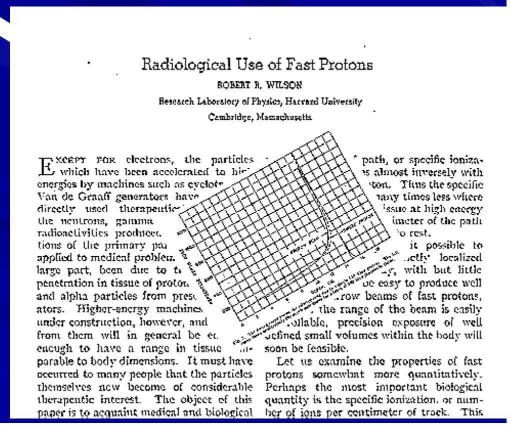
Ernest O. Lawrence and his First cyclotron 1932

1934 - Artificial radioactivity
Irène and Fréderic Jolio Curie



Hadron therapy

1946 – R.R.Wilson
The origin of particle therapy
Using the Bragg peak discovery (1903)



Radiological Use of Fast Protons

ROBERT R. WILSON

Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts

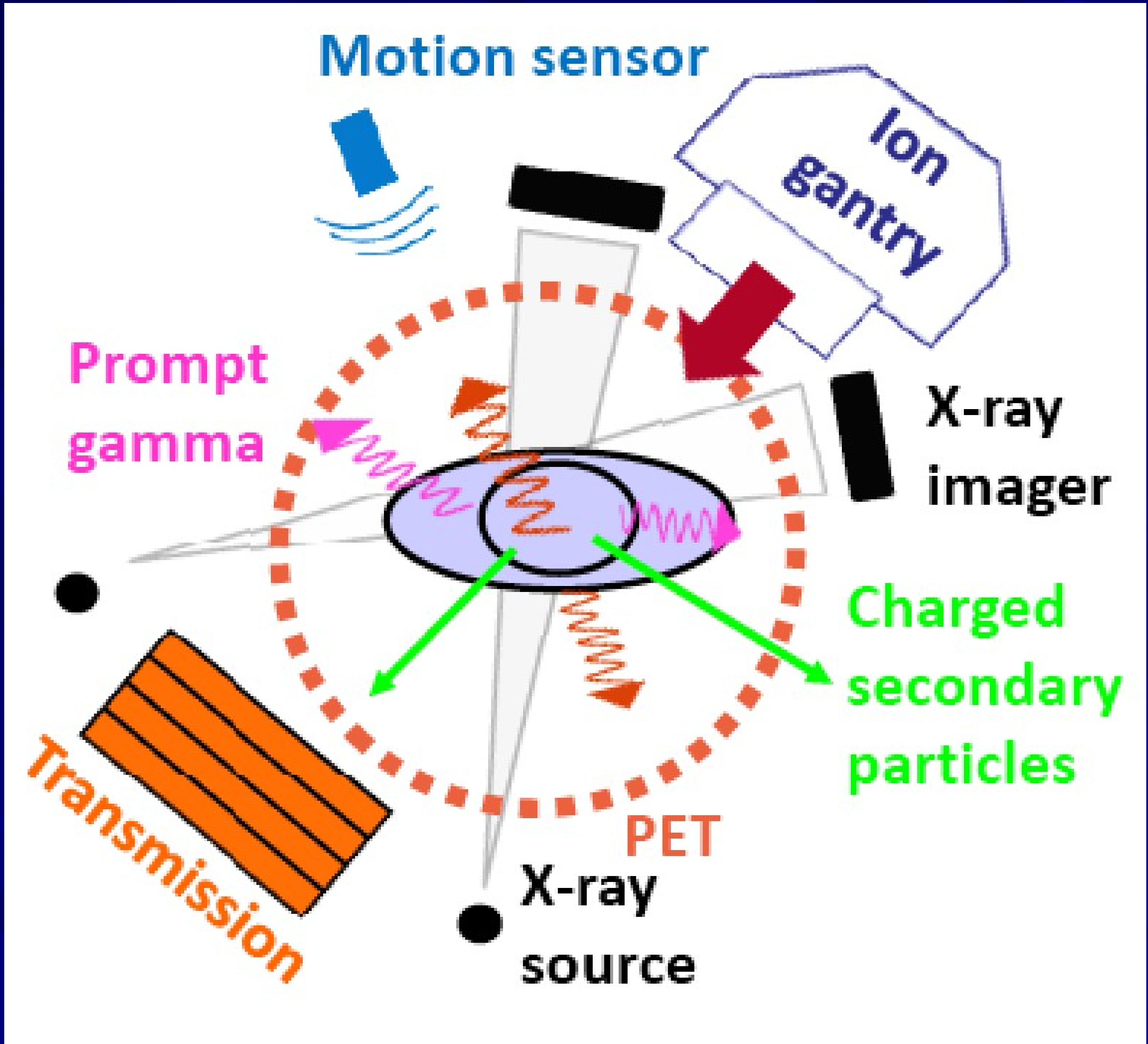
EXCEPT FOR electrons, the particles
which have been accelerated to hi
energies by machines such as cyclot
Van de Graaff generators have
directly used therapeutic
the neutrons, gamma
radioactivities produced.
tions of the primary pa
applied to medical problem.
large part, been due to t
penetration in tissue of proton
and alpha particles from prese
ators. Higher-energy machines
under construction, however, and
from them will in general be e
enough to have a range in tissue
parable to body dimensions. It must have
occurred to many people that the particles
themselves now become of considerable
therapeutic interest. The object of this
paper is to acquaint medical and biological

path, or specific ioniza-
s almost inversely with
ton. Thus the specific
any times less where
issue at high energy
imeter of the path
o rest.
it possible to
ctly localized
y, with but little
be easy to produce well
row beams of fast protons,
the range of the beam is easily
ollable, precision exposure of well
defined small volumes within the body will
soon be feasible.

Let us examine the properties of fast
protons somewhat more quantitatively.
Perhaps the most important biological
quantity is the specific ionization, or num-
ber of ions per centimeter of track. This

The discovery of artificial radioactivity in combination with the cyclotron open the door to the production of useful radio indicators. Practically any element could be bombarded in the cyclotron to generate radioactive isotopes.

Particle therapy environment



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

Courtesy Katia Parodi

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 ….

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

Particle therapy: The Context

- *Why Radiotherapy X is NOT 100 % efficient?*

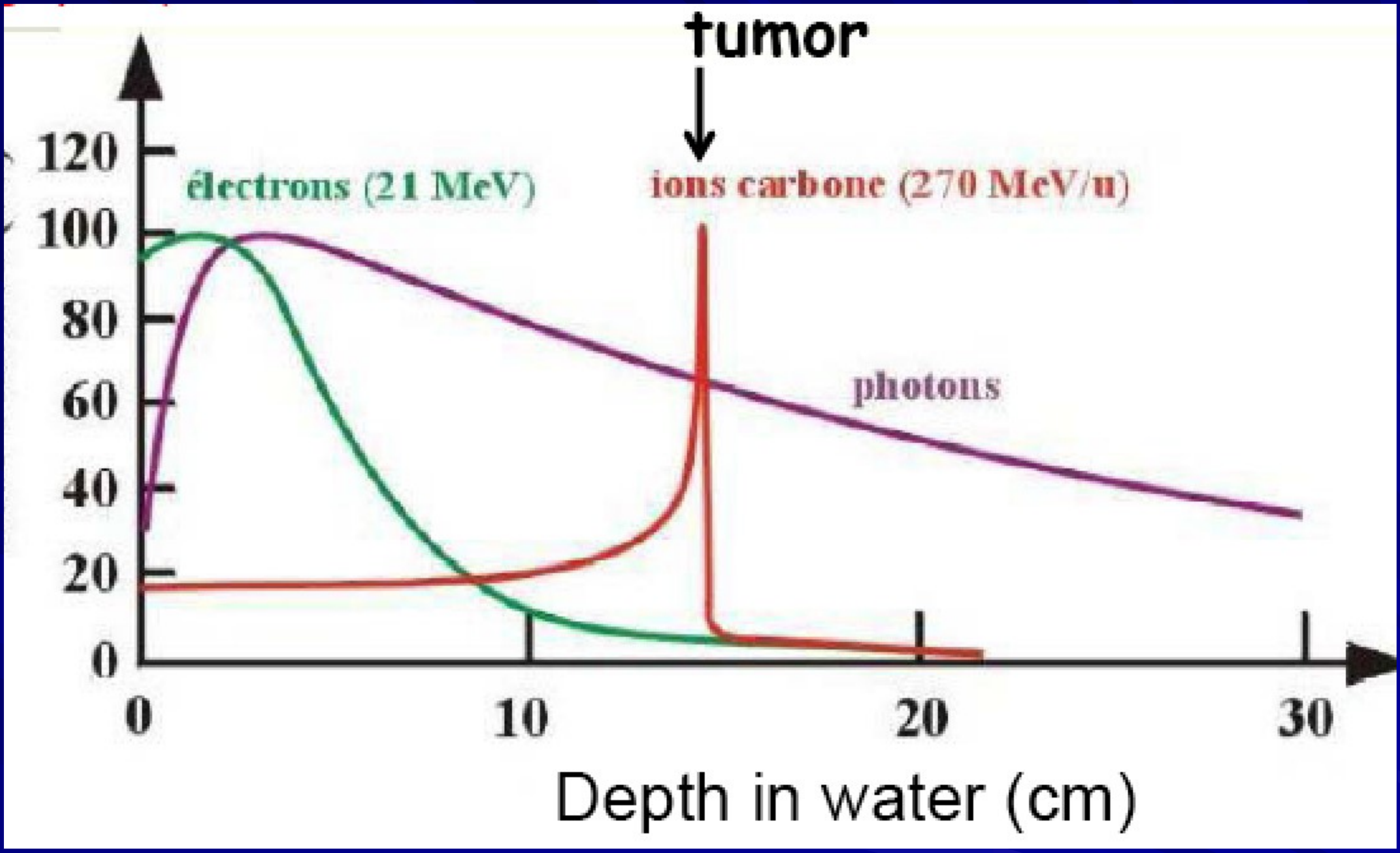
  -Complication < 5 %
  -Tolerance of saine tissue is the limiting factor
  - Close to Organ at Risk

  -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

Hadrontherapy principle (C ion)

Absorbed dose

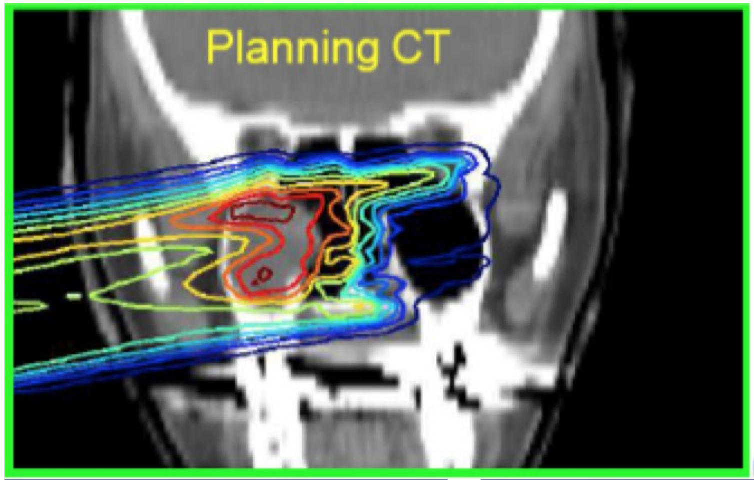


Electron : most of the energy released in first cm

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

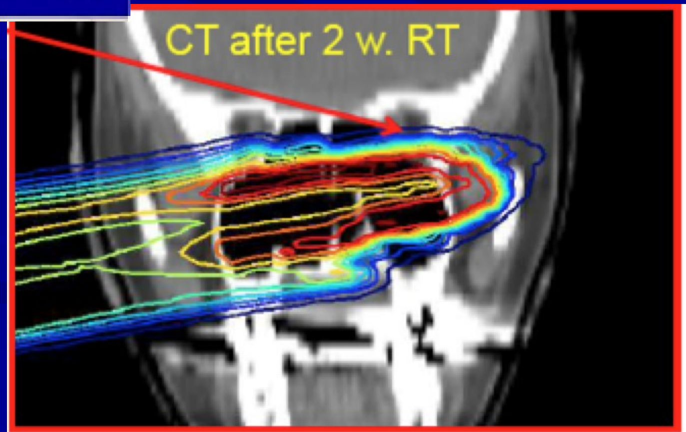
C ions : heavy charged particle : most of the energy lost at the end of path (Braggs peak)

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)



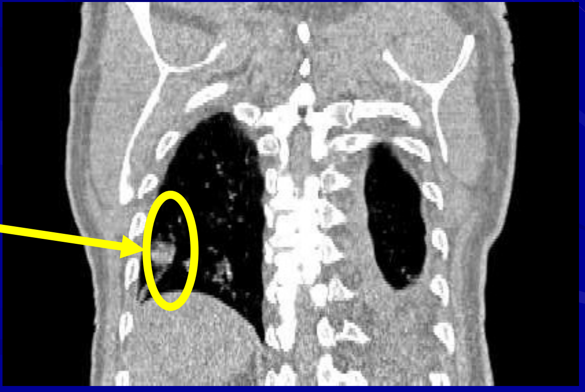
W. Enghardt et al.: Radiother. Oncol 73 (2004) S96

- ***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



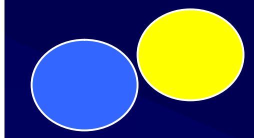
What is the dose deposited ?
How to verify the treatment?

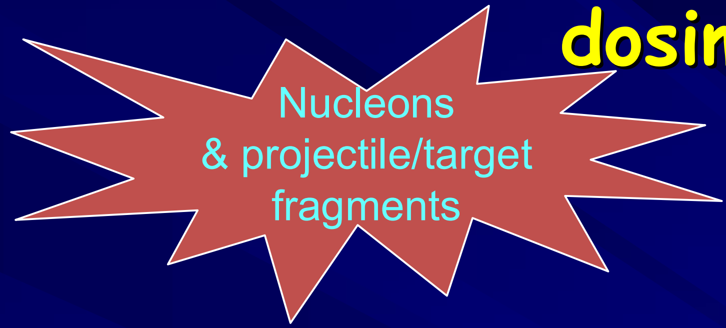
The two 'simultaneous' challenges

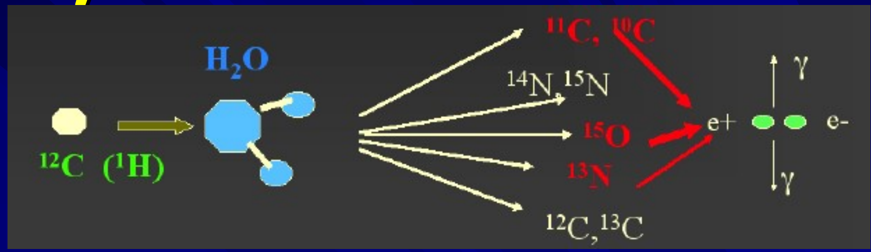
- Reducing error means → Real Time imaging
  - 3D in vivo dosimetry and tomography
    - *Use fragments of beam projectile reactions in the biological matter emerging from the tumor target volume*
- Verification using Computed Tomography/Radiography:
  - CT imaging in charged Particle therapy is needed 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







10^{-21} 10^{-18} 10^{-15} 10^{-12} 10^{-9} 10^{-6} 10^{-3} 10^{0} 10^{3}

Time (s) after collision

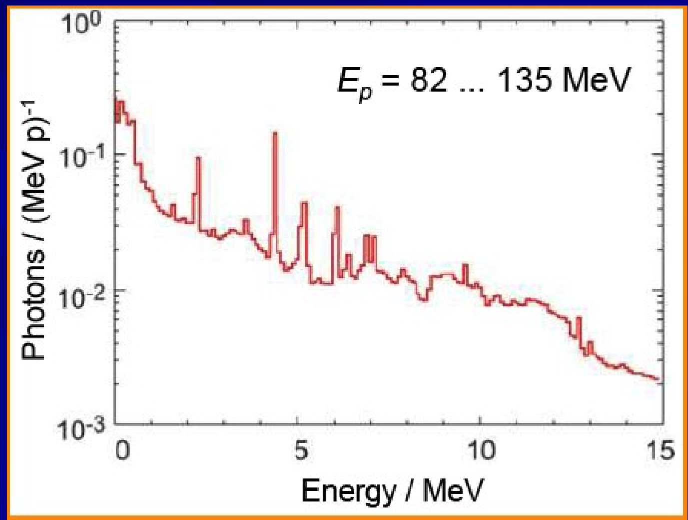
Particles

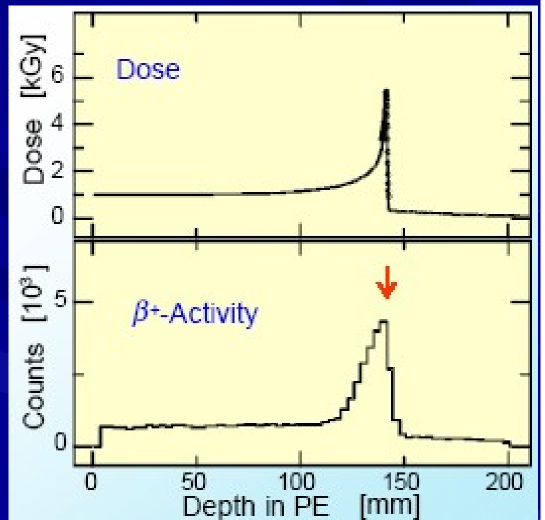
Prompt γ-rays

β^+ - emitter decay

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:	$2 \cdot 10^{-5}$	($2 \cdot 10^5$)

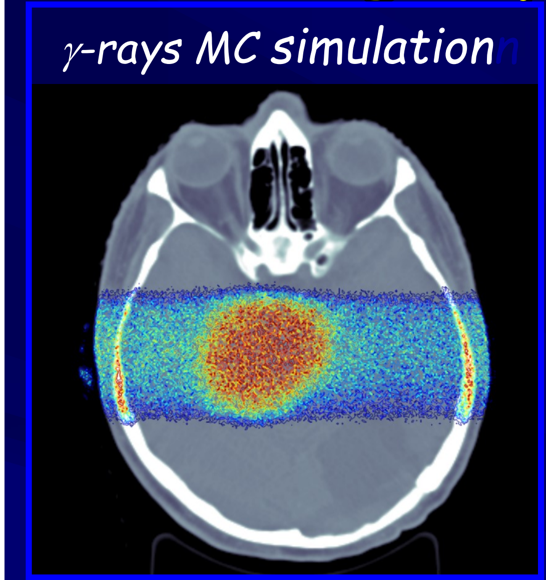




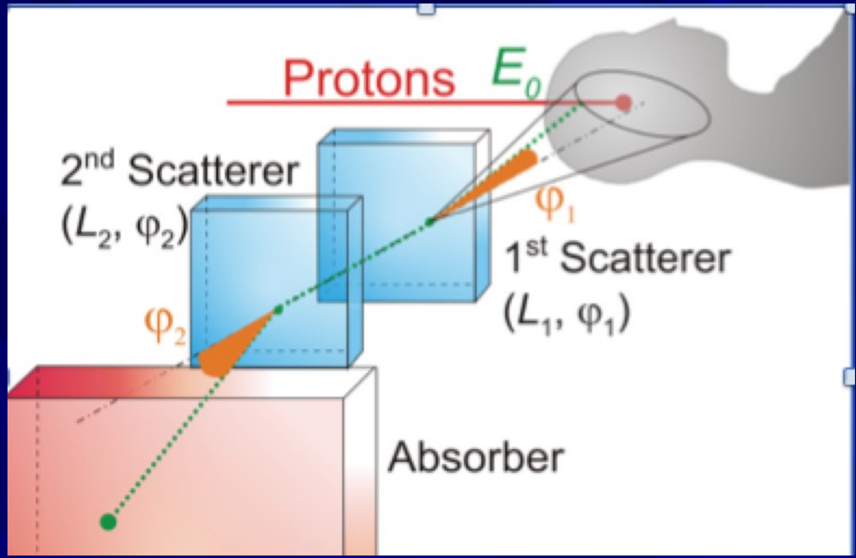
- *However the photon energy different from standard medical (Anger) SPECT camera*

Relation between dose and β+ activities

Single photon: in vivo Compton Camera

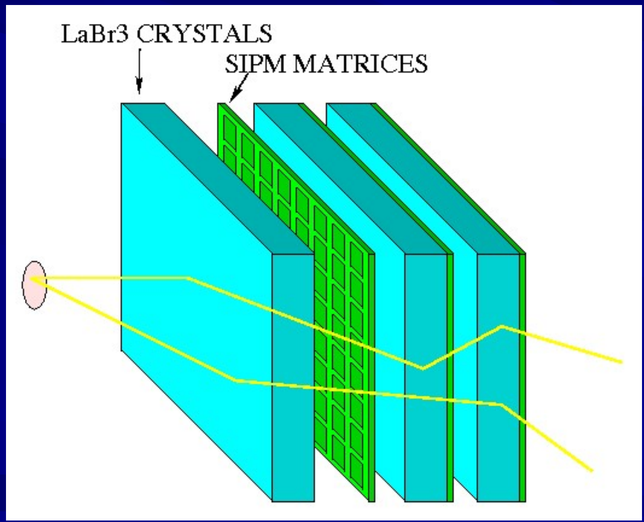


(A.Muller,TU Dresden)

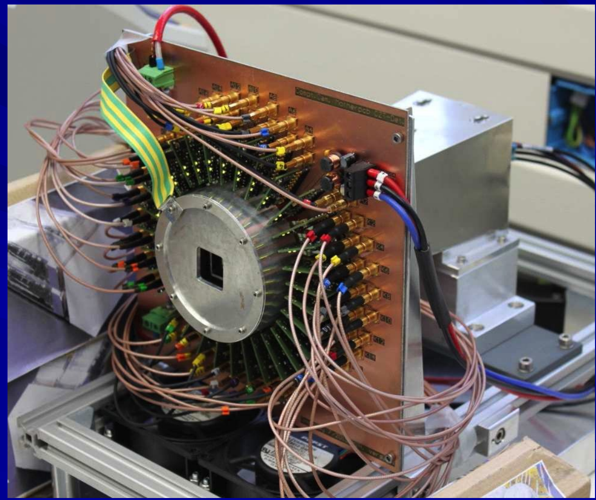


- Required devices:
  - Hodoscope (x,y,t)
  - Scatterer (x,y,E)
  - Absorber (x,y,z,E,t)

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

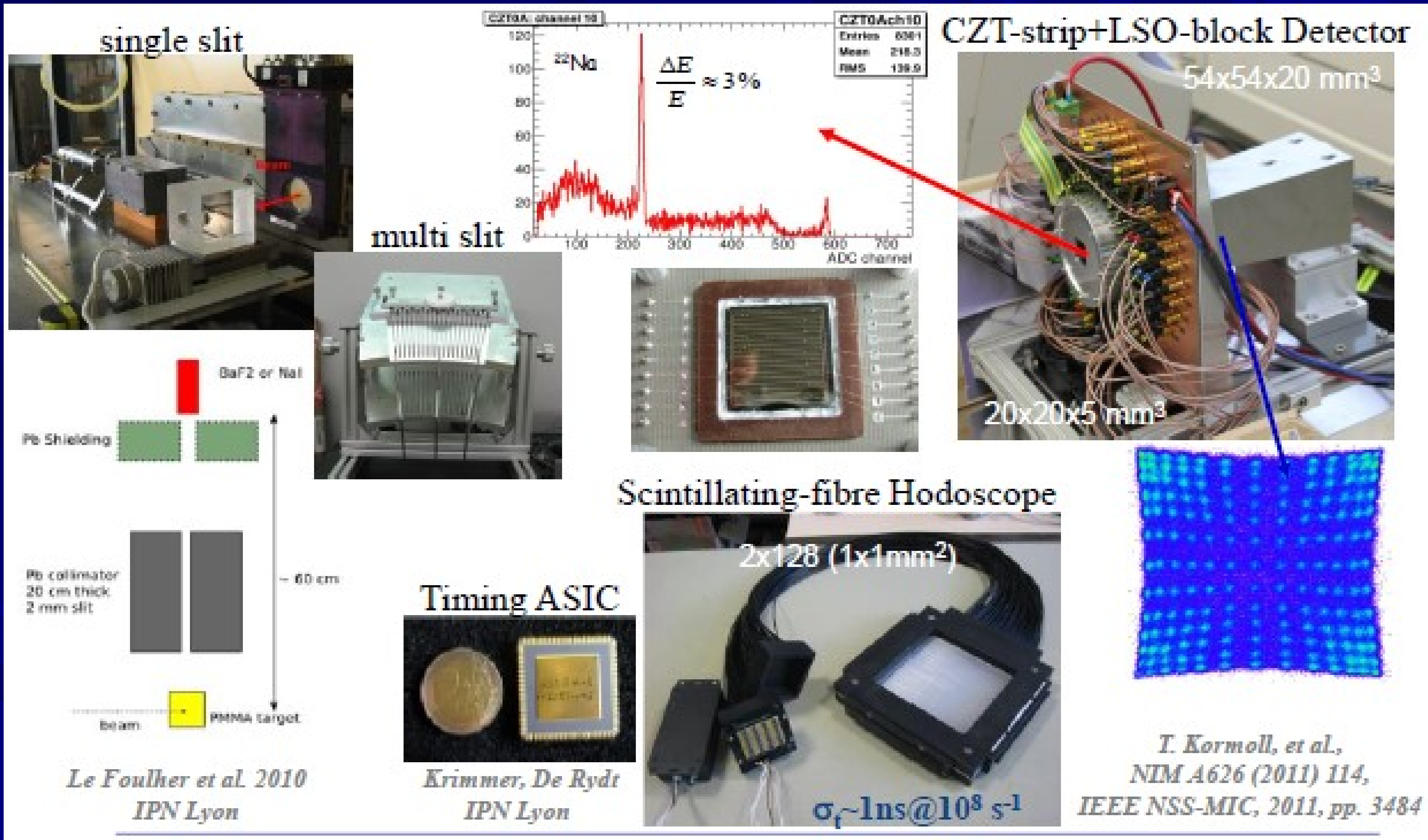


C.Llosa, IFIC



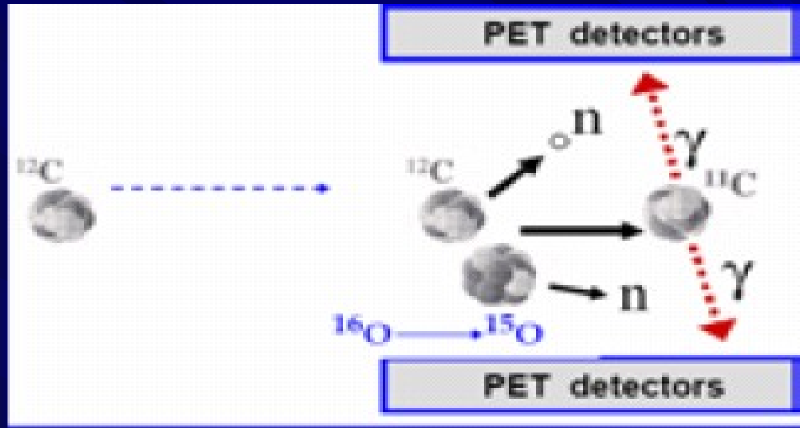
CZT-strip+LYSO-block Detector F.Fiedler et al. Dresden

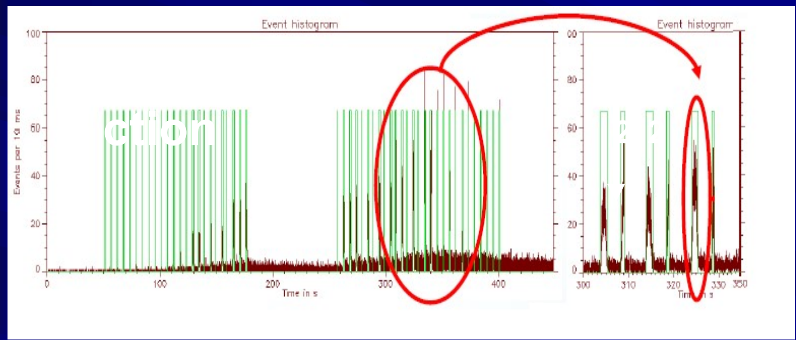
Exemple of Single photon: in vivo SPECT



Present examples: in beam PET

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



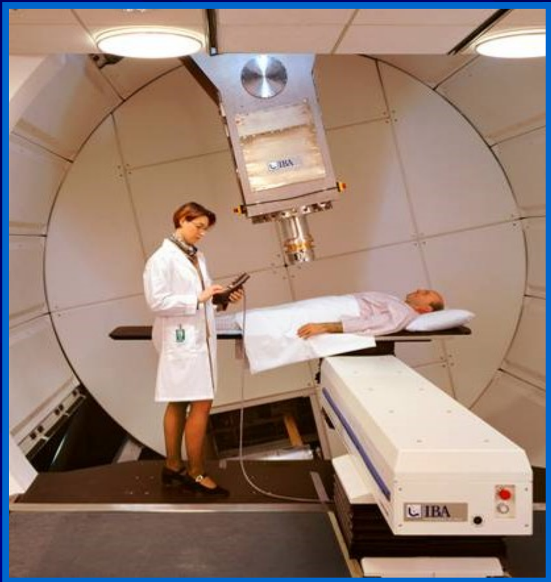


^{1}H-therapy at the National Cancer Center, Kashiwa, Japan

- 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*

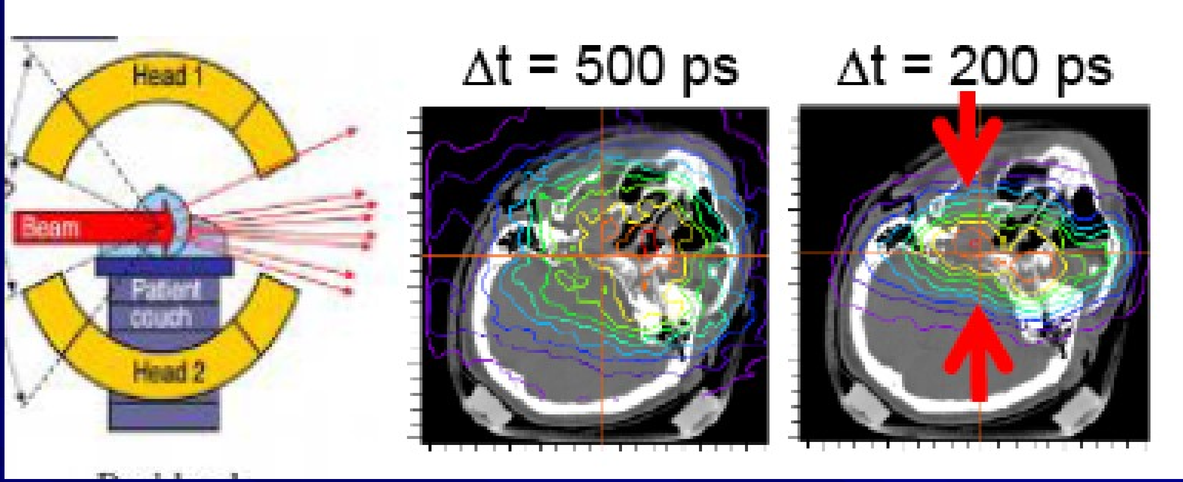
☹ *In-vivo dosimetry & real-time image guidance*

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

Mature technology

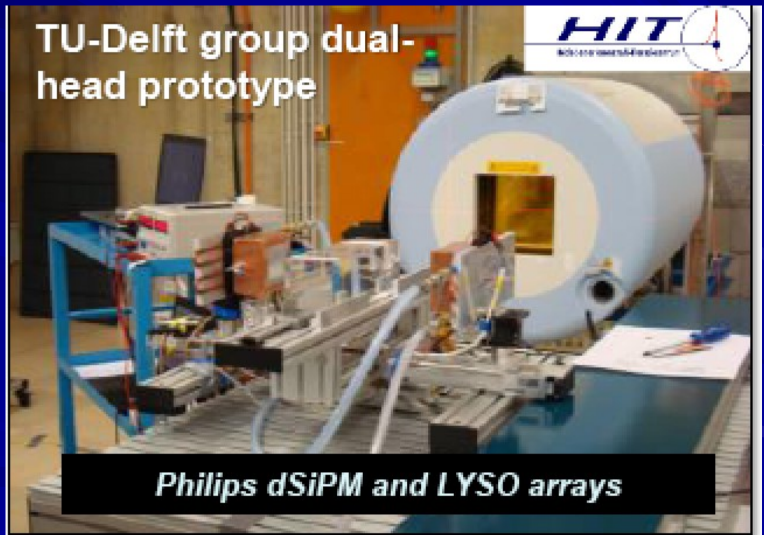
Courtesy W. Enghardt / OncoRay

In vivo PET recent developments

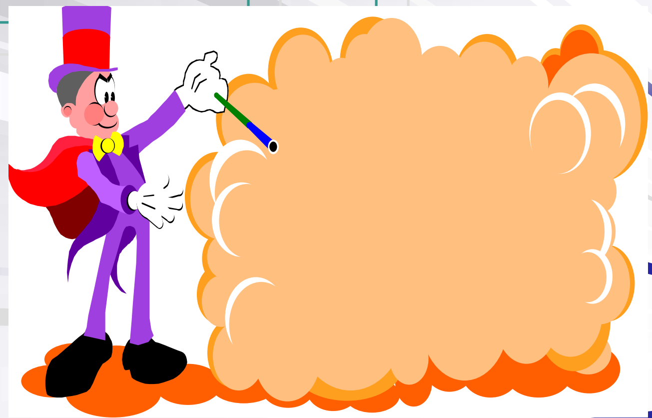


MGH

Courtesy T. Yamaya, NIRS Japan
Presented at IEEE MIC 2014

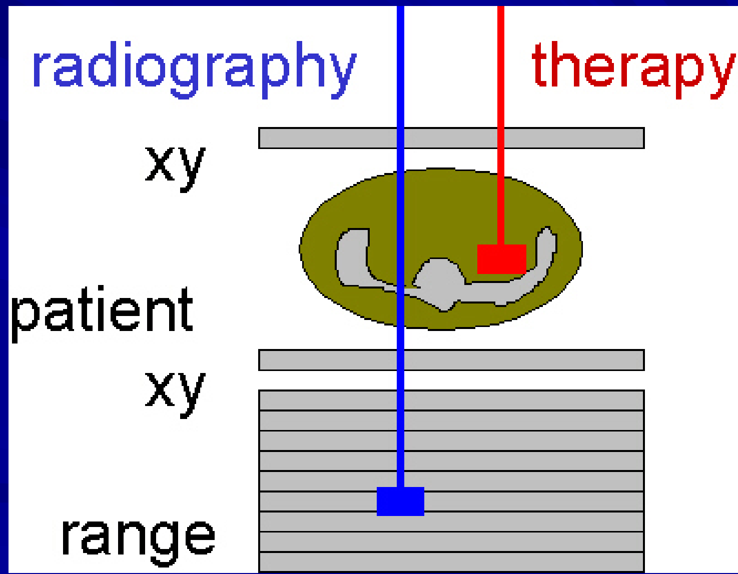


Another dream
The Proton CT



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*

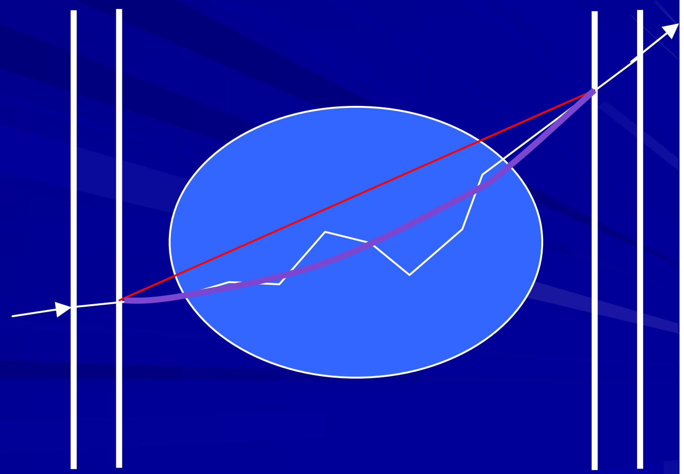


The protons go through the patient
Higher energy, small dose

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*

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



Radiograph of a phantom
Uwe Schneider PhD thesis
(1978,PSI)
A tribute to G.Charpak

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

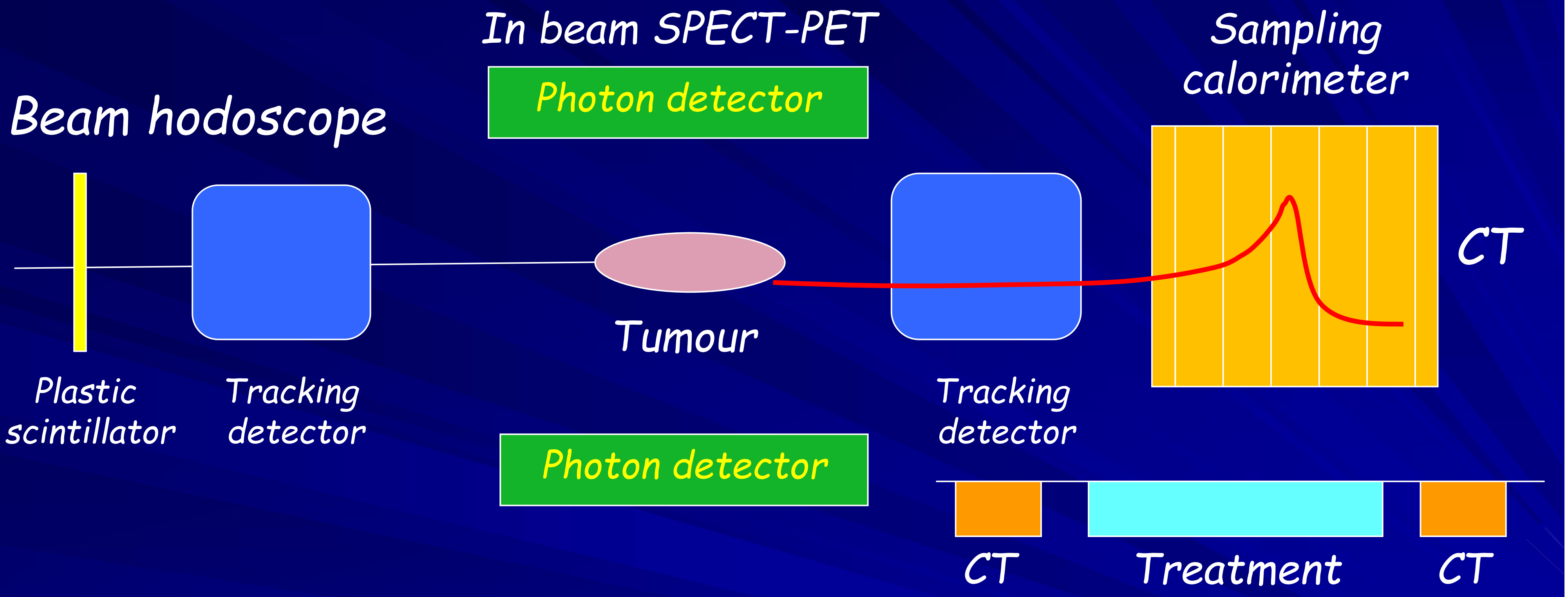
Tumor site	X-rays	IMXT	Protons
Oesoph. & stomach	0.15	0.11	0.00
Colon	0.15	0.07	0.00
Breast	0.00	0.00	0.00
Lung	0.07	0.07	0.01
Thyroid	0.18	0.06	0.00
Bone & soft tissue	0.03	0.02	0.01
Leukemia	0.07	0.05	0.03
All	0.75	0.43	0.05
Compared to X-rays	1	0.6	0.07

The Basics Ingredients

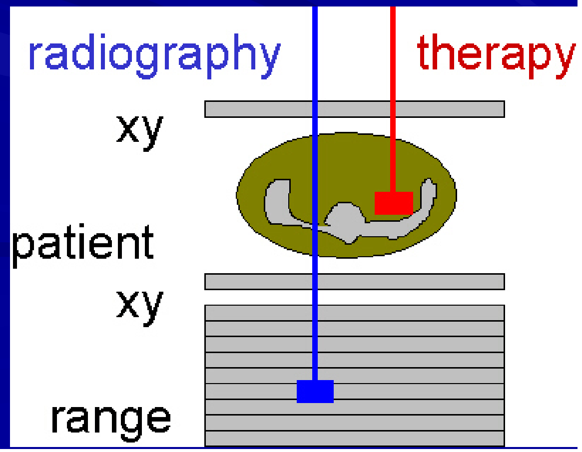
- Beam
  - Measurement (position and direction) particle per particle
- Photon detectors
  - In beam selection of
    - single photon → compton camera (SPECT)
    - two photons → in Beam TOF-PET
- Proton (ion) CT
  - Measure the energy (position, energy and time) of the diffracted particle in an imaging 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)

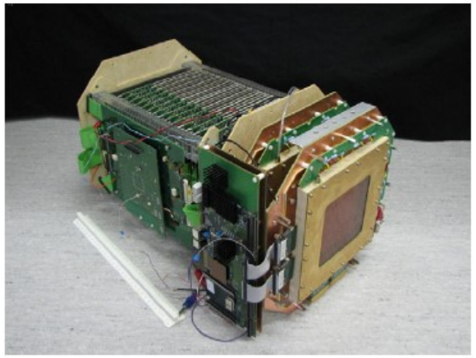
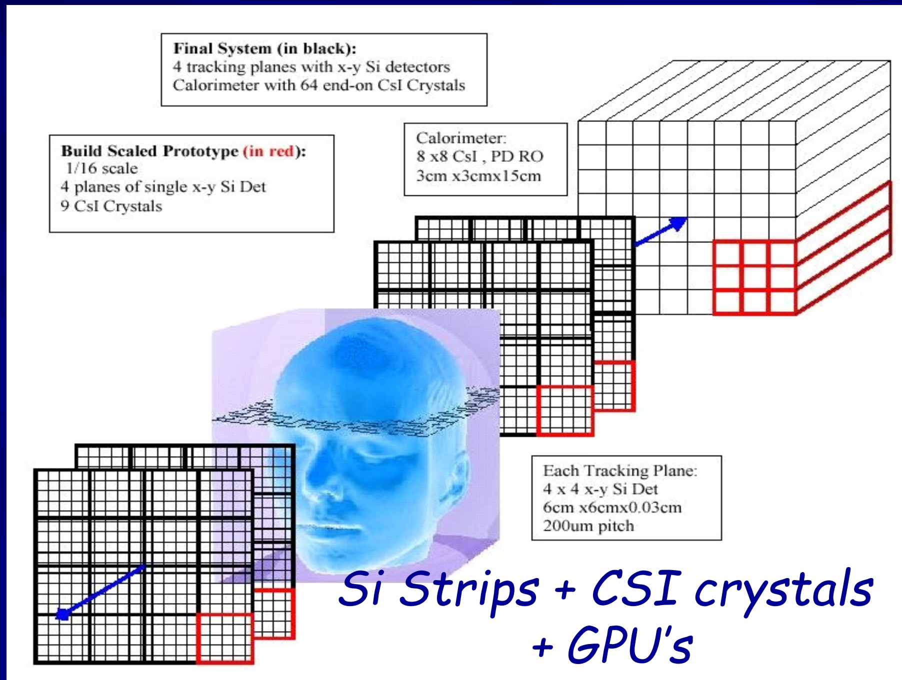
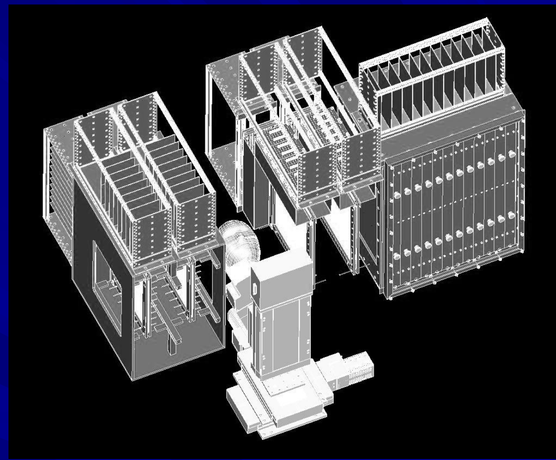


Fig. 1. The Proton Range Radiography setup.

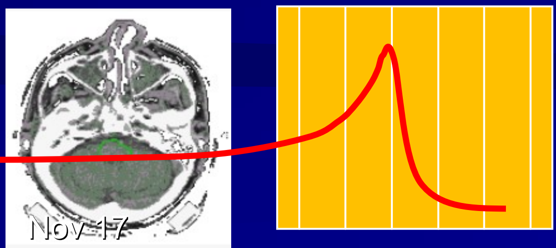
AQUA-CNAO
Scint/MPPC/GEM



Si Strips + CSI crystals
+ GPU's

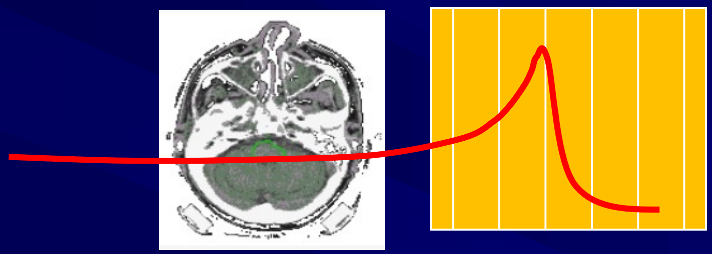


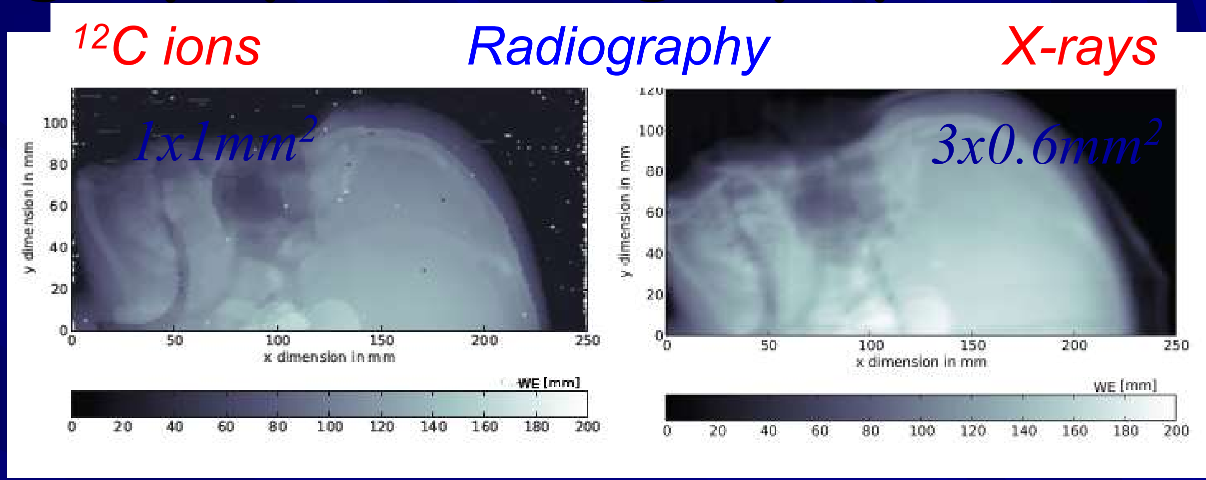
NIU/FNAL
Scint/WLS+SiPM
GPU farm



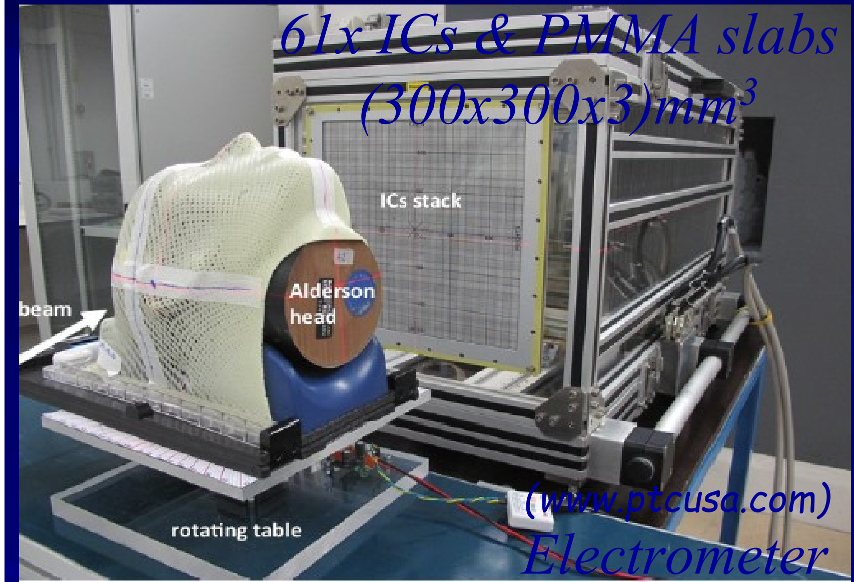
- *Ion Transmission Imaging*
  - *→ See talk from B.Voss*

Primary-Ion Radiography / Tomography

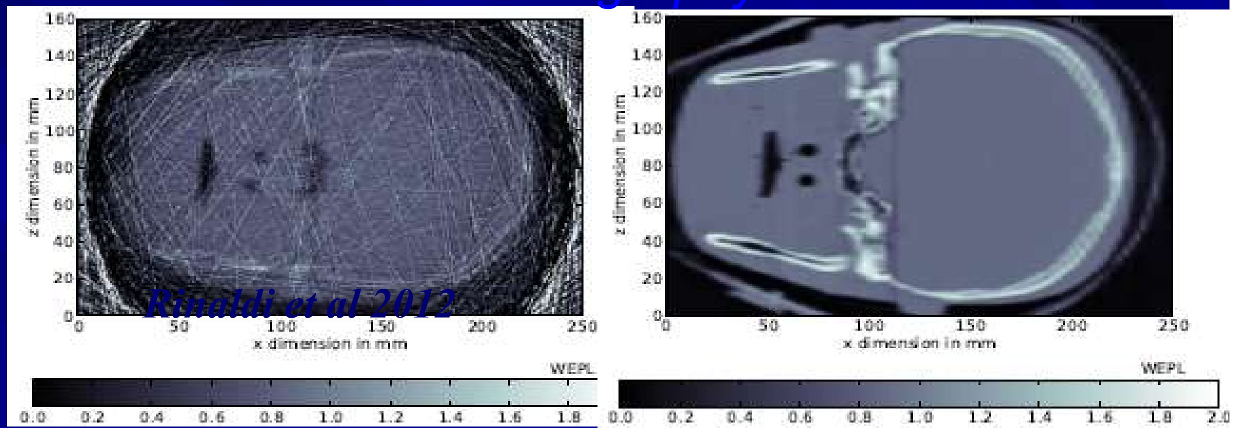




Water equivalent thickness



Tomography



Water equivalent path length

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

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

Thanks to

- D.Townsend (U. Singuapor)
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- S.Majewski (WVU)
- K.Parodi (HIT)
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- Pr. J.P. Gerard (Nice)
- … and many others

Thank you
for your attention