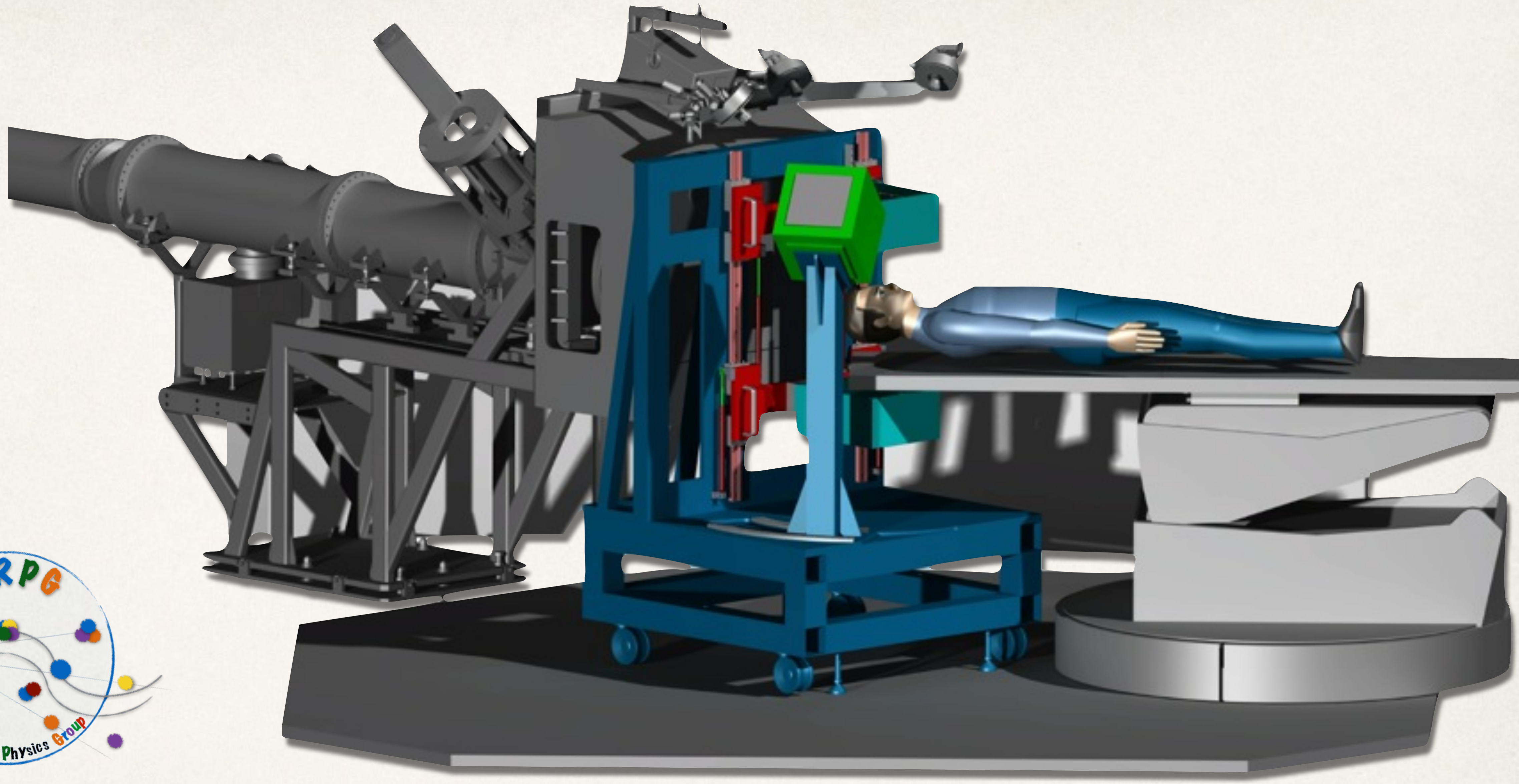

New online methods to monitor dose profiling in particle therapy treatments

Novel particle physics applications in medicine @INFN Roma

November, 17th 2014

Michela Marafini

New online methods to monitor dose profiling in particle therapy treatments

- particle therapy
- dose profile
- monitoring
  - different approaches
  - correlated physics measurements
  - our new online monitor!

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  - **our new online monitor!**

Tumor Treatments

Radiotherapy:

- mainly **photons** and electrons;
- useful for 50-60% of all cancer patients (also together surgery);
- the use of sophisticated imaging (CT), the superposition of several beams, computed optimization and multi-leaves collimators increase the power of this technique.

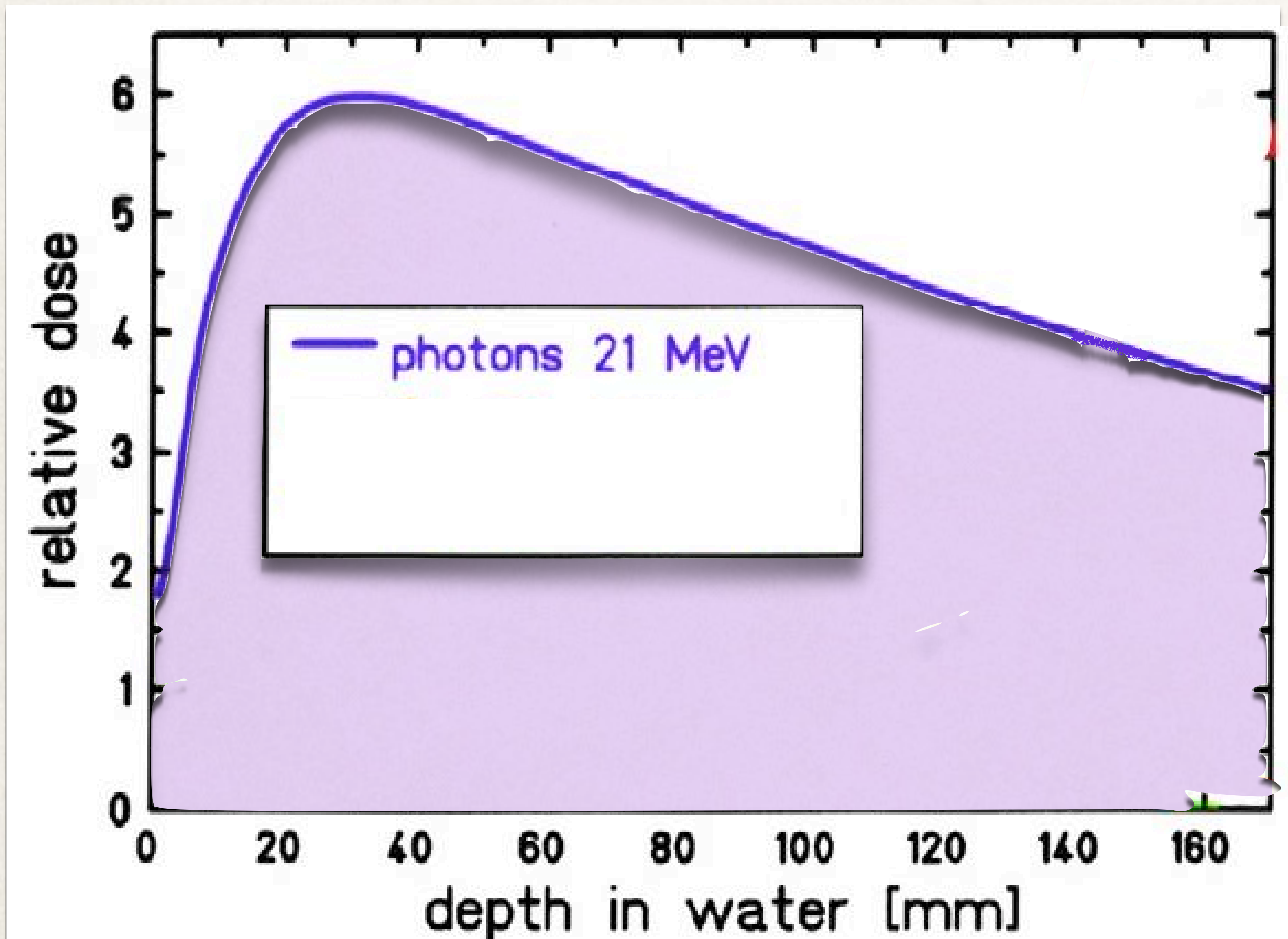
Not so expensive, small, and reliable

BUT

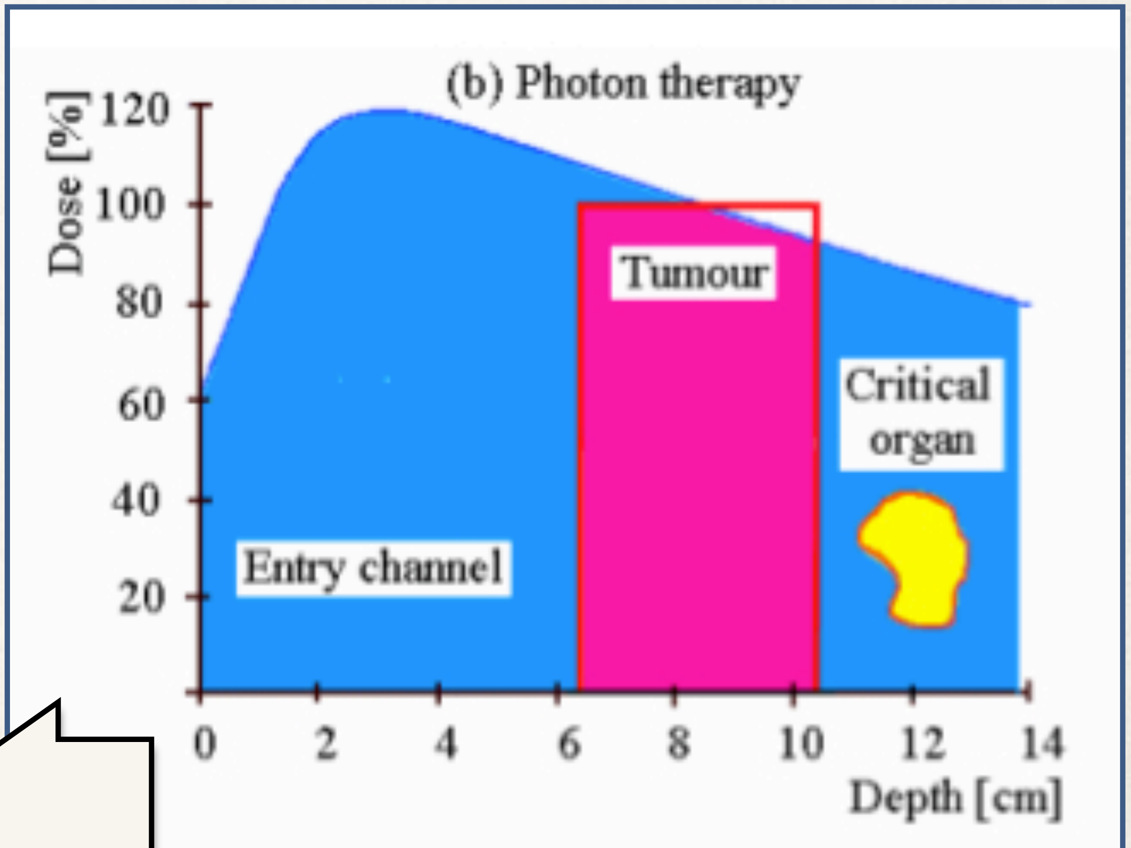
The **energy release shape** is not so suitable to release dose in a deep tumor..

RT: dose distribution

The dose is released in all the tissues crossed by the photons



$$Dose = \frac{dE_{abs}}{dm}$$



The dose distribution of the RT implies a large, and unwanted, dose absorption to the healthy tissues..

Tumor Treatments

Many tumors are not treated:

- Radio-resistent tumor;
- Position close to organ at risk (OAR)

Hadron RT was proposed by Robert Wilson in 1946

..the first PT treatment started only in the sixties in USA with protons!

Particle Therapy can be a viable solution to increase cure thanks to its better **localized dose distribution** and its greater **efficiency** in killing tumor cells

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 ~~plied to medical problems. This has, in ~~e part, been due to the very short ~~ation in tissue of protons, deu~~ ~~ particles from prese~~ ~~r-energy mach~~ ~~ how~~

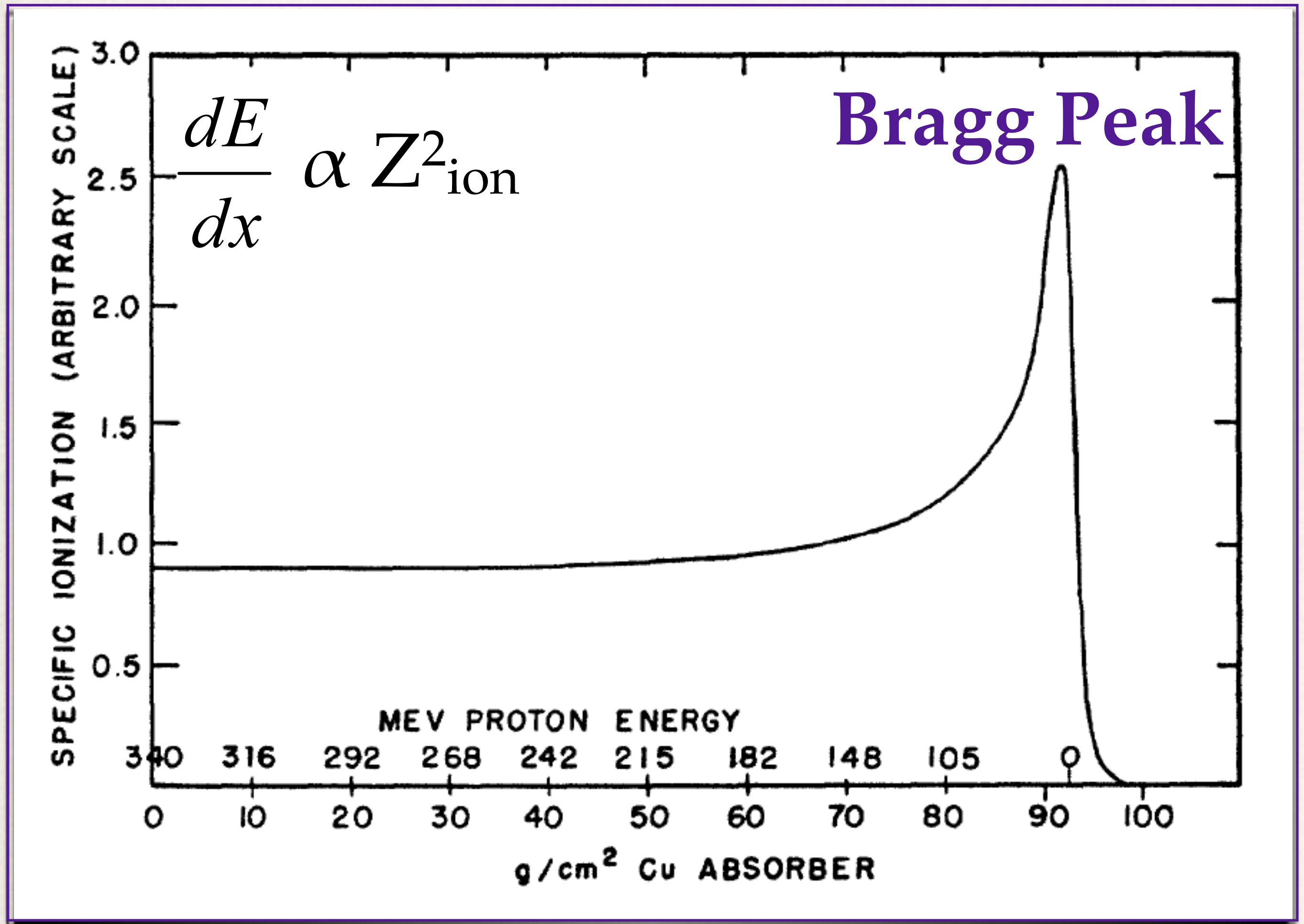
per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

These properties make it possible to irradiate inter~~ly a strictly localized region ~~

Radiology 47: 487-491, 1946

"Foreword to the Second International Symposium on Hadrontherapy" U.Amaldi et al. Excerpta Medica, Elsevier, International Congress Series 1144: ix-xiii (1997)

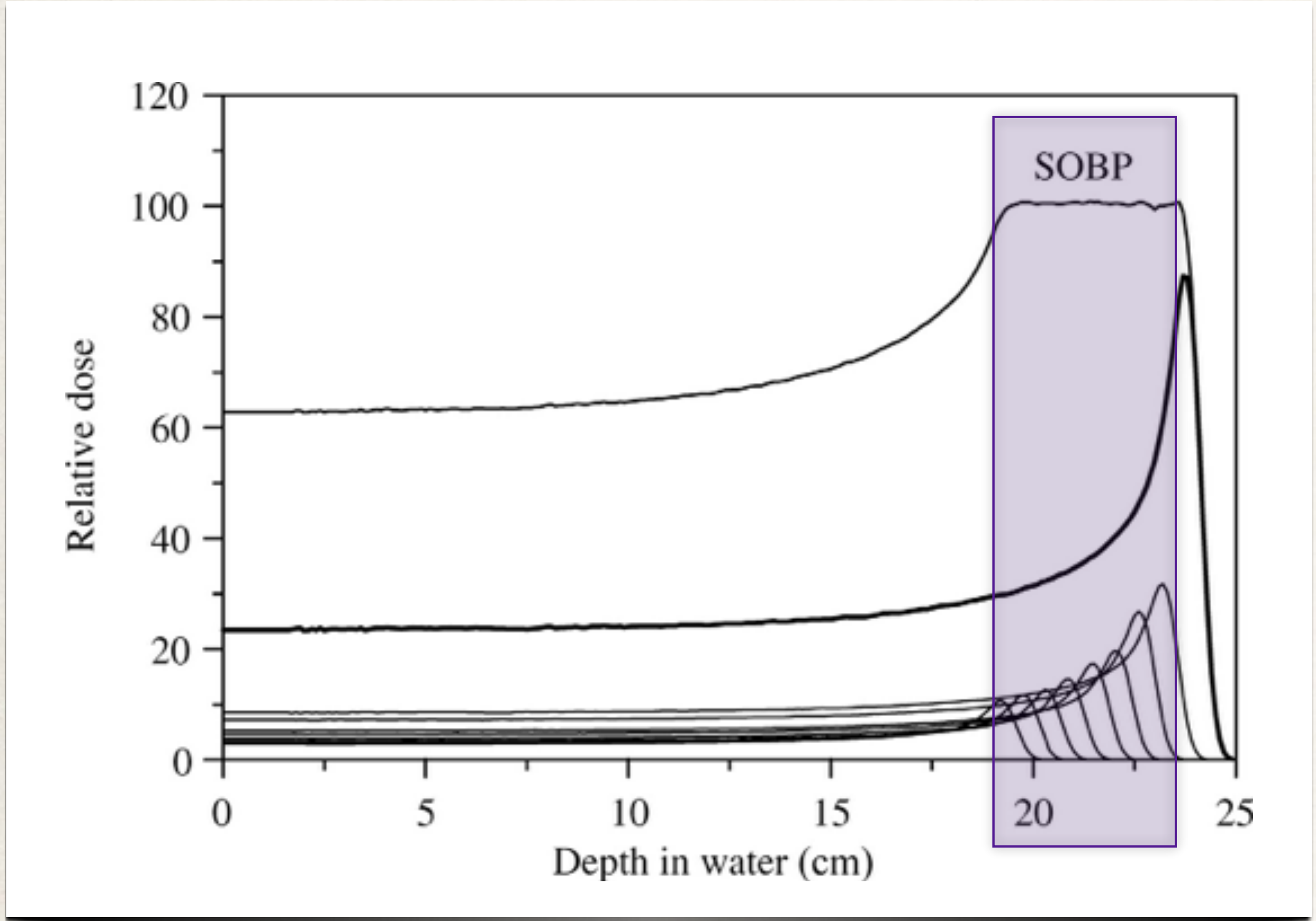
PT: dose distribution



PT allows to concentrate the energy in a specific region preserving the surrounding tissues

The position is a function of:
- beam energy;
- density of the material;

PT: dose distribution



Several pencil beams can be combined in order to “shape” the maximum dose release region.

Localized dose distribution

Spread-out-Bragg Peak

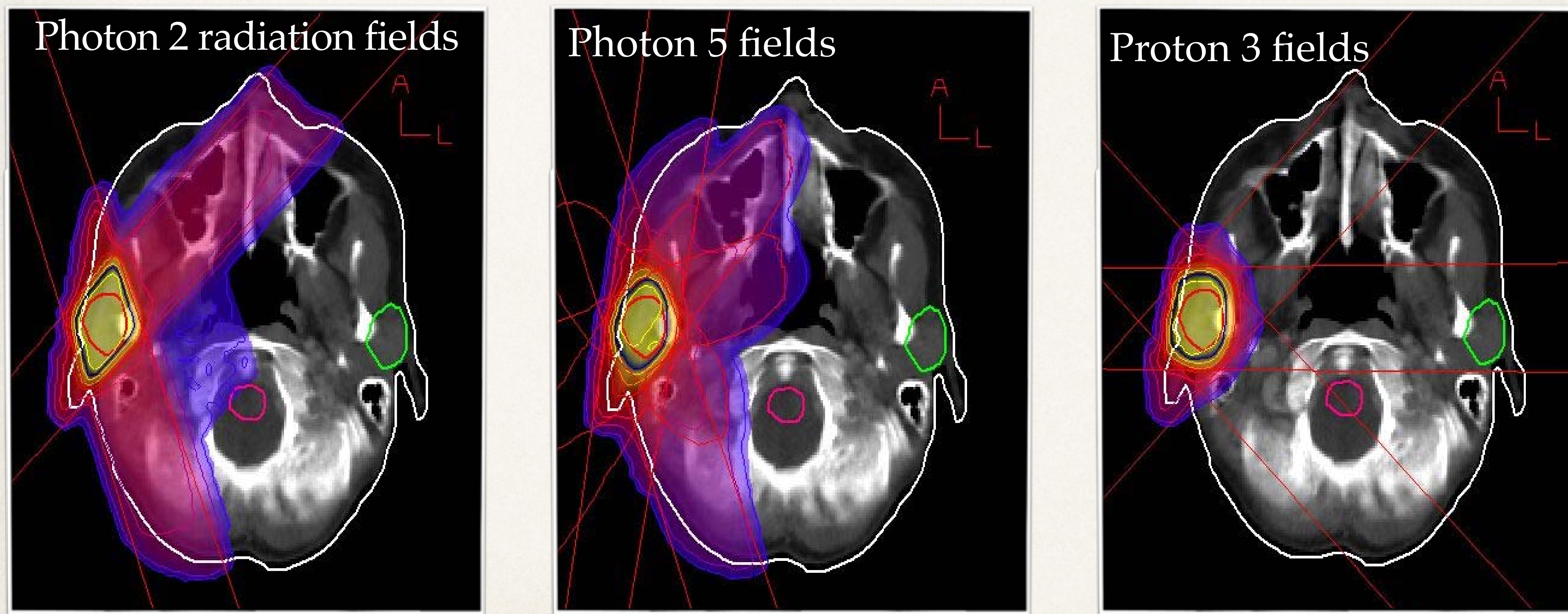
The position is a function of:

- beam energy;

- density of the material;

PT: dose distribution

The combination of many radiation fields allows improving the performances for loco-regional tumors => preserve the healthy tissues.

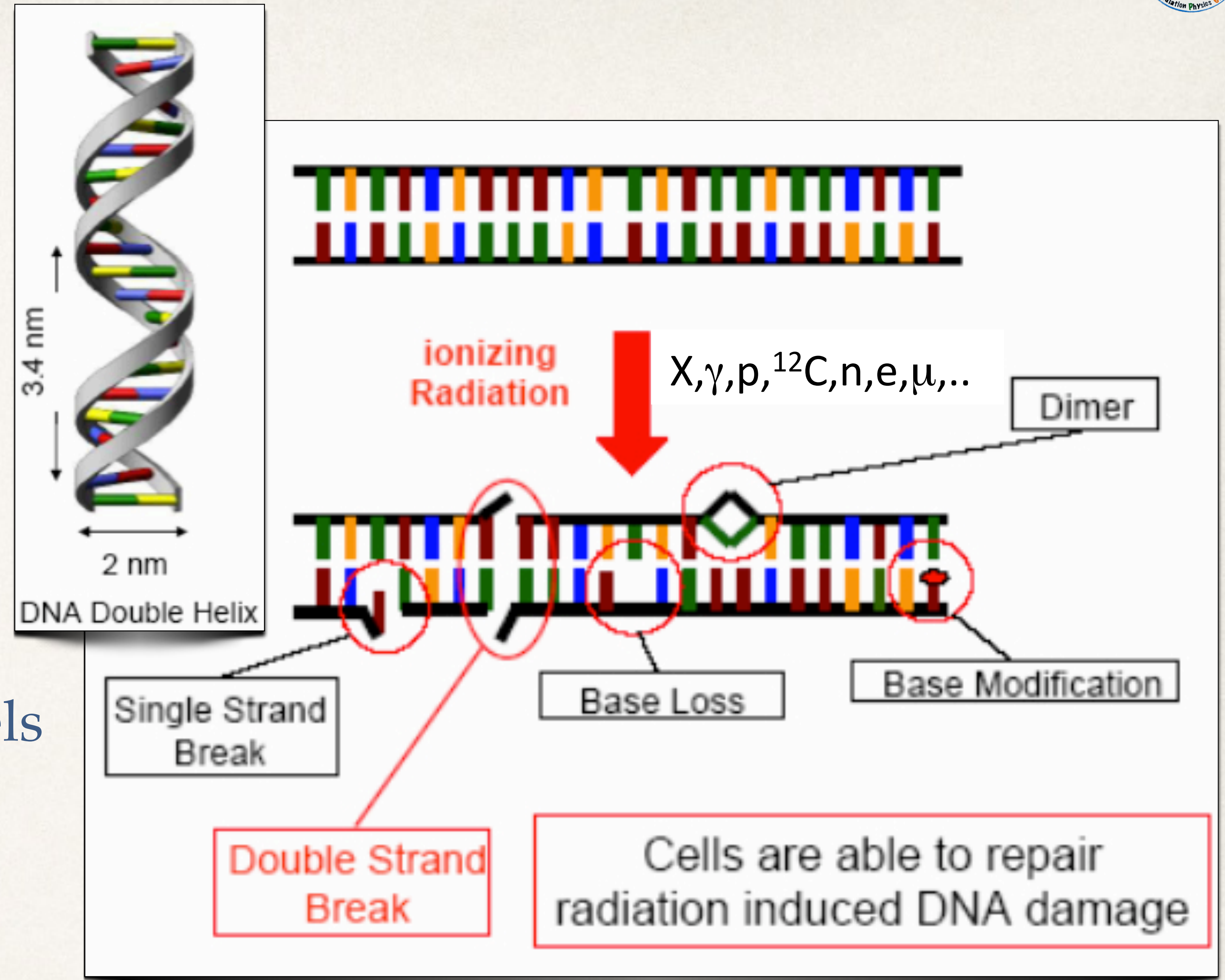


Universitätsklinik für Strahlentherapie und Strahlenbiologie, AKH, Wien

PT: LET

LET ~ ΔE/Δx

Linear Energy Transfer



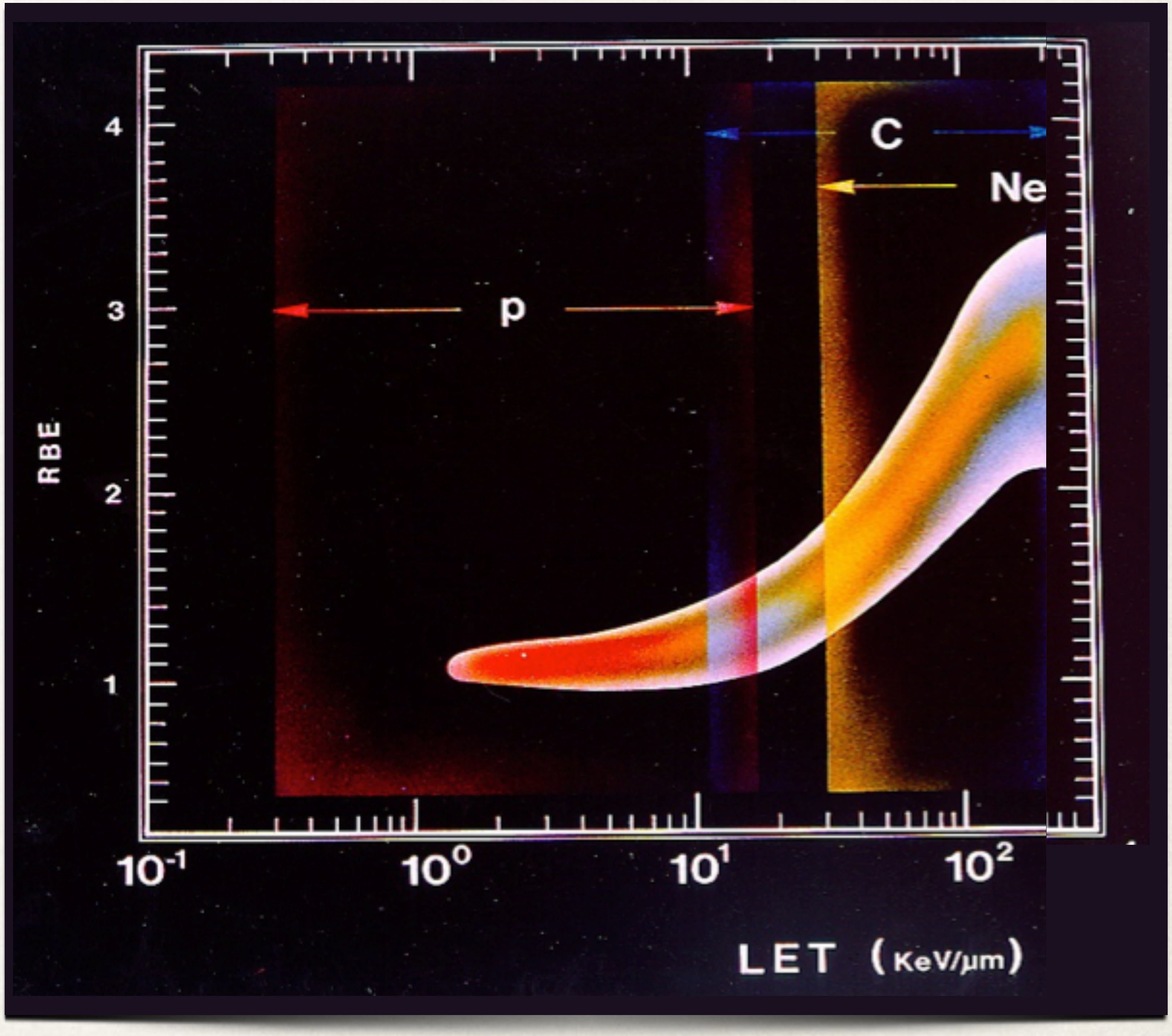
Indirect damage:
the radiation induce (mainly in water) free radicals that break the cels

Direct damage:
the radiation breaks directly the DNA

Because of their high LET carbon ions (and ions in general) are able to induce direct damage => higher Relative Biological Effectiveness

PT: LET

Carbon ions are much better at killing the tumor cells with respect to the X rays for a given dose released => **high RBE**

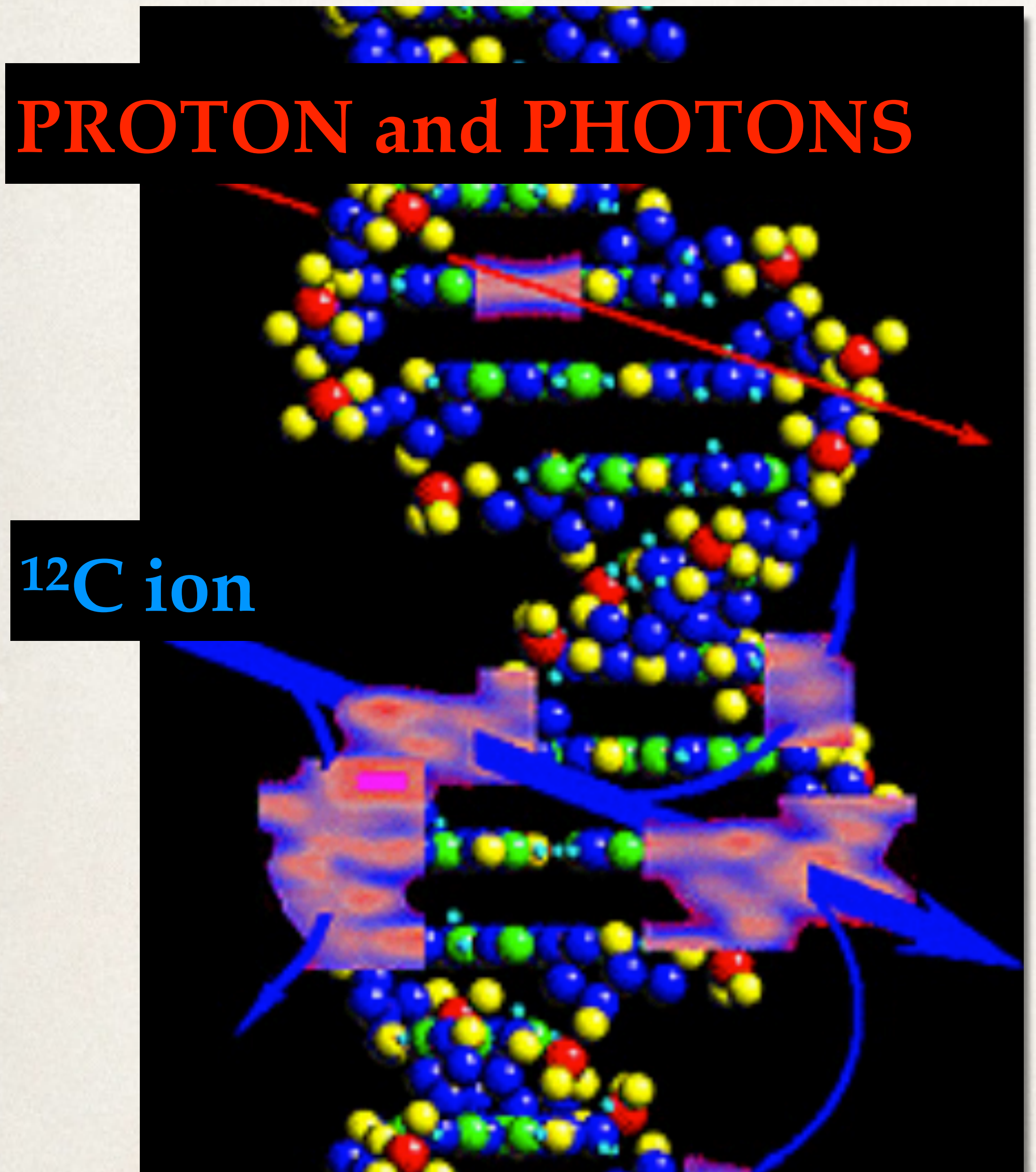


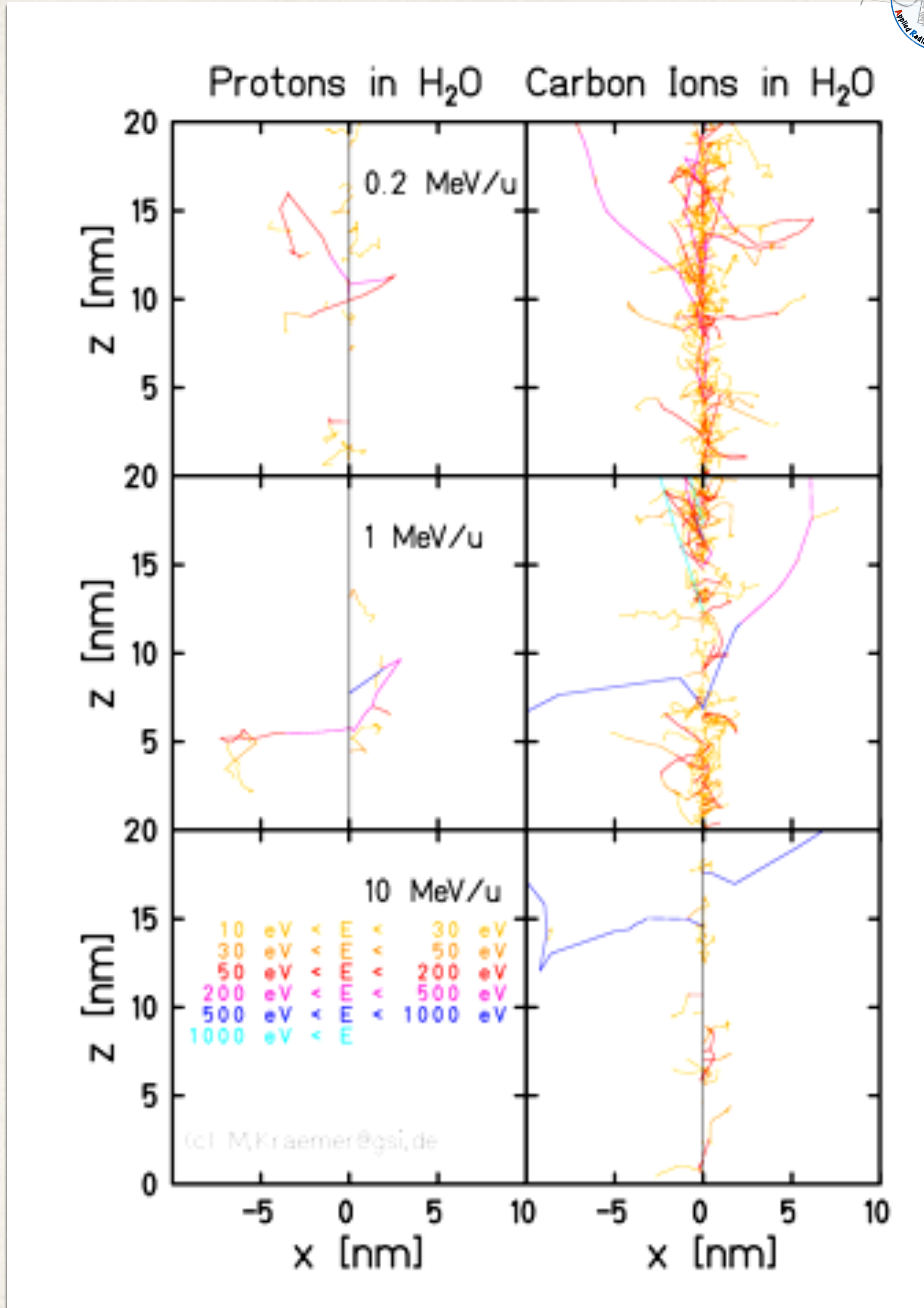
Relative Biological Effectiveness

$$RBE = [\frac{D_\gamma}{D_{ion}}]_{Isoeffect}$$

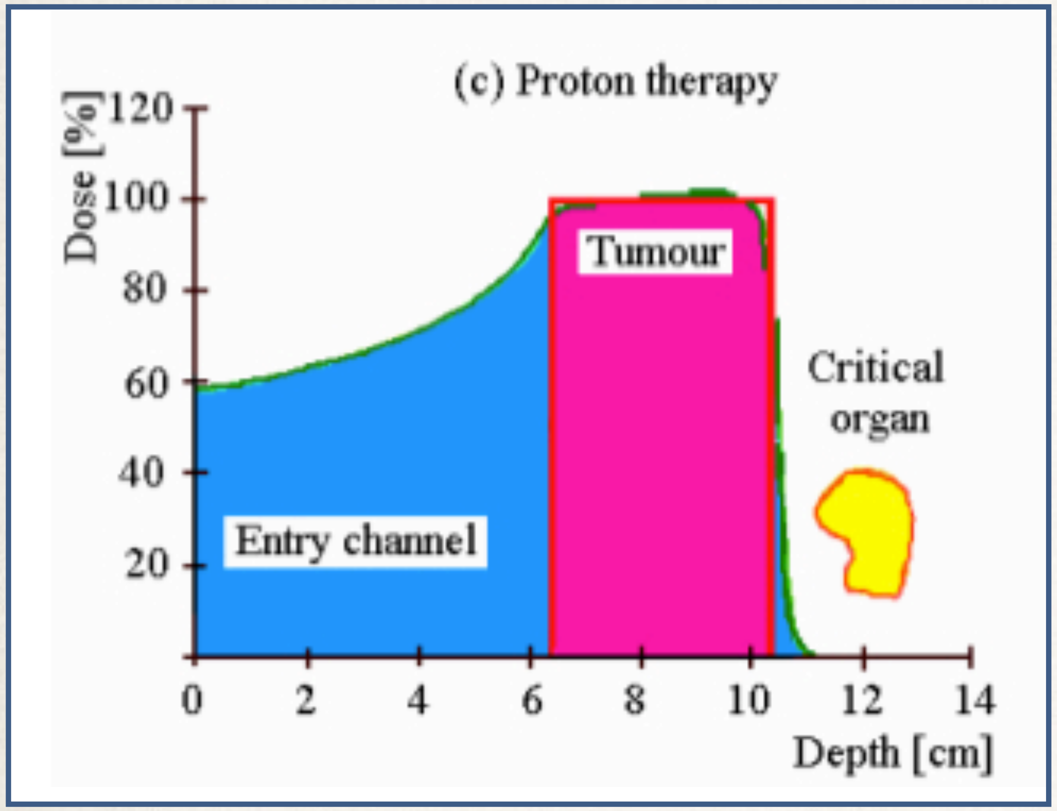
PT: LET

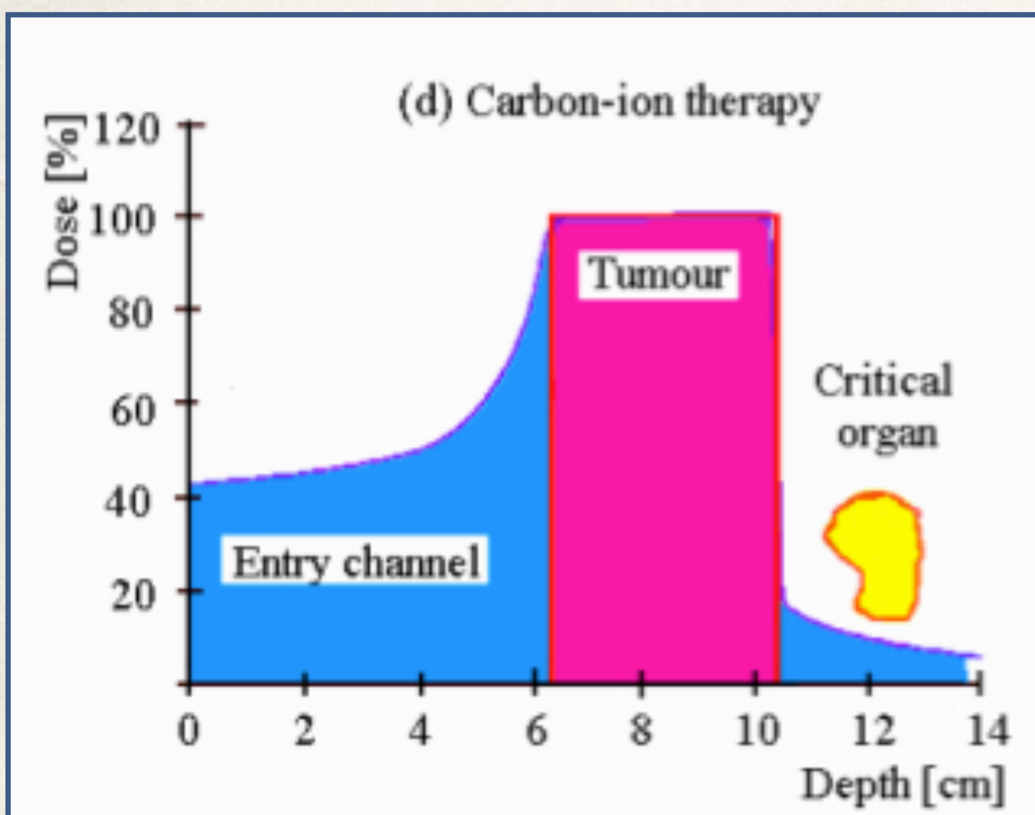
The high ionization density of ^{12}C induces easily DSB in DNA helix





PT: dose distribution



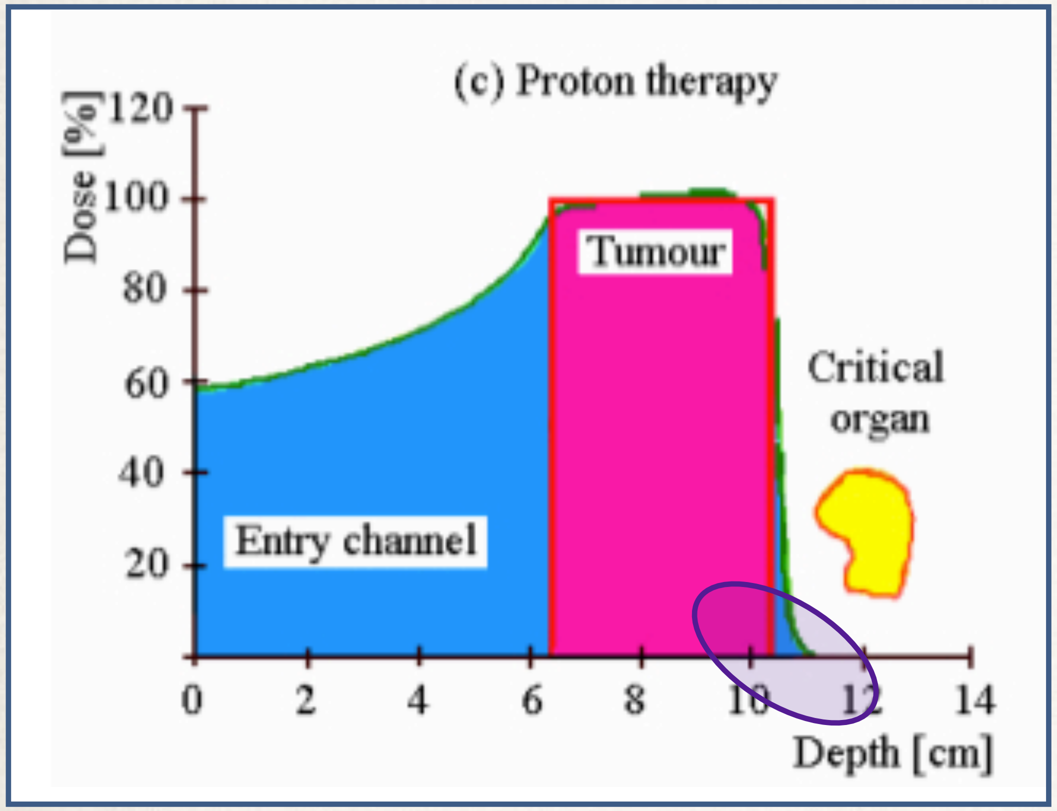


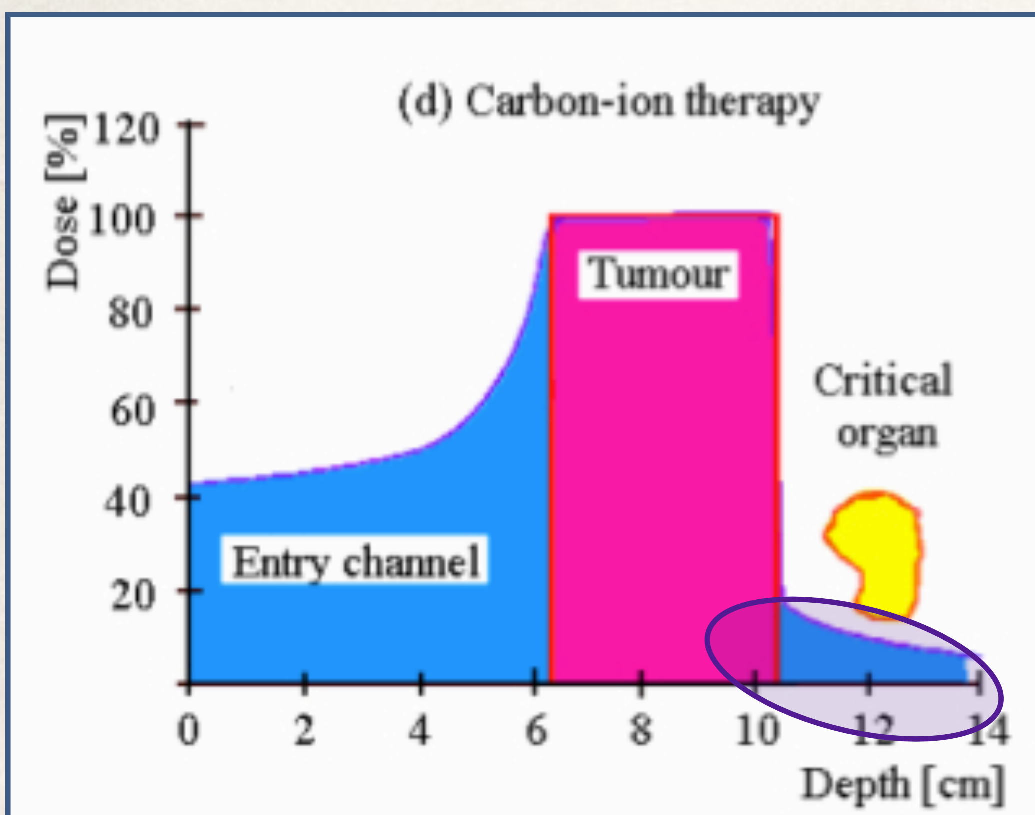
The dose distribution depends also from the type of the beam. 12C ion and proton beams, for example, have different characteristics:

- Proton

- Carbon

PT: dose distribution





The dose distribution depends also from the type of the beam. 12C ion and proton beams, for example, have different characteristics:

- Proton: Reduced **fragmentation**

- Carbon: Reduced Multiple Scattering

PT: dose distribution

FUTURE BEAMS

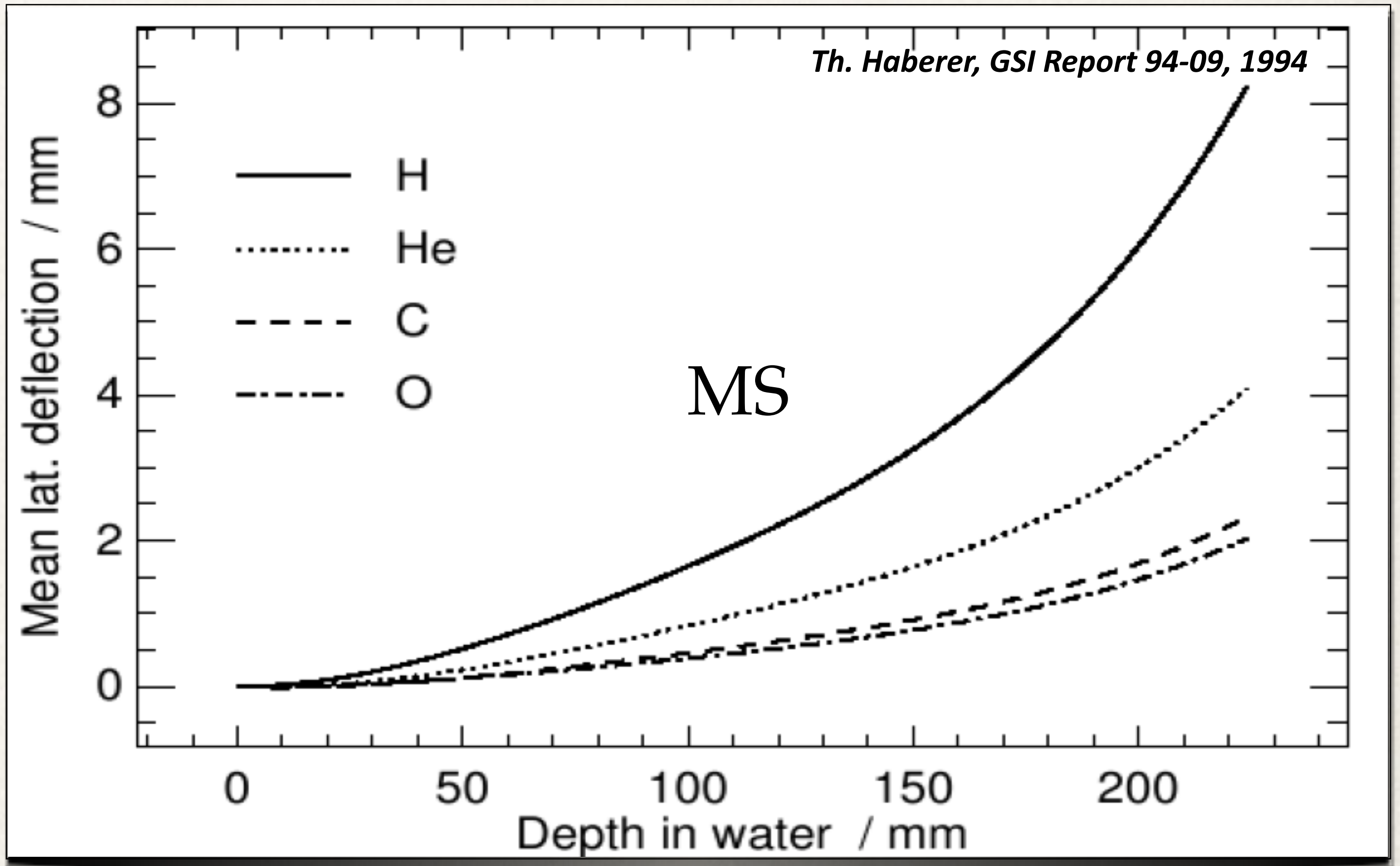
- **Helium**
  - less MS than p
  - reduced fragmentation compared to C;
- **Oxygen**
  - hight RBE

(ipoxit or strongly radioresistent tumors)

The dose distribution depends also from the type of the beam. 12C ion and proton beams, for example, have different characteristics:

- Proton: Reduced **fragmentation**

- Carbon: Reduced Multiple Scattering



Particle therapy

http://www.ptcog.ch/index.php/particle-therapy-literature

Particle Therapy Patient Statistics (per end of 2013)

WHERE COUNTRY	SITE	PARTICLE	FIRST (-LAST) PATIENT	PATIENT TOTAL	DATE OF TOTAL	
Belgium	Louvain-la-Neuve	p	1991 (-1993)	21	1993	ocular tumors only
Canada	Vancouver (TRIUMF)	π^-	1979 (-1994)	367	1994	ocular tumors only
Canada	Vancouver (TRIUMF)	p	1995	175	Dec-13	ocular tumors only
Czech Rep.	Prag (PTCCZ)	p	2012	140	Dec-13	
China	Wanjie (WPTC)	p	2004	1078	Dec-13	
China	Lanzhou	C ion	2006	213	Dec-13	
England	Clatterbridge	p	1989	2446	Dec-13	ocular tumors only
France	Nice (CAL)	p	1991	4936	Dec-13	ocular tumors only
France	Orsay (CPO)	p	1991	6432	Dec-13	5082 ocular tumors
Germany	Darmstadt (GSI)	C-ion	1997 (-2009)	440	2009	
Germany	Berlin (HMI)	p	1998	2312	Dec-13	ocular tumors only
Germany	Munich (RPTC)	p	2009	1811	Dec-13	
Germany	HIT, Heidelberg	C ion	2009	1368	Dec-13	
Germany	HIT, Heidelberg	p	2009	503	Dec-13	
Germany	WPE, Essen	p	2013	32	Dec-13	
Italy	Catania (INFN-LNS)	p	2002	293	Nov-12	ocular tumors only
Italy	Pavia (CNAO)	p	2011	76	Dec-13	
Italy	Pavia (CNAO)	C ion	2012	105	Dec-13	
Japan	Chiba	p	1979 (-2002)	145	2002	ocular tumors only
Japan	Tsukuba (PMRC, 1)	p	1983 (-2000)	700	2000	
Japan	Chiba (HIMAC)	C ion	1994	8073	Dec-13	377 with scanning
Japan	Kashiwa (NCC)	p	1998	1226	Mar-13	
Japan	Hyogo (HIBMC)	p	2001	4223	Dec-13	
Japan	Hyogo (HIBMC)	C ion	2002	1935	Dec-13	
Japan	WERC	p	2002 (-2009)	62	2009	
Japan	Tsukuba (PMRC, 2)	p	2001	2967	Dec-13	
Japan	Shizuoka	p	2003	1590	Dec-13	
Japan	Koriyama-City	p	2008	2306	Dec-13	
Japan	Gunma	C ion	2010	985	Dec-13	
Japan	Ibusuki (MMRI)	p	2011	919	Dec-13	
Japan	Fukui City (Prefectural Hospital)	p	2011	428	Dec-13	
Japan	Nagoya PTC, Nagoya, Aichi	p	2013	199	Dec-13	
Japan	Tosu (Saga-HIMAT)	p	2013	62	Dec-13	

Particle therapy

http://www.ptcog.ch/index.php/particle-therapy-literature

Poland	Krakow	p	2011	39	Dec-13	ocular tumors only
Russia	Dubna (1)	p	1967 (-1996)	124	1996	
Russia	Moscow (ITEP)	p	1969	4320	Dec-13	
Russia	St. Petersburg	p	1975	1386	Dec-12	
Russia	Dubna (JINR, 2)	p	1999	995	Dec-13	
South Africa	iThemba LABS	p	1993	521	Dec-13	
South Korea	Ilsan, Seoul (NCCR)	p	2007	1266	Dec-13	
Sweden	Uppsala (1)	p	1957 (-1976)	73	1976	
Sweden	Uppsala (2)	p	1989	1356	Dec-13	
Switzerland	Villigen PSI (Piotron)	π^-	1980 (-1993)	503	1993	
Switzerland	Villigen PSI (OPTIS 1)	p	1984 (-2010)	5458	2010	ocular tumors only
Switzerland	Villigen-PSI, incl OPTIS2	p	1996	1581	Dec-13	695 ocular tumors
USA, CA.	Berkeley 184	p	1954 (-1957)	30	1957	
USA, CA.	Berkeley	He	1957 (-1992)	2054	1992	
USA, NM.	Los Alamos	π^-	1974 (-1982)	230	1982	
USA, CA.	Berkeley	ions	1975 (-1992)	433	1992	
USA, MA.	Harvard (HCL)	p	1961 (-2002)	9116	2002	
USA, CA.	Loma Linda (LLUMC)	p	1990	17829	Dec-13	
IN., USA	Bloomington (MPRI, 1)	p	1993 (-1999)	34	1999	ocular tumors only
USA, CA.	UCSF - CNL	p	1994	1621	Dec-13	ocular tumors only
USA, MA.	Boston (NPTC)	p	2001	7345	Dec-13	
USA, IN.	Bloomington (IU Health PTC)	p				
USA, TX.	Houston (MD Anderson)	p				
USA, FL	Jacksonville (UFPTI)	p				
USA, OK.	Oklahoma City (ProCure PTC)	p				
USA, PA.	Philadelphia (UPenn)	p				
USA, IL.	CDH Warrenville	p				
USA, VA.	Hampton (HUPTI)	p				
USA, NY.	New Jersey (ProCure PTC)	p				
USA, WA	Seattle (SCCA ProCure PTC)	p				
USA, MO.	St. Louis (S. Lee King PTC)	p				

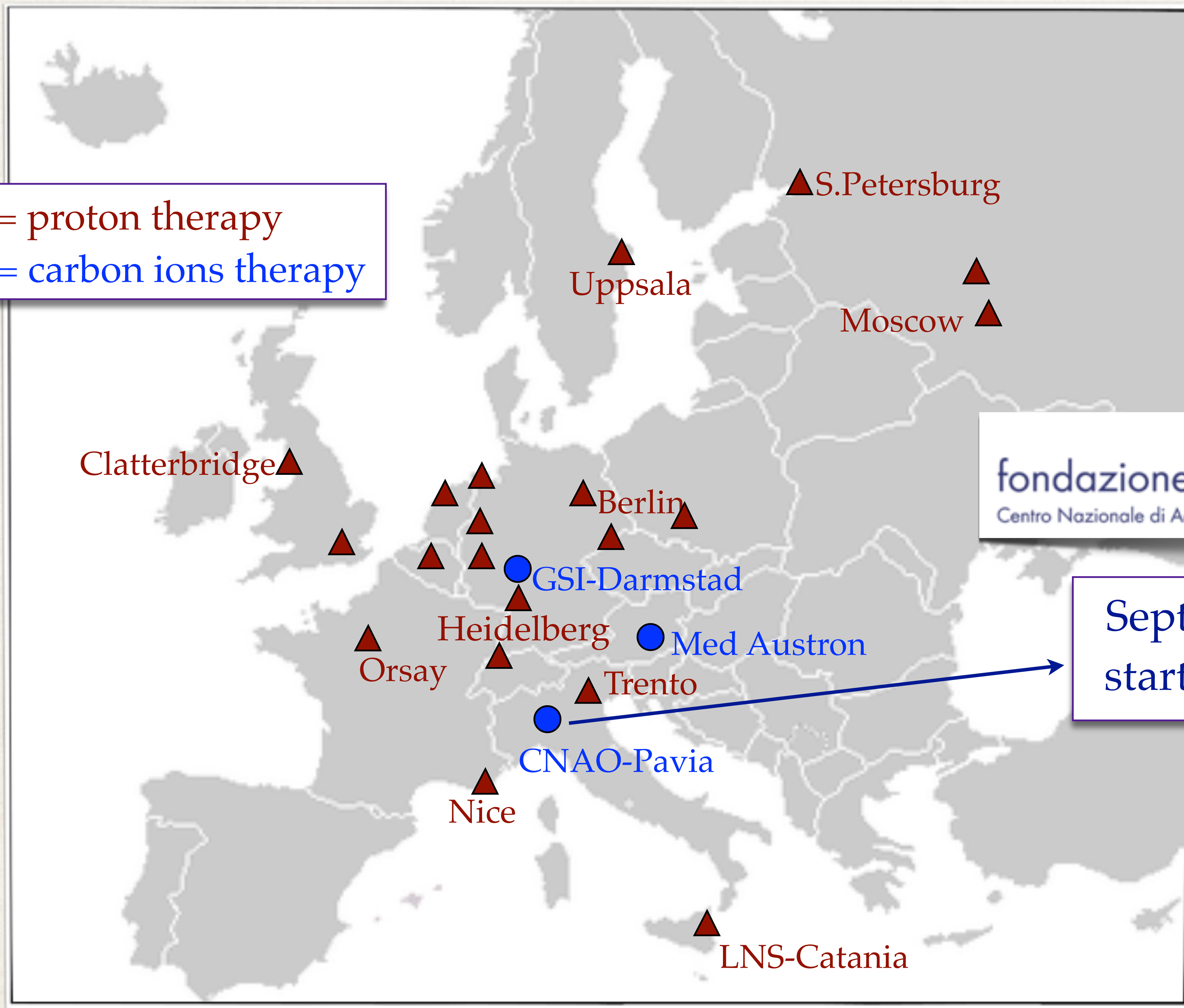
Total for all facilities (in operation and out of operation):

2054 He
1100 pions
13119 C-ions
433 other ions
105743 protons
122449 Grand Total

More than 50 operative centers.. and other are under construction!

PT in EUROPE

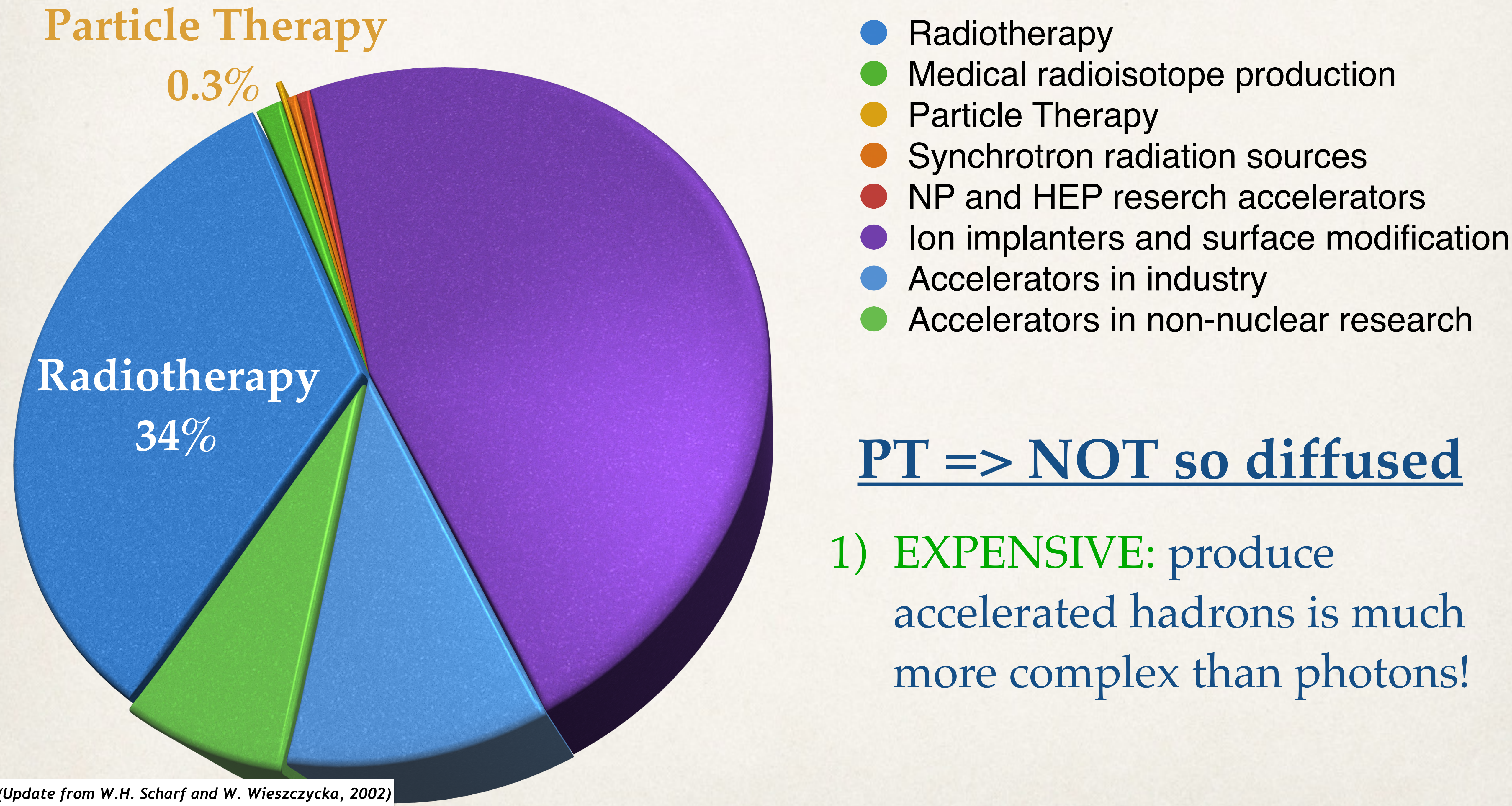
▲ = proton therapy
● = carbon ions therapy



fondazione CNAO
Centro Nazionale di Adroterapia Oncologica per il trattamento dei tumori

September 22nd 2011 start clinical activity.

Treatment uncertainties in Ion Beam Therapy



(Update from W.H. Scharf and W. Wieszczycka, 2002)

PT => NOT so diffused

1) EXPENSIVE: produce accelerated hadrons is much more complex than photons!

Treatment uncertainties in Ion Beam Therapy

- Radiotherapy
- Medical radioisotope production
- Particle Therapy
- Synchrotron radiation sources
- NP and HEP reserch accelerators
- Ion implanters and surface modification
- Accelerators in industry
- Accelerators in non-nuclear research

PT => NOT so diffused

1) EXPENSIVE: produce accelerated hadrons is much more complex than photons!
2) POWER!

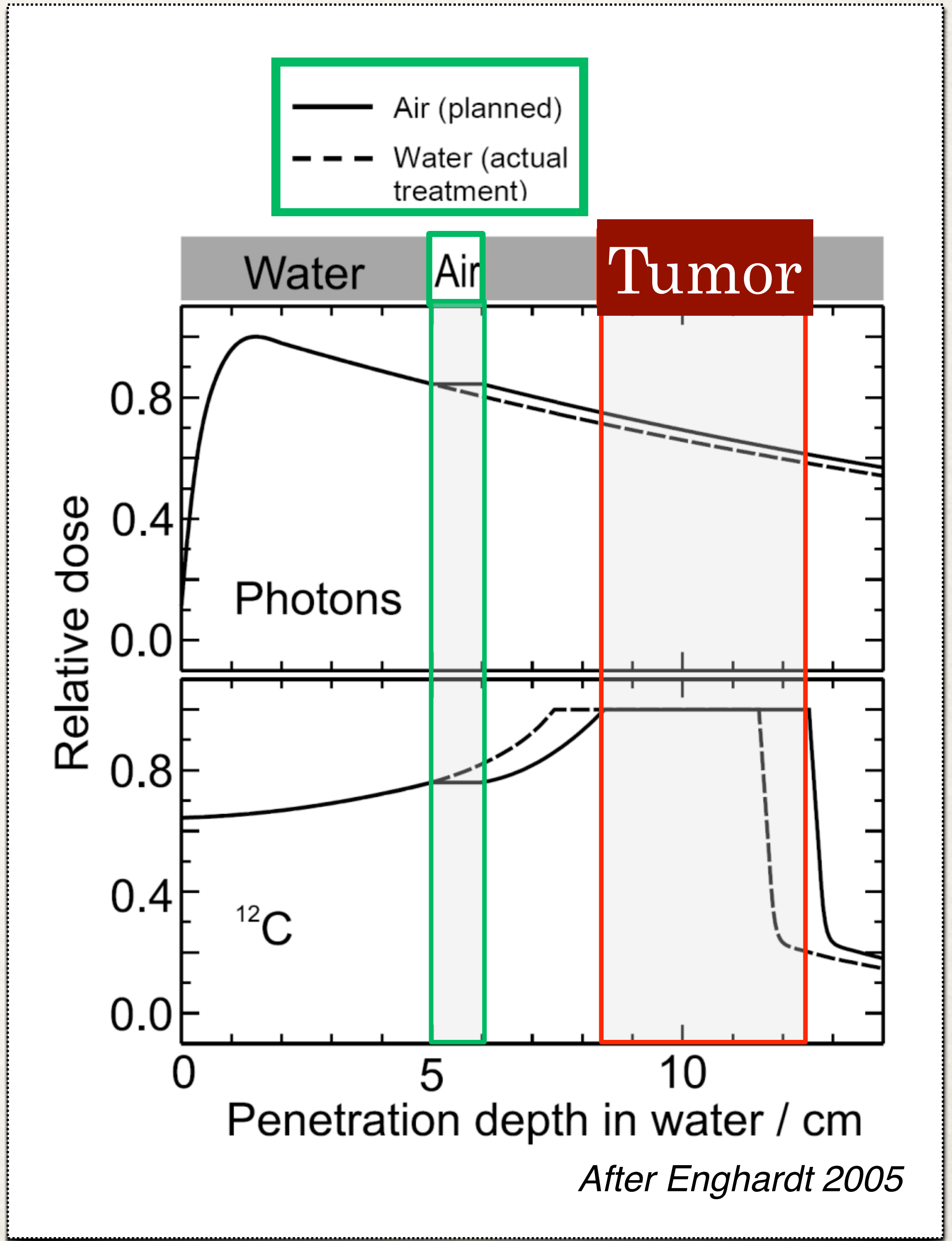
Treatment uncertainties in Ion Beam Therapy

Courtesy of K.Parodi

- TPS dose calculation errors
  - Inhomogeneities, metallic implants
  - Conversion HU ion range
  - CT artifacts

- Difference TP / delivery
  - Daily setup variation
  - Internal organ motion
  - Anatomical / physiological changes

- Daily practice of compromising dose conformity for safe delivery



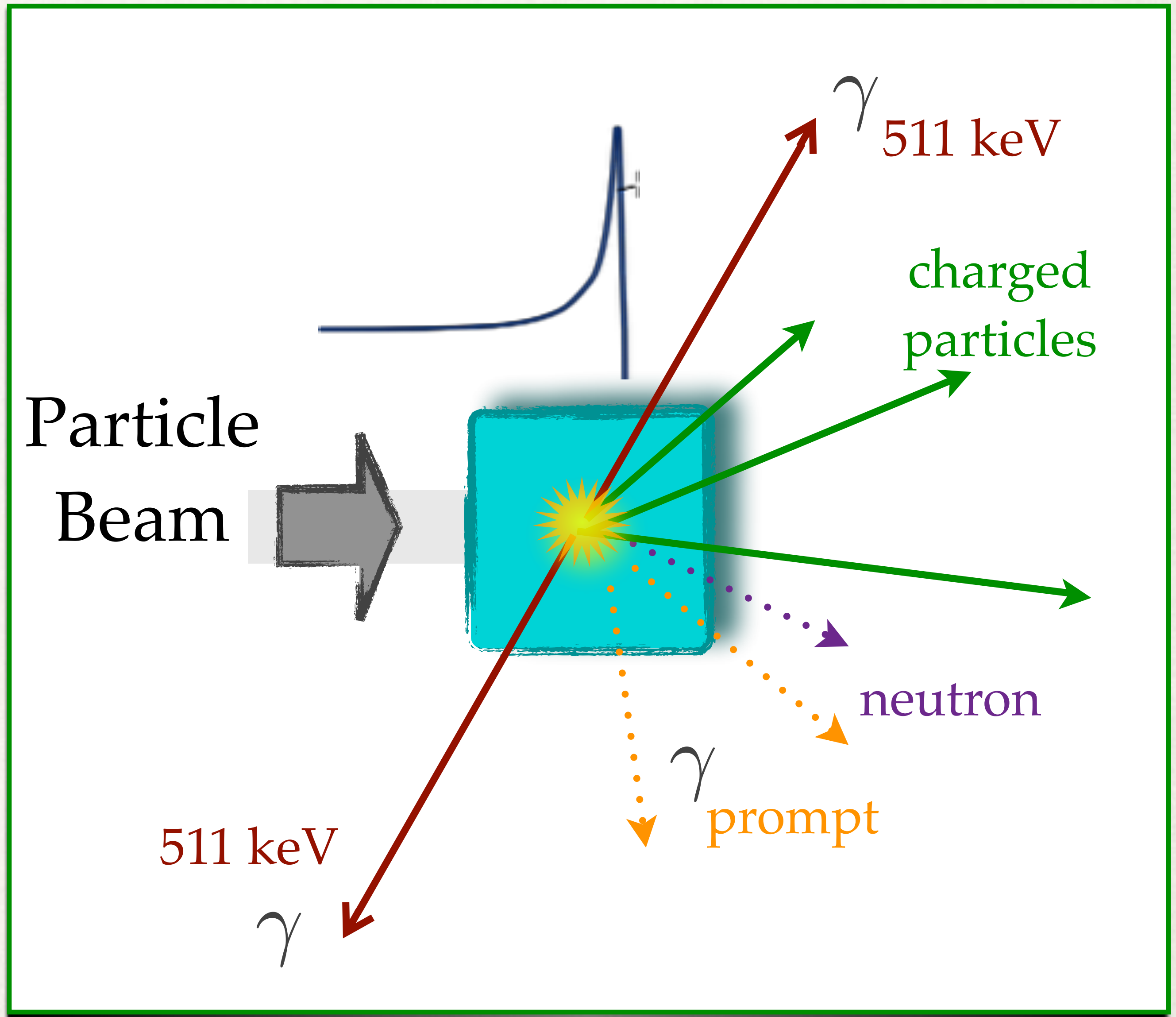
Treatment uncertainties in Ion Beam Therapy

To increase the development of particle therapy and make it safer is crucial to **monitor *on line* the rage of the beam**

Monitoring

In conventional RT (i.e. with photons), the beam crosses the patient body and can be used for monitoring. In PT the beam is absorbed inside the patient.
An ideal PT monitor device should:

- **Check shape** (compulsory) and absolute value (desirable);
- Exploit as signal the **secondary particles**, generated by the beam, coming out from the patient, dealing with the background of the other secondaries;
- Measurements and feed-back should be provided **during the treatment** (in-beam). Best, in active system, if the monitor can follow "on line" the irradiation scan (!)

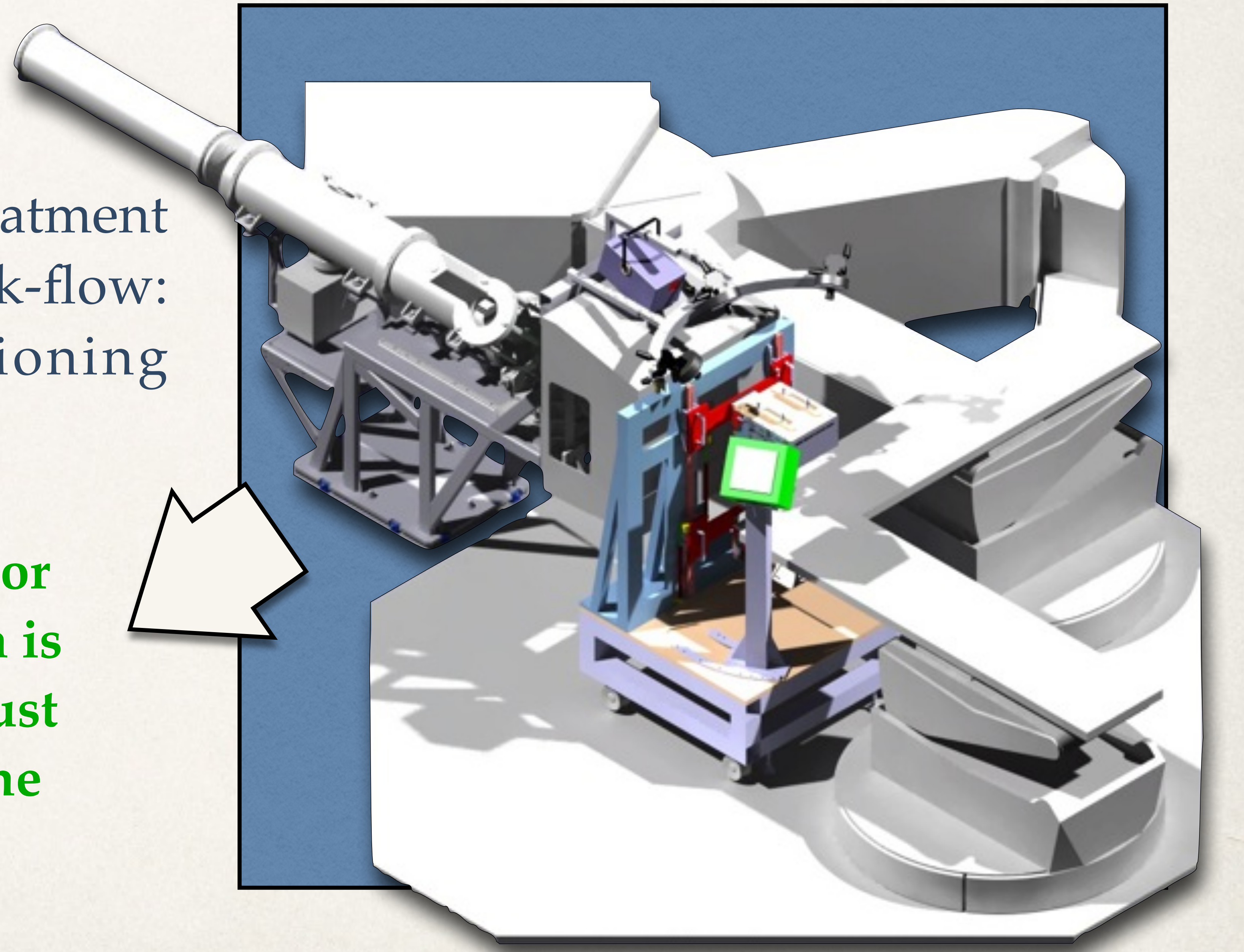


Monitoring

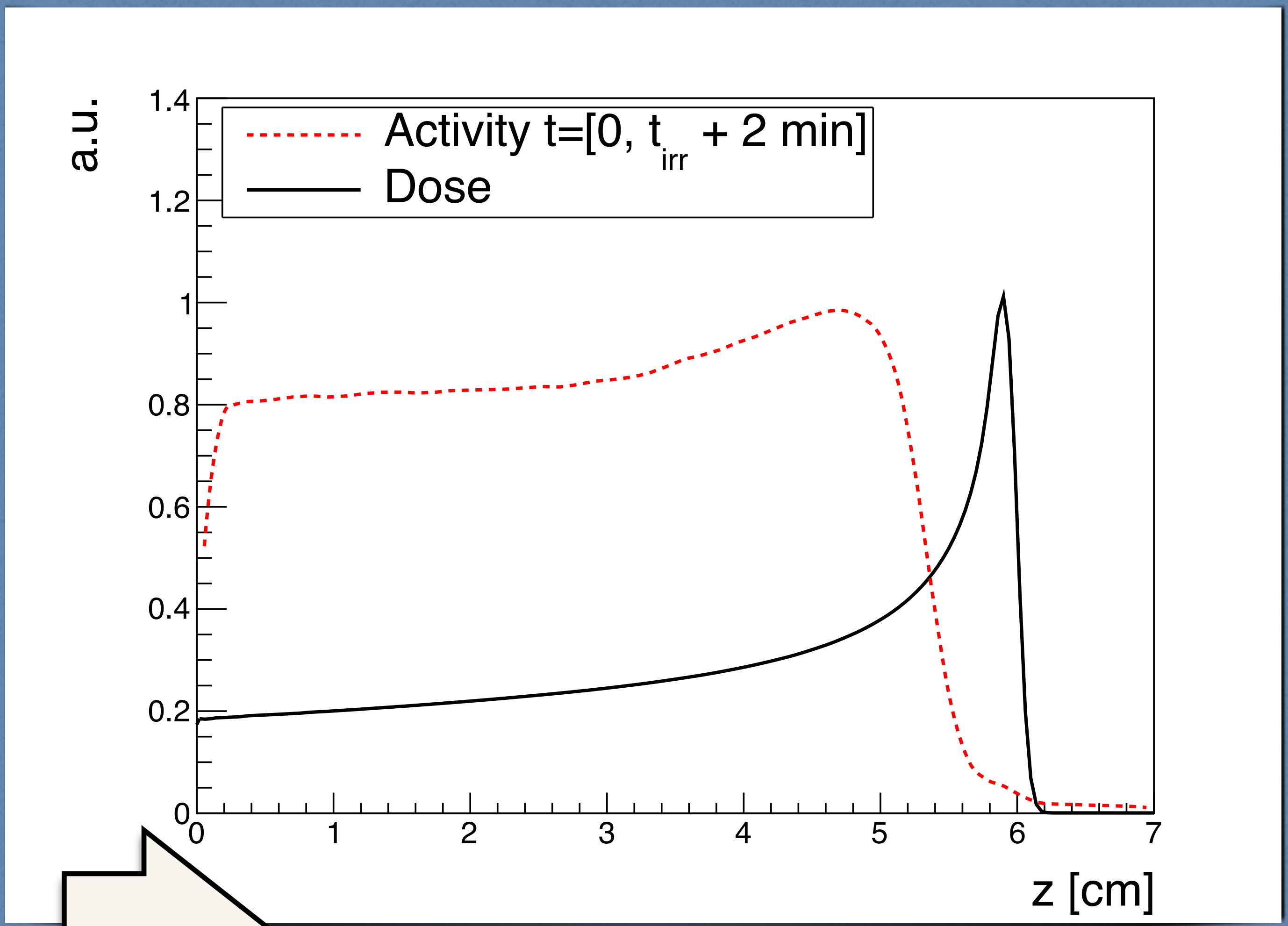
In conventional RT (i.e. with photons), the beam crosses the patient body and can be used for monitoring. In PT the beam is absorbed inside the patient.
An ideal PT monitor device should:

- Must be integrated in the treatment environment and work-flow: nozzle, couch, positioning system, controls…

The integration of the monitor system in the treatment room is a very important task and must be accomplished BEFORE the detector design definition



Monitoring: β^+ Activity



FLUKA simulation. Proton 95 MeV beam

β^+ produced in the dis-excitation of isotopos (C, O..) produced by the beam interaction with tissues.

The β^+ activity emission shape is correlated with the dose distribution (ant to the Bragg Peak position). The β^+ emits a positron that produce two (back-to-back) 511 keV photons during its annihilations.

Monitoring: β$^+$ Activity

FEATURES

a.u.

- Isotopes of short lifetime ^{11}C (20 min), ^{15}O (2 min), ^{10}C (20 s) with respect to conventional PET (hours);
  - Low activity asks for quite a long acquisition time (some minutes at minimum) with difficult in-beam feedback;
  - fondo prompt
- Metabolic wash-out -> the β$^+$ emitters are blurred by the patient metabolism;

z [cm]

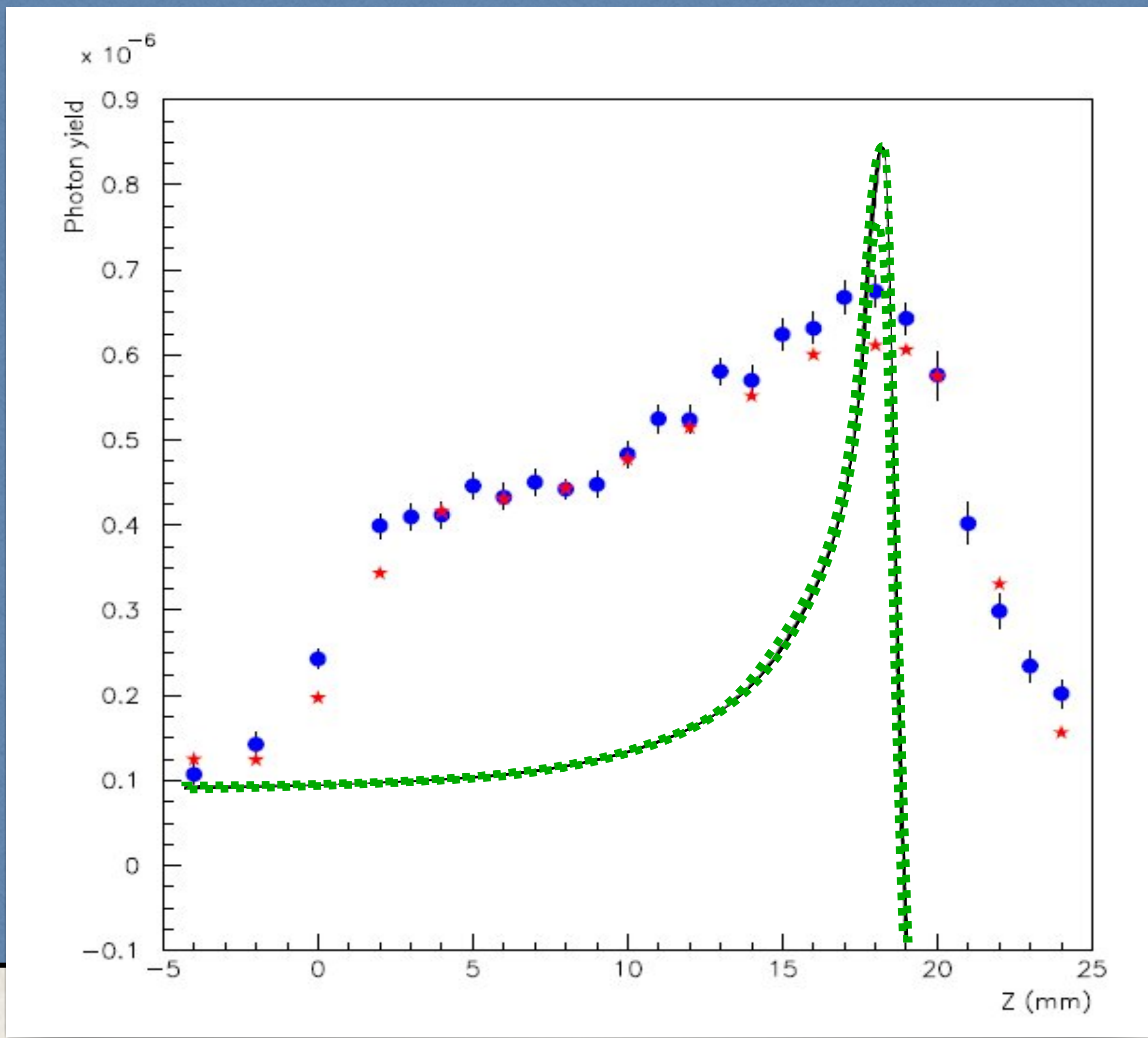
FLUKA simulation. Proton 95 MeV beam

Monitoring: Prompt γ

G4

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	($1 \cdot 10^{7}$)
α-particles:	$2 \cdot 10^{-5}$	($2 \cdot 10^{5}$)



A.Ferrari and FLUKA collaboration
(73 MeV/u C ion)

- There is a huge background due to neutrons & uncorrelated gamma produced by neutrons. This background is beam, energy and site specific;
- It's not simple back-pointing the γ direction: take profit by the SPECT technique… but the energy of these γ is in the 1-10 MeV range-> much more difficult to stop and collimate!!

- multislit;
- knife-edge;
- Compton camera;

R&D

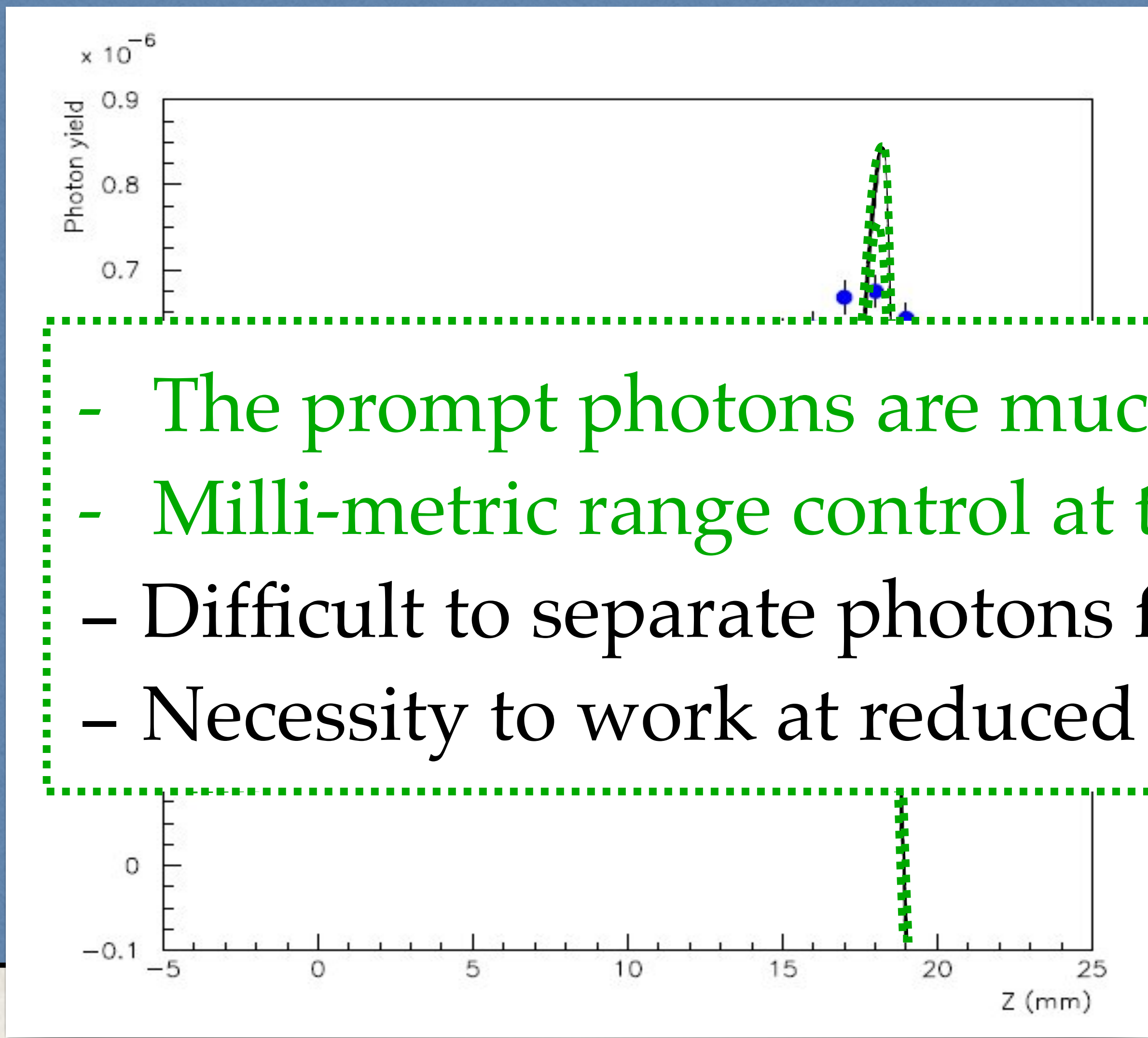
Monitoring: Prompt γ

G4

Balance of promptly emitted particles outside the target:

Incident protons:	1.0	(~10^{10})
γ-rays:	0.3	($3 \cdot 10^9$)
Neutrons:	0.09	($9 \cdot 10^8$)
Protons:	0.001	($1 \cdot 10^7$)
α-particles:	[illegible]	[illegible]

FEATURES



A.Ferrari and FLUKA collaboration
(73 MeV/u C ion)

- There is a huge backg...

- The prompt photons are much more abundant than other secondaries;
- Milli-metric range control at the pencil-beam scale for protons;
- Difficult to separate photons from neutron background;
- Necessity to work at reduced intensity;

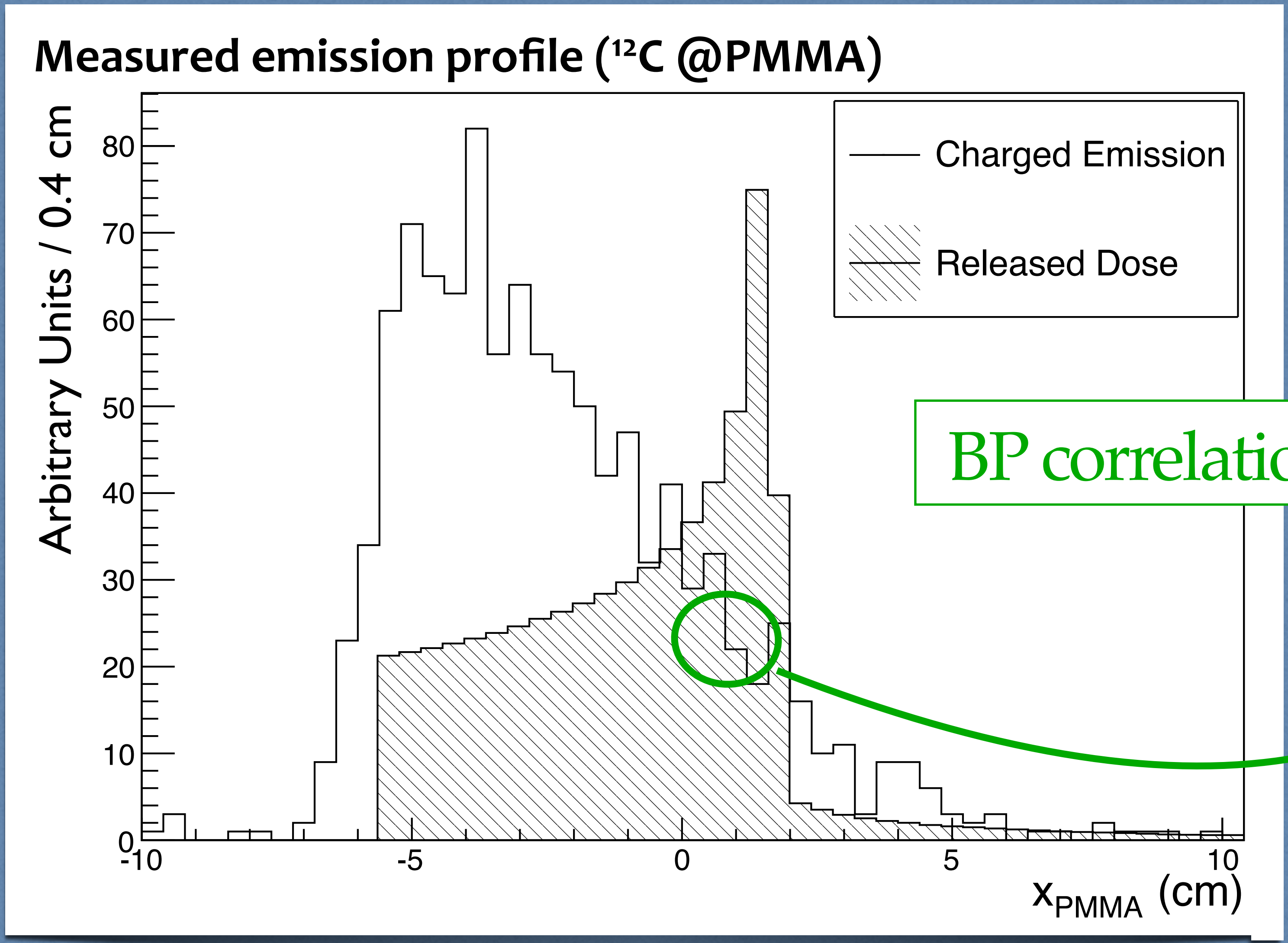
energy of these γ is in the 1-10 MeV range-> much more difficult to stop and collimate!!

- multislit;
- knife-edge;
- Compton camera;

R&D

Monitoring: charged particles

Charged secondary particles: protons, deutons and tritium..

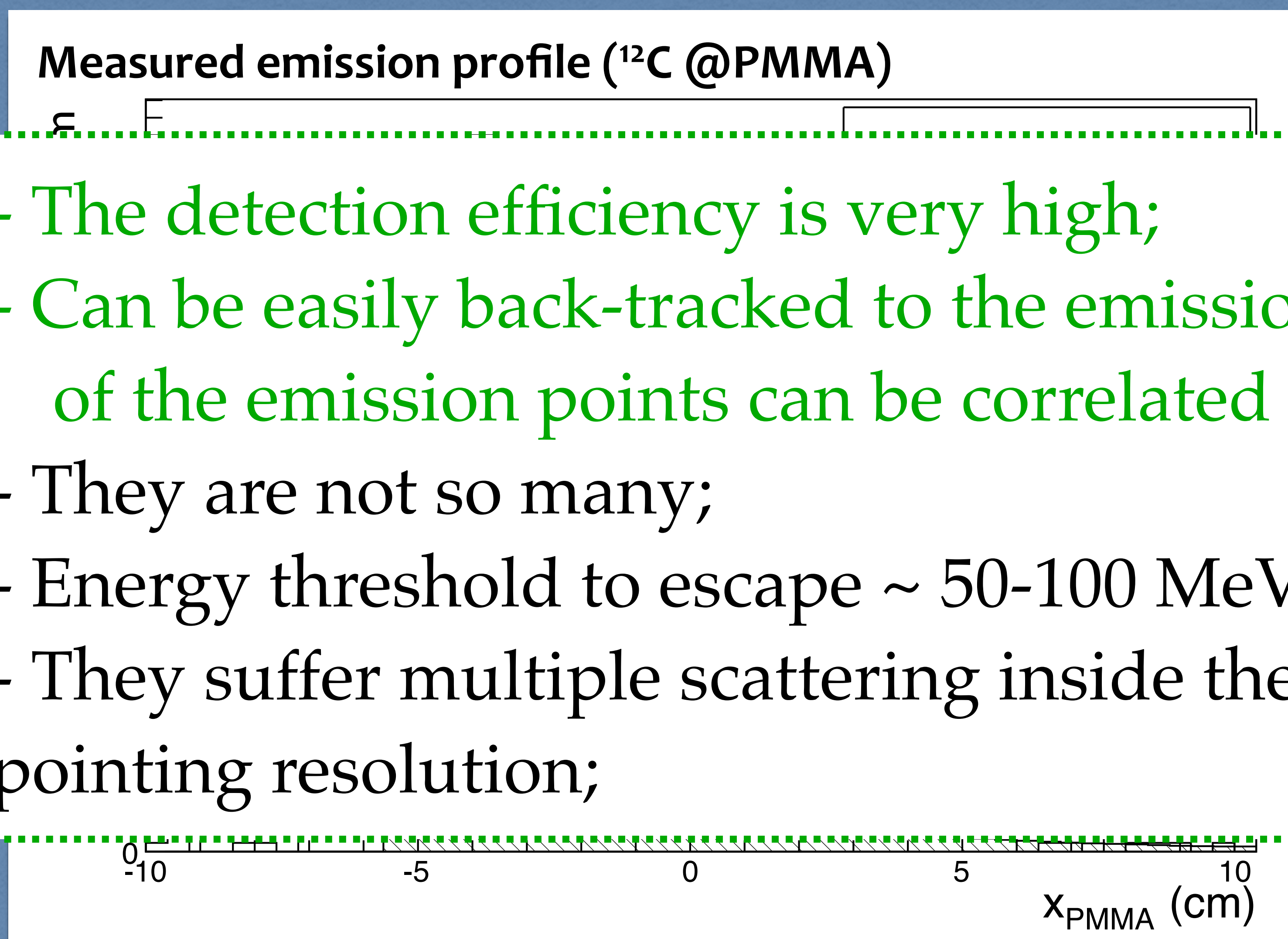


L. Piersanti et al. Phys. Med. Biol. 59 1857

Charged secondary particles are mainly produced before the Bragg Peak. The emission shape can be correlated with the BP position.

BP correlation with emission profile

Monitoring: charged particles



L. Piersanti et al. Phys. Med. Biol. 59 1857

Charged secondary particles
a ... fore

FEATURES

- The detection efficiency is very high;
- Can be easily back-tracked to the emission point => the distribution of the emission points can be correlated to the beam profile;
- They are not so many;
- Energy threshold to escape ~ 50-100 MeV;
- They suffer multiple scattering inside the patient -> worsen the back-pointing resolution;

Secondary particles: measurements

The **fluxes of secondary particles are largely unknown:**
MonteCarlo simulation not reliable => need of measurements

- PET Photons

flux and profile for different energies:
- 80 MeV/u ^{12}**C** beam
- 102,125,144 MeV/u ^{4}**He** beam

- Prompt Photons

flux and spectrum for different energies:
- 80, 220 MeV/u ^{12}**C** beam
- 50-300 MeV/u ^{16}**O** beam
- 50-300 MeV/u ^{4}**He** beam

$60^o, 90^o, 120^o$

- Fragmentation (charged particles)

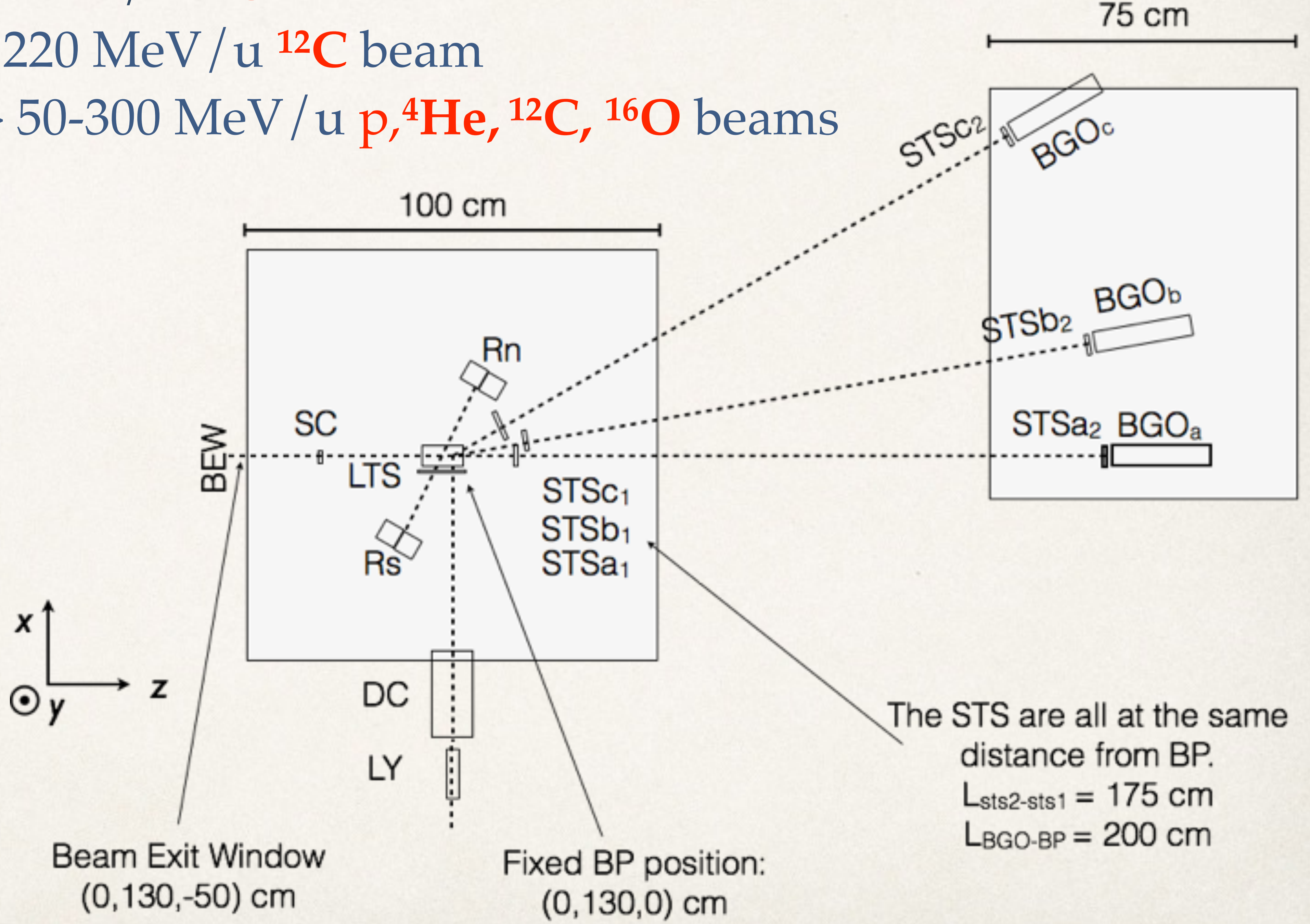
flux and spectrum for different energies:
- 80, 220 MeV/u ^{12}**C** beam — $60^o, 90^o$
- 50-300 MeV/u ^{16}**O** beam
- 50-300 MeV/u ^{4}**He** beam

$0^o, 5^o, 10^o 20^o, 30^o$

Secondary particles: measurements

Several experiments with different beams on PMMA target:

LNS (Catania) -> 80 MeV/u ^{12}**C** beam
GSI (Darmstadt) -> 220 MeV/u ^{12}**C** beam
HIT (Heidelberg) -> 50-300 MeV/u p, ^{4}**He**, ^{12}**C**, ^{16}**O** beams



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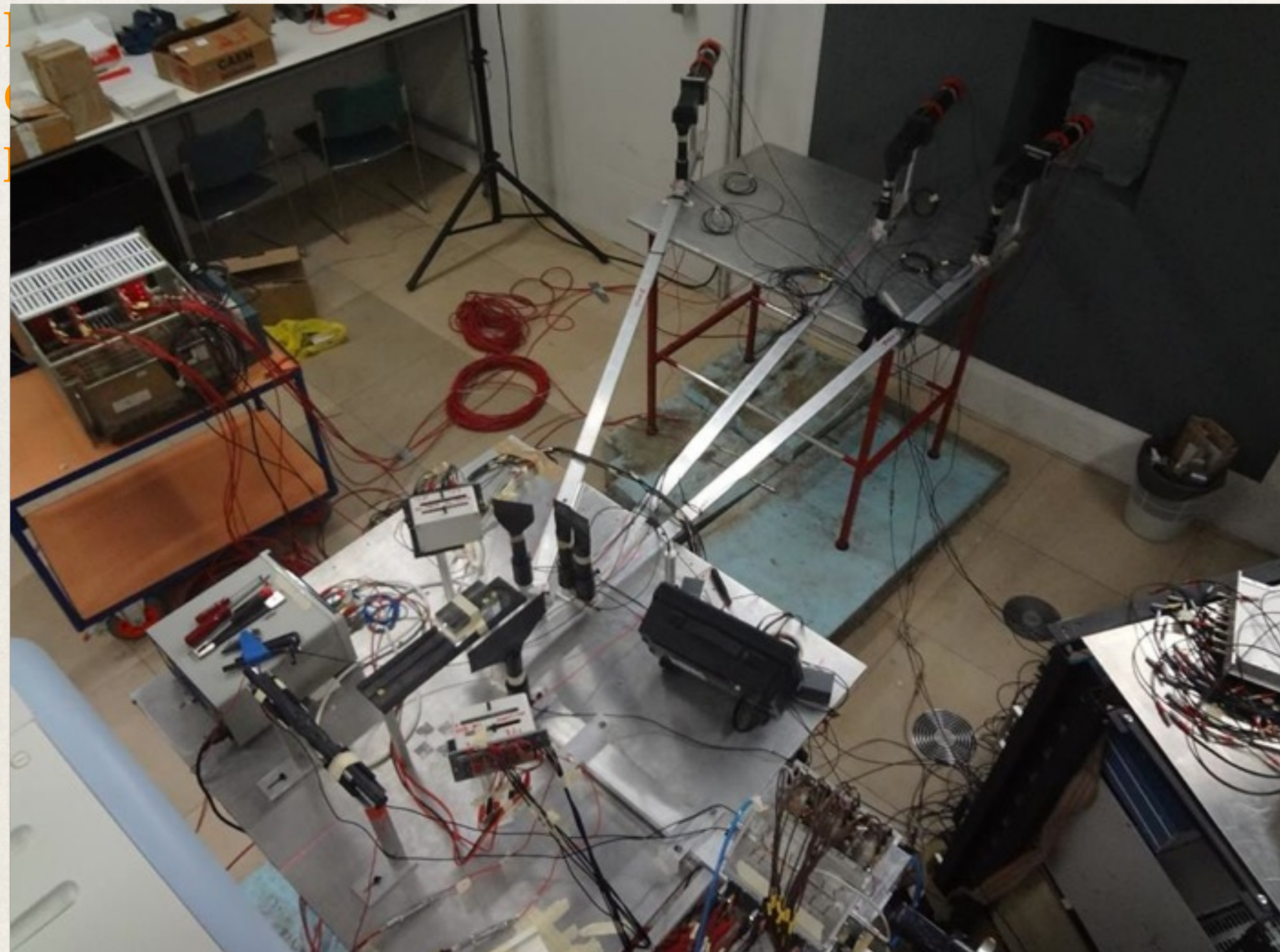
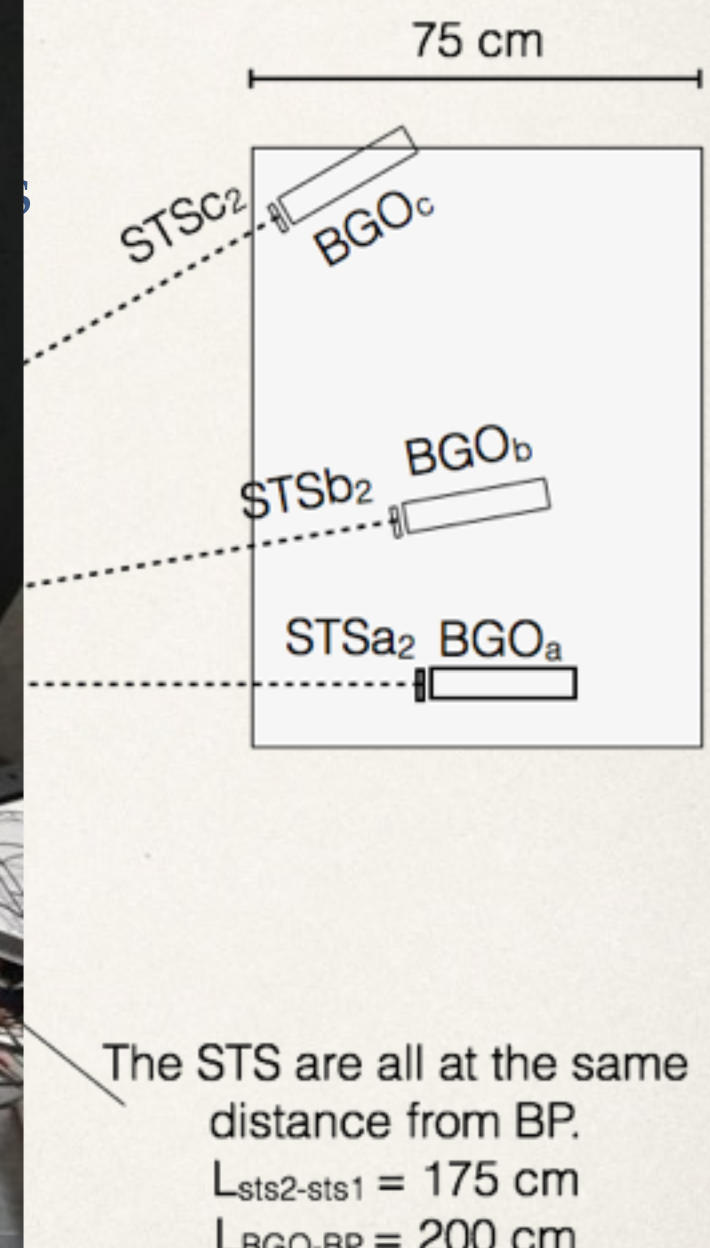
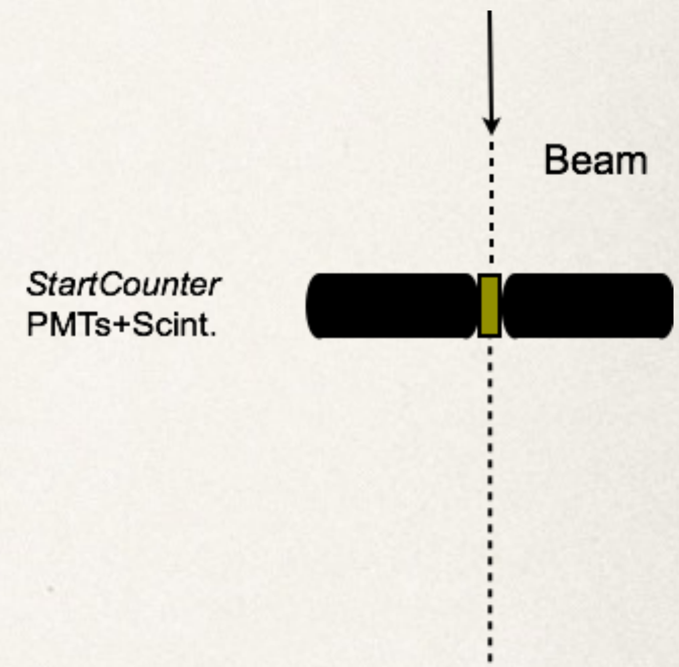


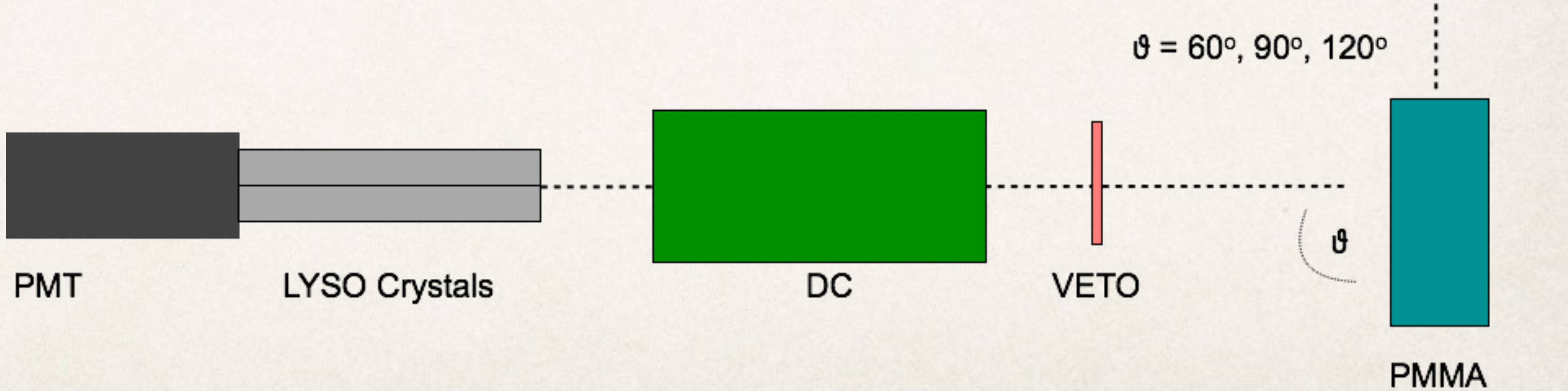


Secondary particles: PROMPT PHOTONS

Carbon ion on PMMA target:

We measure the prompt photons flux and spectrum
for different energies: 80, 220, 50-300 MeV/u



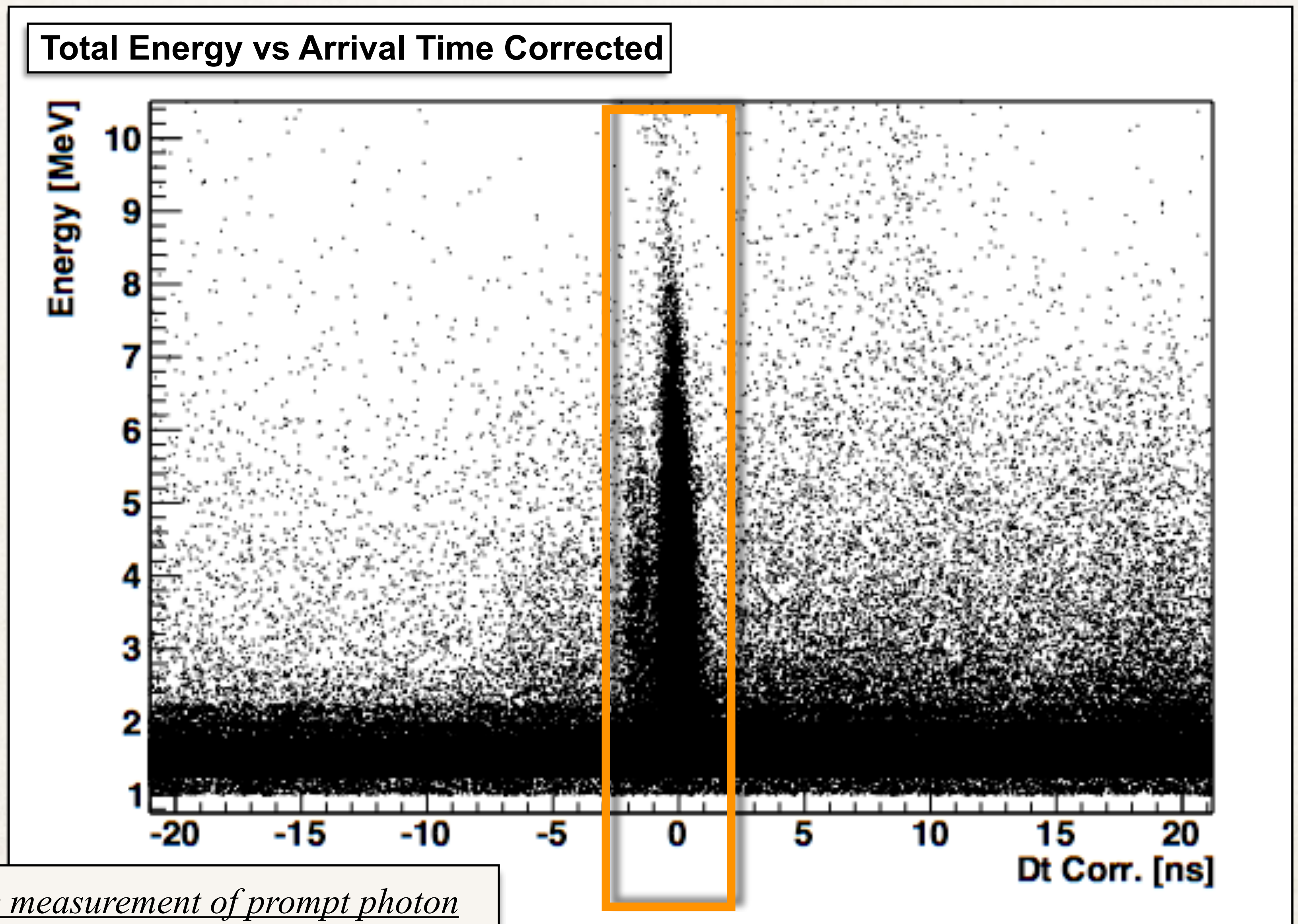


Secondary particles:

PROMPT PHOTONS

Carbon ion on PMMA target:

We measure the prompt photons flux and spectrum
for different energies: 80, 220, 50-300 MeV/u



C. Agodi, *et al.* *"Precise measurement of prompt photon emission from 80 MeV/u carbon ion beam irradiation"* , **JINST 7 (2012) P03001**

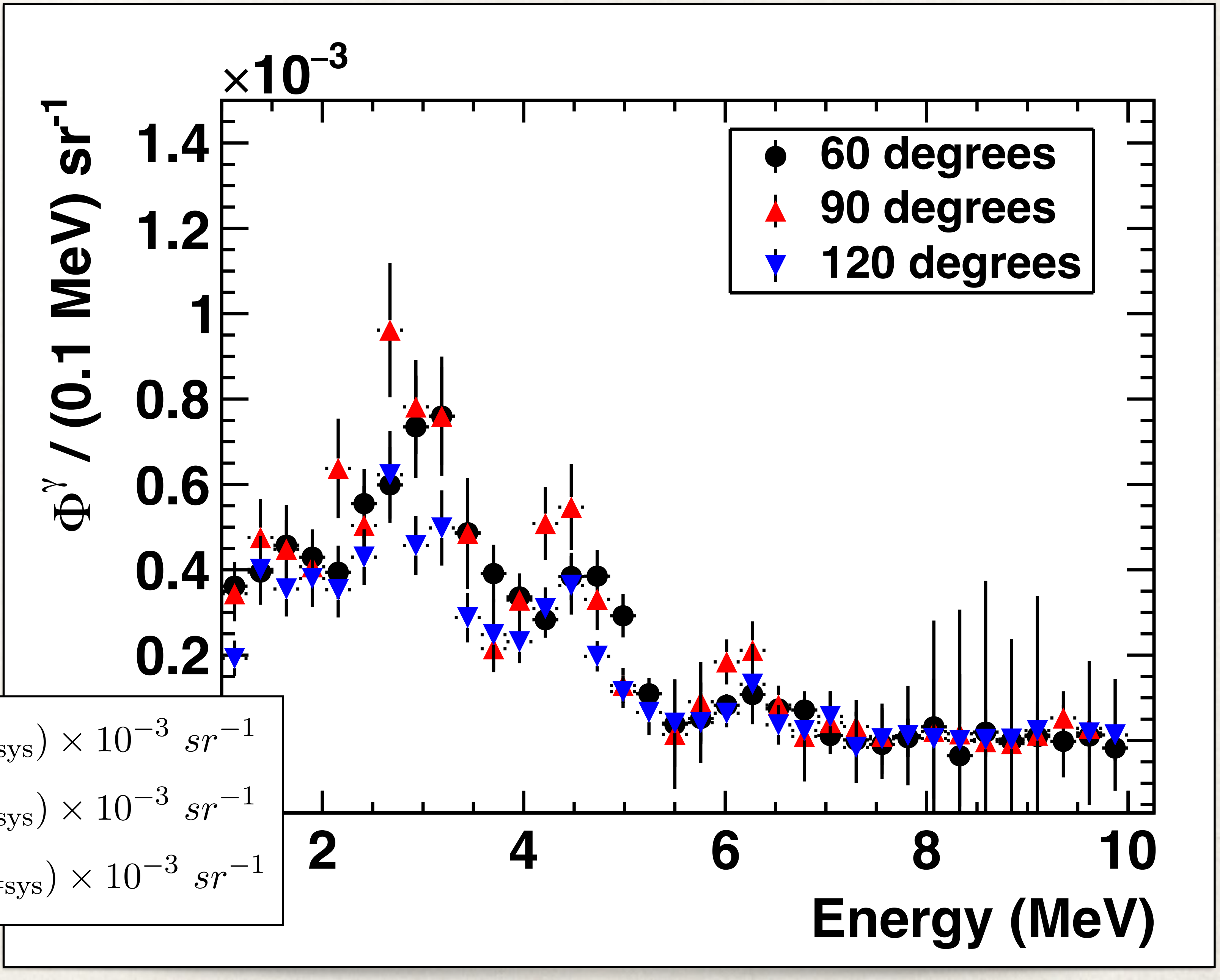
Secondary particles: PROMPT PHOTONS

Carbon ion on PMMA target:

GSI (Darmstadt, Germany) -> 220 MeV/u ^{12}**C** beam;

Under Construction. *"Precise measurement of prompt photon emission from 220 MeV/u carbon ion beam irradiation"*

prompt photon spectrum



$$\Phi^{\gamma}(E > 2\ \mathrm{MeV}\ @60^{\circ}) = (6.59 \pm 0.22_{\mathrm{stat}} \pm 1.07_{\mathrm{sys}}) \times 10^{-3}\ sr^{-1}$$

$$\Phi^{\gamma}(E > 2\ \mathrm{MeV}\ @90^{\circ}) = (7.39 \pm 0.38_{\mathrm{stat}} \pm 1.27_{\mathrm{sys}}) \times 10^{-3}\ sr^{-1}$$

$$\Phi^{\gamma}(E > 2\ \mathrm{MeV}\ @120^{\circ}) = (5.02 \pm 0.24_{\mathrm{stat}} \pm 1.34_{\mathrm{sys}}) \times 10^{-3}\ sr^{-1}$$

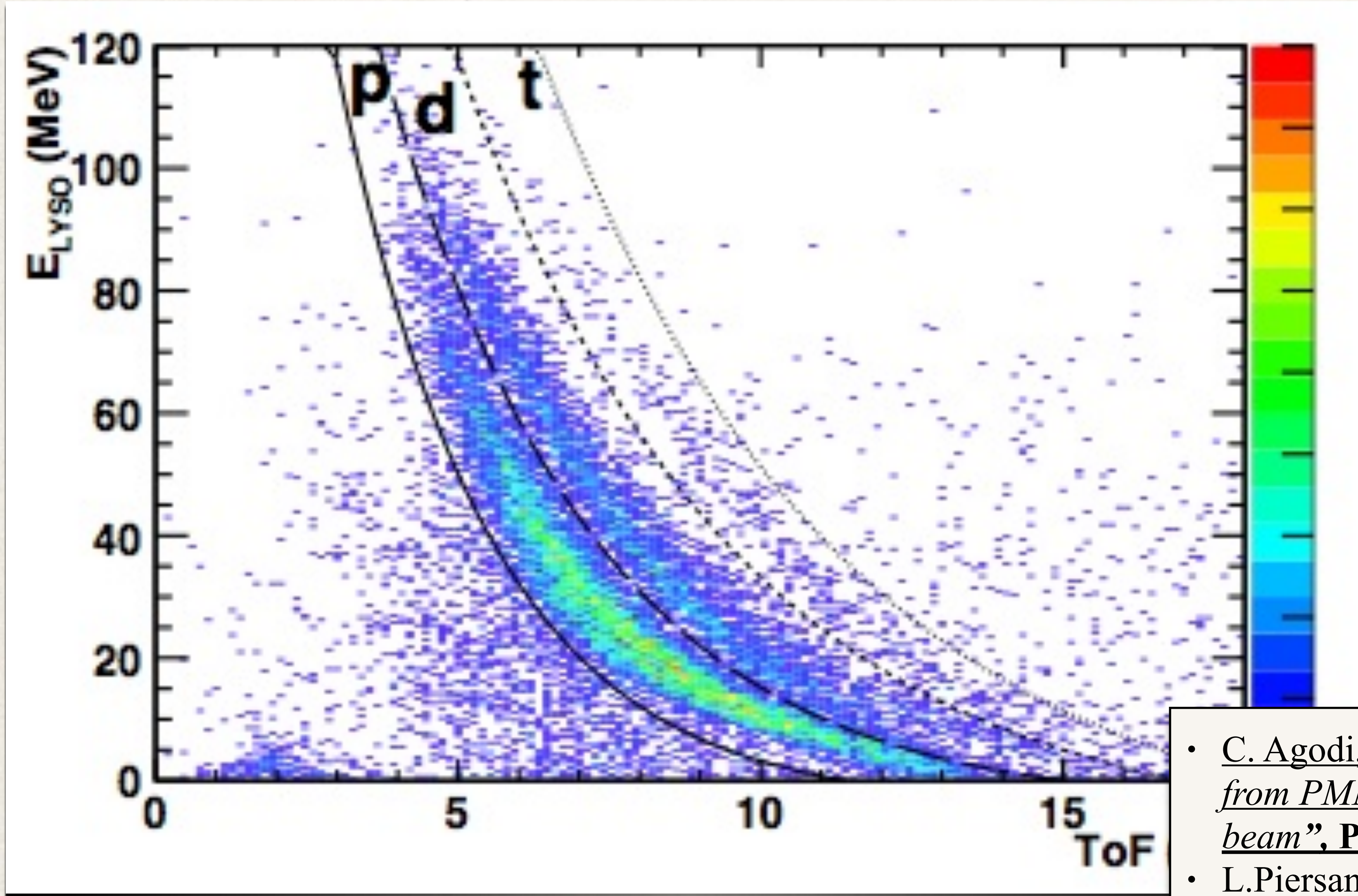
Secondary particles:

CHARGED PARTICLES

Carbon ion on PMMA target:

We measure the charged particles flux for different energies: 80, 220, 50-300 MeV/u

GSI (Darmstadt, Germany) -> 220 MeV/u ^{12}**C** beam;



Fragmentation at 90^{o} exist!!

- C. Agodi, *et al. "Charged particle's flux measurement from PMMA irradiated by 80 MeV/u carbon ion beam"*, **PMB. 57 (2012) 5667**
- L.Piersanti et al. *"Measurement of charged particles yields from PMMA irradiated by 220 MeV/u ^{12}C beam"* **PMB 59 (2014) 1857-1872**

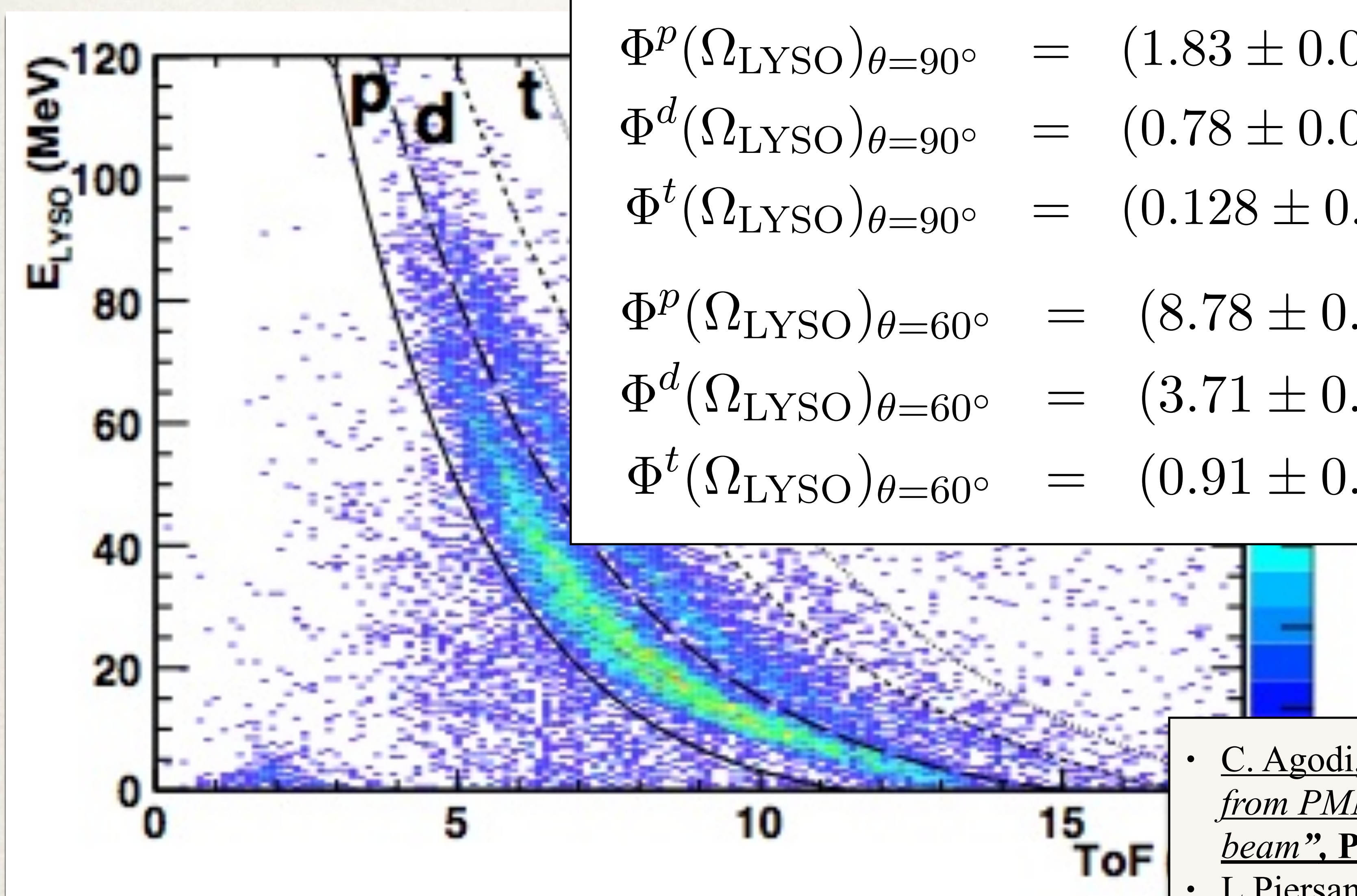
Secondary particles:

CHARGED PARTICLES

Carbon ion on PMMA target:

We measure the charged particles flux for different energies: 80, 220, 50-300 MeV/u

GSI (Darmstadt, Germany) -> 220 MeV/u ^{12}**C** beam;



$$\Phi^p(\Omega_{\mathrm{LYSO}})_{\theta=90^\circ} = (1.83 \pm 0.02_{\mathrm{stat}} \pm 0.14_{\mathrm{sys}}) \times 10^{-3}\ sr^{-1}$$
$$\Phi^d(\Omega_{\mathrm{LYSO}})_{\theta=90^\circ} = (0.78 \pm 0.01_{\mathrm{stat}} \pm 0.09_{\mathrm{sys}}) \times 10^{-3}\ sr^{-1}$$
$$\Phi^t(\Omega_{\mathrm{LYSO}})_{\theta=90^\circ} = (0.128 \pm 0.005_{\mathrm{stat}} \pm 0.028_{\mathrm{sys}}) \times 10^{-3}\ sr^{-1}$$

$$\Phi^p(\Omega_{\mathrm{LYSO}})_{\theta=60^\circ} = (8.78 \pm 0.07_{\mathrm{stat}} \pm 0.64_{\mathrm{sys}}) \times 10^{-3}\ sr^{-1}$$
$$\Phi^d(\Omega_{\mathrm{LYSO}})_{\theta=60^\circ} = (3.71 \pm 0.04_{\mathrm{stat}} \pm 0.37_{\mathrm{sys}}) \times 10^{-3}\ sr^{-1}$$
$$\Phi^t(\Omega_{\mathrm{LYSO}})_{\theta=60^\circ} = (0.91 \pm 0.01_{\mathrm{stat}} \pm 0.21_{\mathrm{sys}}) \times 10^{-3}\ sr^{-1}$$

- C. Agodi, *et al. "Charged particle's flux measurement from PMMA irradiated by 80 MeV/u carbon ion beam"*, **PMB. 57 (2012) 5667**
- L.Piersanti et al. *"Measurement of charged particles yields from PMMA irradiated by 220 MeV/u ^{12}C beam"* **PMB 59 (2014) 1857-1872**

Secondary particles:

CHARGED PARTICLES

Carbon ion on PMMA target:

GSI (Darmstadt, Germany)
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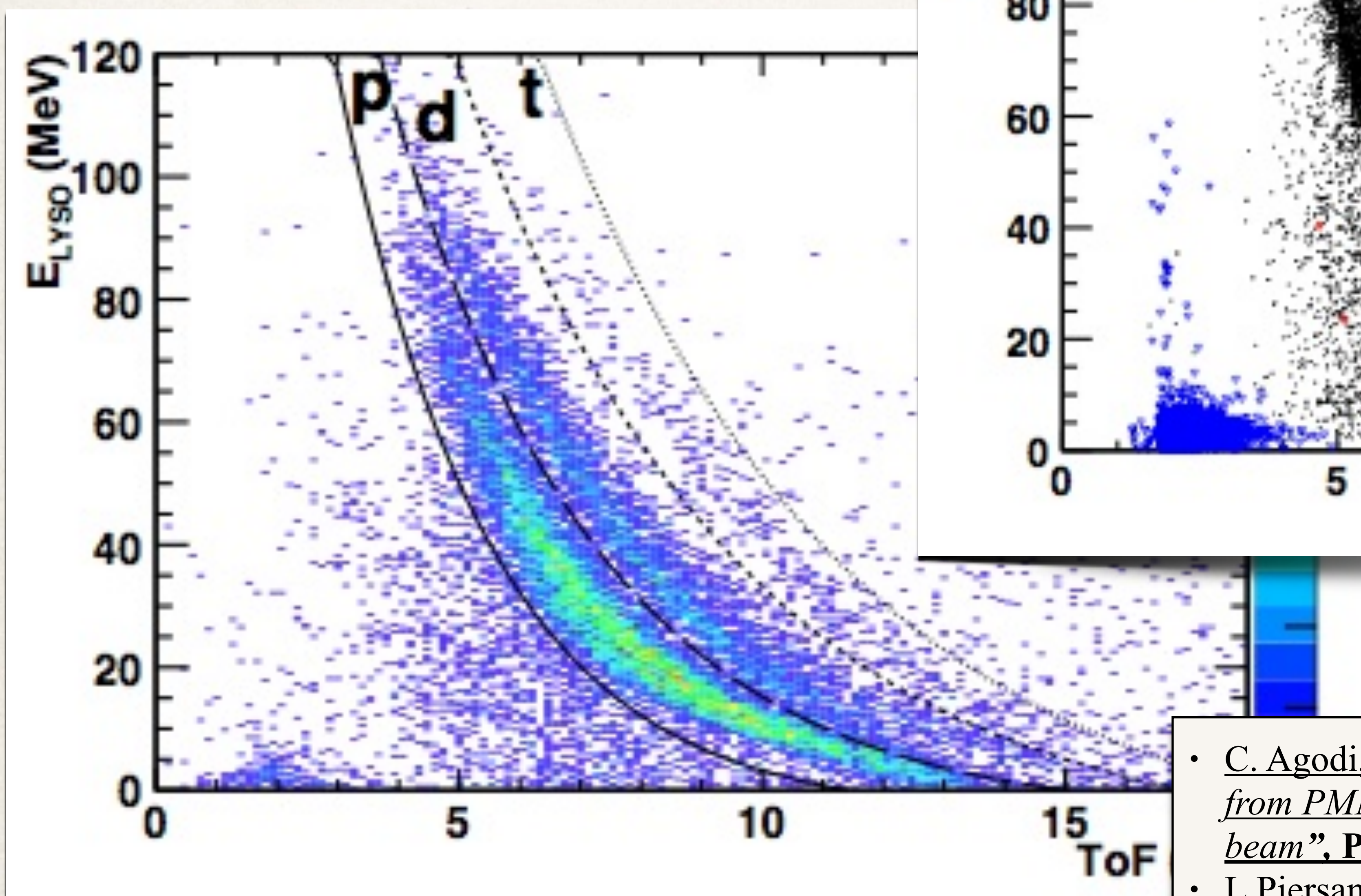
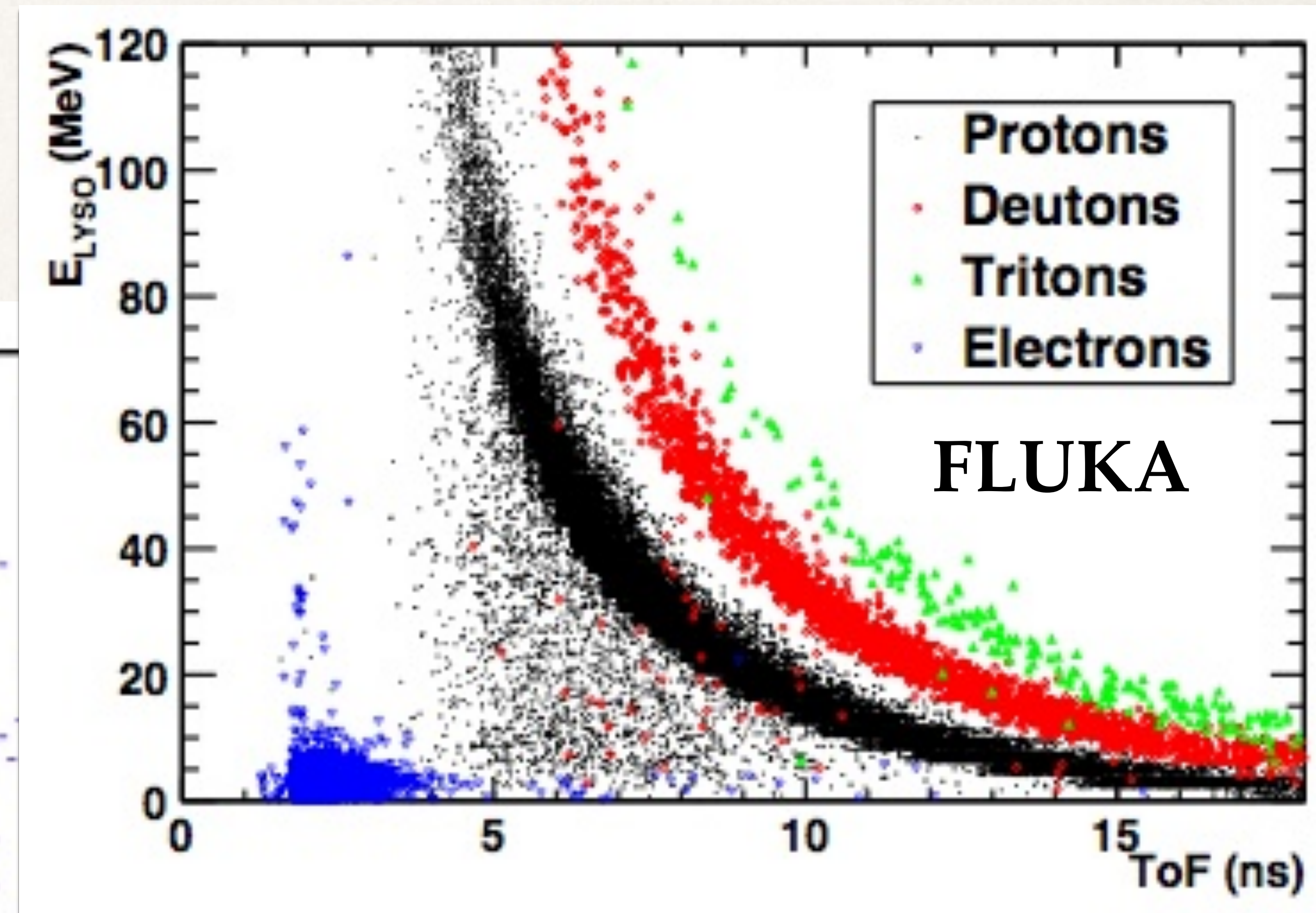
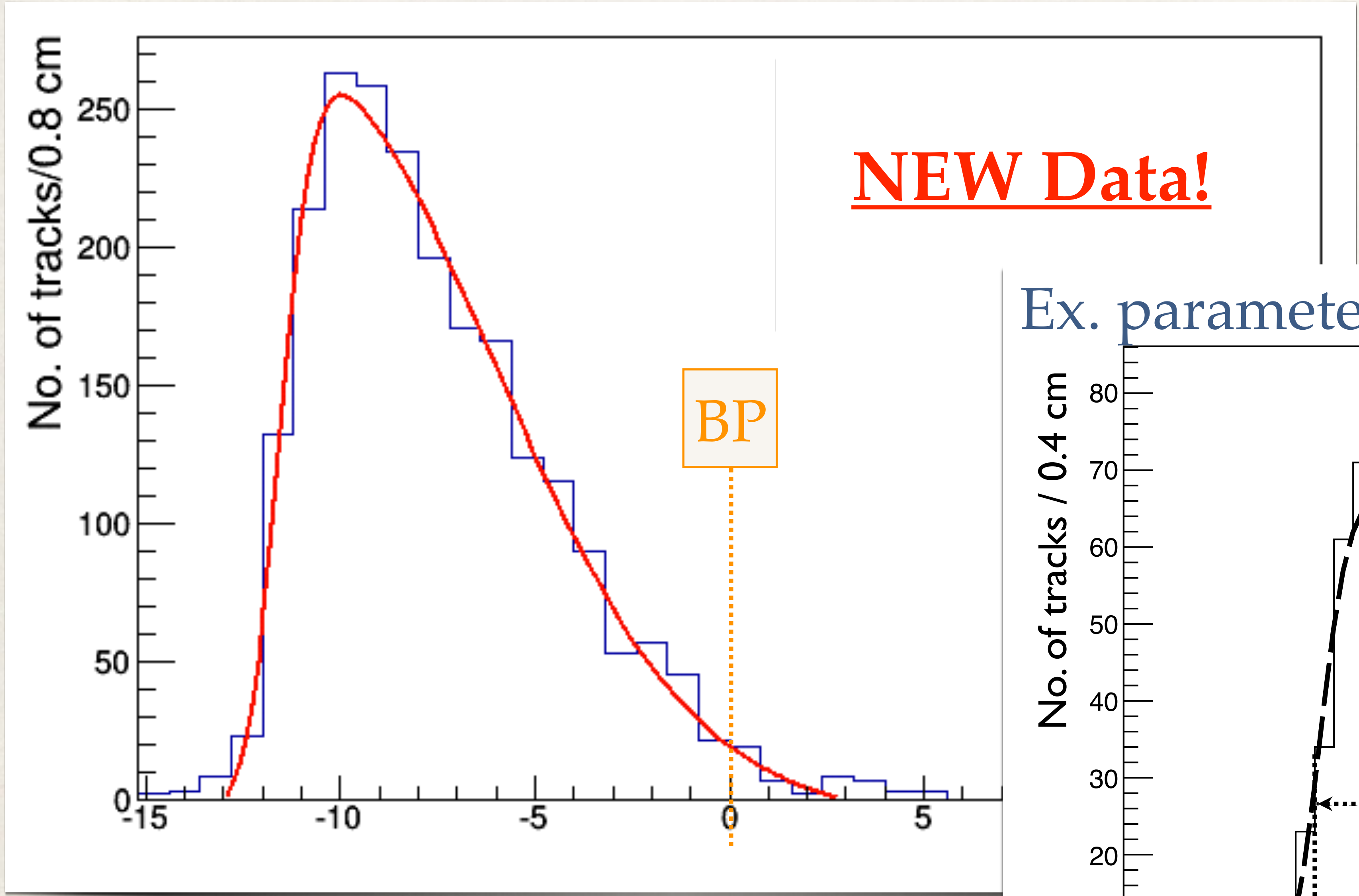




- C. Agodi, *et al. "Charged particle's flux measurement from PMMA irradiated by 80 MeV/u carbon ion beam"*, **PMB. 57 (2012) 5667**
- L.Piersanti et al. *"Measurement of charged particles yields from PMMA irradiated by 220 MeV/u ^{12}C beam"* **PMB 59 (2014) 1857-1872**

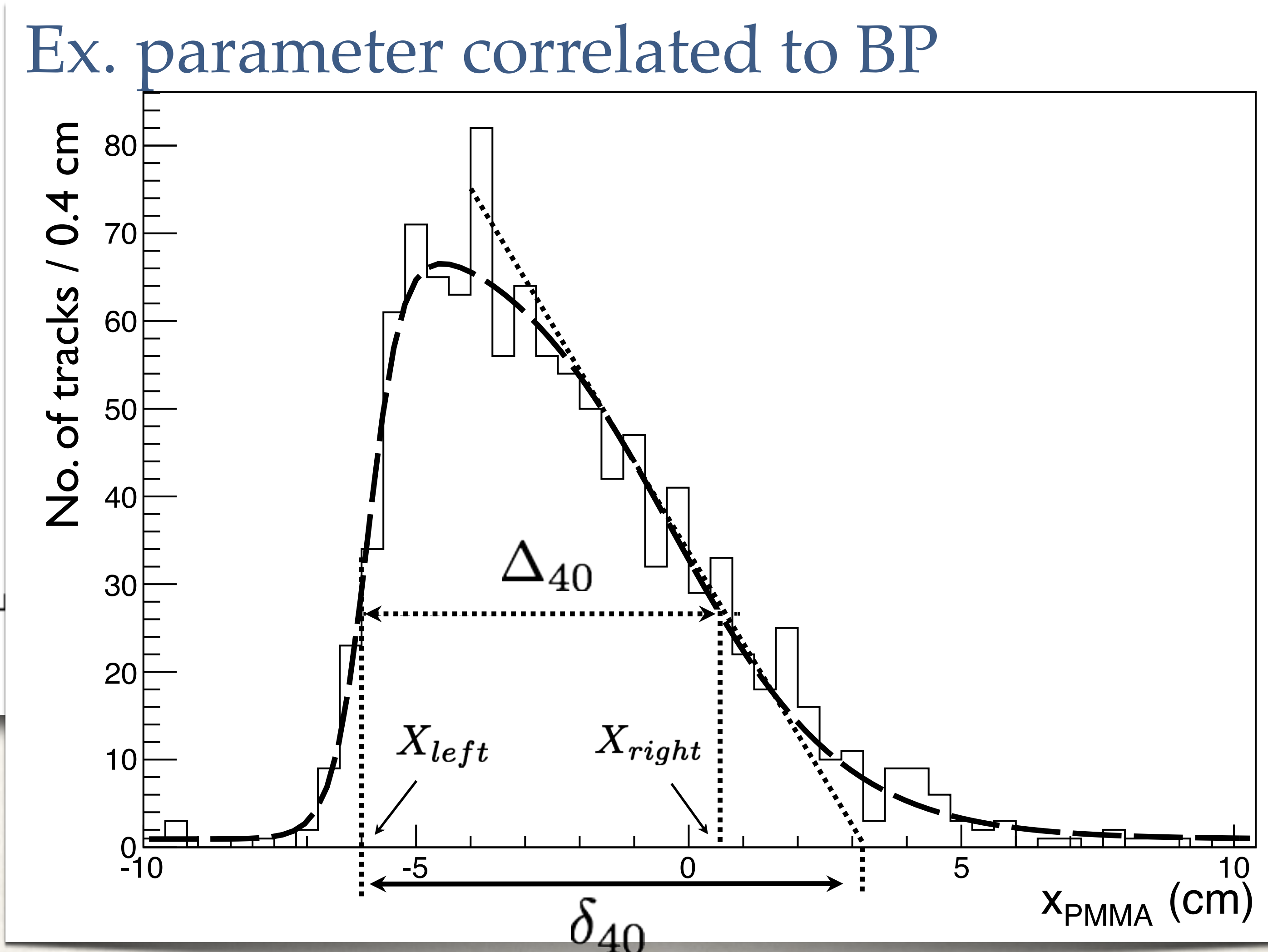
Secondary particles: CHARGED PARTICLES

HIT (Heidelberg) -> 125 MeV/u ^{4}He beam: **detector @90°**



He fragments!!

Ex. parameter correlated to BP



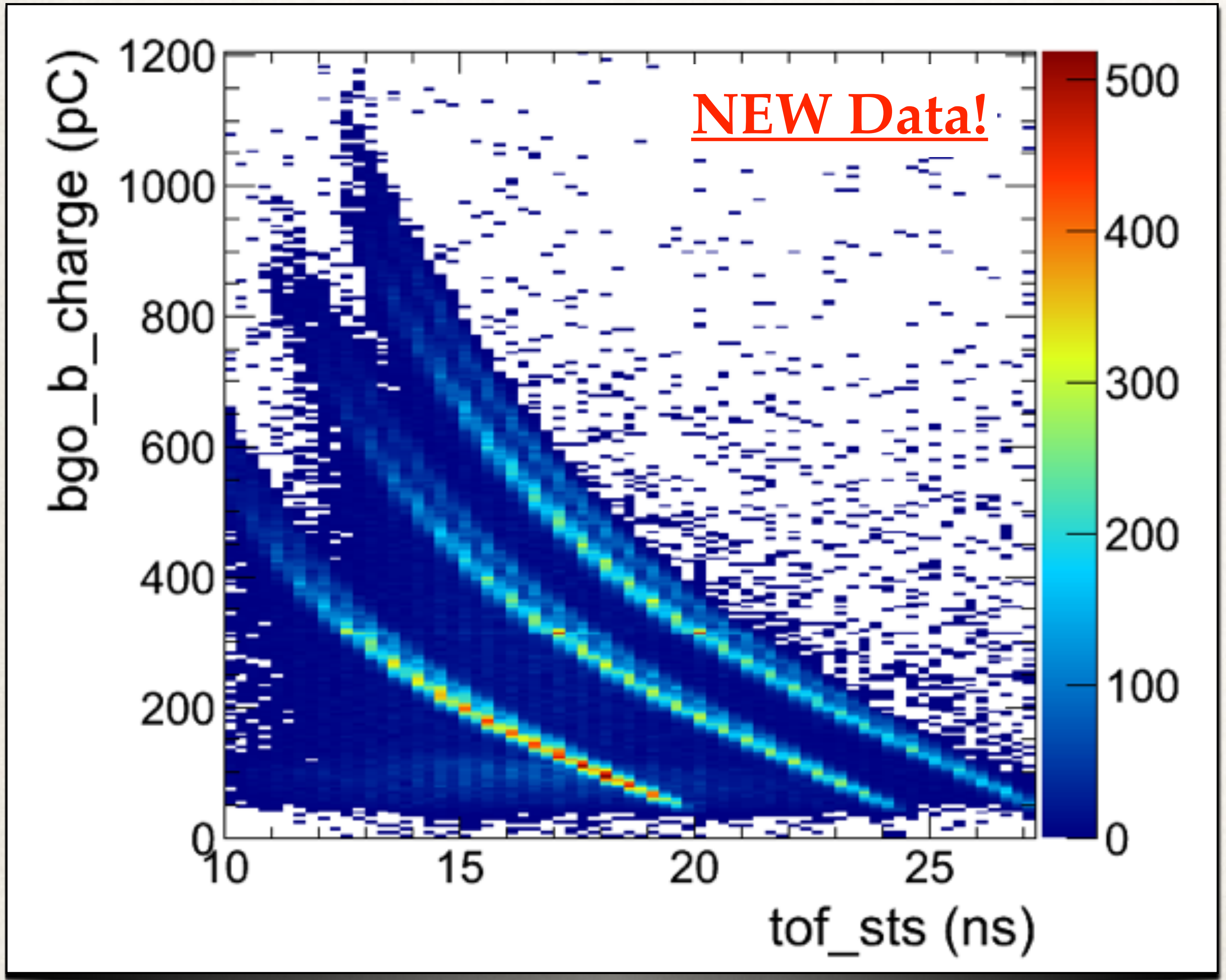
Analysis on going

Secondary particles: CHARGED PARTICLES

Beam on PMMA target:

He fragments!!

HIT (Heidelberg) -> 125 MeV/u ^{4}**He** beam: **detector @10°**



The protons, deutons and tritiums produced in the fragmentation of the PMMA are measured with forward BGO crystal detectors

Analysis on going

New Monitor: exploiting secondary particles

From what we measured we can estimate the expected flux of charged secondary particles on a dose monitor detector:

Very Conservative considerations @90º:

- single pencil beam (2 Gy dose),
- small detector (10x10 cm^2 @ 35 cm)
- deep tumor (MS σ_{MS} ~ 3.16 rad)

~ 4 mm resolution

.. we decide to propose something..

The INSIDE Project

PRIN MIUR 2010-2011 -2010P98A75

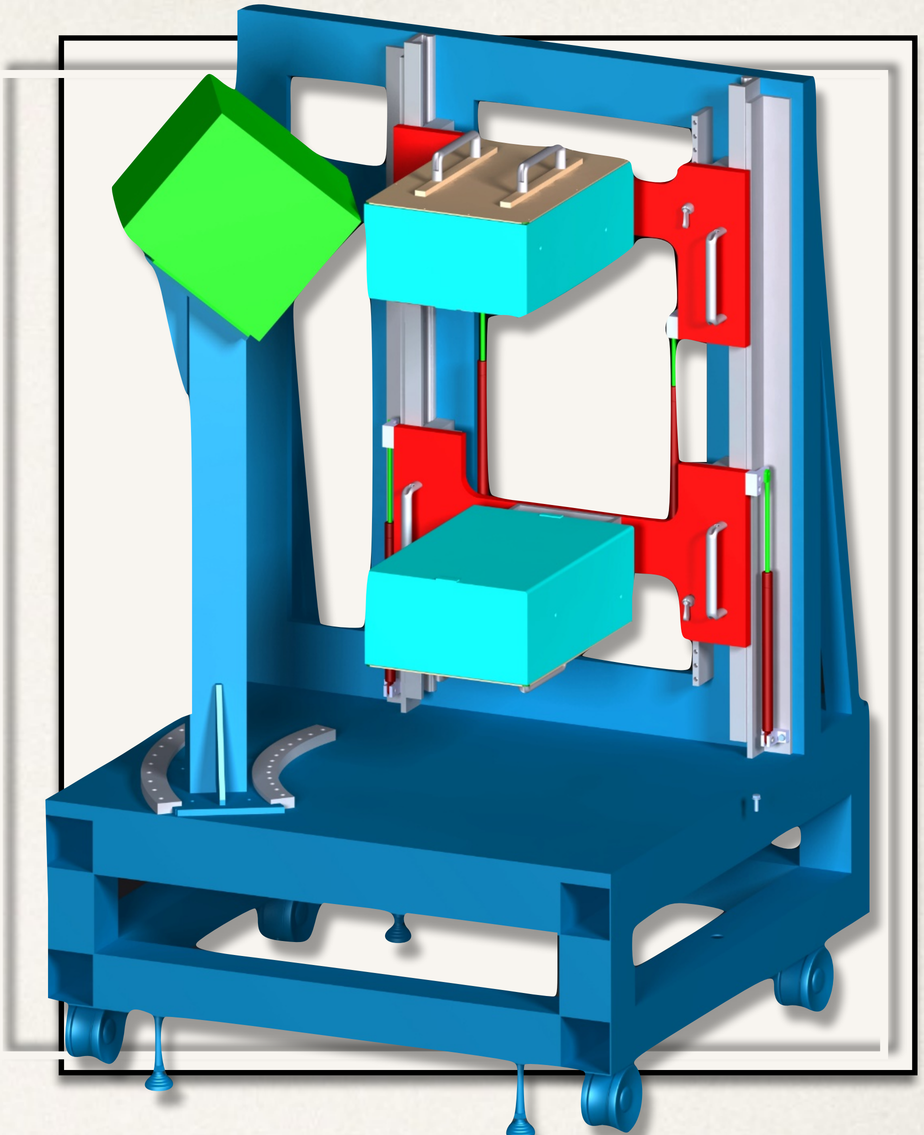
INFN RDH project

Centro Fermi project

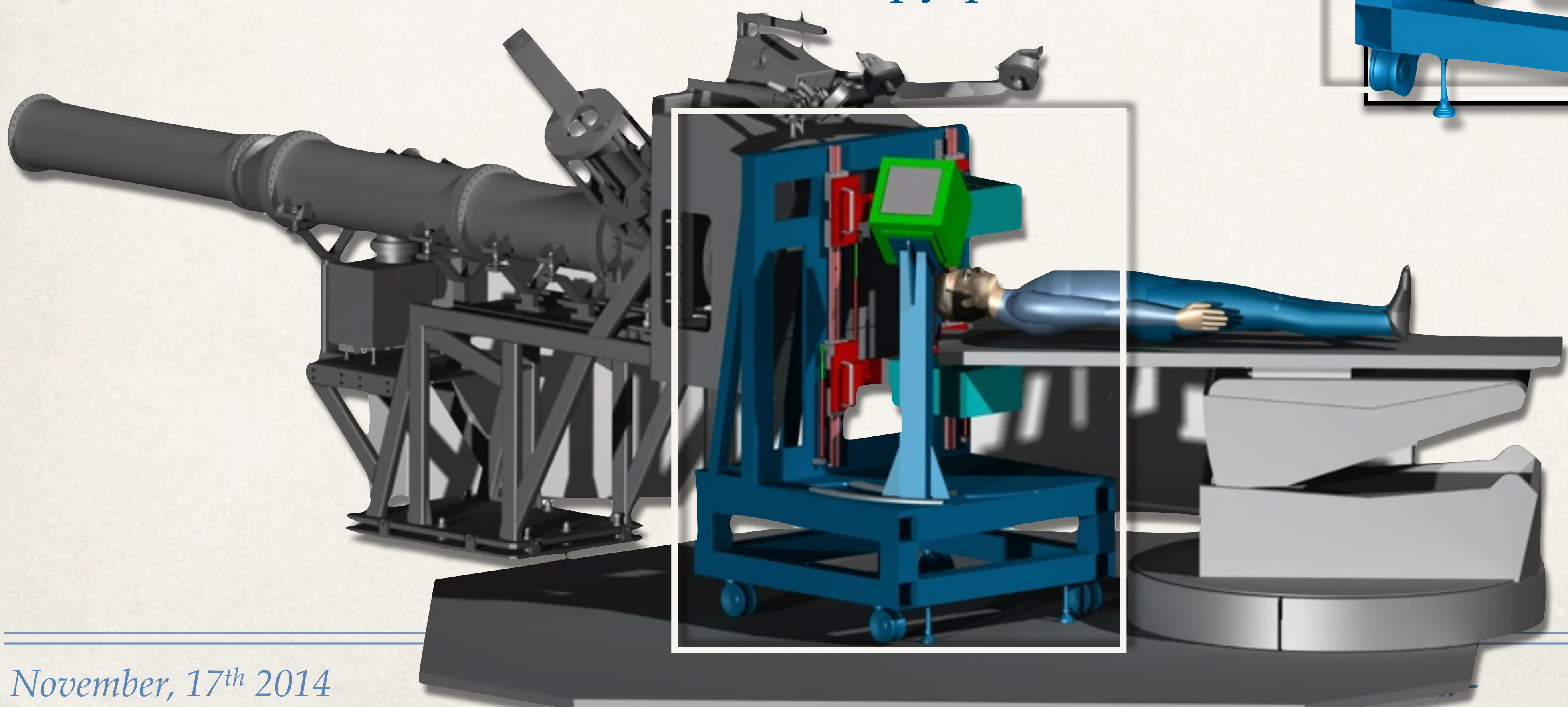
INnovative Solutions for In-beam DosimEtry in Hadrontherapy

The INSIDE Project

The project addresses the dose monitoring on line problem: two **PET-heads** to β^+ activity measurements and a **Dose Profiler** for the reconstruction of the charged secondary particles emission distribution.

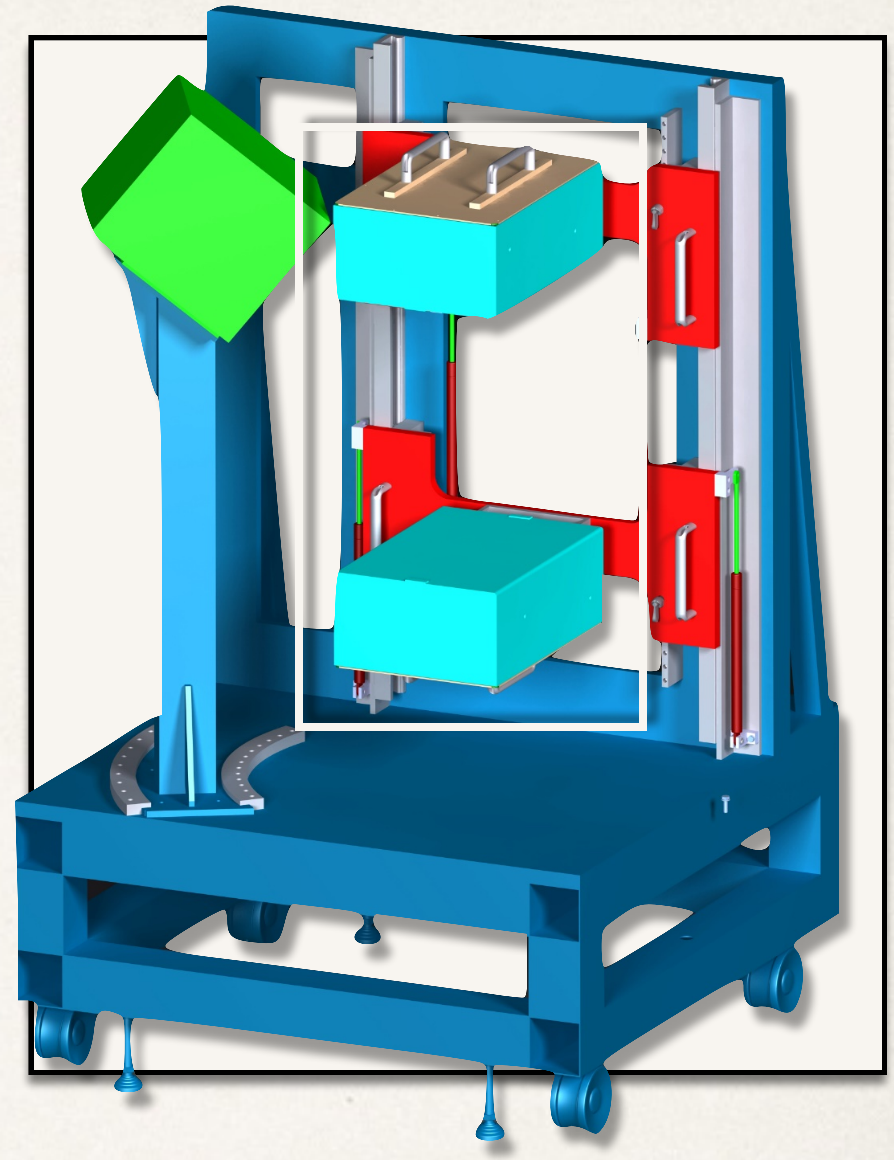


For the **CNAO** measurements we design a cart in order to hold up the detectors minimizing the interferences with therapy procedures



The INSIDE Project

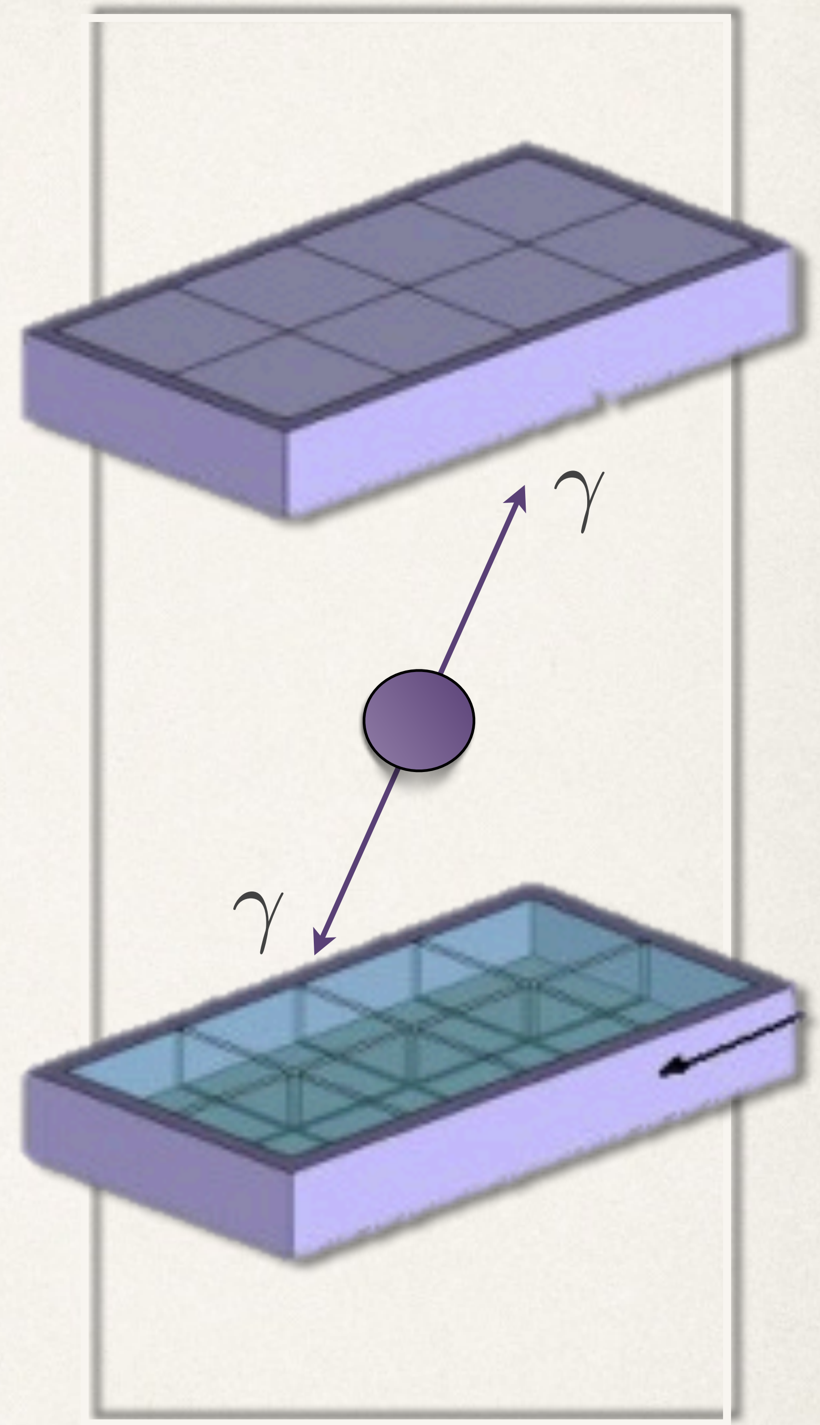
- Detectors to measure the 511 keV photons in order to reconstruct the β^+ activity map;
- Full in-beam PET system able to sustain annihilation, prompt photon and neutron rates during the beam irradiation (in-beam and inter-spill);



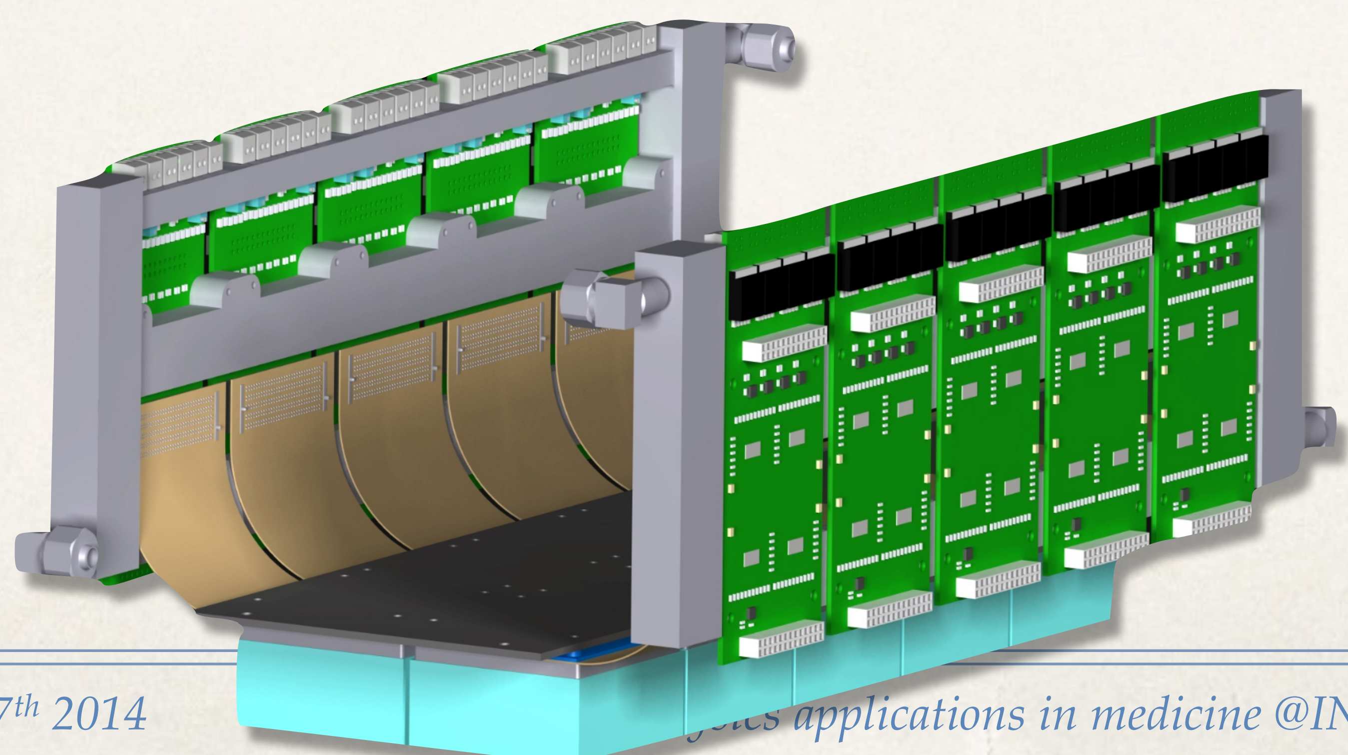
Total sensitive area of a module: 5 cm x 5 cm

The INSIDE Project

- Detectors to measure the 511 keV photons in order to reconstruct the β^+ activity map;
- Full in-beam PET system able to sustain annihilation, prompt photon and neutron rates during the beam irradiation (in-beam and inter-spill);
- Two planar panels: 10 cm x 20 cm wide => 2 x 4 detection modules;



=> 511 keV back-to-back

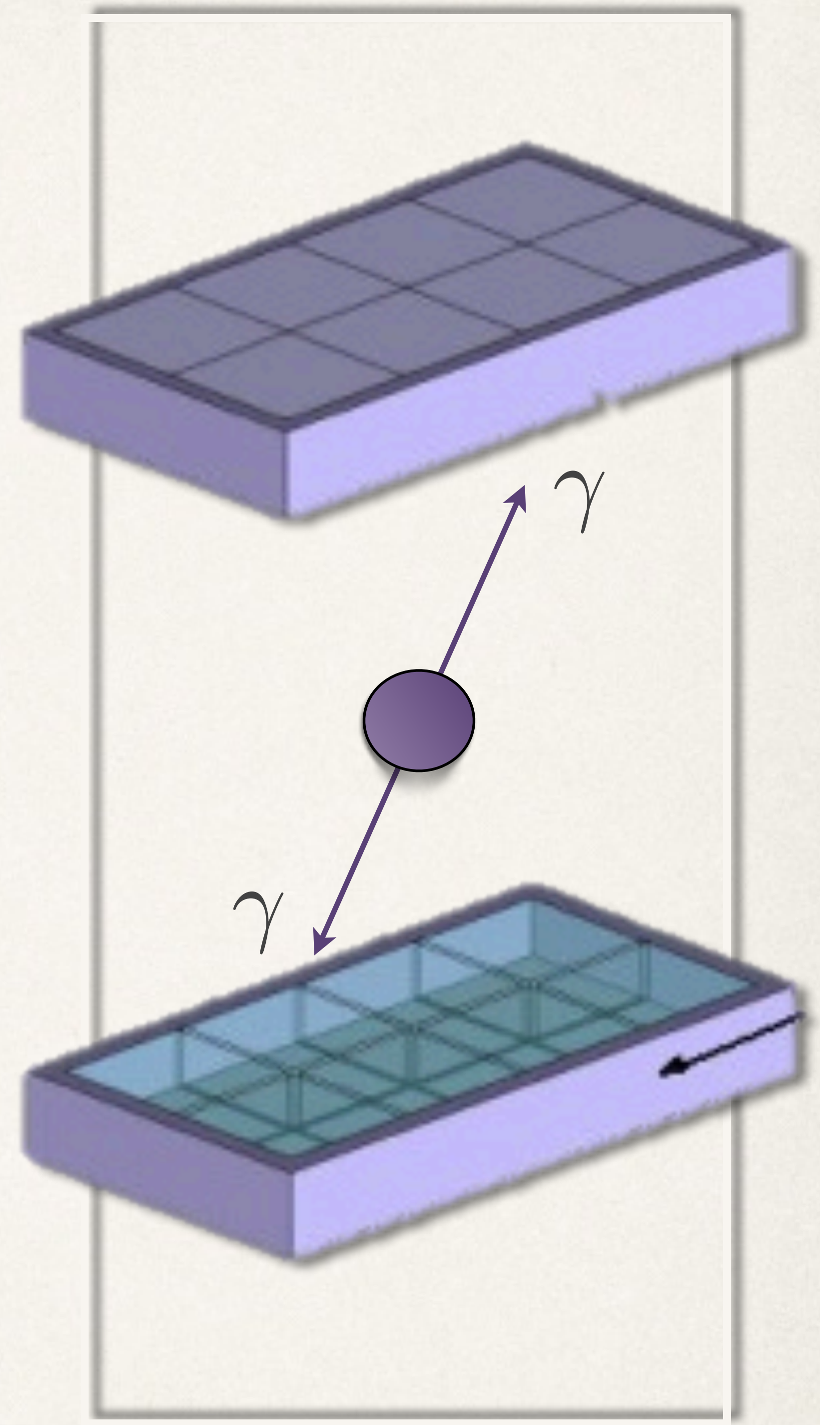


The INSIDE Project

- Detectors to measure the 511 keV photons in order to reconstruct the β^+ activity map;
- Two planar panels: 10 cm x 20 cm wide => 2 x 4 detection modules;

  - Each module is composed of a pixelated LYSO matrix 16 x 16 pixels, 3 mm x 3 mm crystals (pitch 3.1mm);
  - LYSO matrix readout: array of SiPM (16x16 pixels) coupled one-to-one.

The **resolution** of the two PET heads system in the β^+ activity reconstruction map is expected to be between 1 and **2 mm (FWHM)** in beam direction.

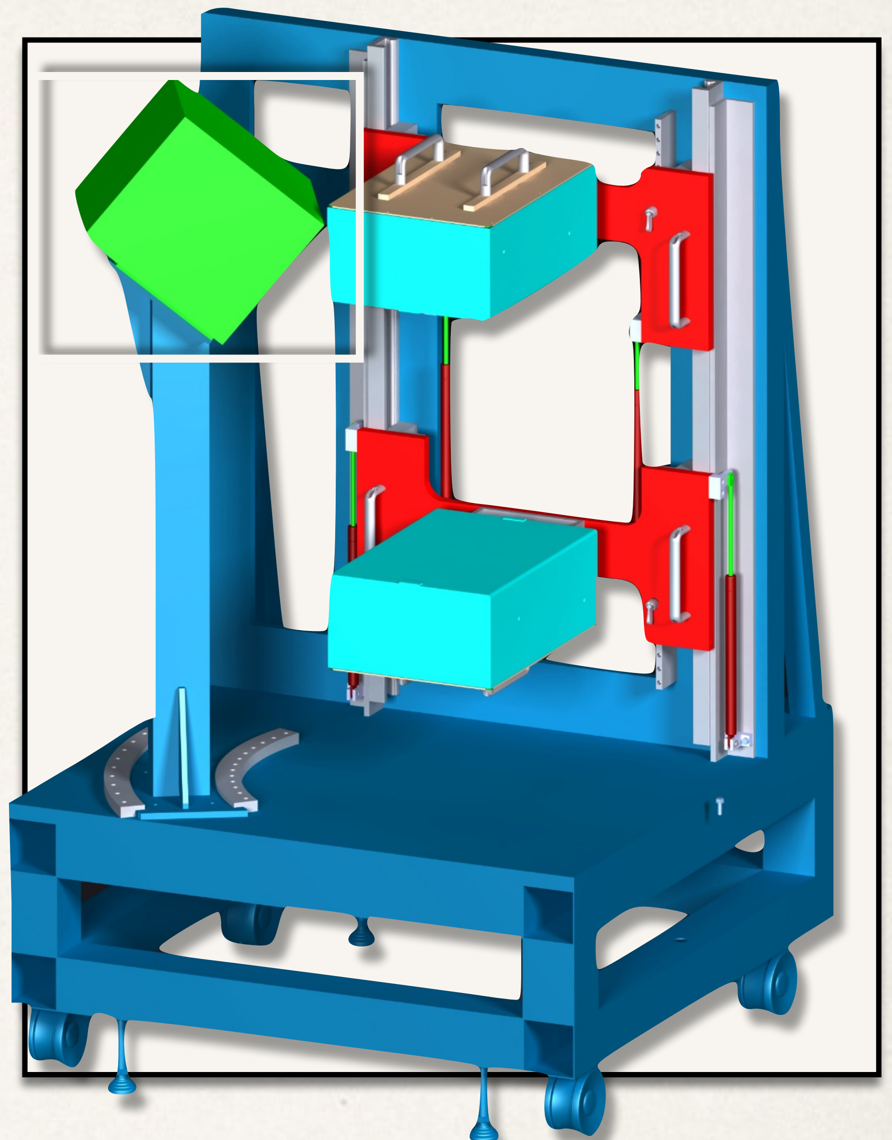


=> 511 keV back-to-back

The INSIDE Project: Dose Profiler

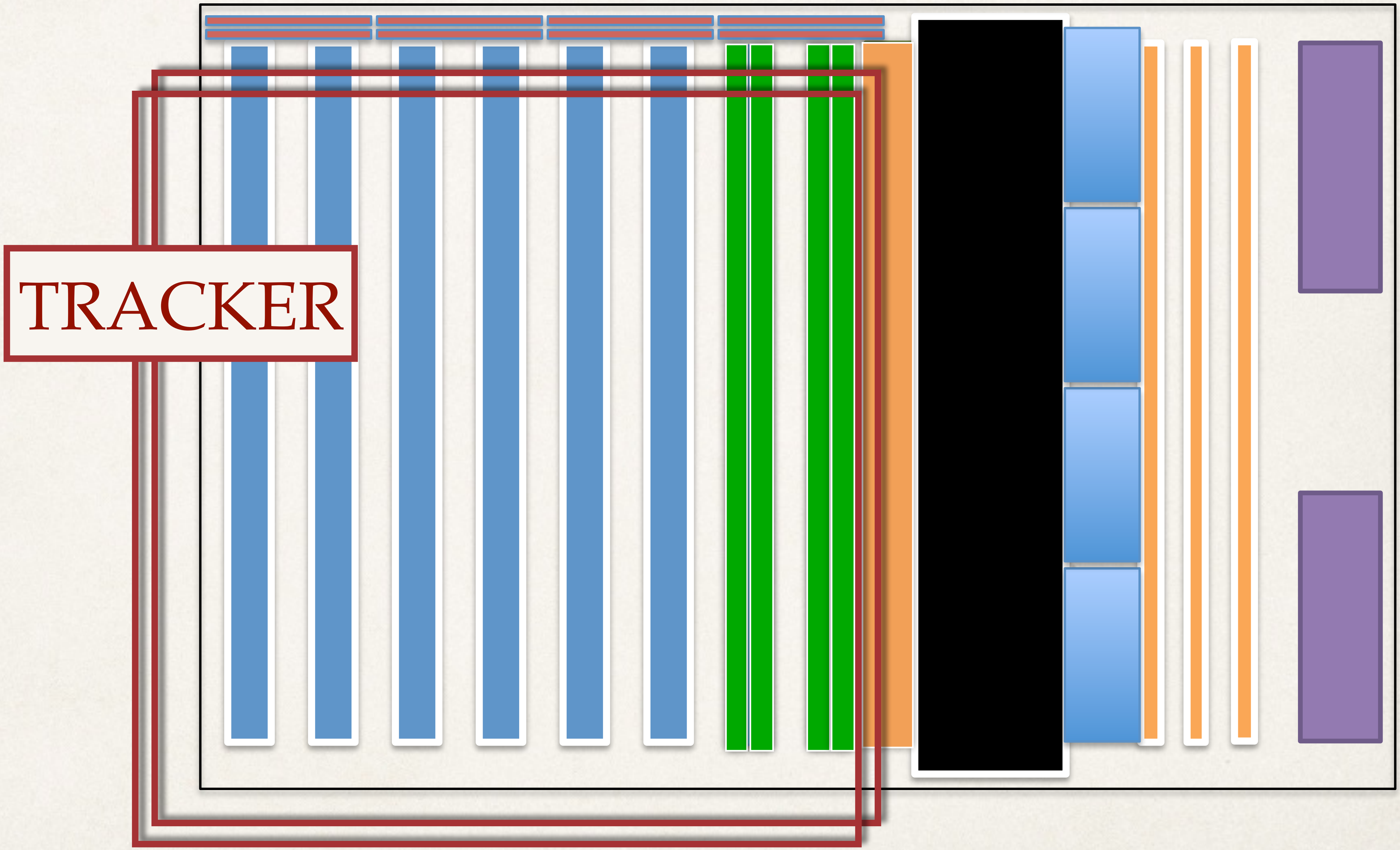
- The Dose Profiler aim is to back tracks the secondary particles (p,d,t and prompt photons) and reconstruct their emission point together with their flux.

detector at 60° to increase the secondary charged particles rate



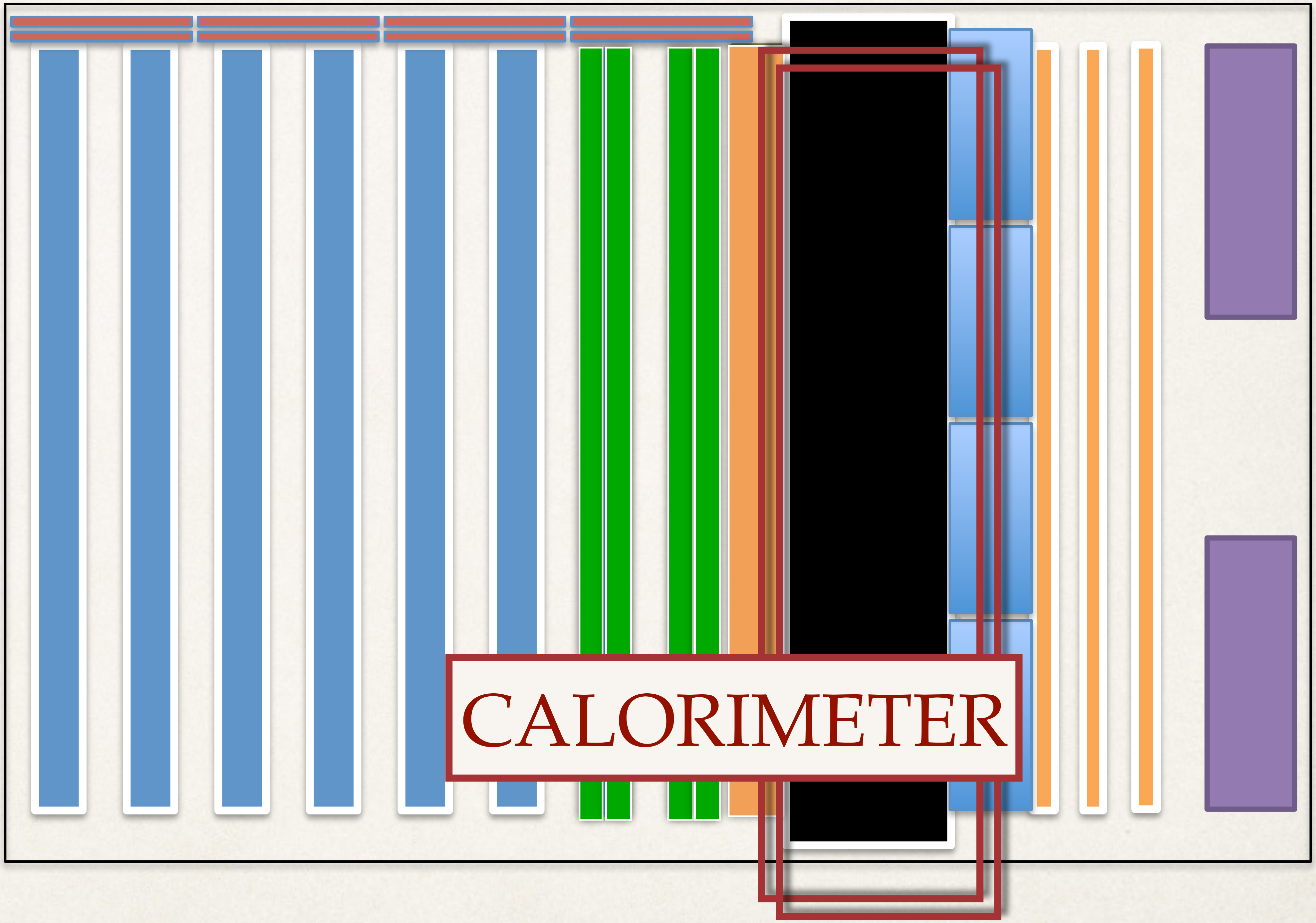
The INSIDE Project: Dose Profiler

The detector is divided in two parts:

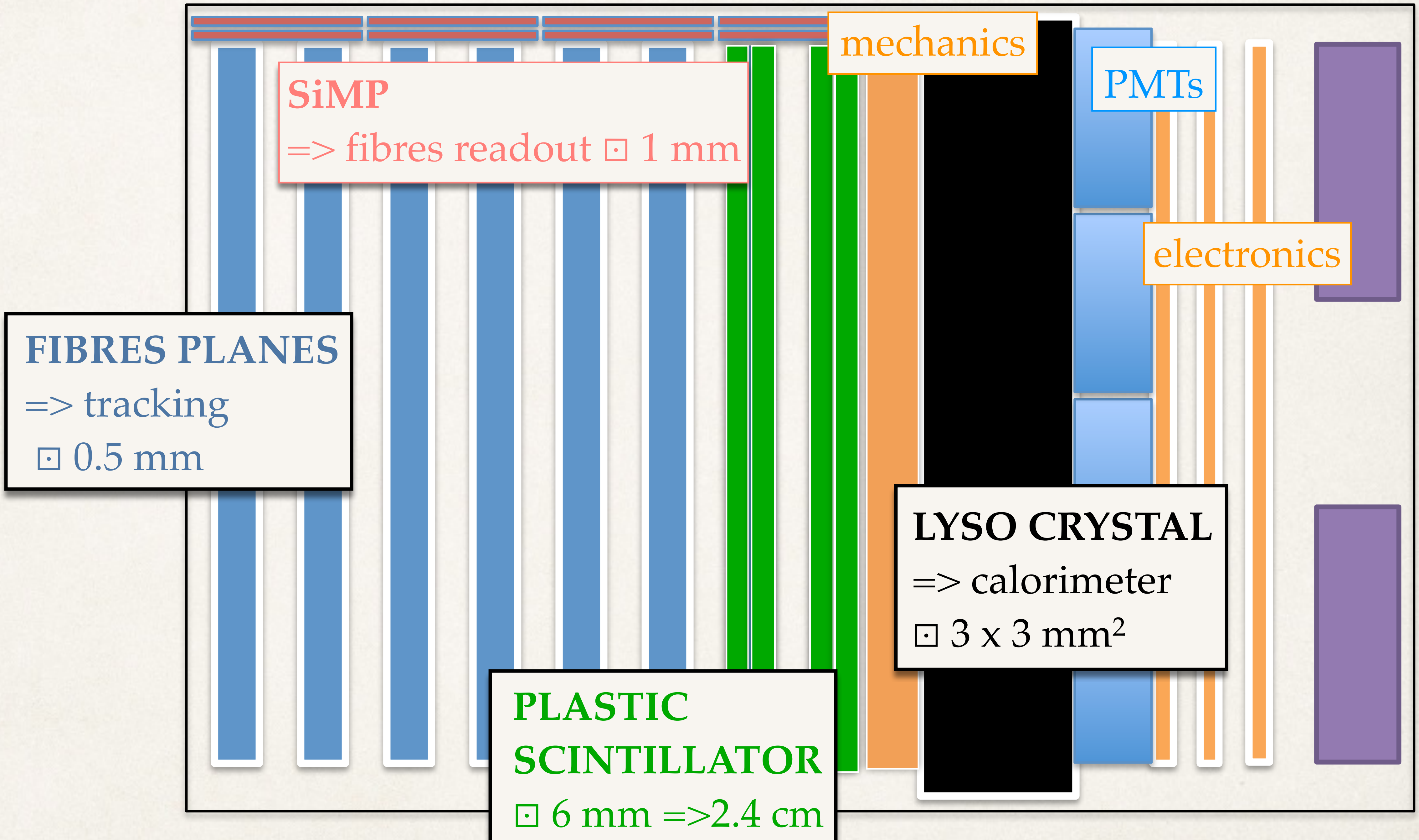


The INSIDE Project: Dose Profiler

The detector is divided in two parts:

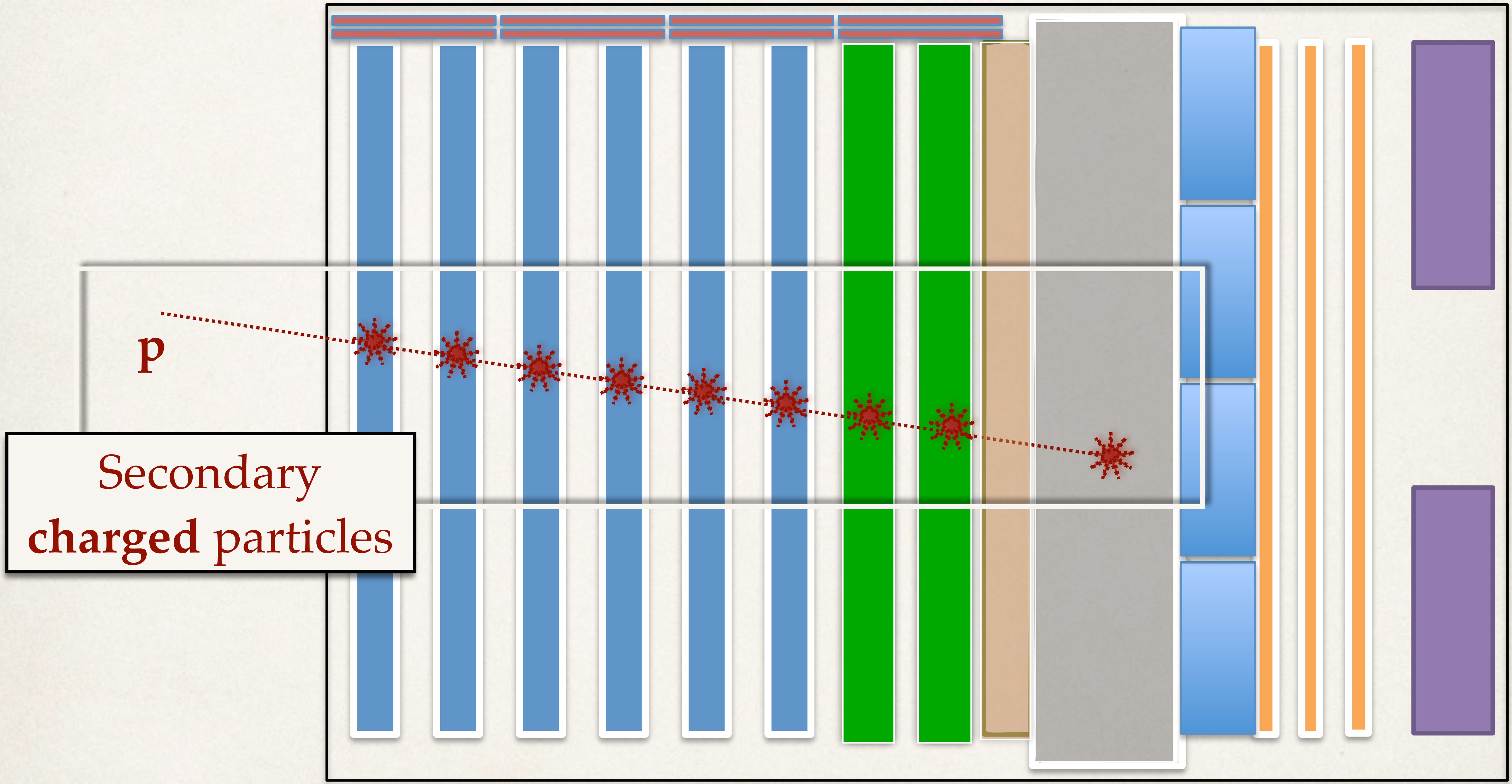


The INSIDE Project: Dose Profiler

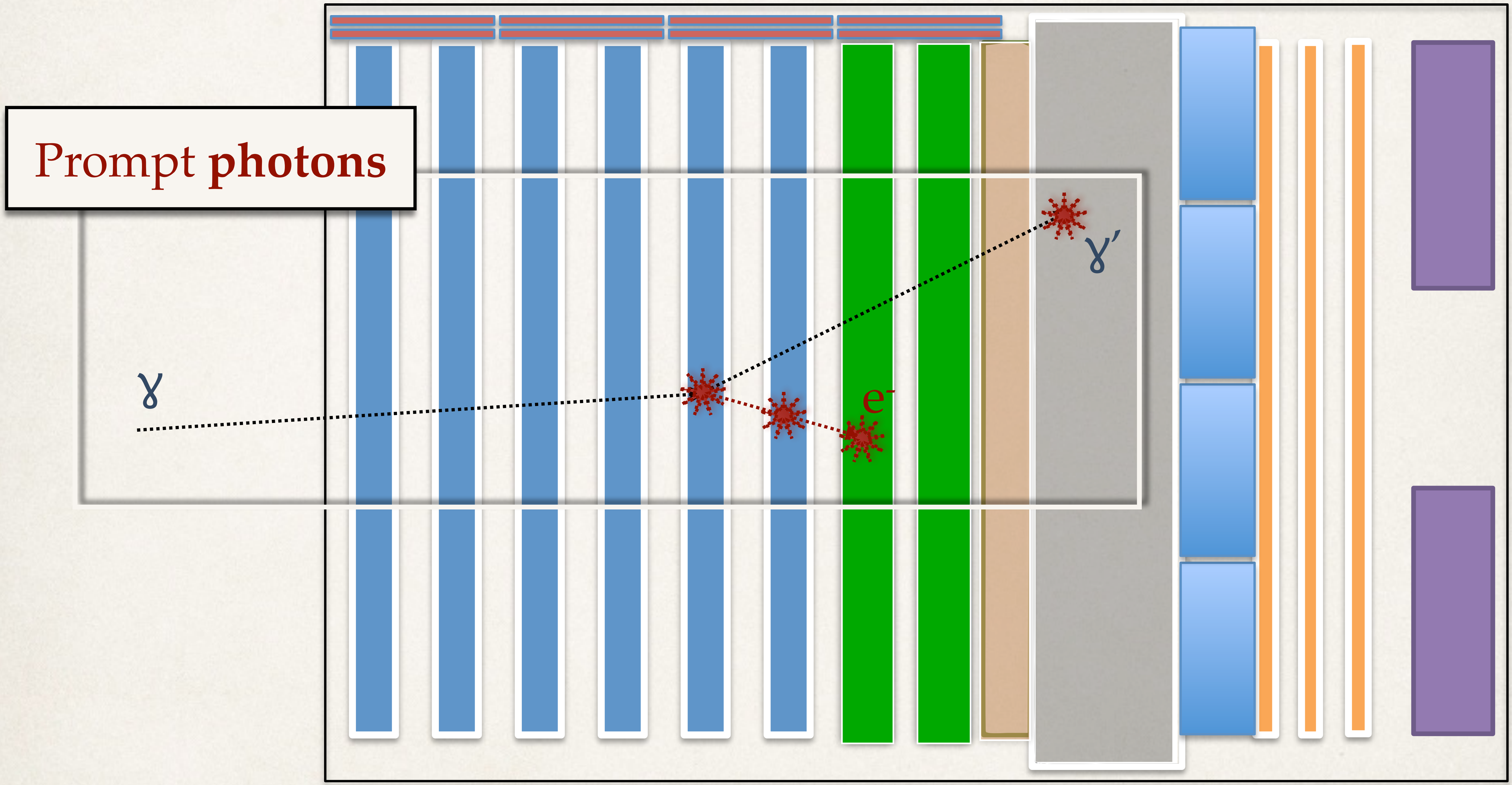


The INSIDE Project: Dose Profiler

For protons of E_K>30 MeV the tracking is "easy": all layers are crossed..

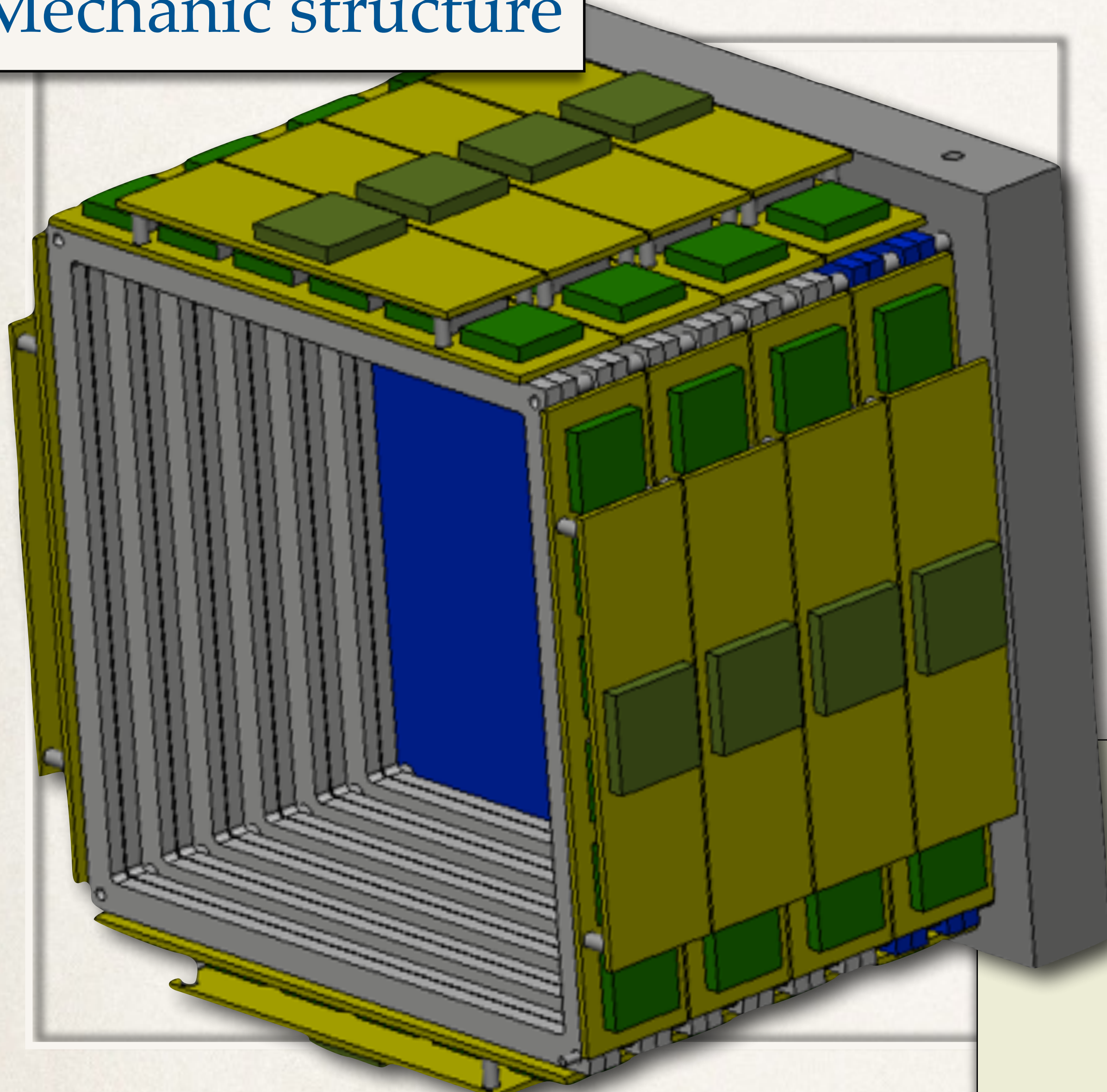


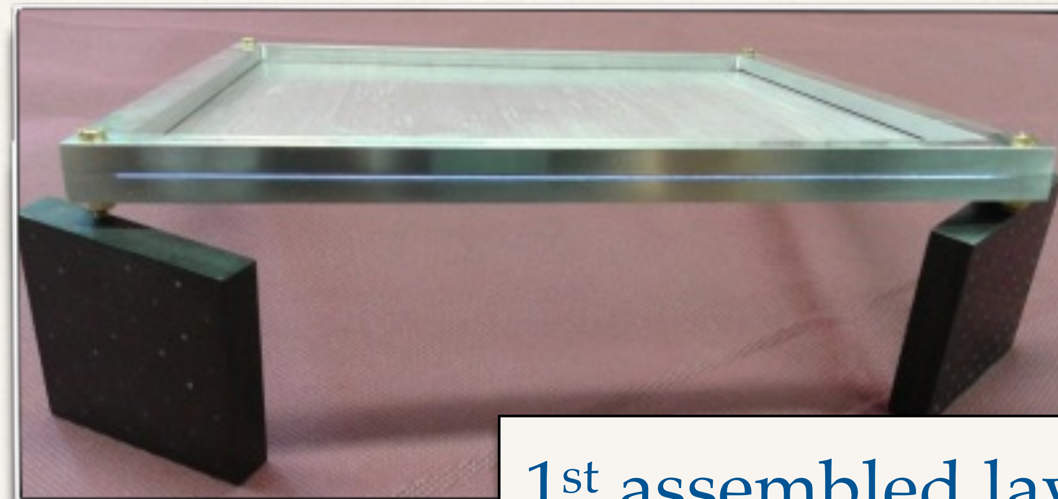
The INSIDE Project: Dose Profiler



The INSIDE Project: Dose Profiler

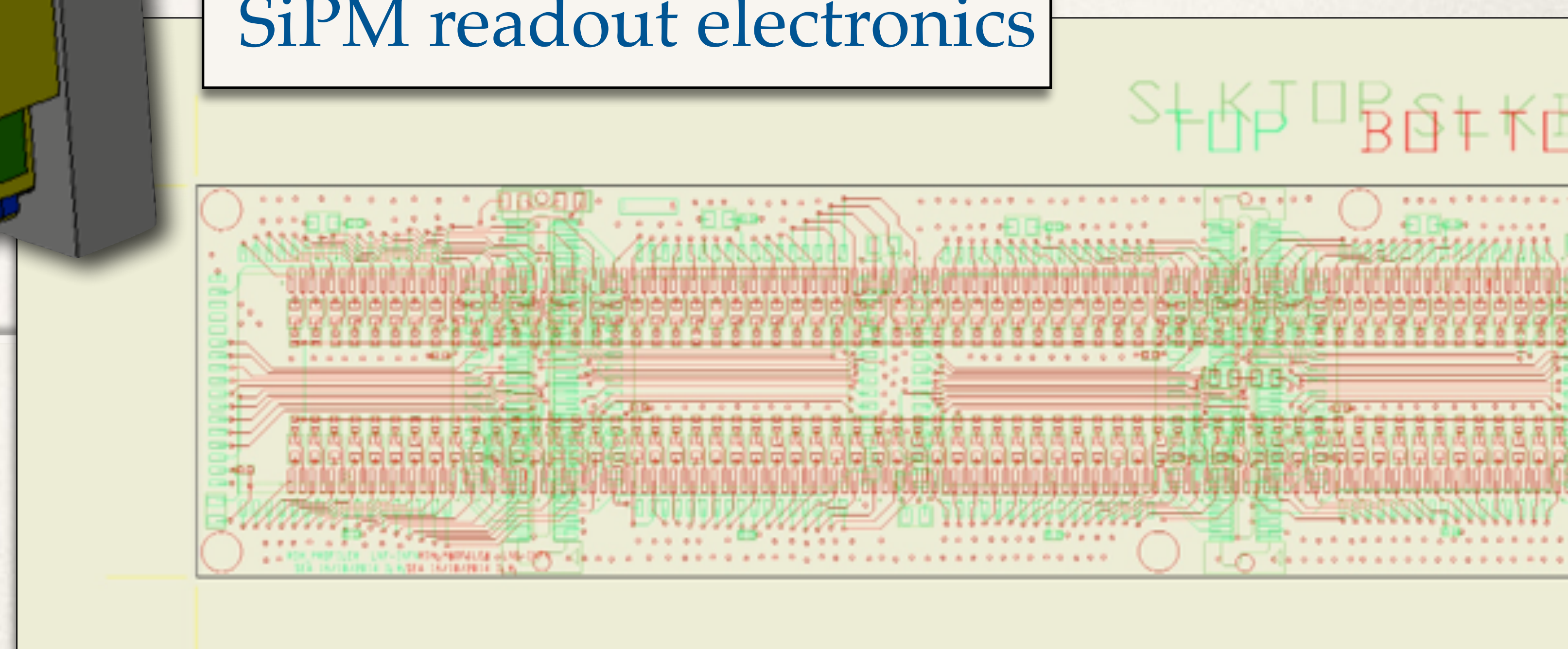
Mechanic structure



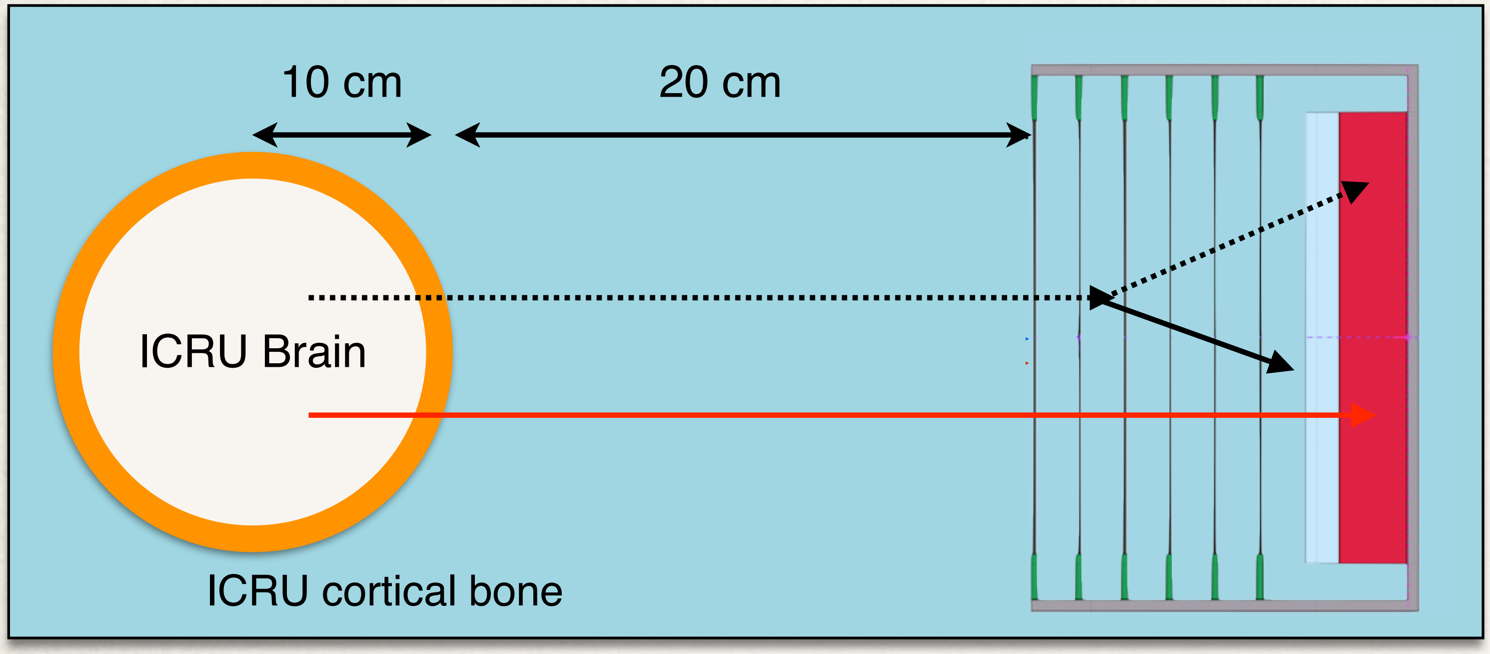


1^{st} assembled layer

SiPM readout electronics

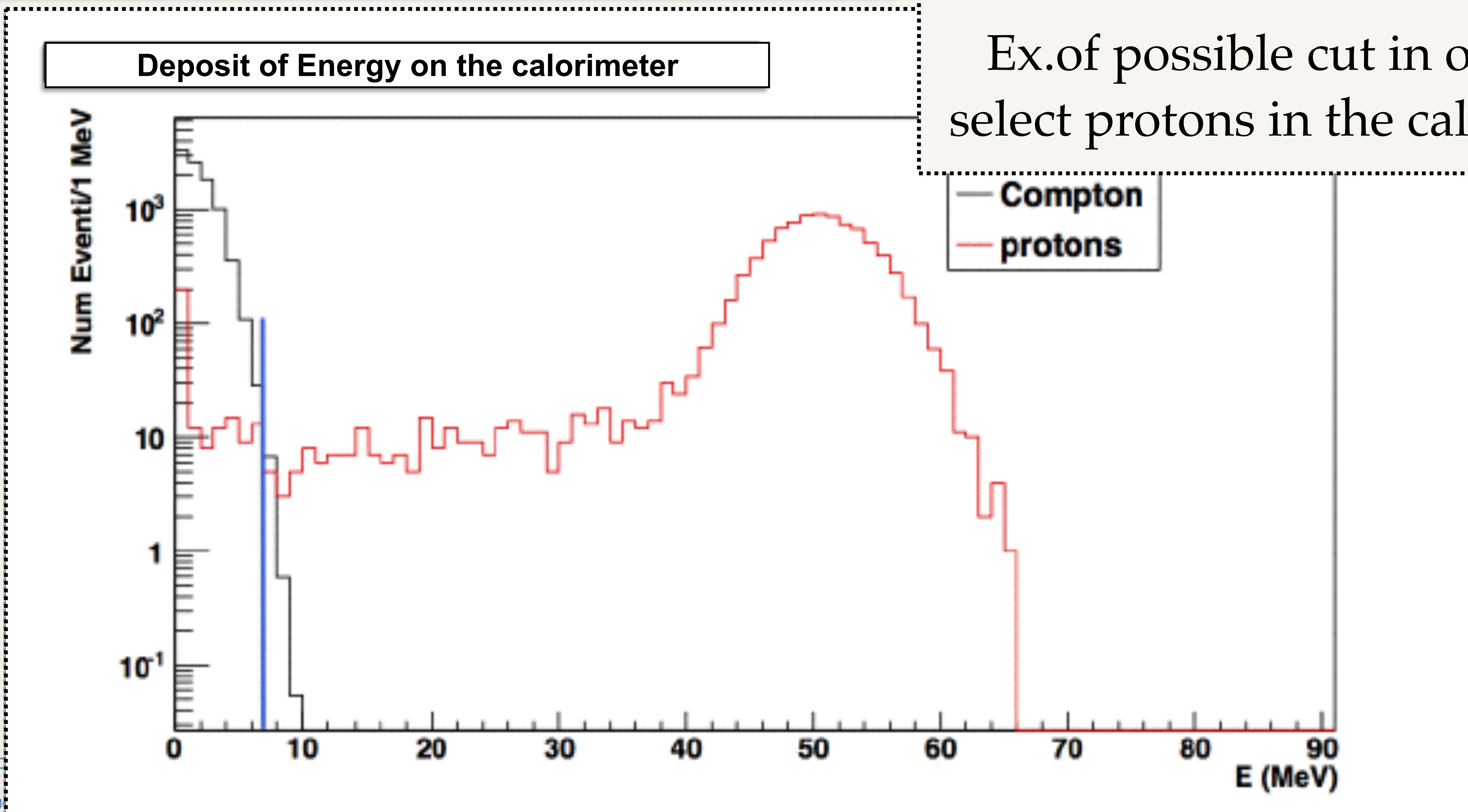


The INSIDE Project: Dose Profiler

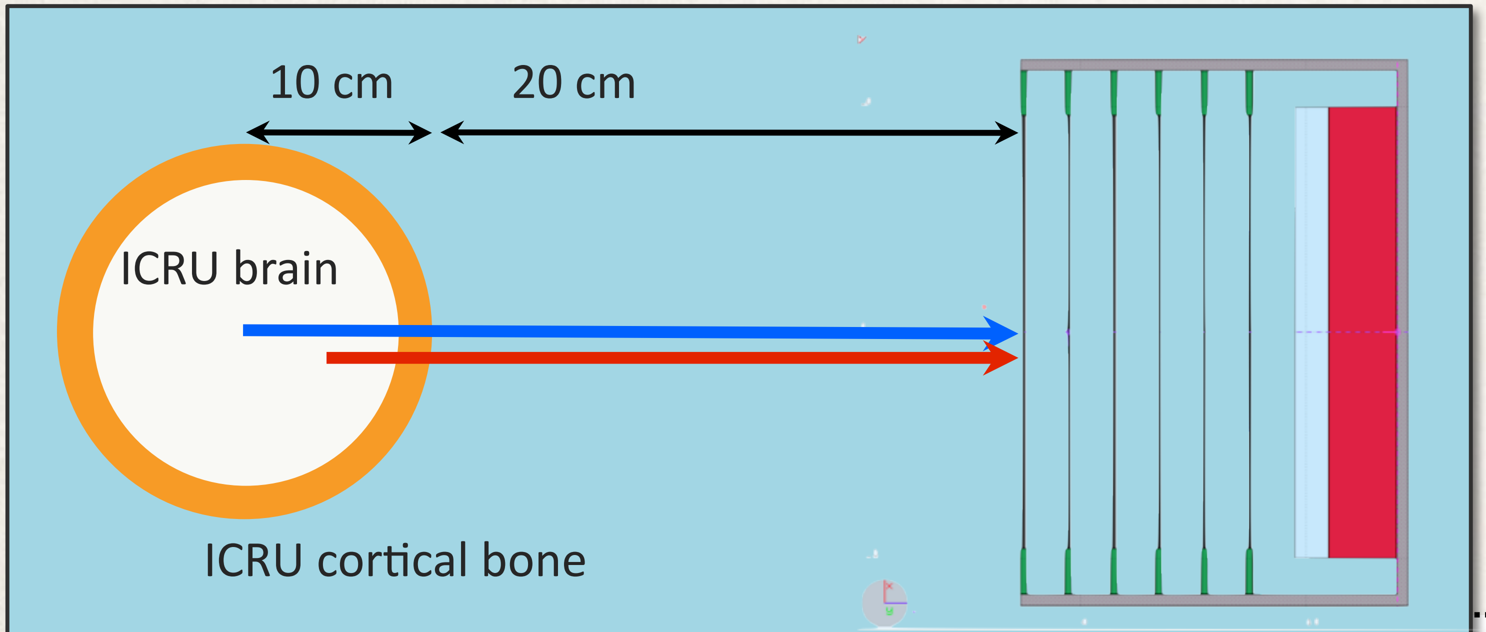


We simulate the detector with FLUKA. The resolution of the DP can be calculated for different tumor depth.

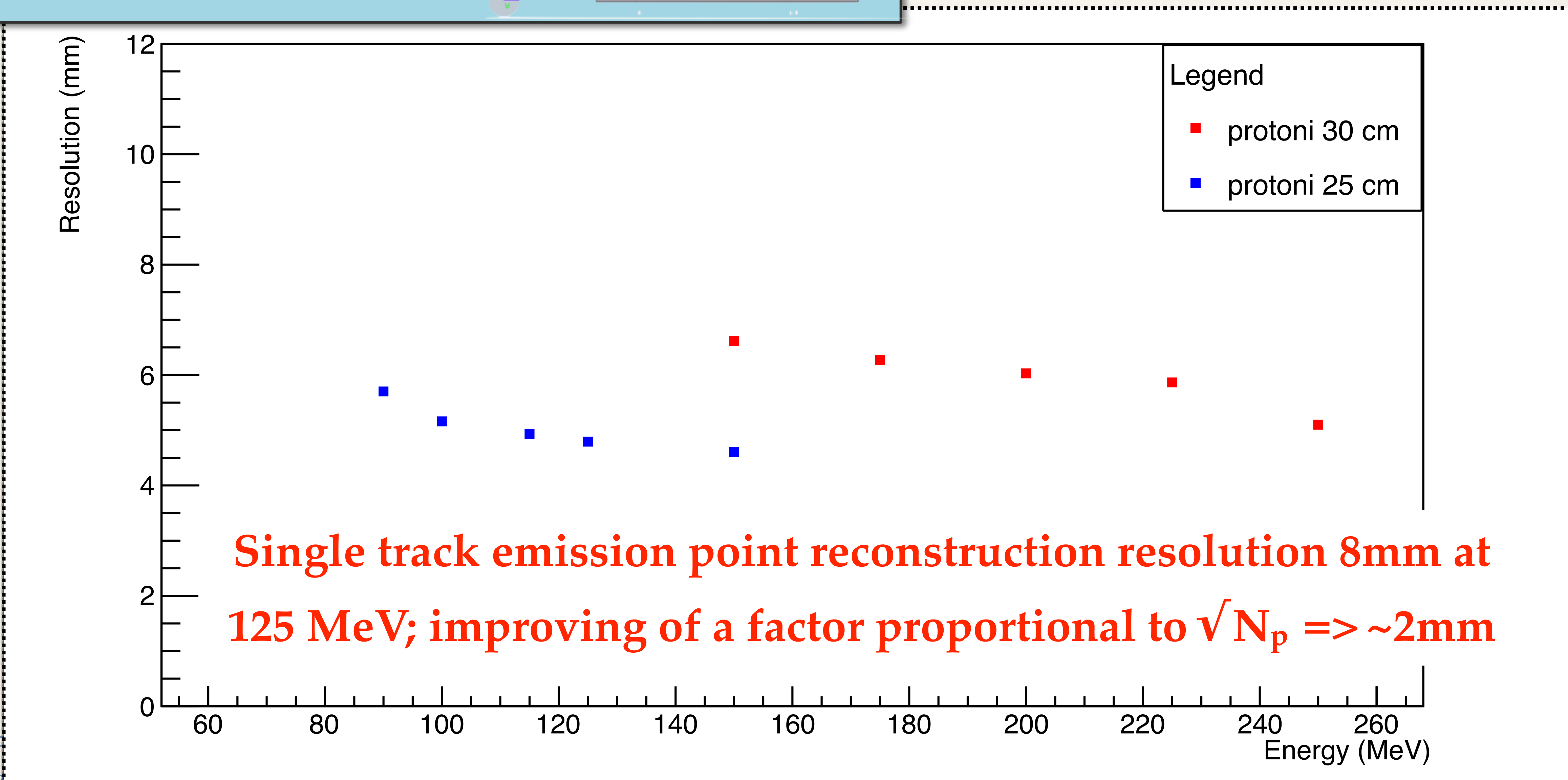
Ex.of possible cut in order to select protons in the calorimeter



The INSIDE Project: Dose Profiler



We simulate the detector with FLUKA. The resolution of the DP can be calculated for different tumor depth.



Single track emission point reconstruction resolution 8mm at 125 MeV; improving of a factor proportional to $\sqrt{N_p}$ => ~2mm

Conclusions

- Particle therapy is very useful to cure loco-regional tumors preserving the surrounding healthy tissues;

- the online range monitoring is crucial => dose realized on treated volume and BP positioning;

- secondary particles produced in the interaction of the beam with the patient can be exploited:

  - Flux and spectrum measurements

  - INSIDE Project ⇨ **test in treatment room at CNAO end of 2016**

    - **Dose Profiler: secondary charged particles and prompt photons**

GRAZIE

Master and and PhD students are very welcome!

- **Prof. Riccardo Faccini**
riccardo.faccini@roma1.infn.it
- **Prof. Vincenzo Patera**
vincenzo.patera@uniroma1.it
- **Michela Marafini**
michela.marafini@roma1.infn.it

Backup

…

OUR GROUP

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1. DIPARTIMENTO DI FISICA, SAPIENZA UNIVERSITÀ DI ROMA, ROME, ITALY;
2. **INFN SEZIONE DI ROMA, ITALY;**
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4. DIPARTIMENTO DI SCIENZE DI BASE E APPLICATE PER INGEGNERIA, SAPIENZA UNIVERSITÀ DI ROMA, ITALY;
5. MUSEO STORICO DELLA FISICA E CENTRO STUDI E RICERCHE 'E. FERMI', ITALY;
6. CENTER FOR LIFE NANO SCIENCE@SAPIENZA, ISTITUTO ITALIANO DI TECNOLOGIA, ITALY;
7. DIPARTIMENTO DI MATEMATICA E FISICA, ROMA TRE UNIVERSITÀ DI ROMA, ITALY;
8. DIPARTIMENTO DI INGEGNERIA MECCANICA E AEROSPAZIALE, SAPIENZA UNIVERSITÀ DI ROMA, ITALY;
9. INFN SEZIONE DI MILANO, ITALY;

Oncological application:

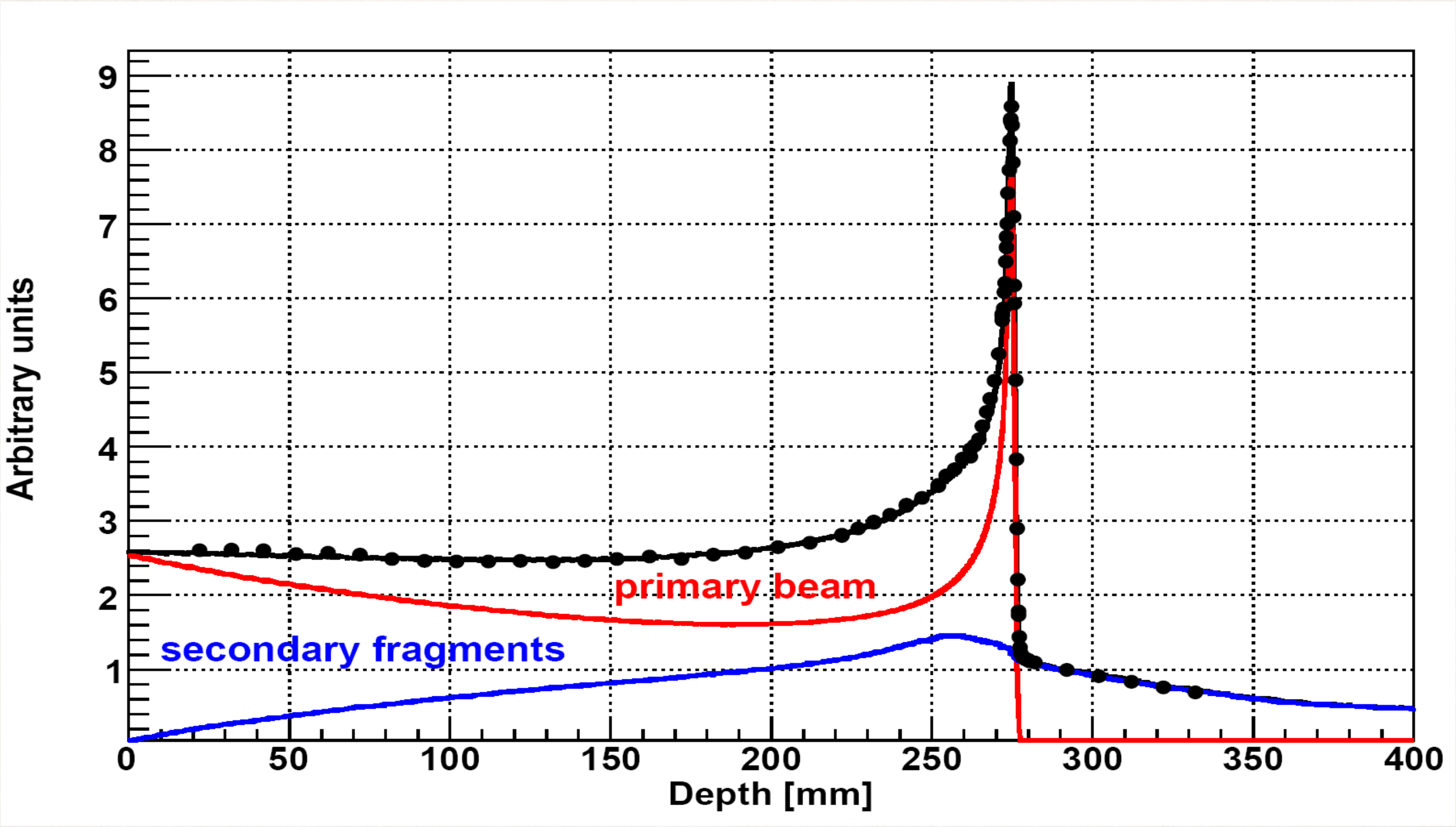
- CHIRONE: Probes for radio-guided surgery

Previous talk: Elena!

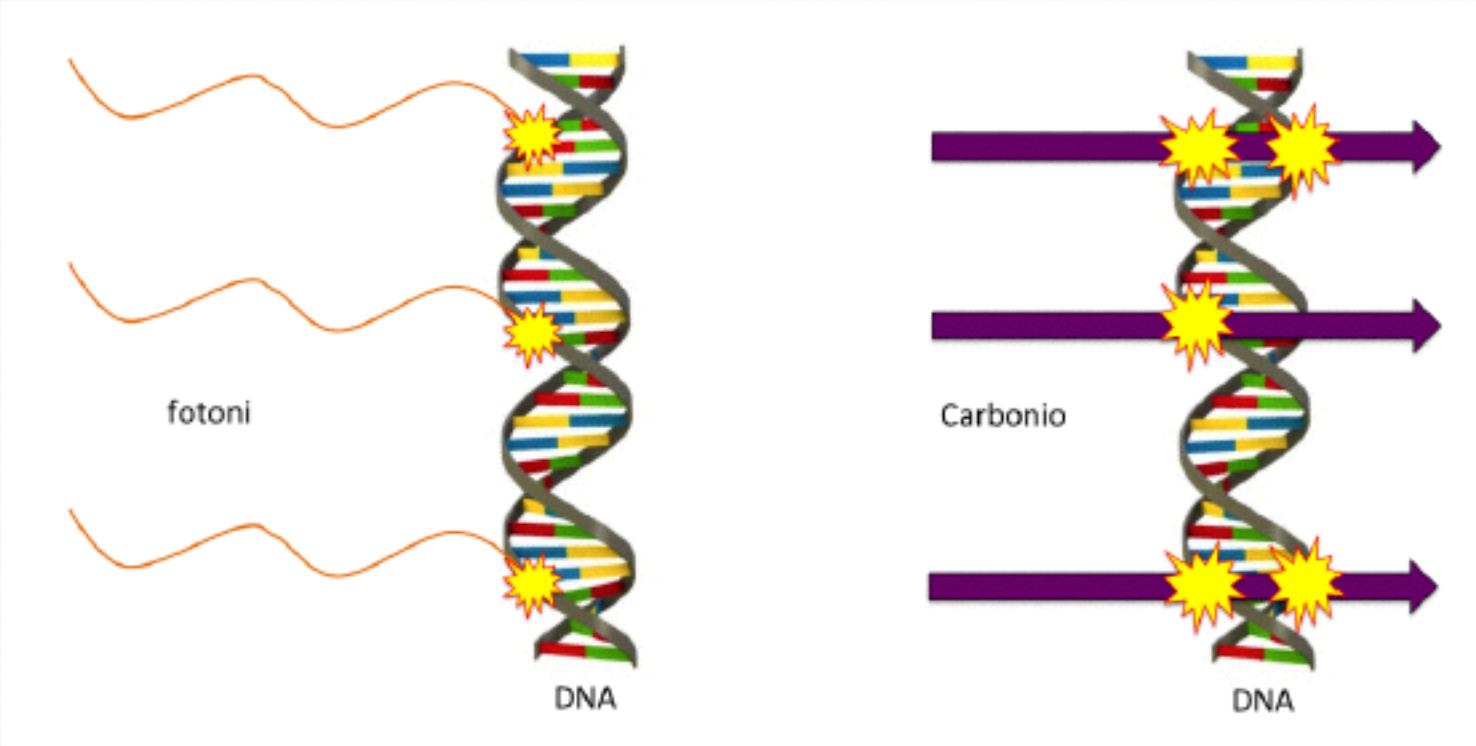
Particle therapy applications:

- flux and spectra measurements for neutral and charged secondary particles;
- INSIDE: dose profiler;
- proposal MONDO: neutron dose measurements;
- PET studies;

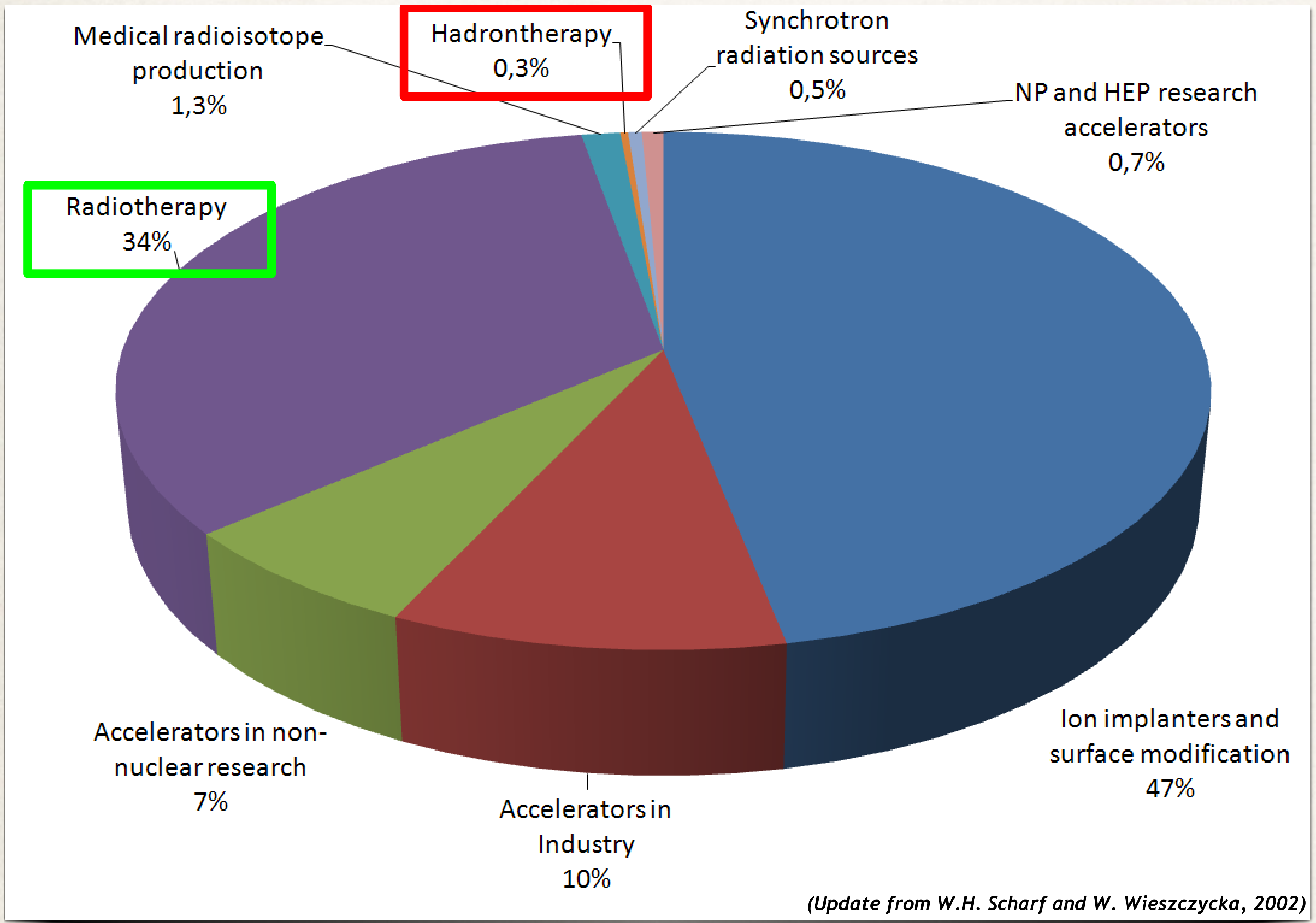
PT: dose distribution



PT: dose distribution

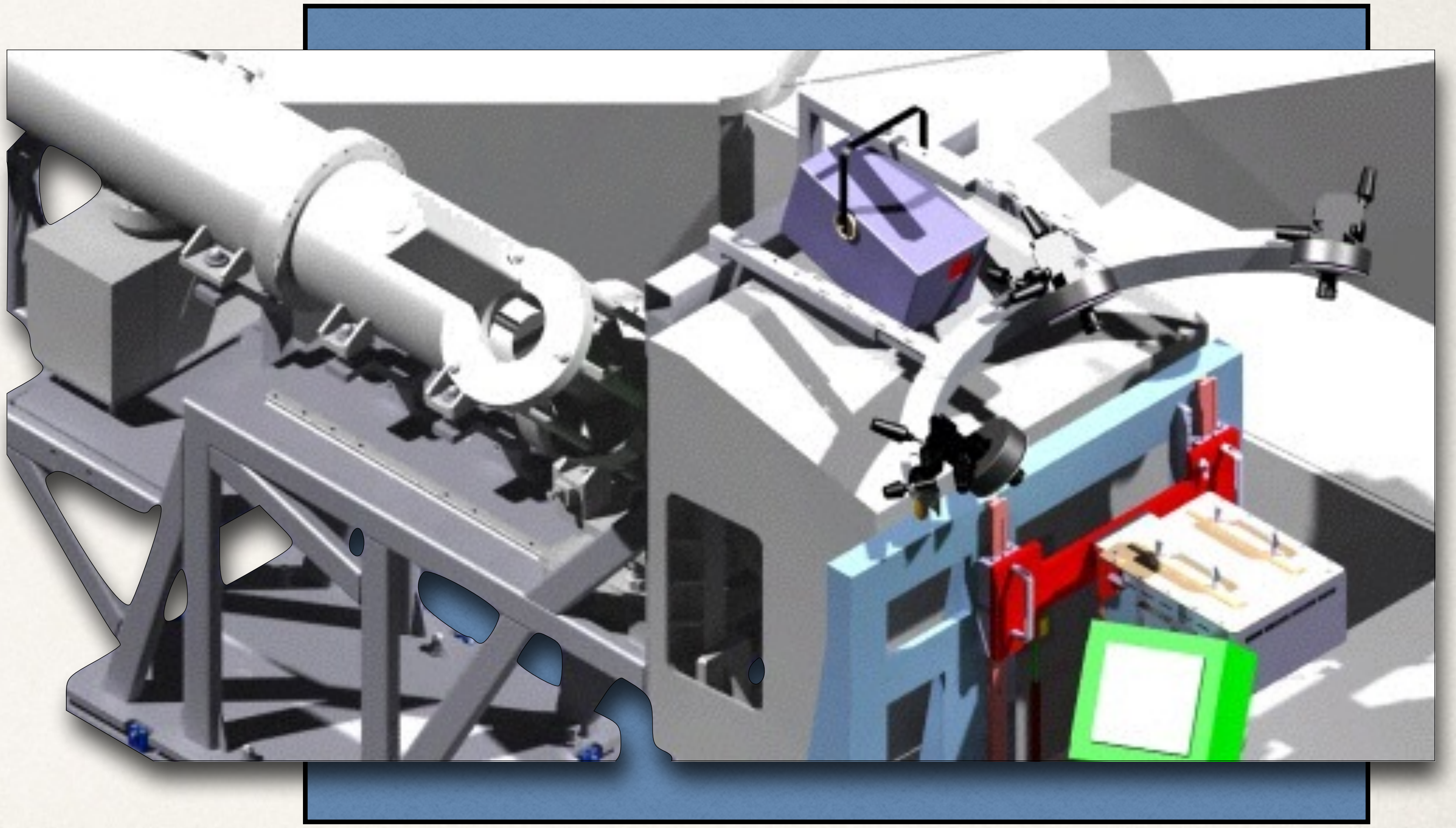


Treatment uncertainties in Ion Beam Therapy

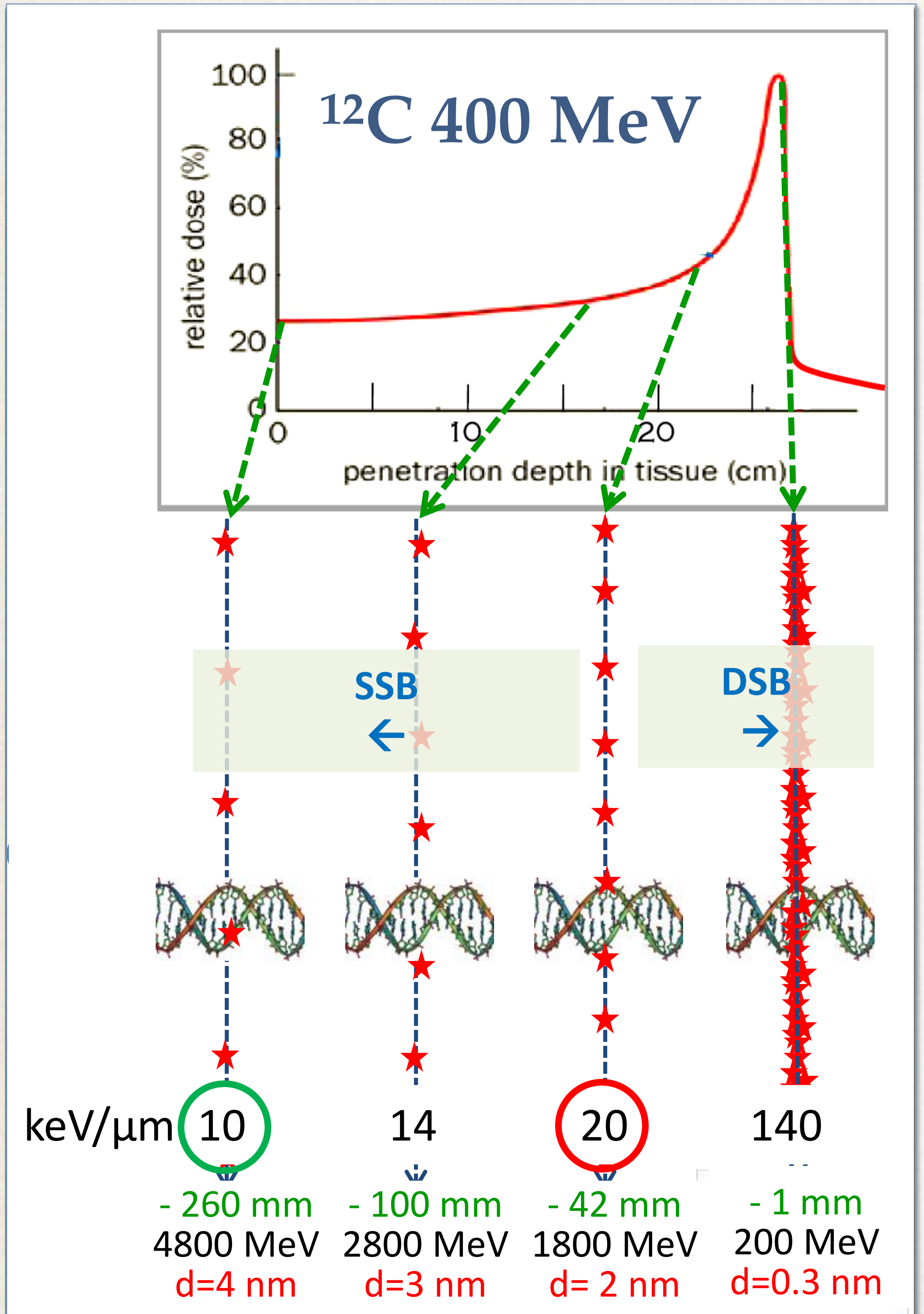


Monitoring

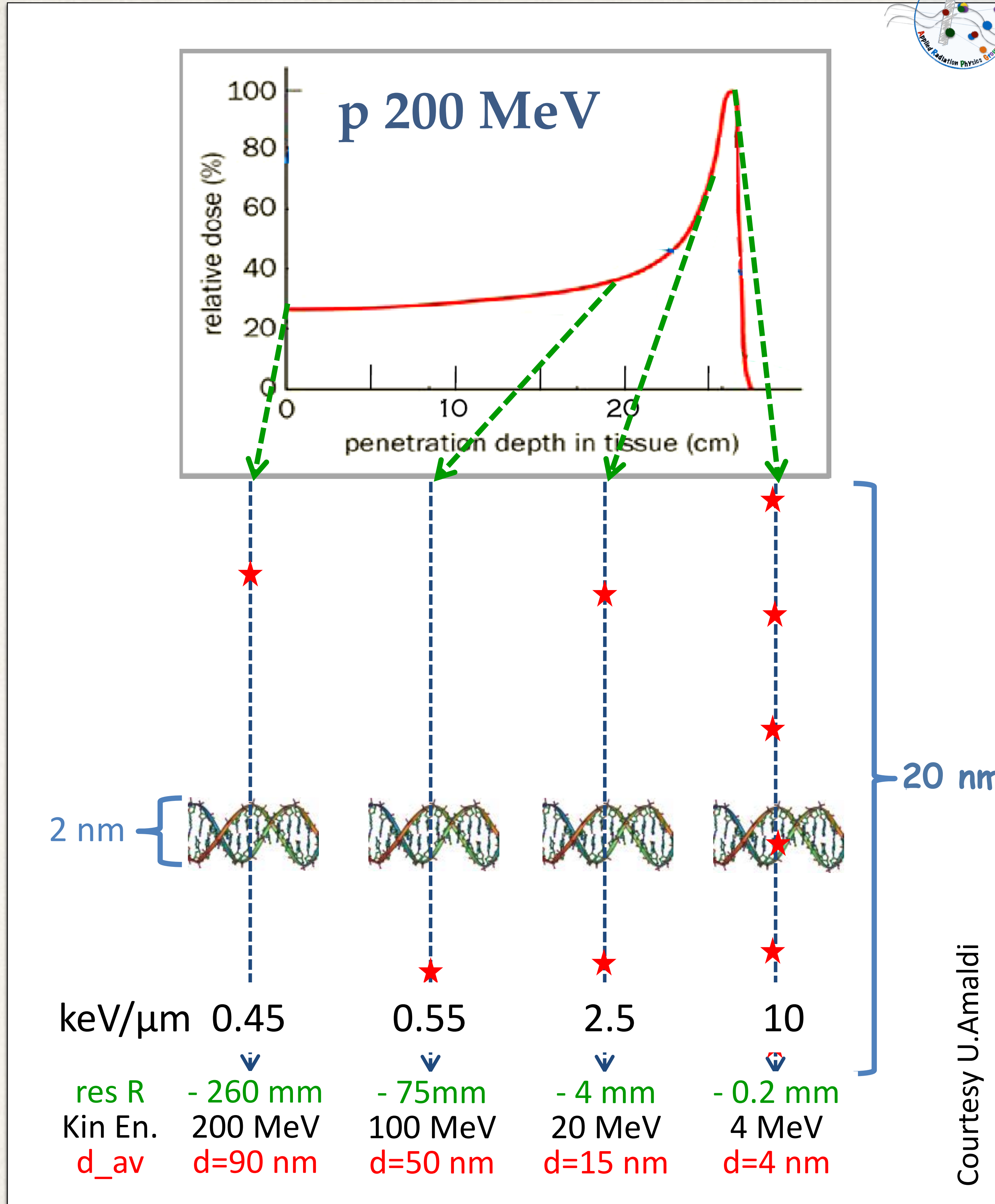
Cameras for optic system



PT: LET



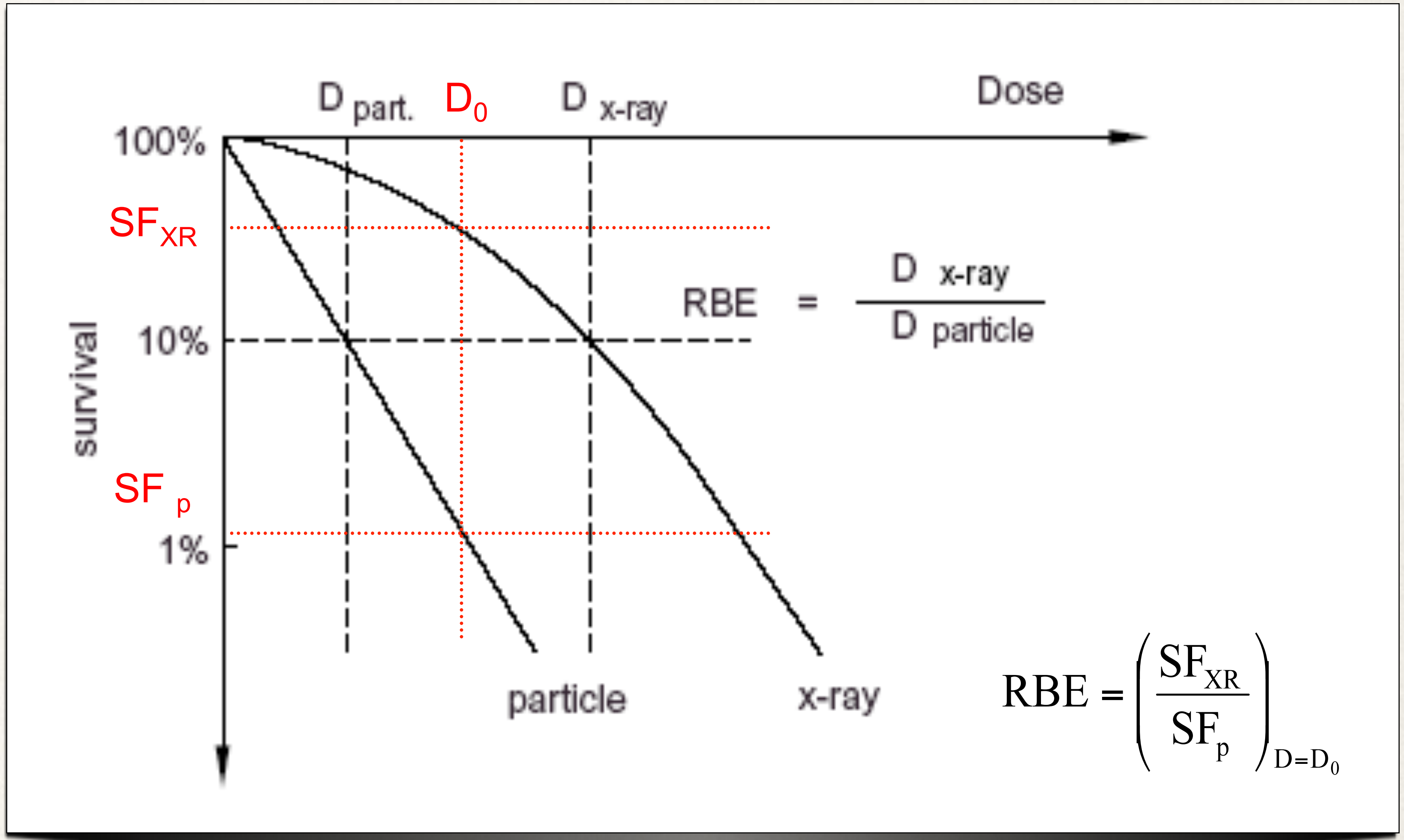
100
80
60
40
20
0
relative dose (%)
¹²C 400 MeV
0
10
20
penetration depth in tissue (cm)
SSB
DSB
keV/µm
10
14
20
140
- 260 mm
4800 MeV
d=4 nm
- 100 mm
2800 MeV
d=3 nm
- 42 mm
1800 MeV
d= 2 nm
- 1 mm
200 MeV
d=0.3 nm



100
80
60
40
20
0
relative dose (%)
p 200 MeV
0
10
20
penetration depth in tissue (cm)
2 nm
20 nm
keV/µm
0.45
0.55
2.5
10
res R
Kin En.
d_av
- 260 mm
200 MeV
d=90 nm
- 75mm
100 MeV
d=50 nm
- 4 mm
20 MeV
d=15 nm
- 0.2 mm
4 MeV
d=4 nm
Courtesy U.Amaldi

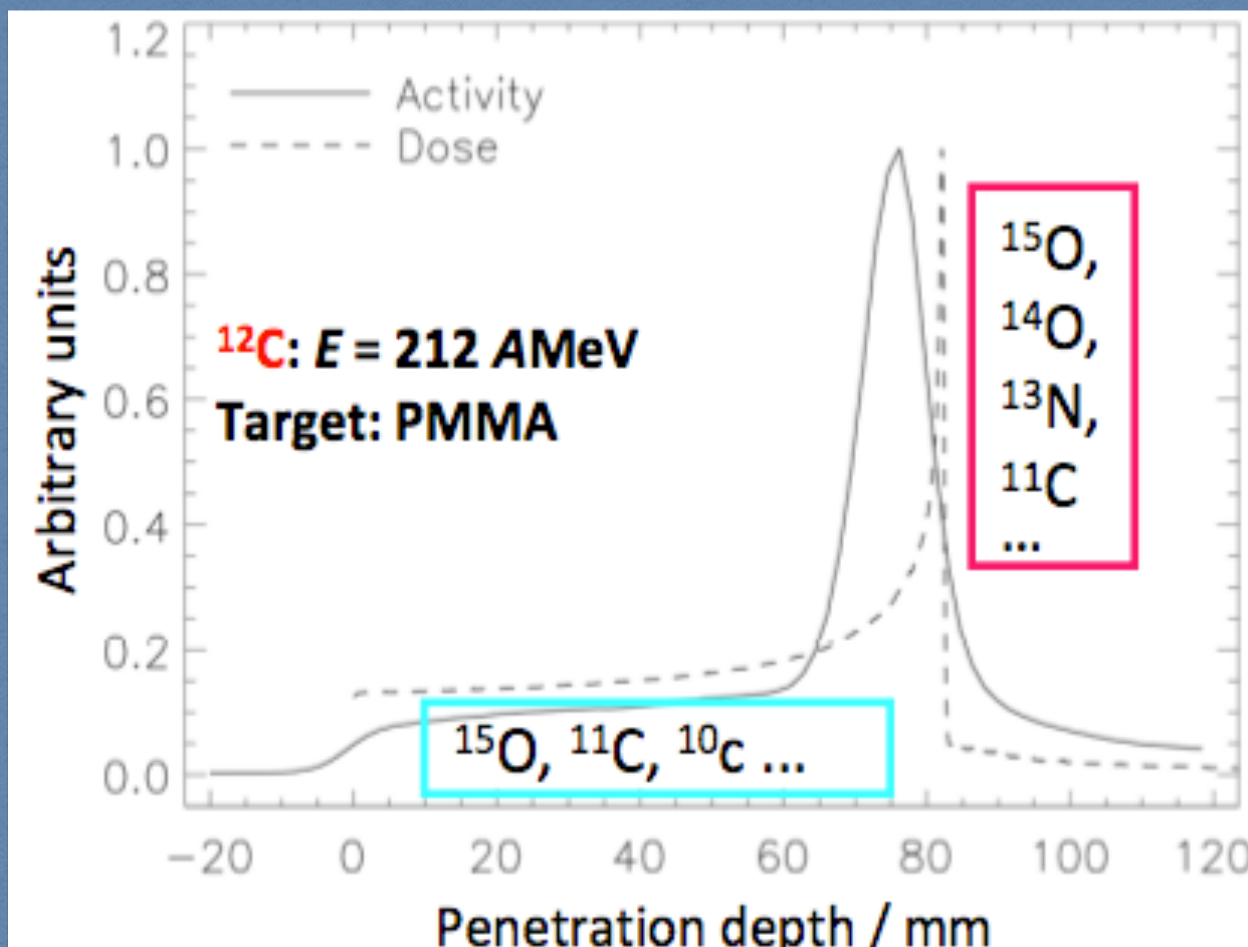
PT: RBE

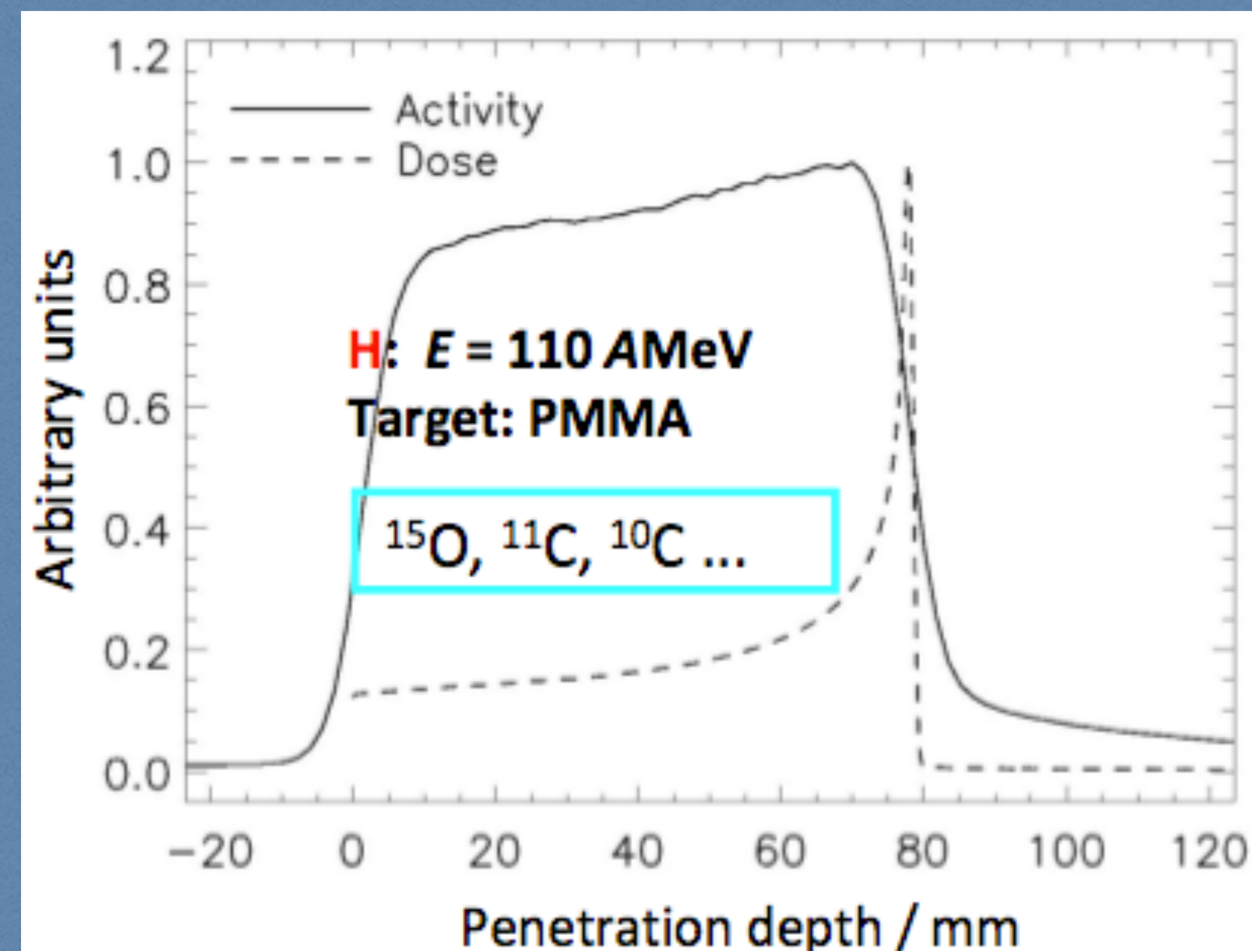
The cell survival probability as a function of realized dose increases for ion beams because of their hight RBE



Relative Biological Effectiveness

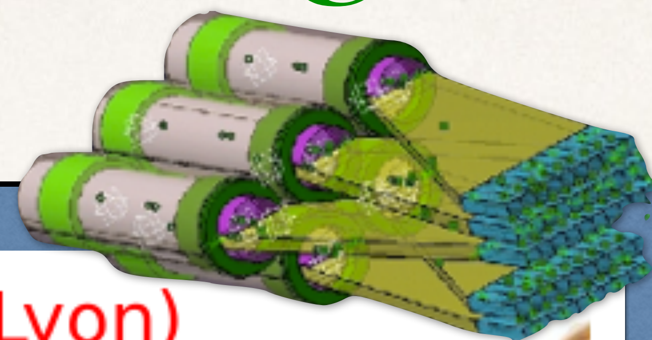
Monitoring: β^+ Activity

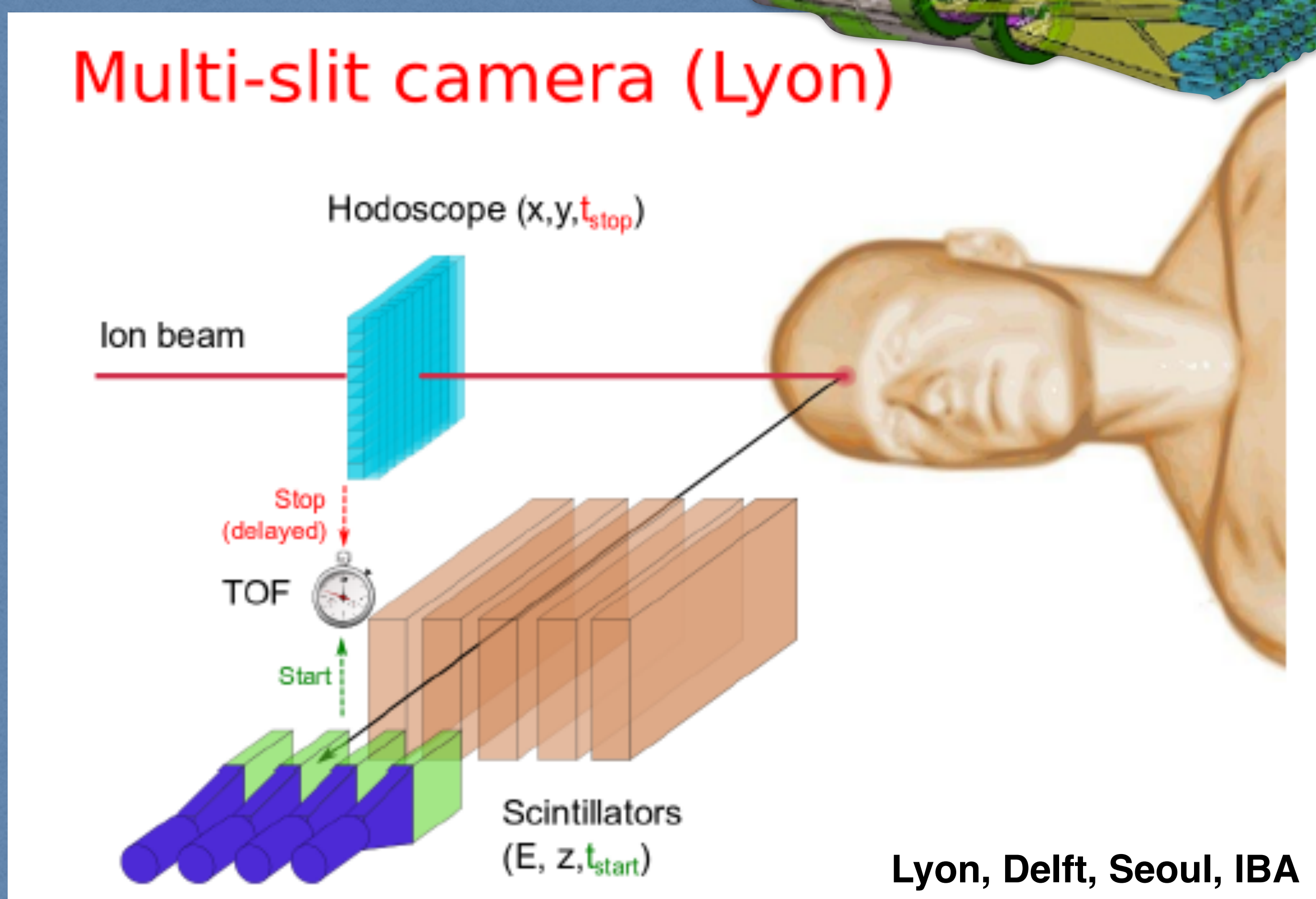




The β^+ activity emission shape is correlated with the dose distribution (ant to the Bragg Peak position). The β^+ emits a positron that produce two (back-to-back) 511 keV photons during its annihilations.

Monitoring: Prompt γ

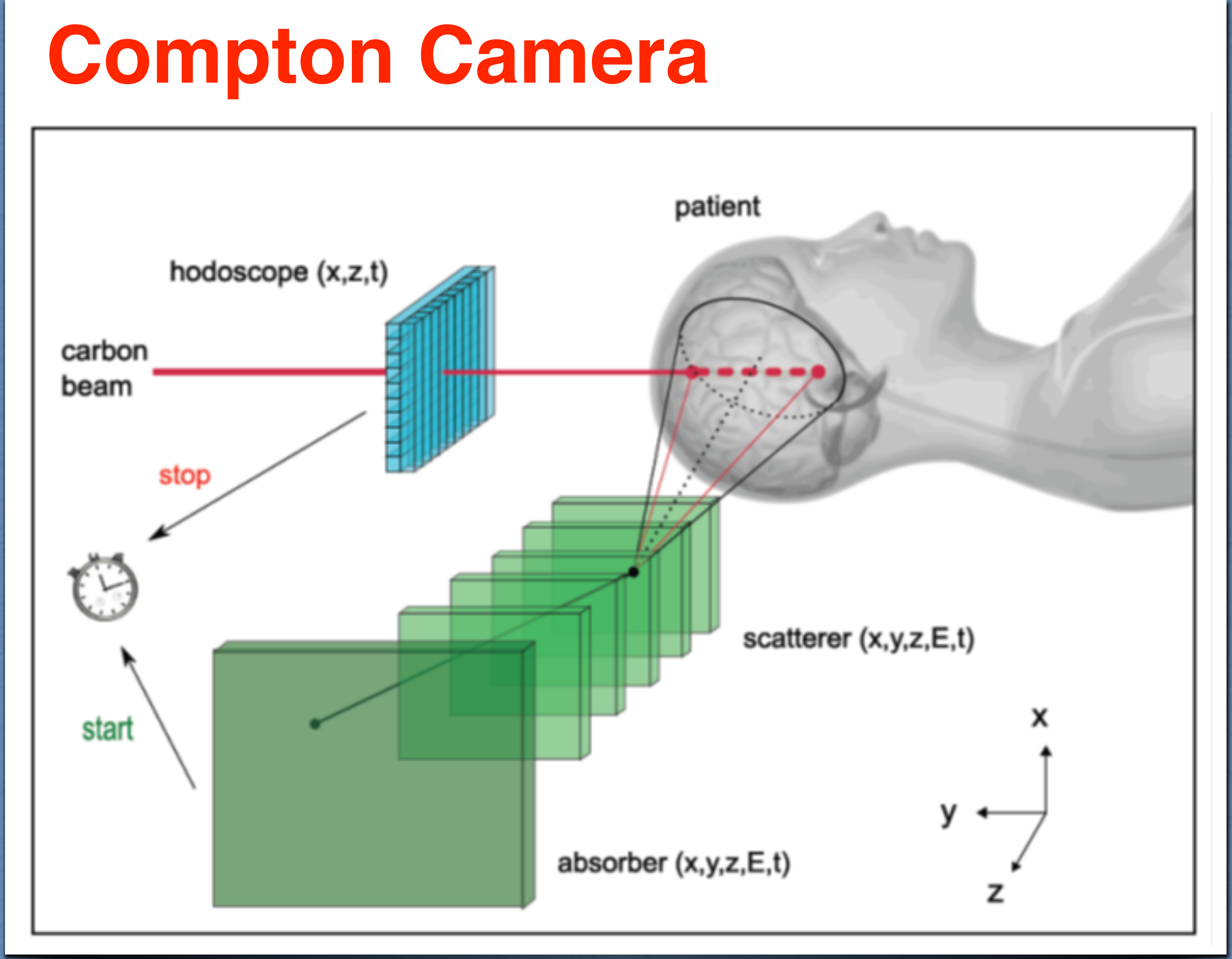




Courtesy of D.Dauvergne PET symposium 2014

Millimetric range-control at the pencil-beam scale for protons

Monitoring: Prompt γ



- No collimation: potentially higher efficiency
- Potentially better spatial resolution (< 1cm PSF)
- If beam position known simplified reconstruction
- 3D-potential imaging (several cameras)

Courtesy of D.Dauvergne PET symposium 2014

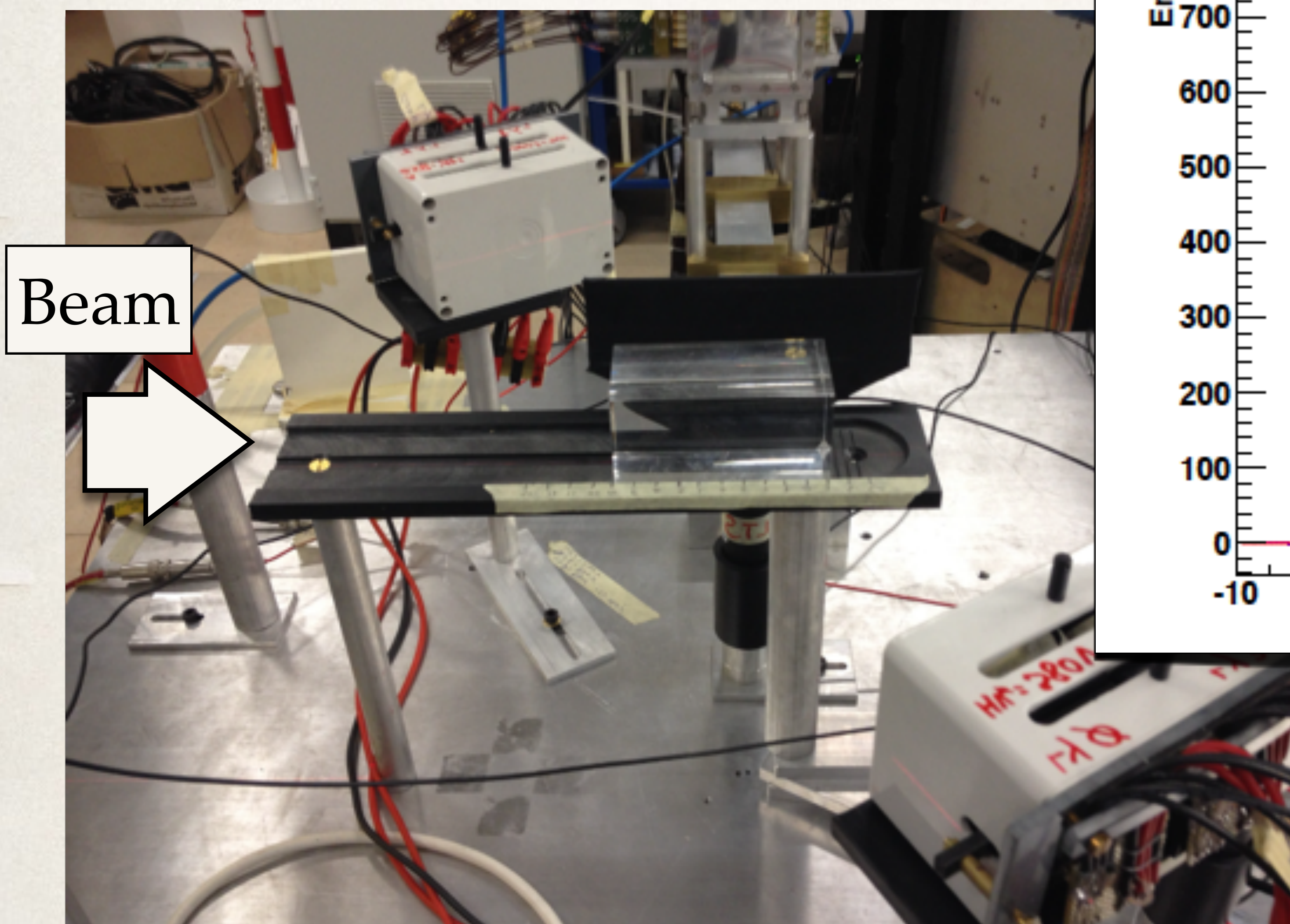
Main issue: necessity to work at reduced intensity

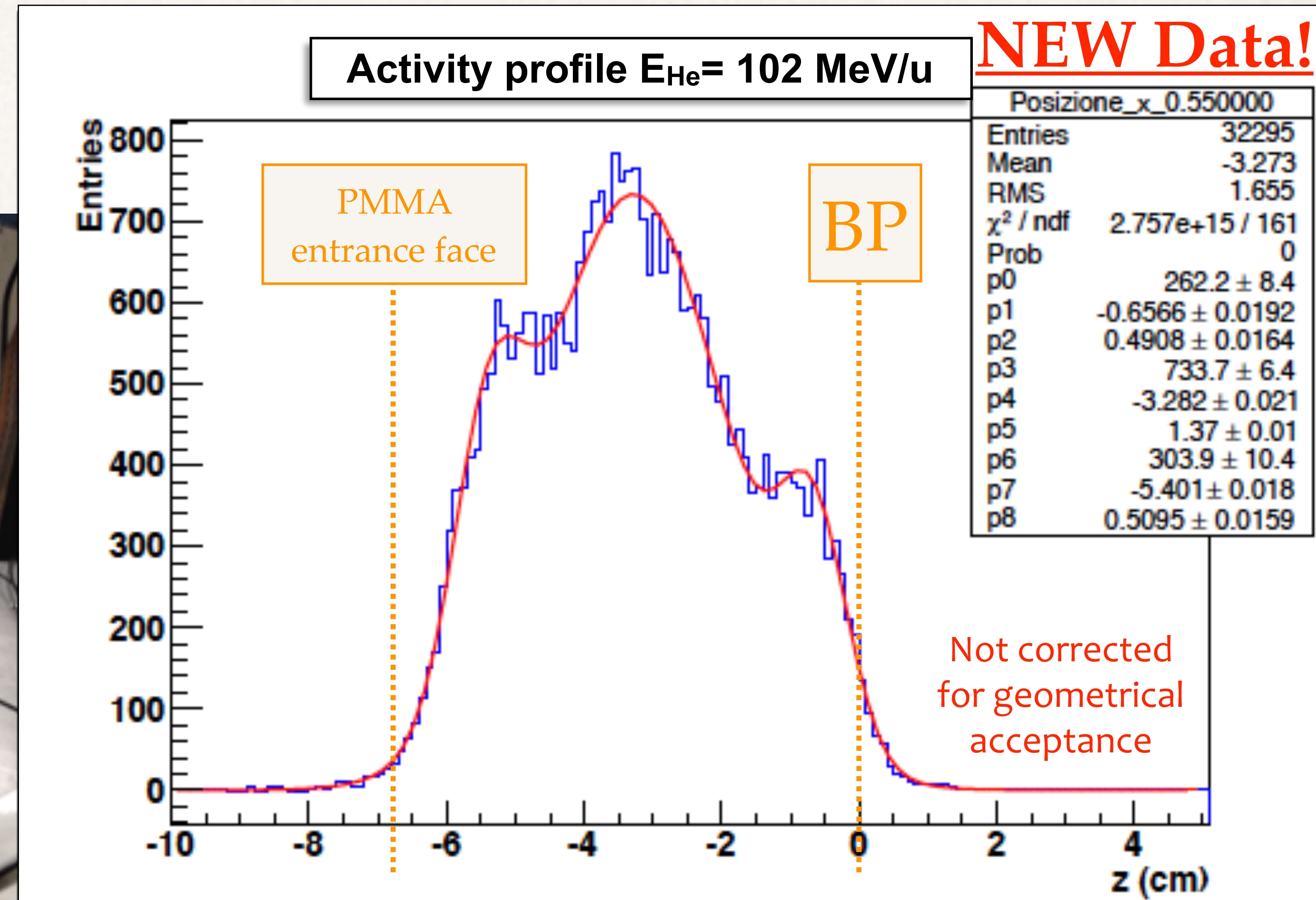
Secondary particles:

PET PHOTONS

We measure the PET photons flux and profile for different energies:

- 80 MeV/u ^{12}C beam
- 102,125,144 MeV/u ^{4}He beam





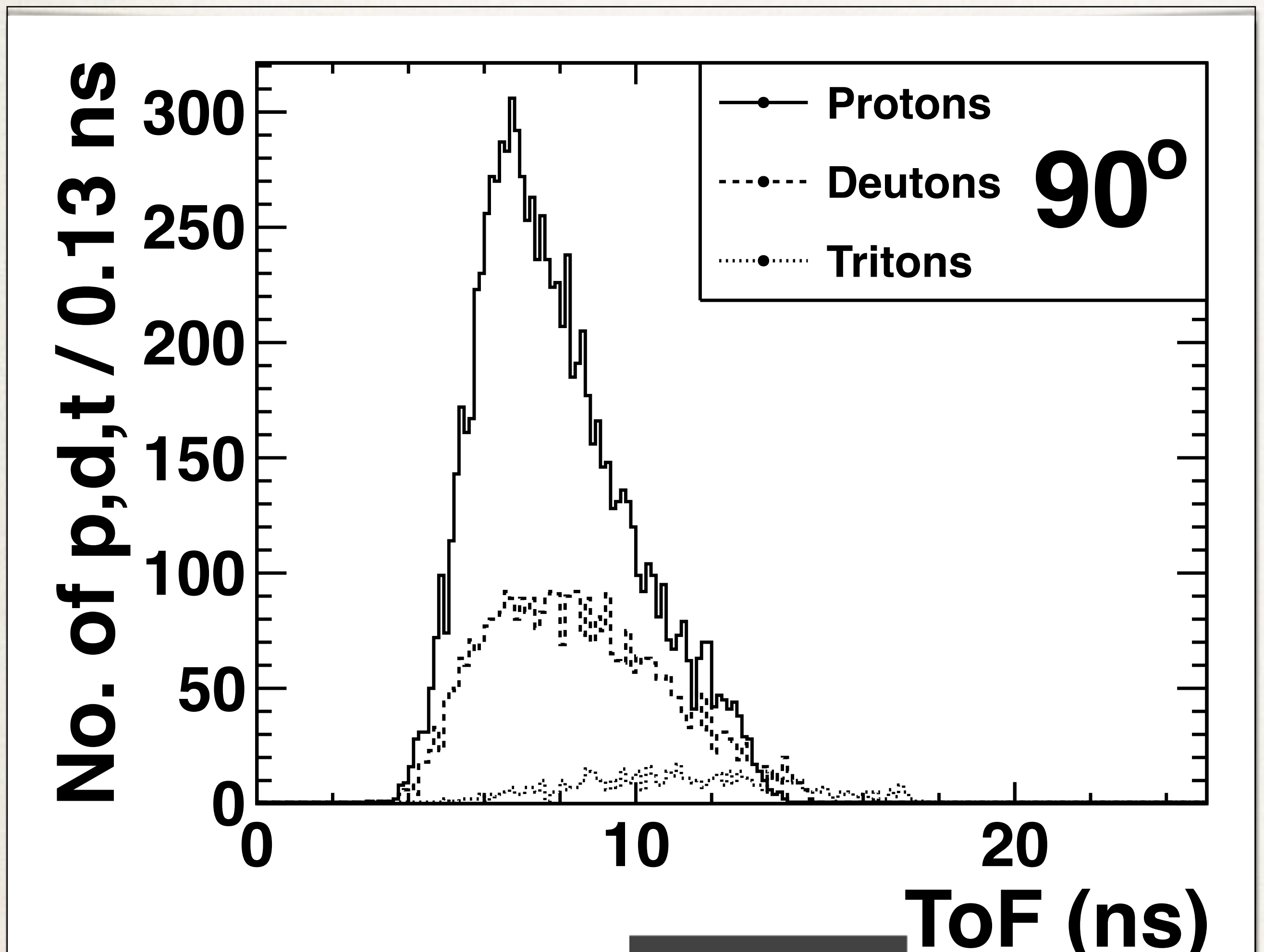
- C.Agodi, *et al.* *"Study of the time and space distribution of β+ emitters from 80 MeV/u carbon ion beam irradiation on PMMA"* **NIM B 58752 (2012)**
- Under construction.. *"Study of the time and space distribution of β+ emitters from … helium ion beam irradiation on PMMA"*

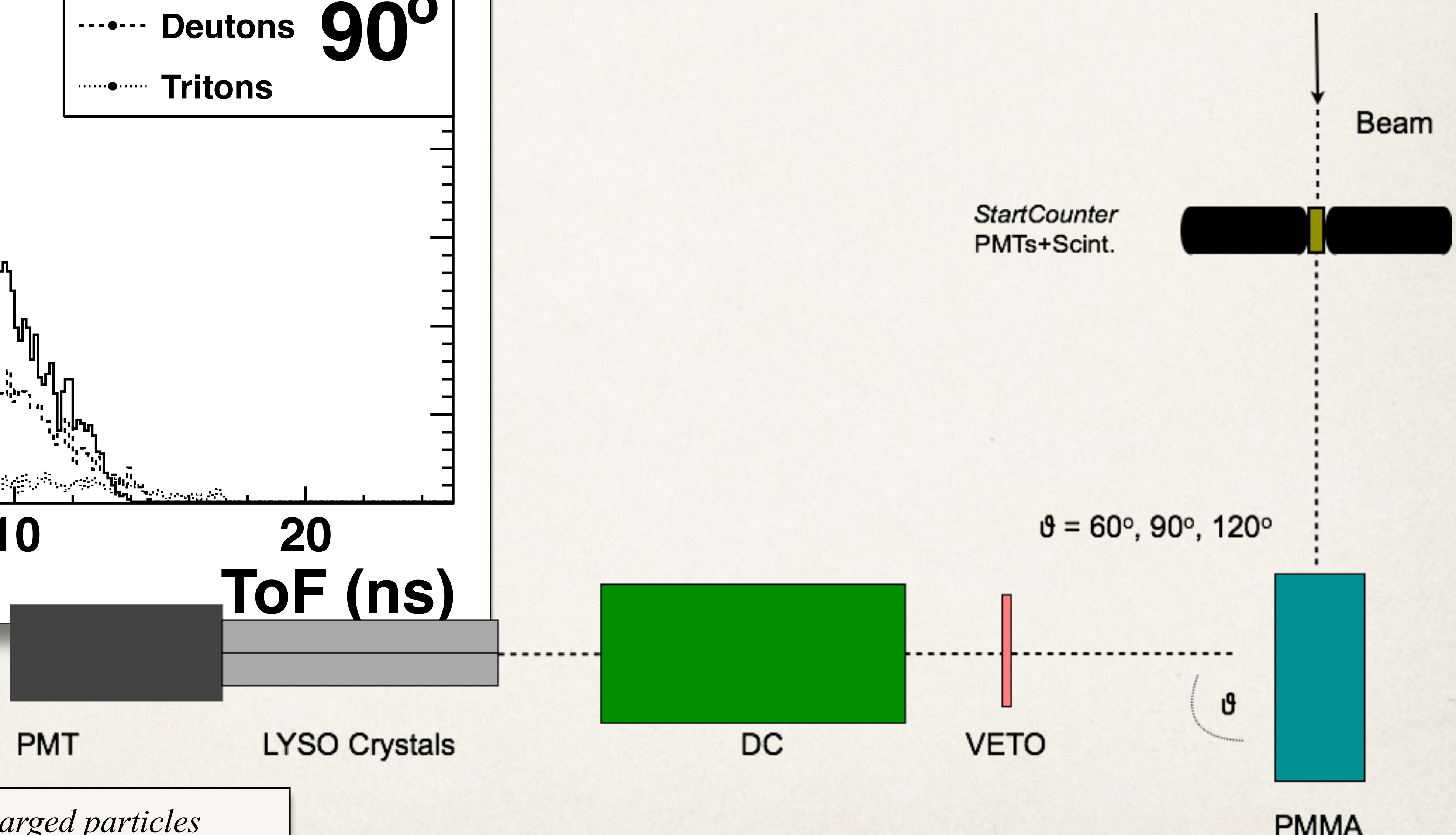
Secondary particles: measurements

Carbon ion on PMMA target:

CHARGED PARTICLES

We measure the charged particles flux for different energies: 80, 220, 50-300 MeV/u

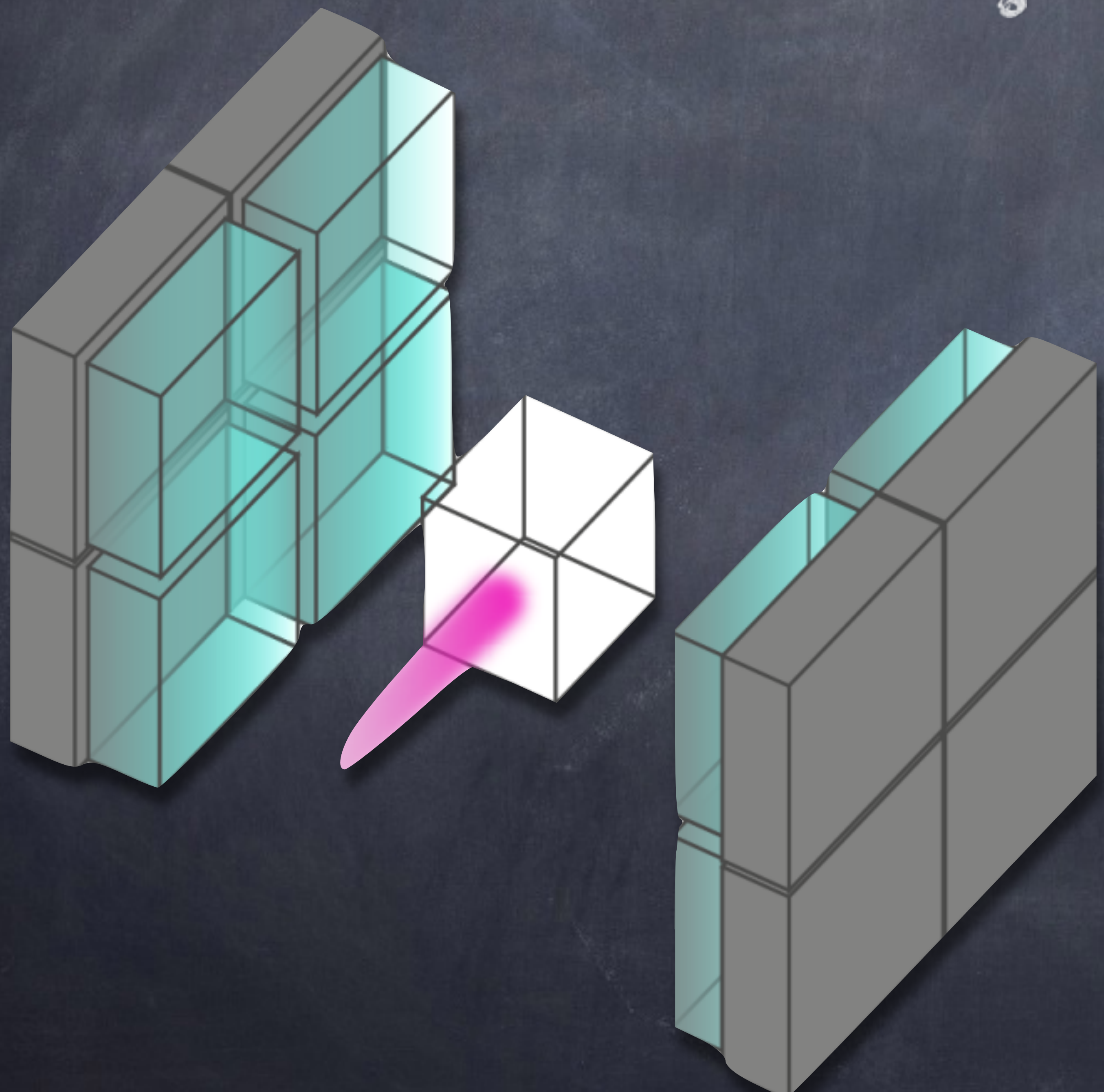




L.Piersanti et al. *"Measurement of charged particles yields from PMMA irradiated by 220 MeV/u ^{12}C beam"*
PMB 59 (2014) 1857-1872

PET HEADS BACKGROUND

DOPET: an in-beam PET monitor for hadrontherapy

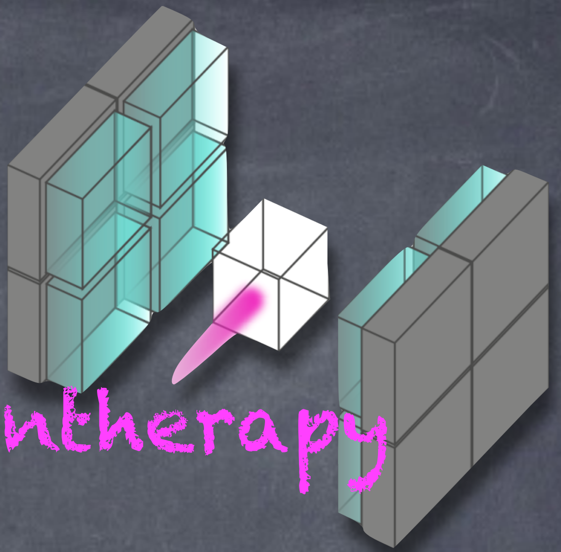


- Two PET heads, each made of 2x2 squared position-sensitive photomultipliers (Hamamatsu H8500) coupled to LYSO:Ce scintillating crystal arrays (2x2x18 mm3 pixel size).

NEW

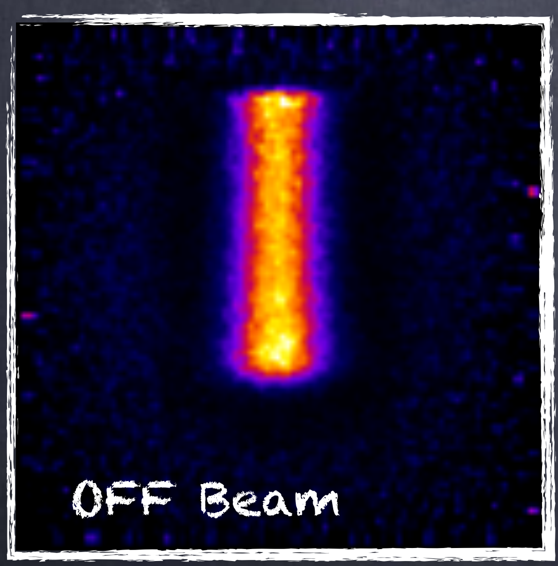
CNAO: 95 MeV proton beam on PMMA in-beam and off-beam acquisition

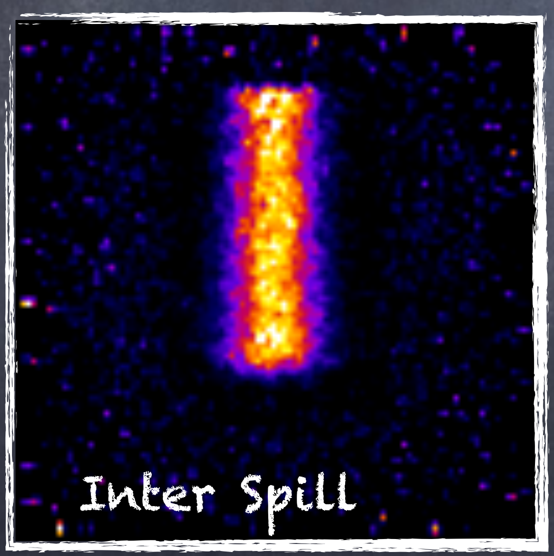
PET HEADS BACKGROUND

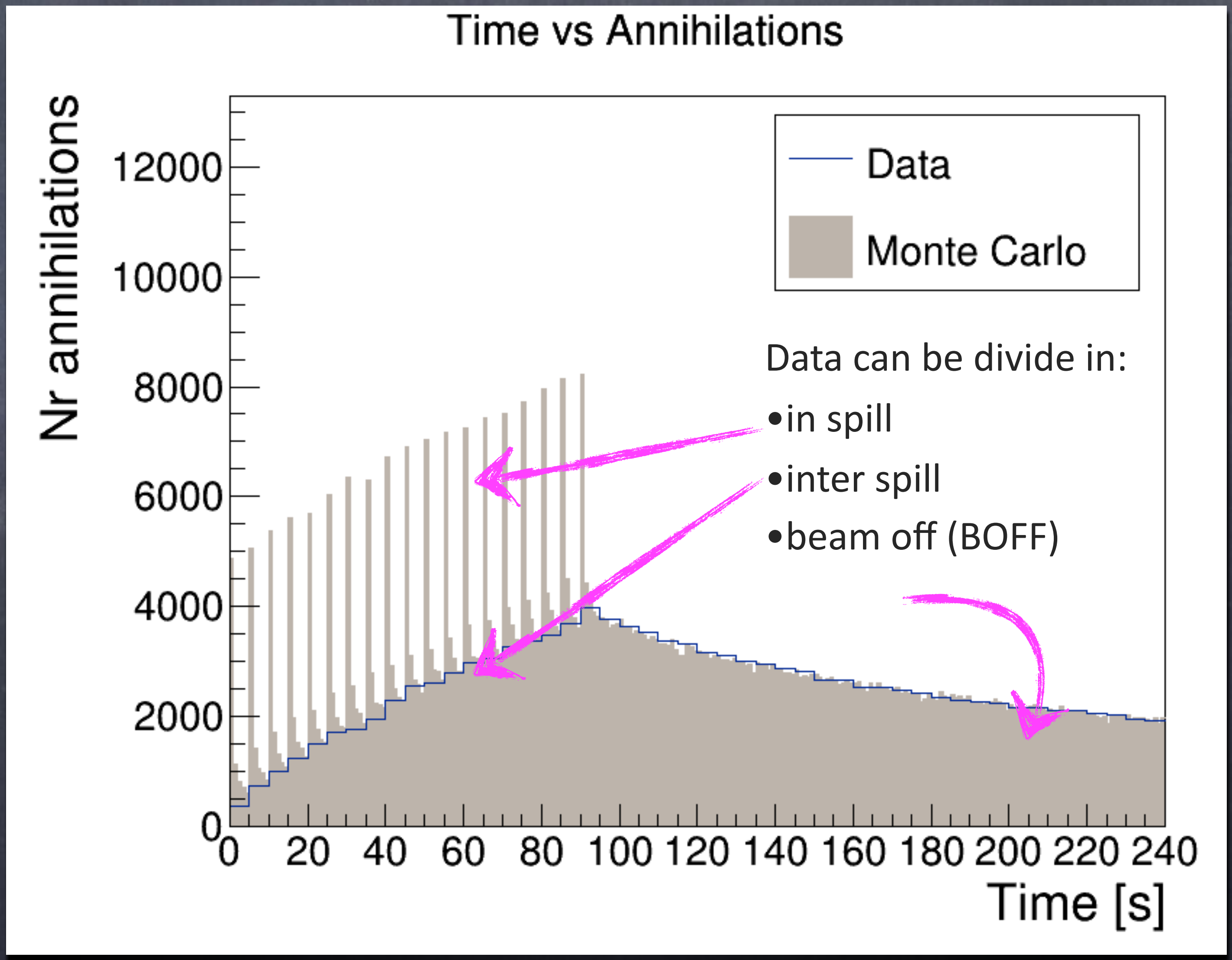


DOPET: an in-beam PET monitor for hadrontherapy

The annihilation map is reconstructed with Maximum Likelihood Estimation Maximization (MLEM) Iterative algorithm







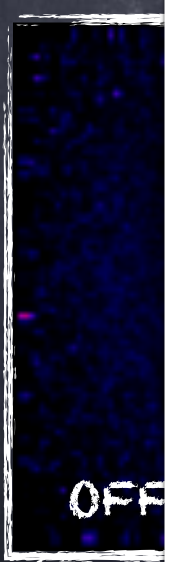
- Beam OFF ~ 550 sec
- Inter-spill ~100 sec
- Beam ON ~120 sec
- In-spill ~20 sec

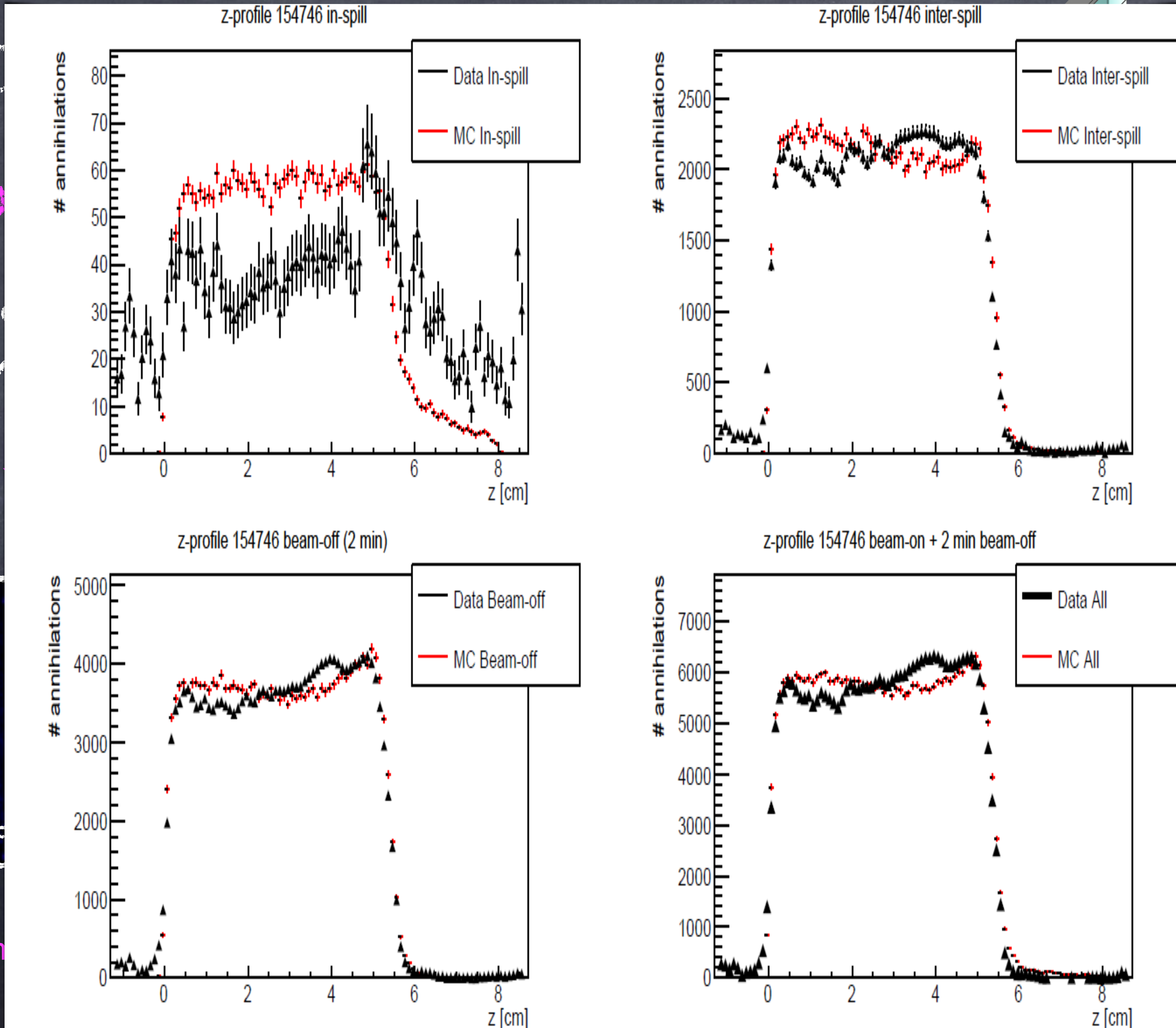
PE

DO

The … hood

Estim





- Bean