Università degli Studi di Pavia

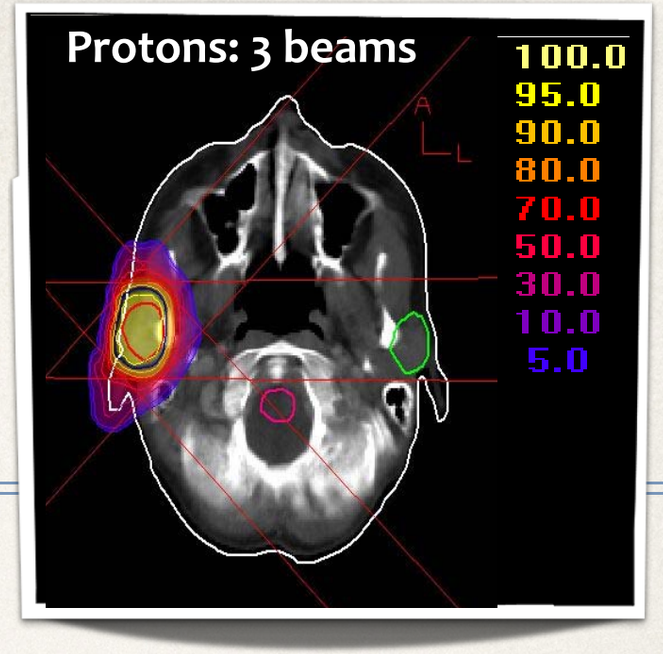
Physics Colloquia

Ilaria Mattei

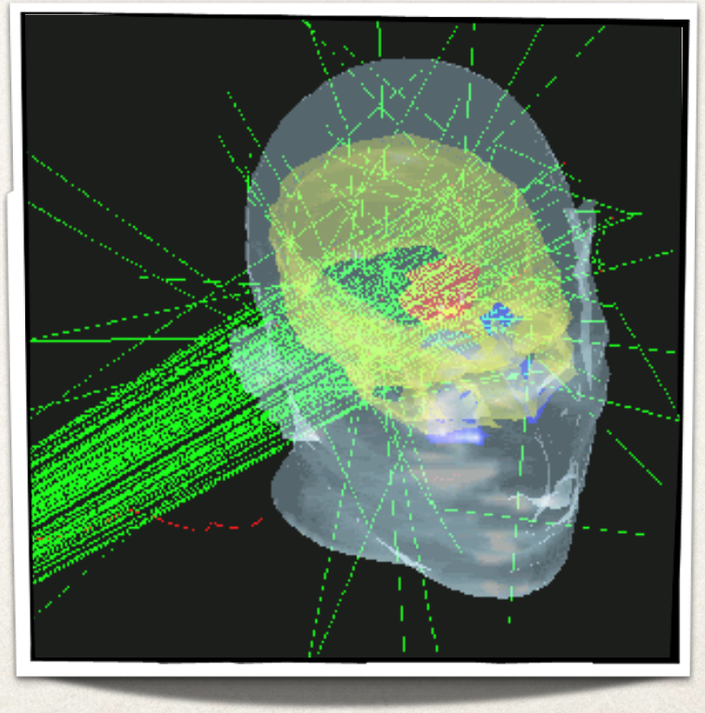
Recent development on range monitoring in Particle Therapy

22-11-2021

Outline



- Introduction to **Particle Therapy**
- **Range Monitoring:**
  - The Dose Profiler detector
  - The PAPRICA project
- **MonteCarlo nuclear DataBase**: the FOOT experiment
- **Upcoming Activities**

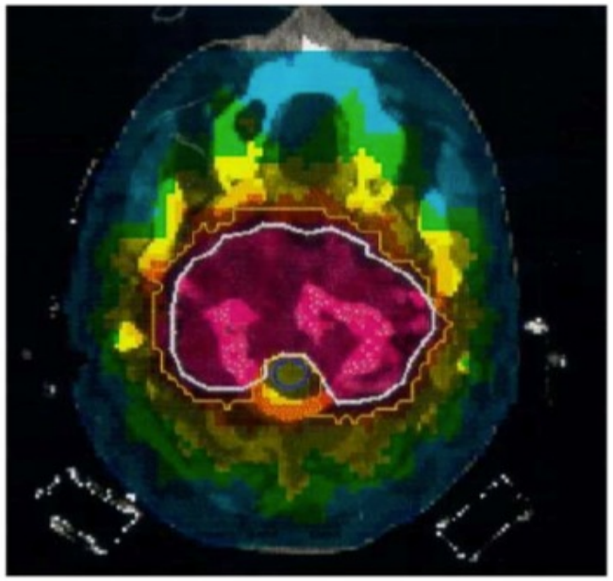


Introduction to Particle Therapy

Tumor Treatment with Radiotherapy

- Mainly **photons** and electrons
- Useful for ~65% of all cancer patients (**localized tumors**), together with surgery
- **Sophisticated imaging** (CT), superimposition of **several beams**, computed **optimization** and **multi-leaves collimators** (**IMRT**)
- **Not** so **expensive** and reliable

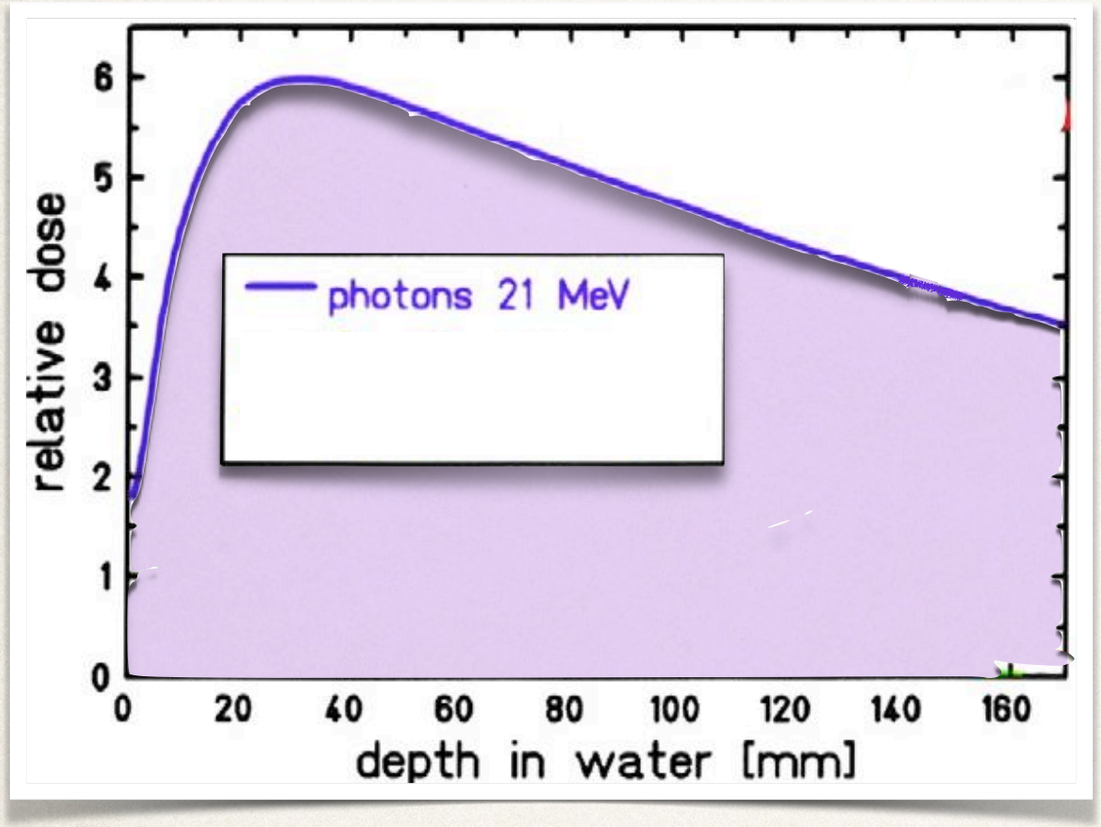
DOSE RELEASED more CONFORMAL to the TUMOR volume



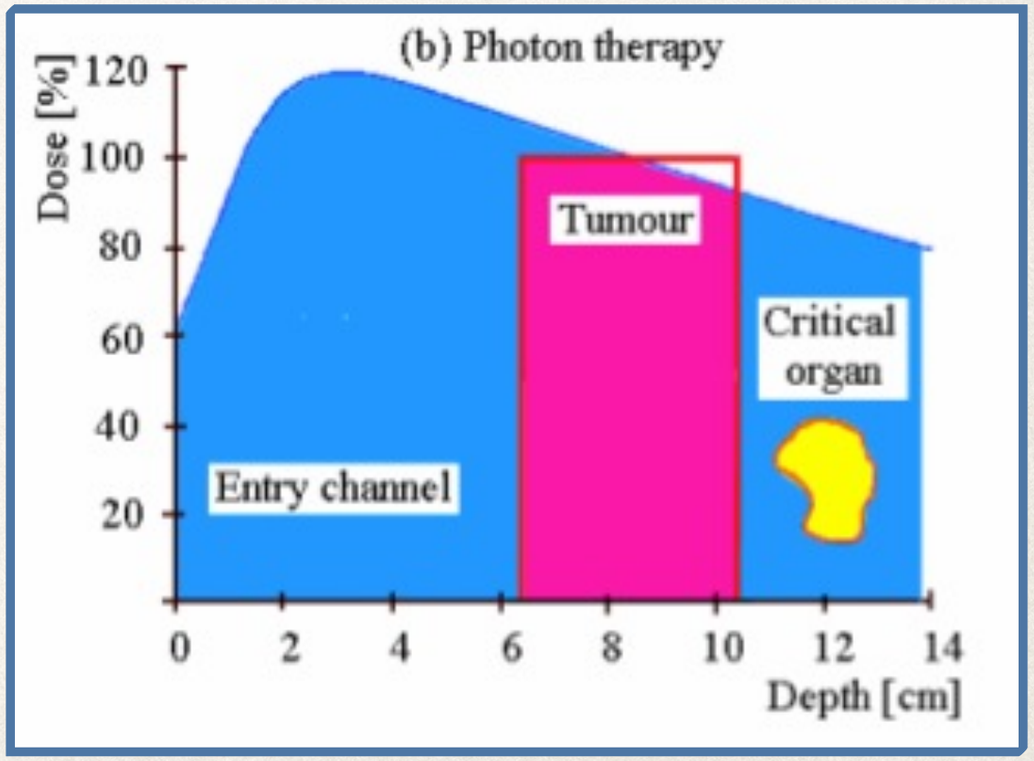
…BUT…

Radiotherapy: Dose Deposition

...BUT the **energy release is not sparing healthy tissues**.



$$Dose = \frac{dE_{abs}}{dm}[Gray]$$

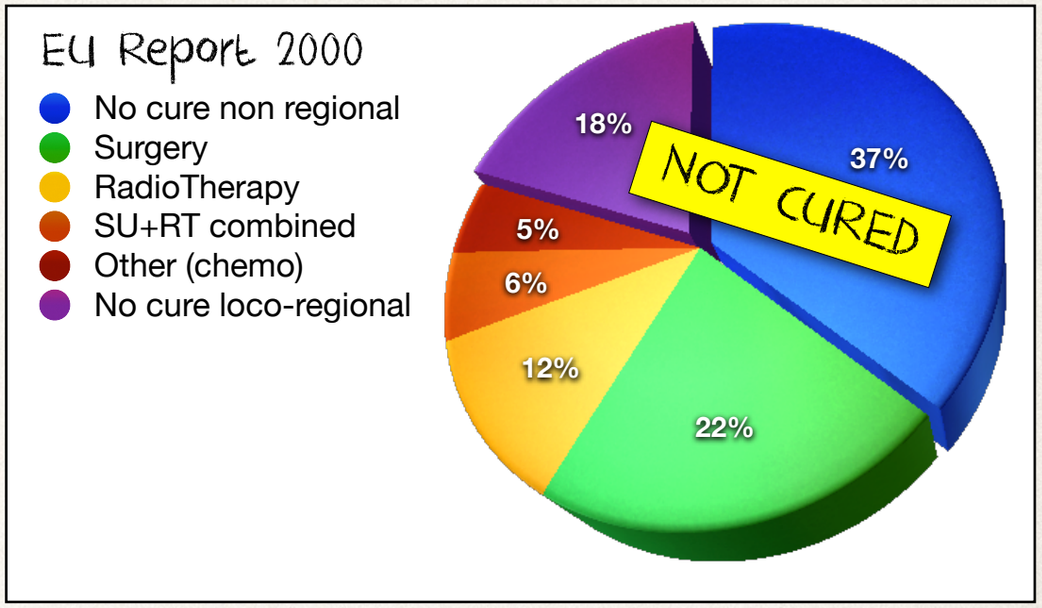


The **RT** dose distribution implies a large and unwanted dose delivered to healthy tissues.

Tumor treatment in EU

Many tumors are not treated…

- **Anatomy** does not permit surgery
- **Radioresistant** tumors
- Tumor position close to Organs At Risk (**OAR**)



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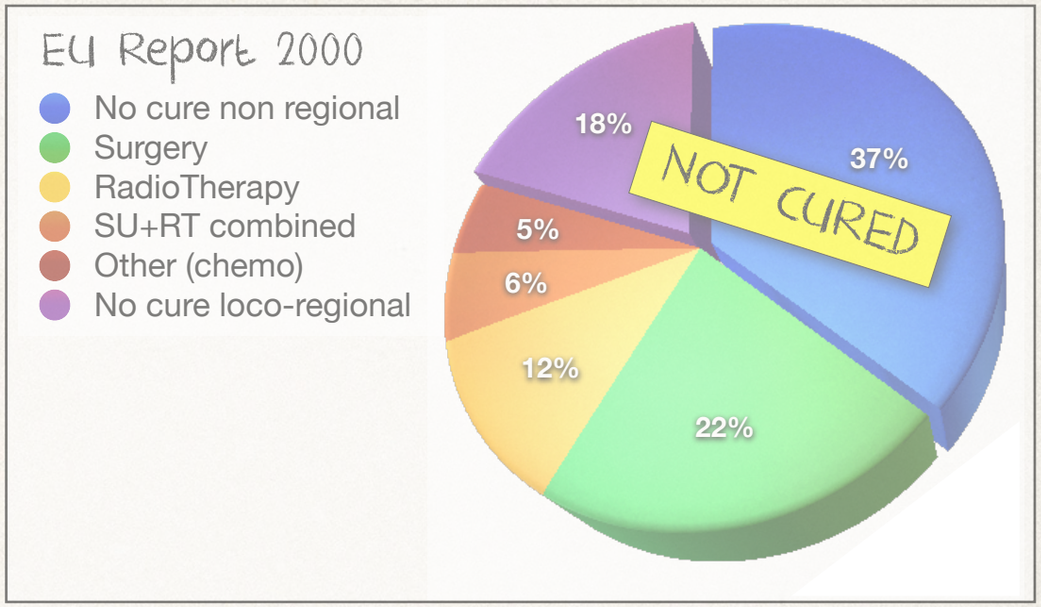
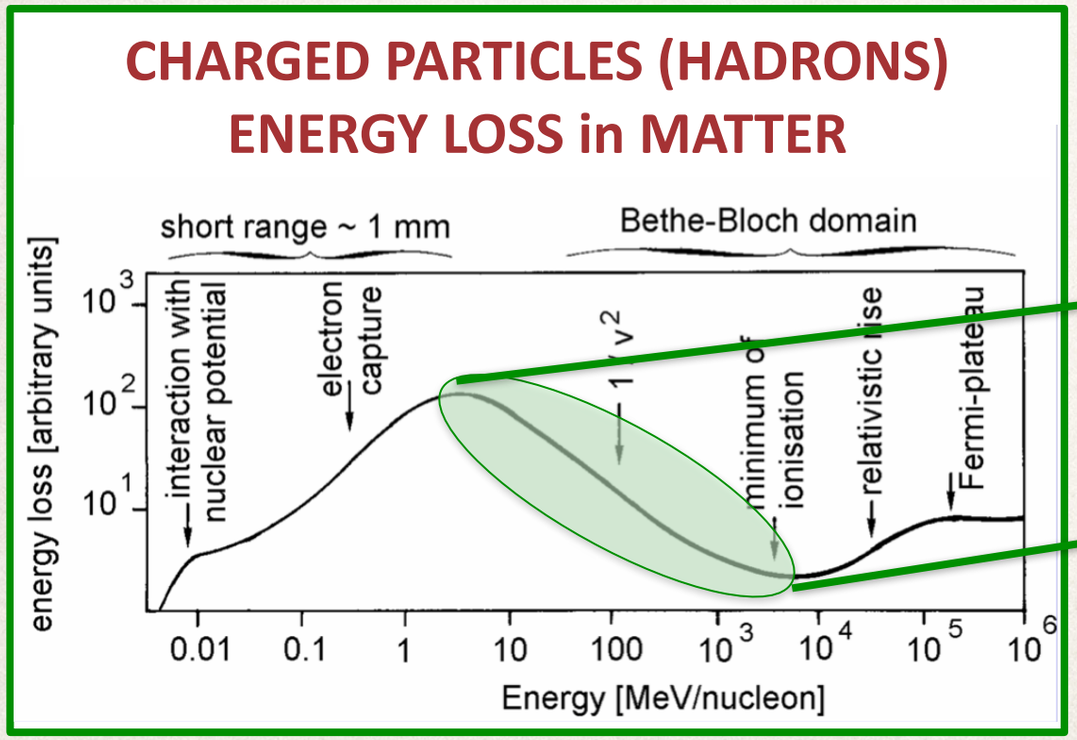
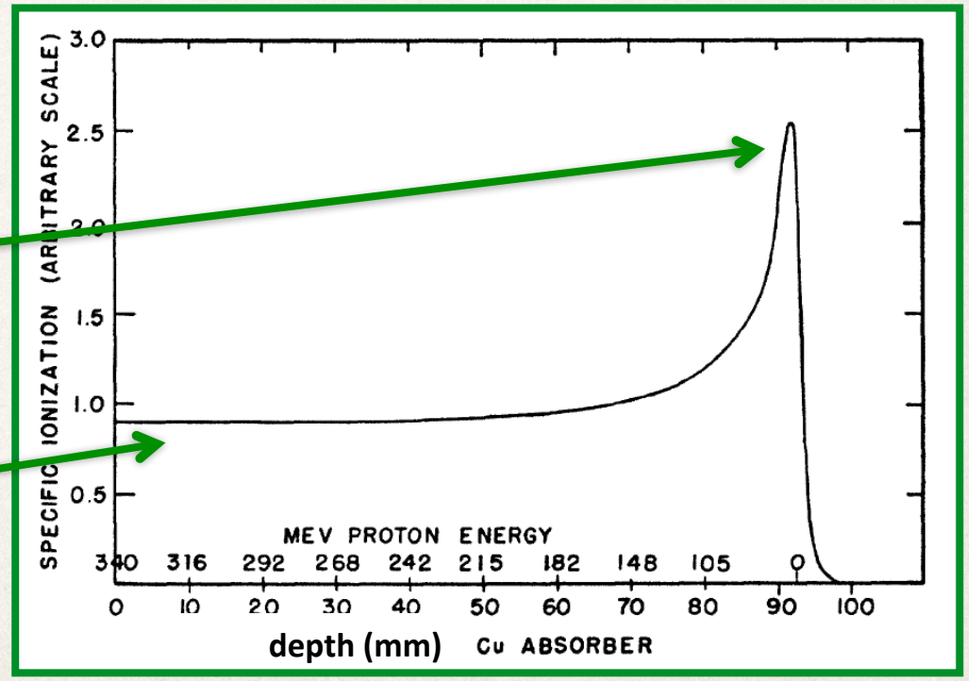


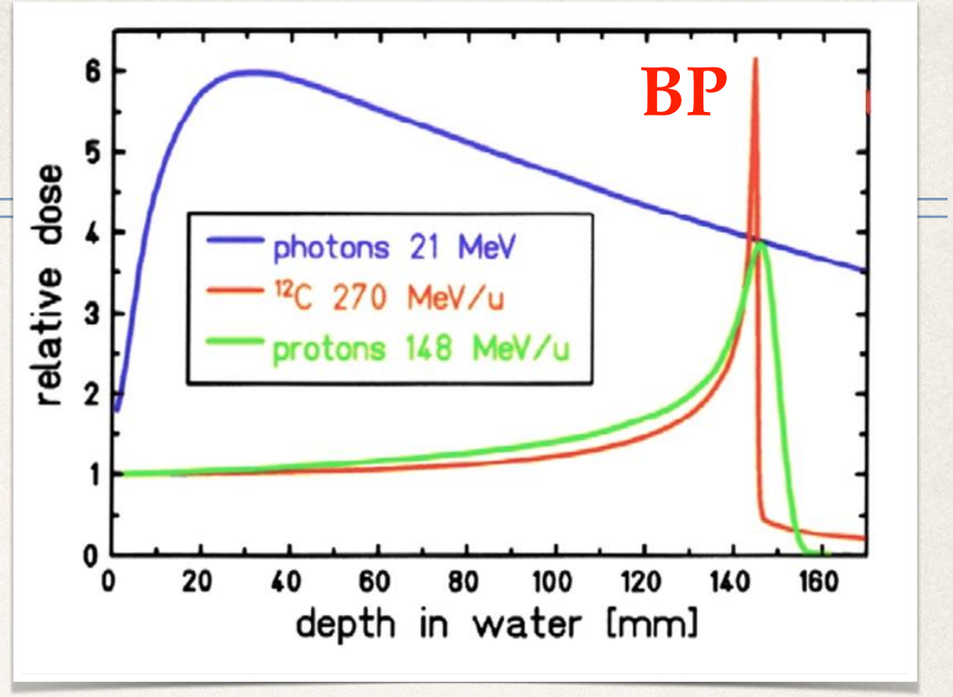
…BUT PHYSICS CAN HELP (Wilson 1964)

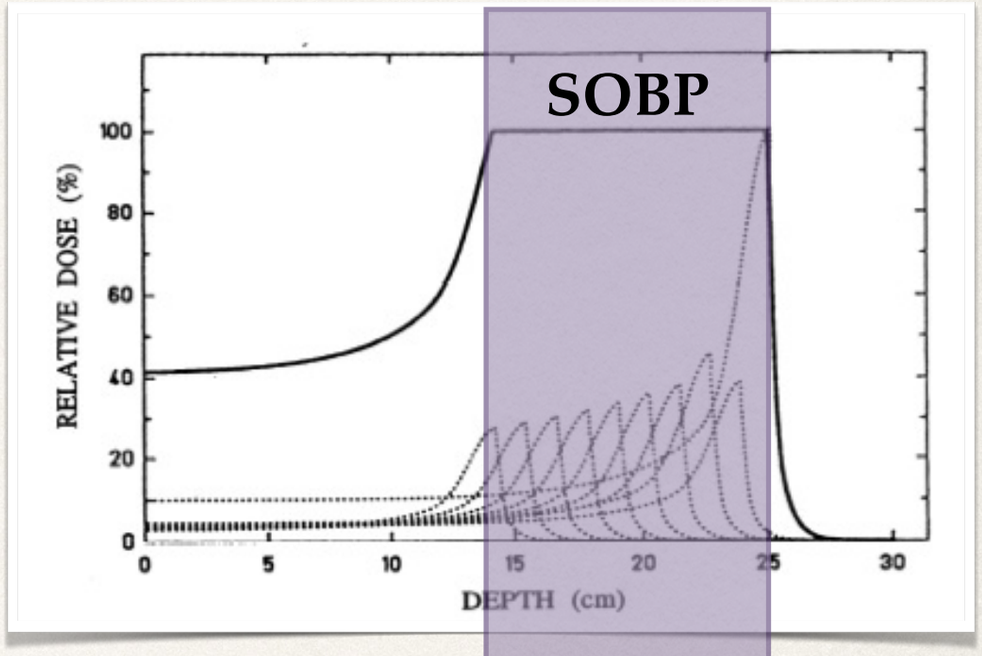




Particle Therapy

- **Hadron beams** (**p**, **^{12}C**, ^{16}O, ^{4}He..)
- Highest dose release (**Bragg peak**) at the end of the particle range, sparing normal tissues
- **Particle range** function of the **beam energy** and **density of crossed material**
- Dose decrease rapidly after the BP
- Several pencil beams can be combined in order to "shape" the maximum dose release region => **Spread Out Bragg Peak (SOBP)**

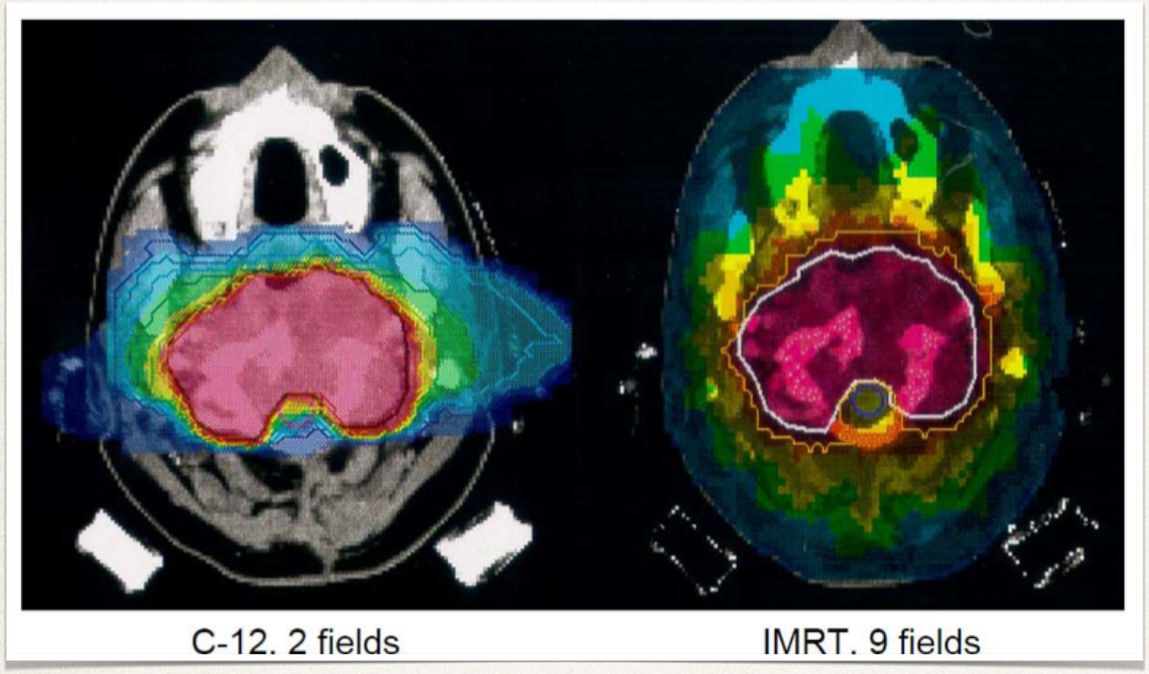




Localized Dose Distribution

Particle Therapy: Dose Deposition

^{12}C (PT) vs **IMRT**



The **dose deposition** can be **very conformal to the tumor volume** both for PT and RT, **but with PT healthy tissues and critical organs are better saved.**

Particle Therapy: Dose Deposition

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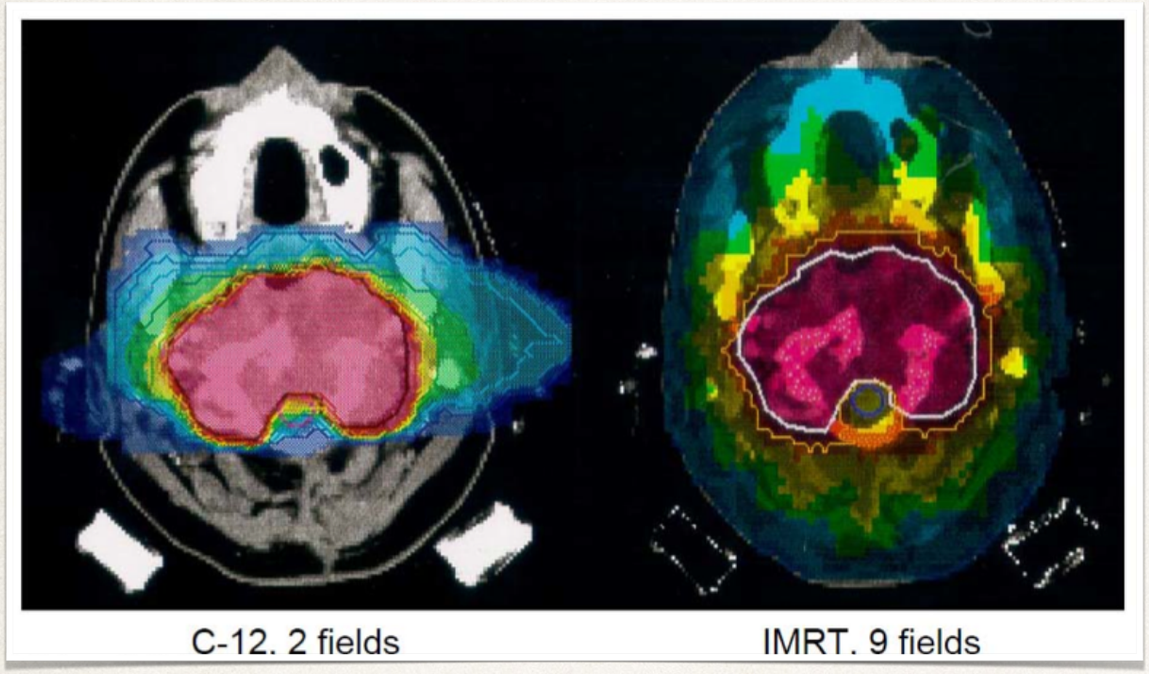

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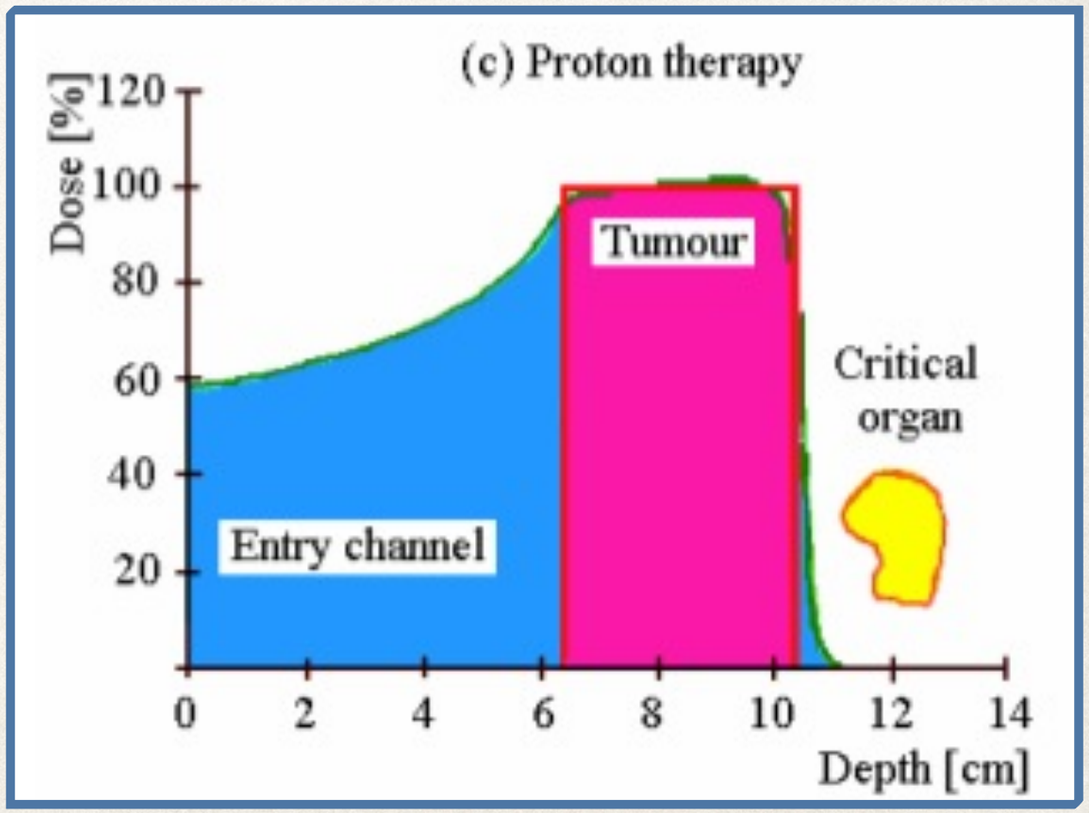
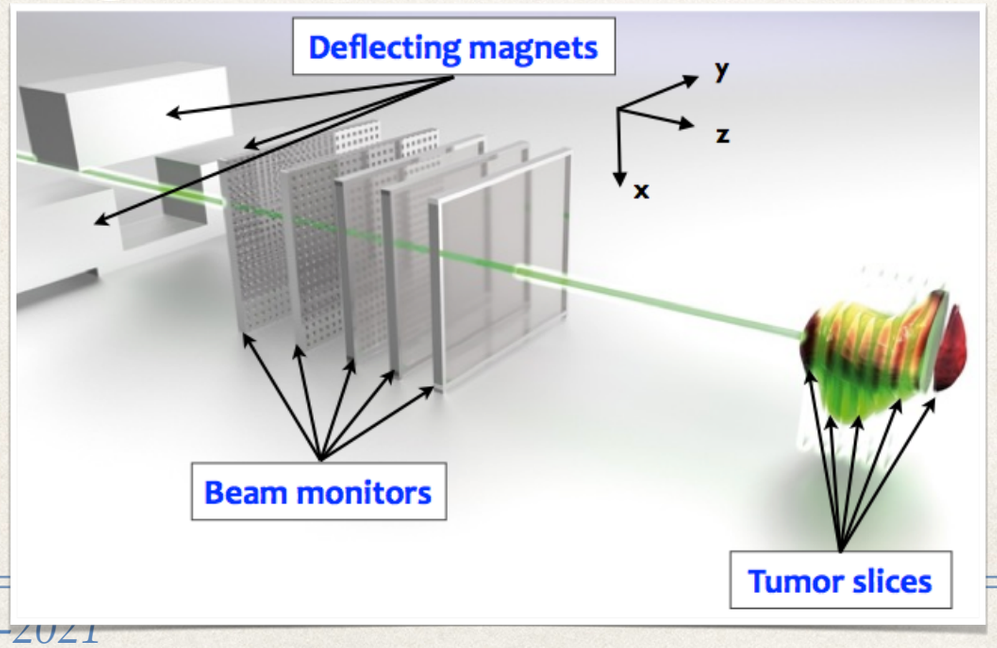
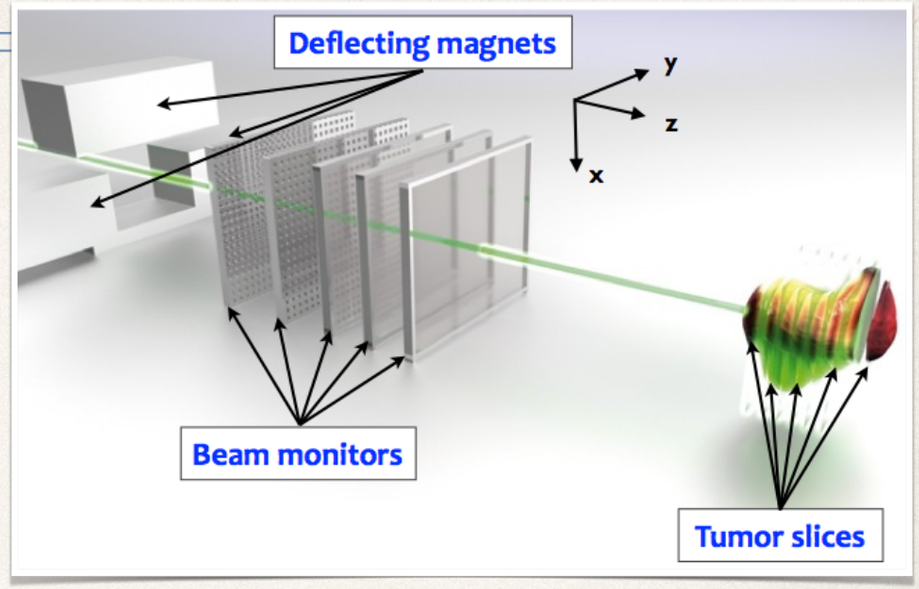


PT pencil beam scanning

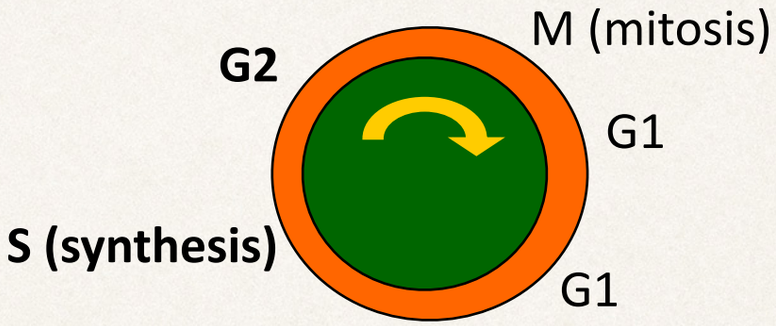


Particle Therapy: Treatment



- p: 50 - 250 MeV
- 12C: 80 - 400 MeV/u
- Total Dose: 20 - 70 Gy
- Treatment delivered in 2 Gy fractions

=> **4R**:
- Reoxygenation
- Redistribution
- Repopulation
- Repair

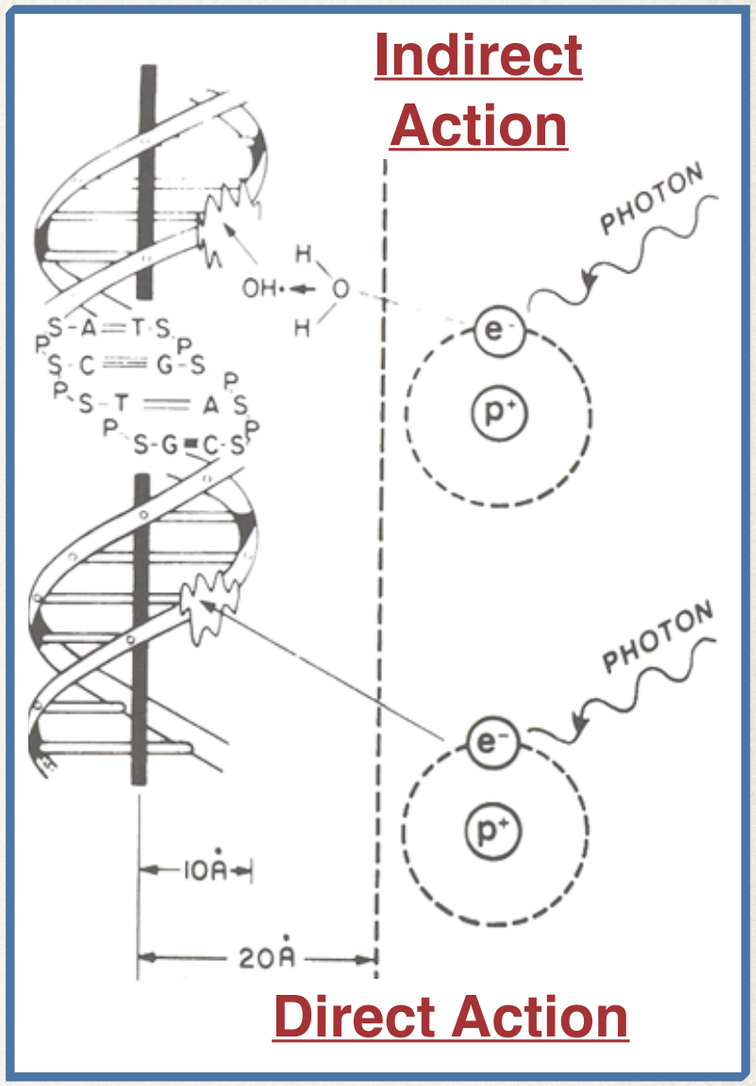


Radiations: Biological Damage

Directly related to the DNA damage:

- **Indirect Action:** by free radicals
- **Direct Action:** the radiation breaks directly the DNA helix (SSB, DSB)

Cells are able to repair DNA damages induced by radiations, EXCEPT for DSB.



The Linear Energy Transfer (LET) gives an estimation of the radiation biological damage

$$LET = \frac{\Delta E}{\Delta x} \; (keV/\mu m)$$

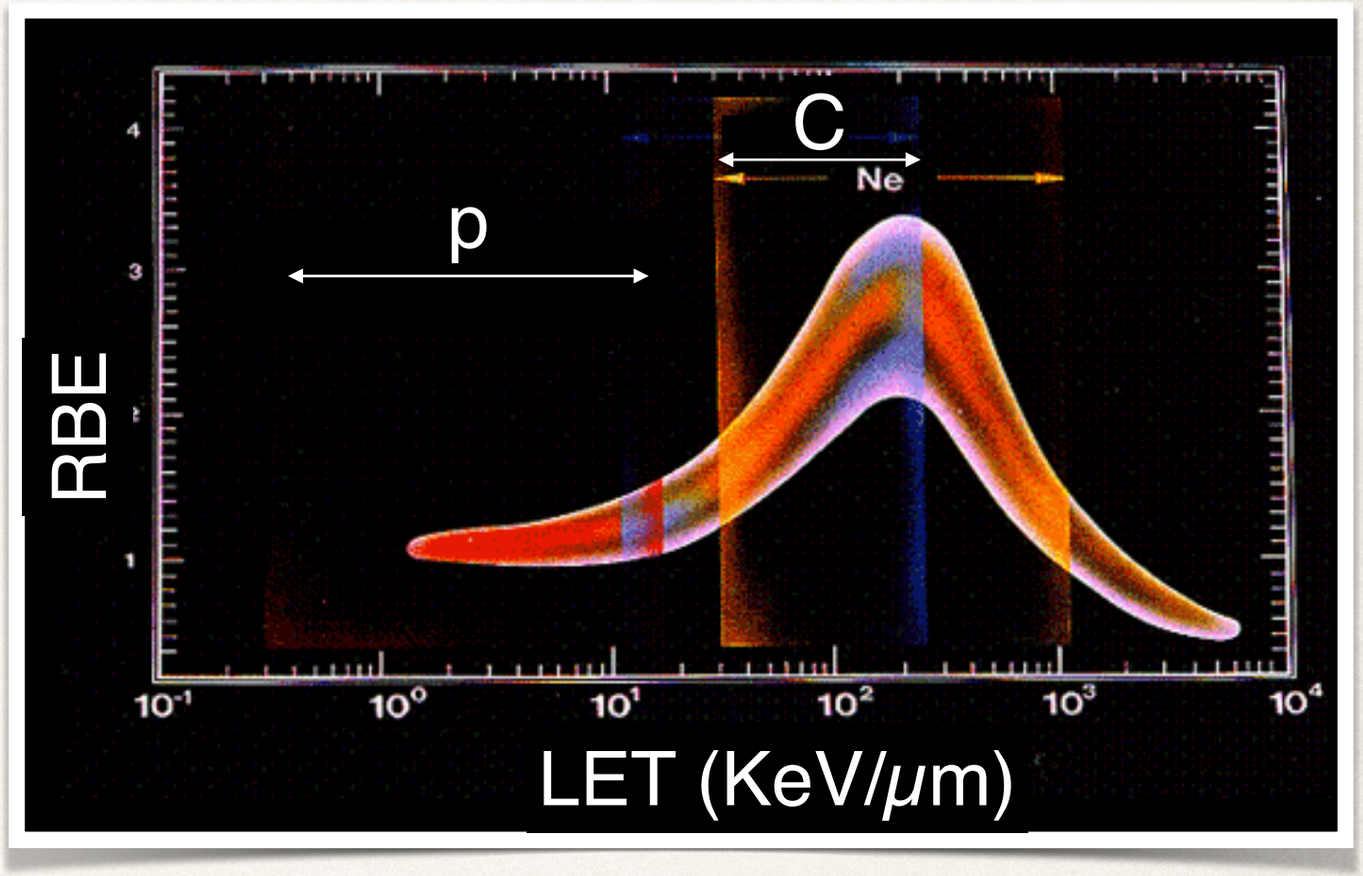
PT: Biological Damage

- **Relative Biological Effectiveness**

$$RBE = \frac{D_\gamma}{D_{ch}}|_{iso}$$

PT allows the use of higher LET particles with respect to photons (RT) inducing more direct DNA damages:

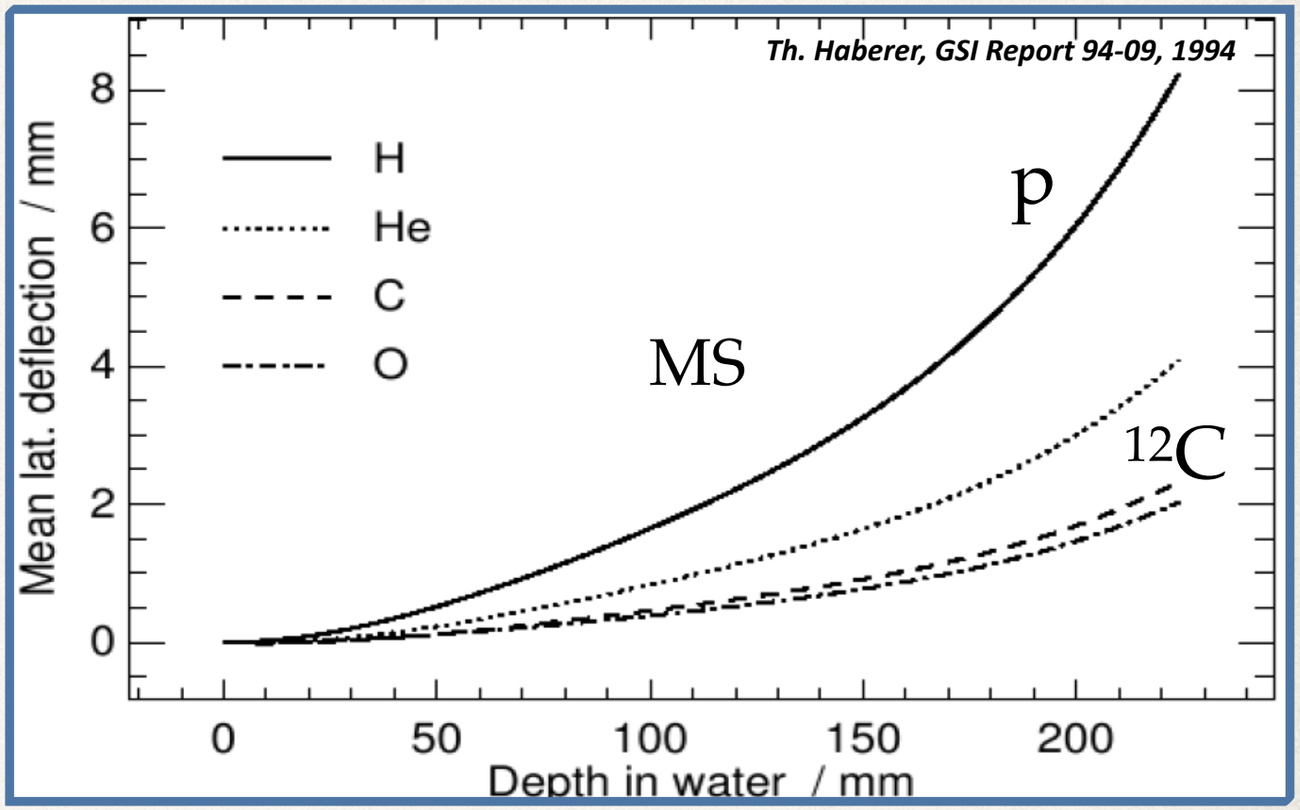
- **high RBE**
- **not sensitive to oxygen** => same effect on hypoxic/well oxygenated tumor regions



PT has a higher radiobiological effectiveness with respect to RT.

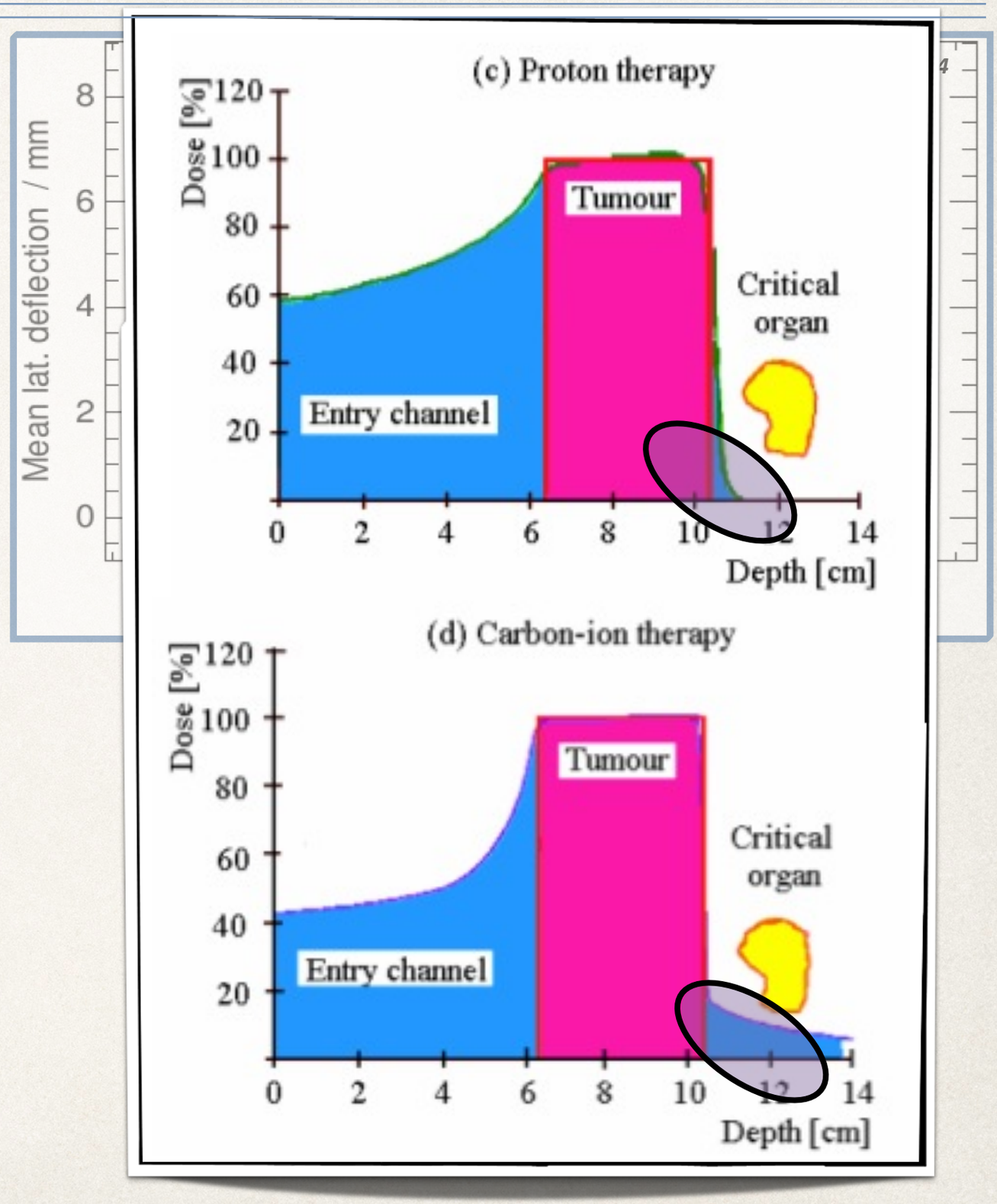
Particle Therapy: features

- Charged particles suffer multiple scattering => lateral beam spread ($\propto Z_{mat}$, $(p\beta c)^{-1}$, $\sqrt{x}$)

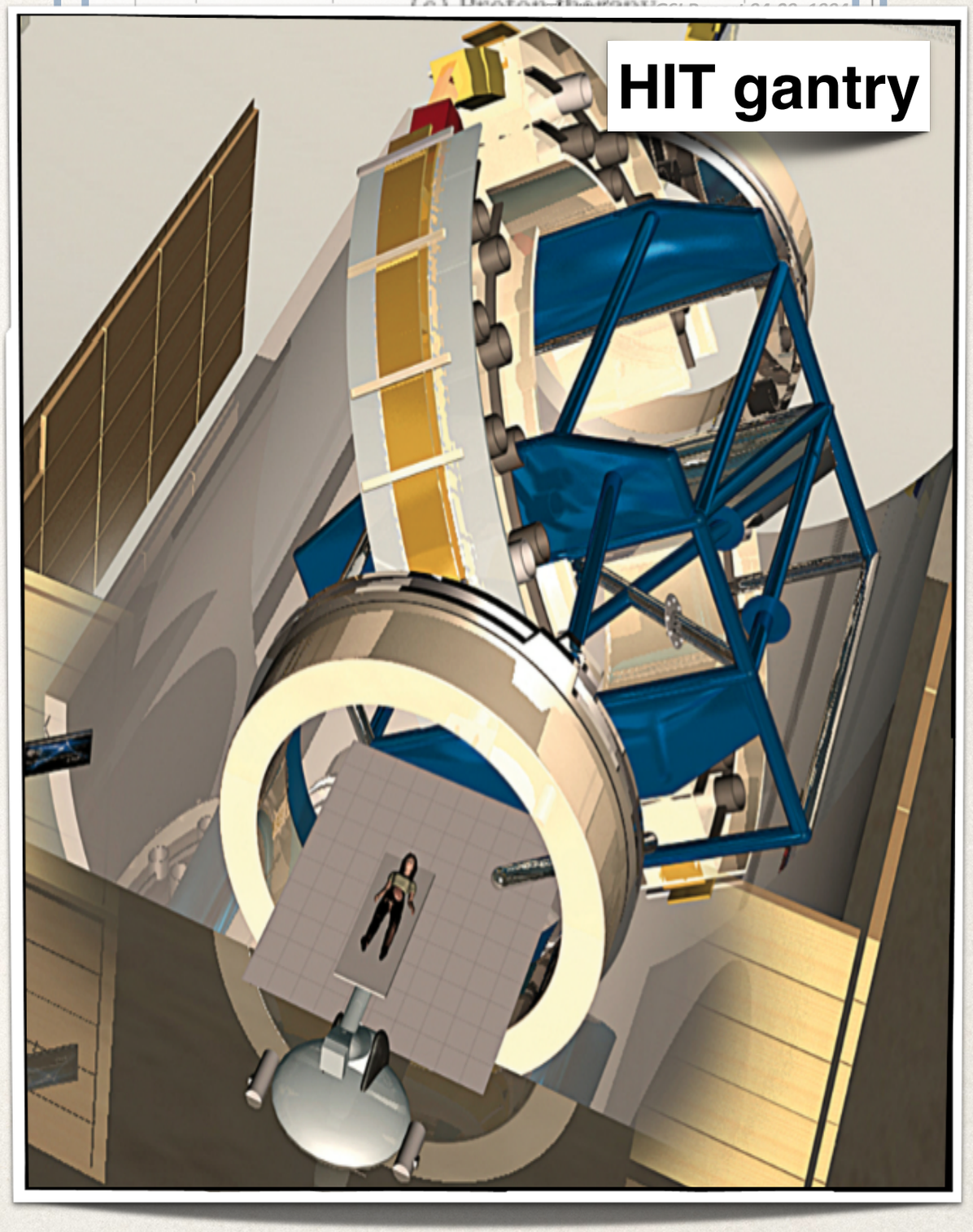


Particle Therapy: features

- Charged particles suffer multiple scattering => lateral beam spread ($\propto Z_{mat}$, $(p\beta c)^{-1}$, $\sqrt{x}$)
- Particles with A > 1 undergo **nuclear fragmentation** => BP tail



Particle Therapy: features



- **PT** is more **expensive** than RT: the beam delivery is a complex work of engineering

Particle Therapy in the World

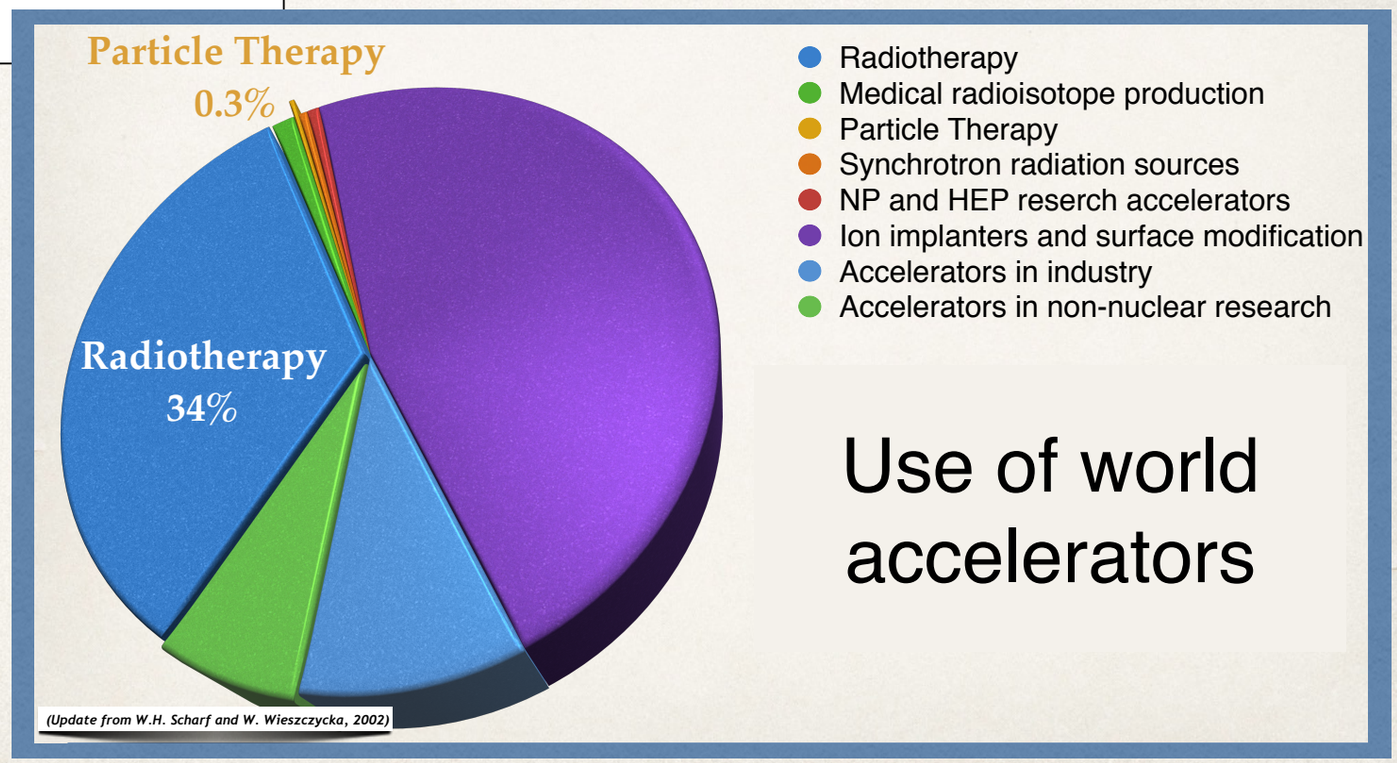
Country	Facilities in operation		Facilities planned (or under construction)		Patients treated (operative facilities)	
	Protons	Light ions	Protons	Light ions	Protons	Light ions
USA	16	0	15	0	44458	
Europe	13	2	15	1	27479	1473
Japan	9	4	3	1	13859	11055
Russia	3	0	2	0	6701	
China	1	2	2	1	1078	249
South Korea	1	0	1	1	1158	
South Africa	1	0	0	0	521	
Canada	1	0	0	0	175	
Taiwan	0	0	2	0		
Saudi Arabia	0	0	1	0		
India			1			

More than 50 PT facilities and others under construction, more than 100000 patients treated…

PT in Italy

- CATANA - Catania
- CNAO - Pavia
- ATreP - Trento

…But only a 0.3% with respect to the 34% of RT.

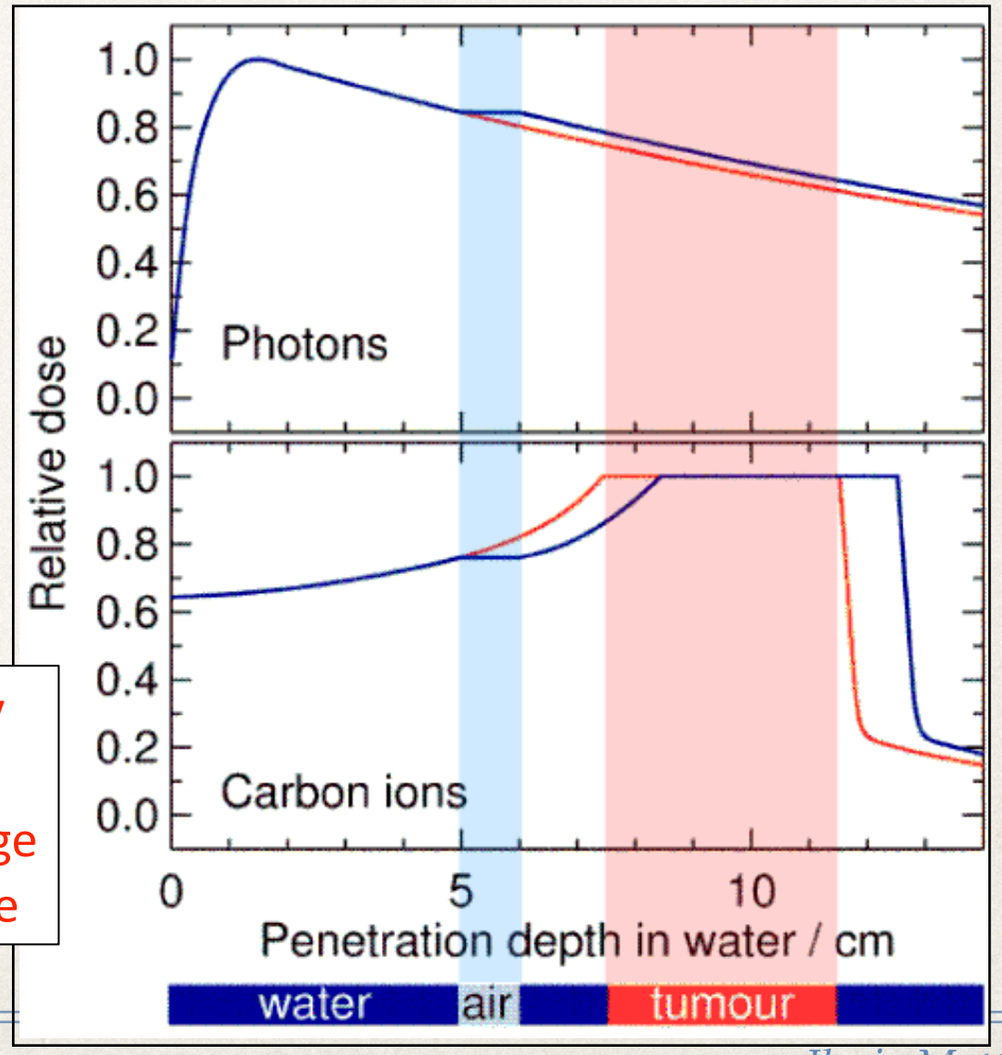


Use of world accelerators

Range Monitoring

Why it is so crucial to monitor the beam range in PT?
It is like firing with a precision rifle!

- 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



A little density mismatch => sensible change in dose release

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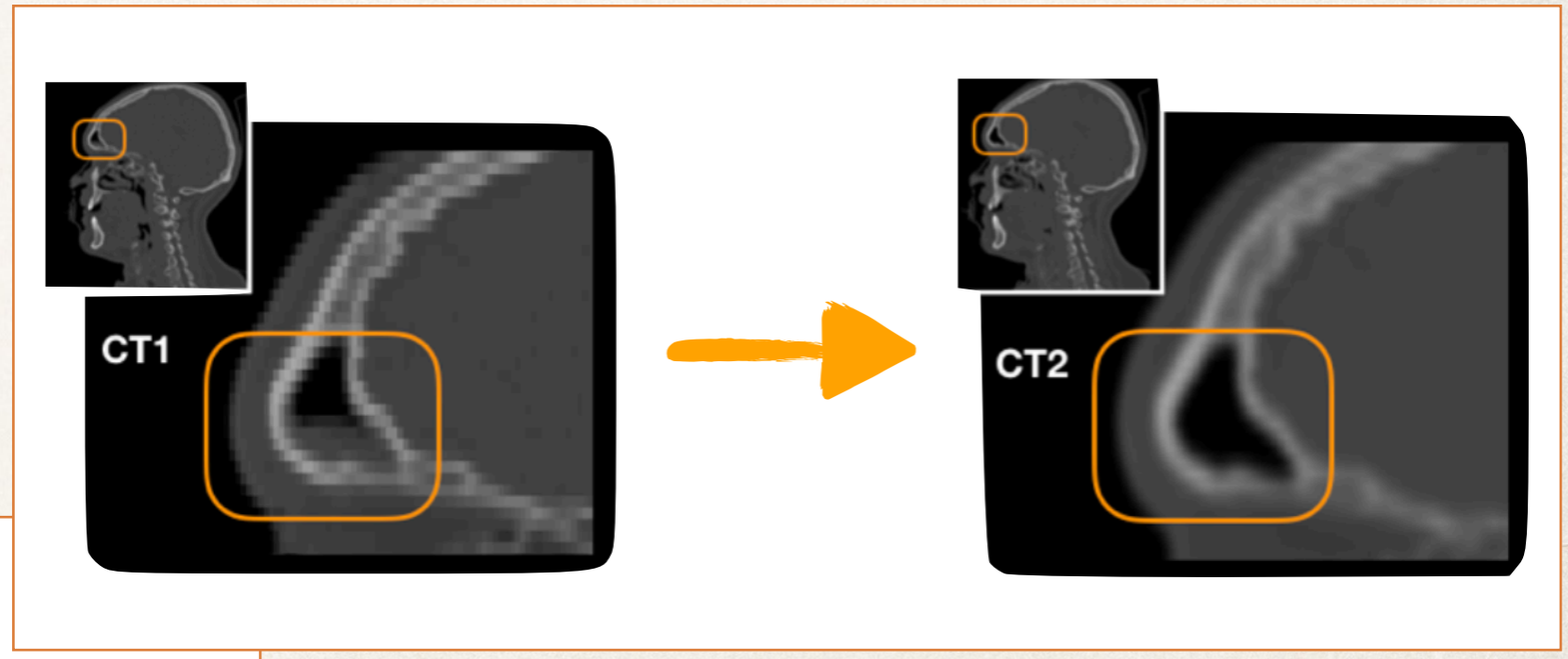


INTER-FRACTIONAL MONITORING

How to monitor the released dose

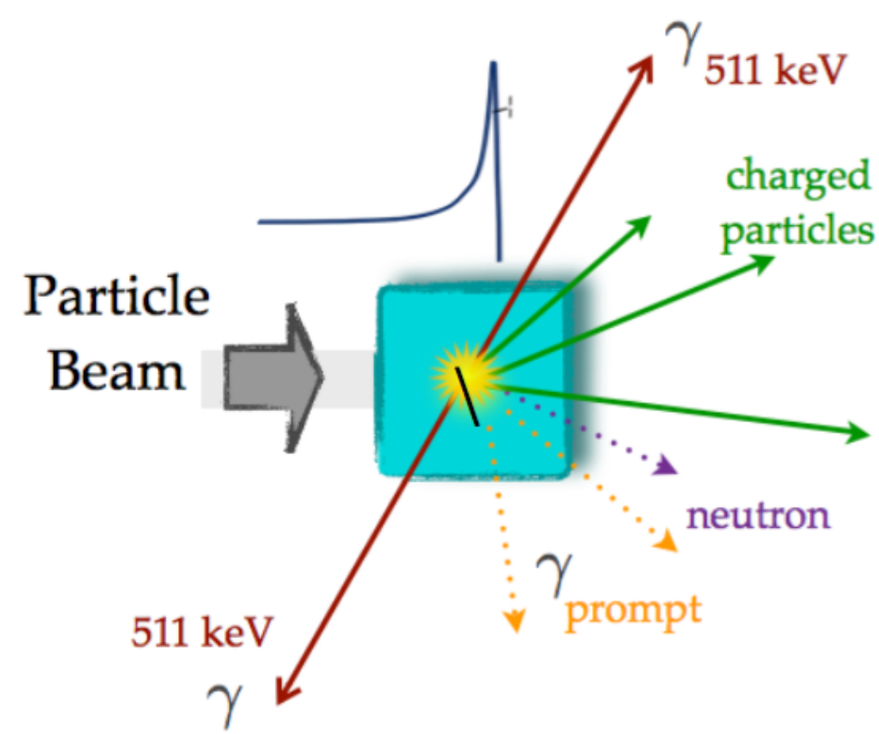
In **conventional RT** (photons) the **beam crosses the patient body** while **in PT the beam is absorbed inside the patient!**

An ideal **PT monitor device**:

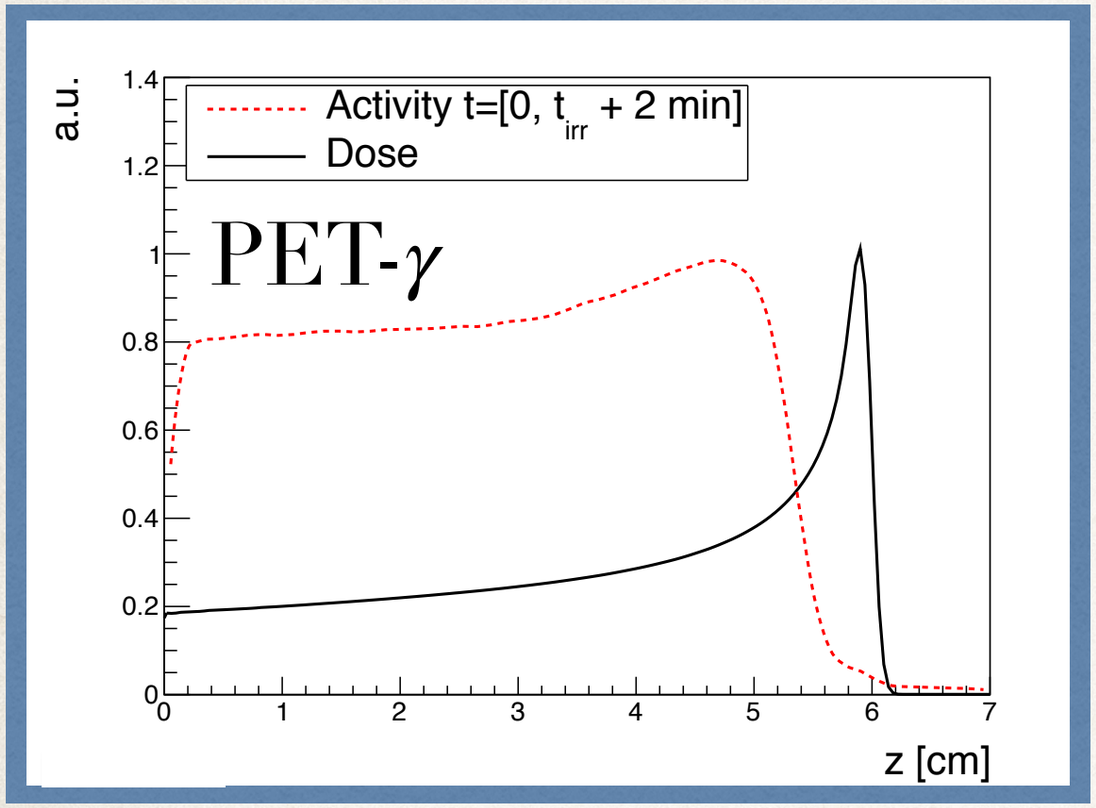
- Must rely on **secondary products** generated by the beam that come out from the patient to spot the dose release position
- Should measure the **dose shape and absolute value** to check the agreement between the planned target volume and the actually irradiated volume
- The **measurement** should be done during the treatment (***on-line***)
- Must be able to **deal with** other secondaries that act like **background**

Different secondary particles are produced.

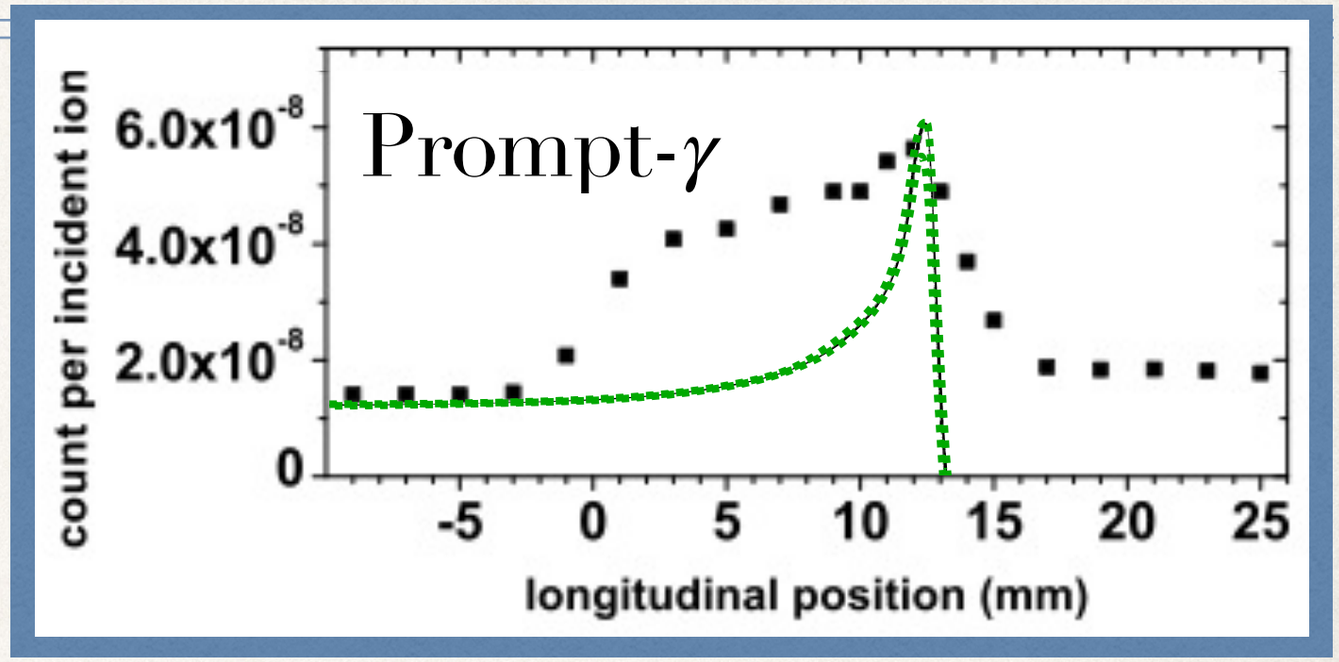
Which ones to choose for monitoring?



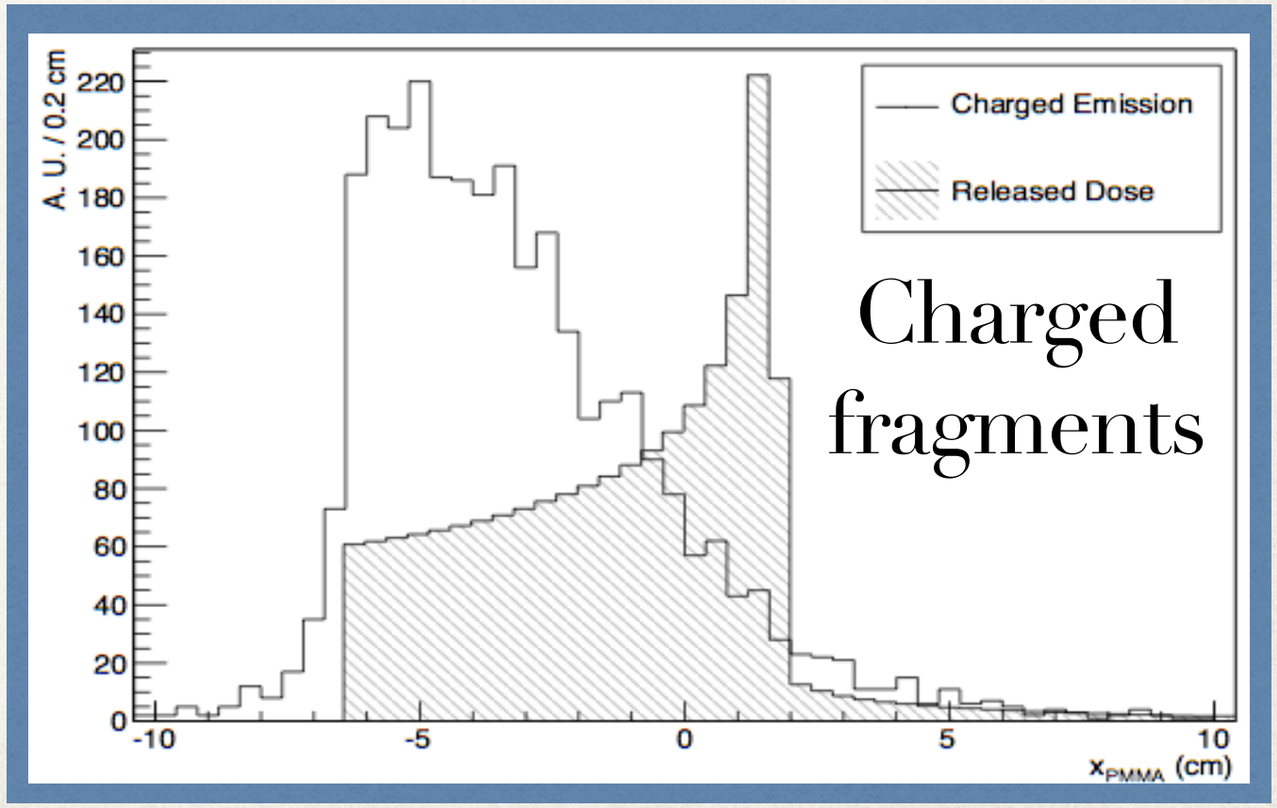
Secondary Products: PET-γ, Prompt-γ, Charged fragments



95 MeV proton beam (FLUKA)

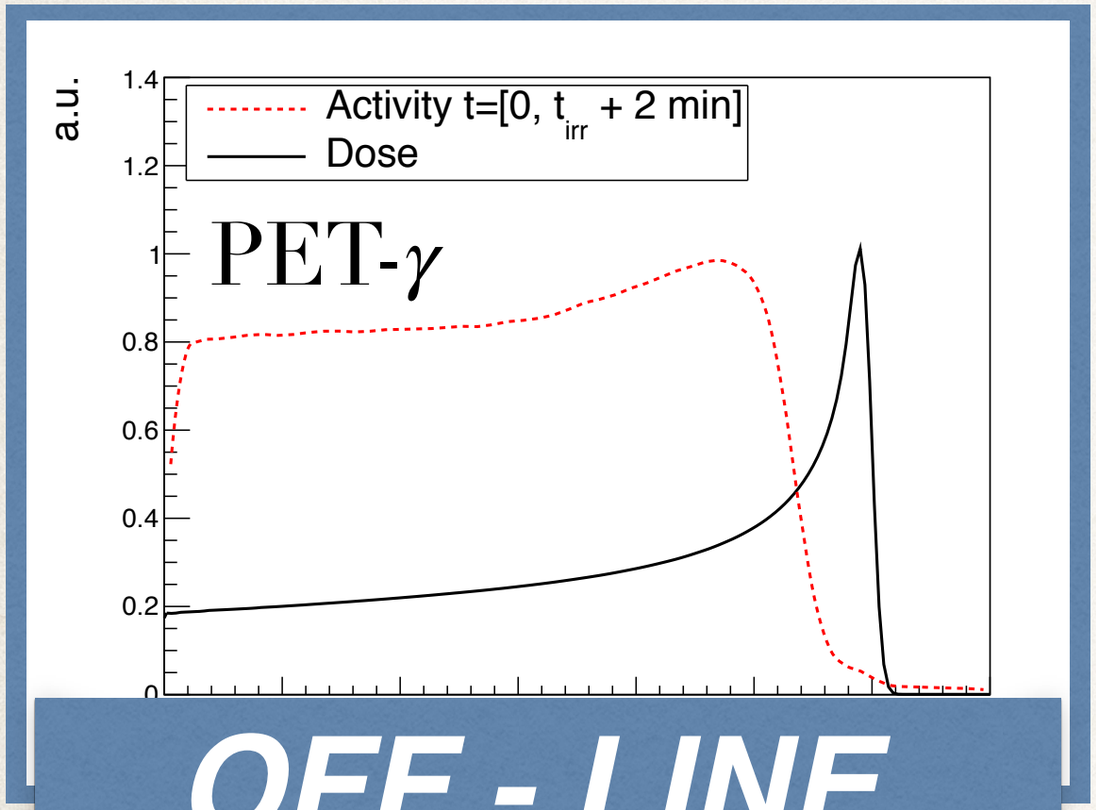


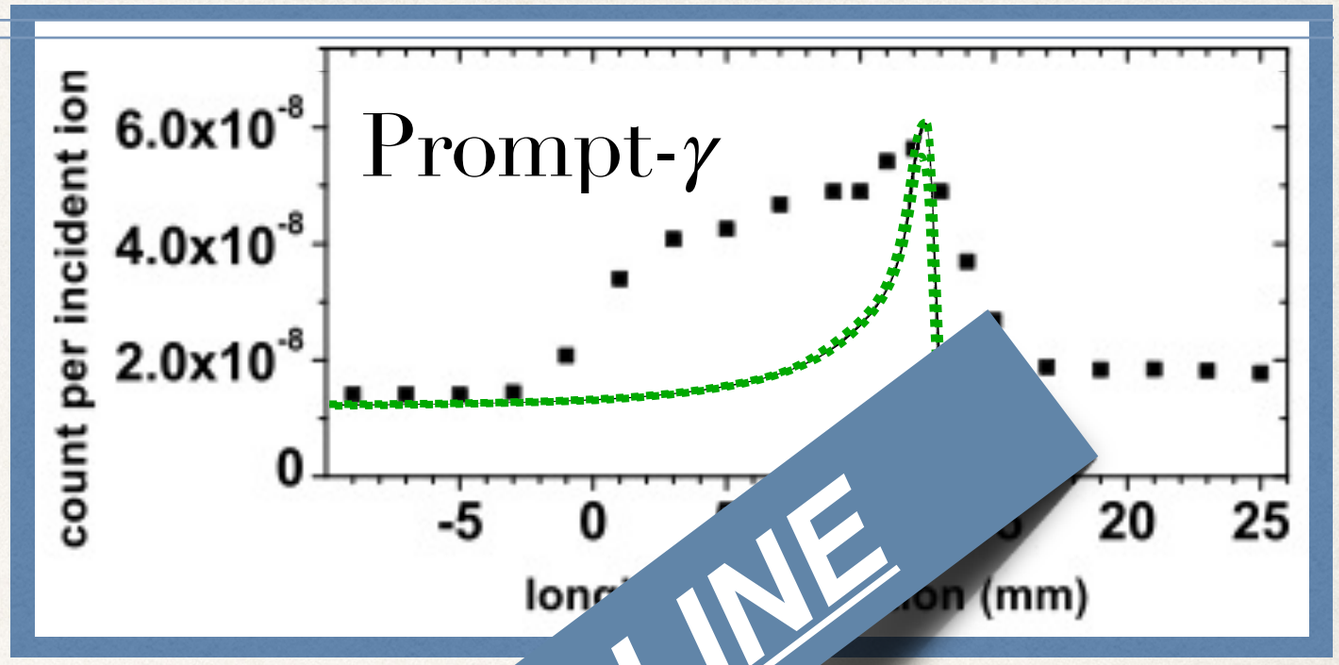
73 MeV/u ^{12}C ion beam (*Testa et al.*)



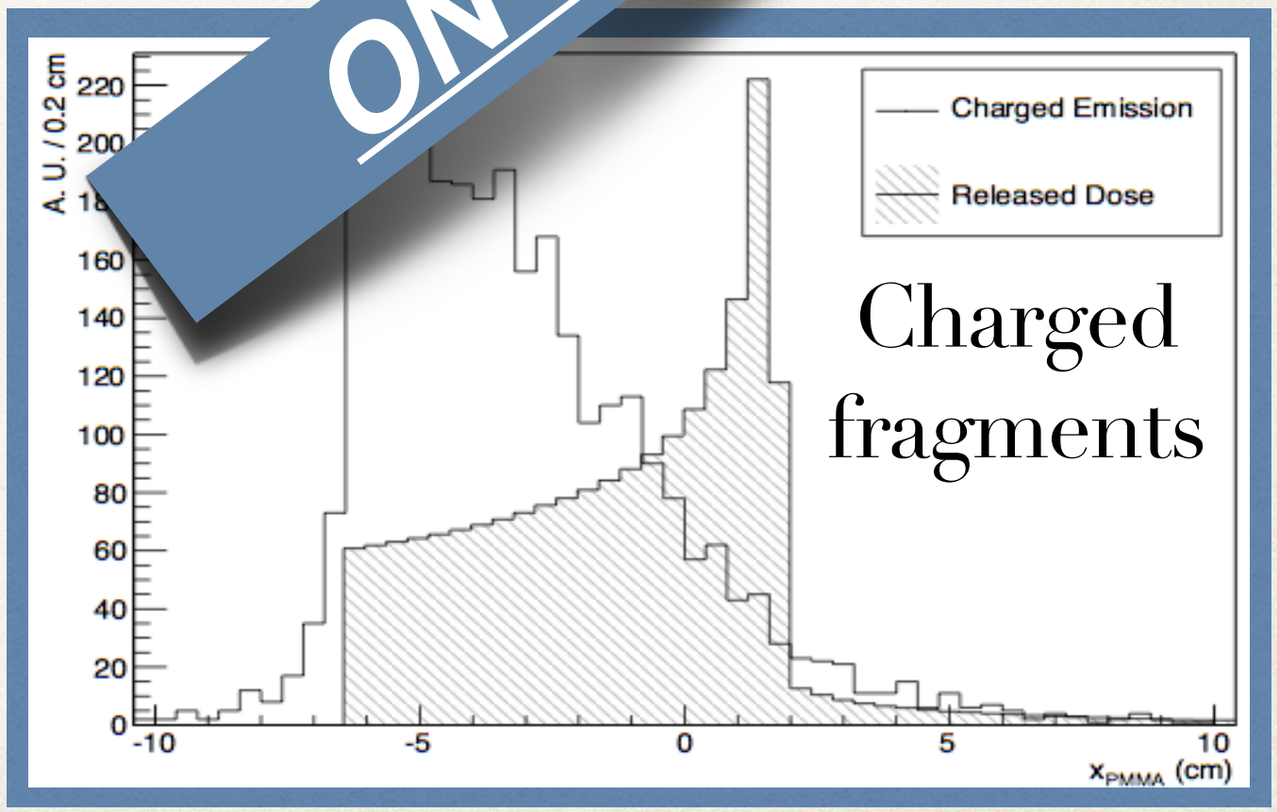
220 MeV/u ^{12}C ion beam (*Piersanti, **Mattei** et al.*)

Secondary Products: PET-γ, Prompt-γ, Charged fragments





73 MeV / u cam (*Testa et al.*)



ON - LINE

OFF - LINE

- β+ isotopes of short lifetime ^{11}C(~20min), ^{15}O(~2min), ^{10}C(~20s)
- Low β+ activity, long acquisition time
- Patient metabolic washout

eam
al.)

The Dose Profiler

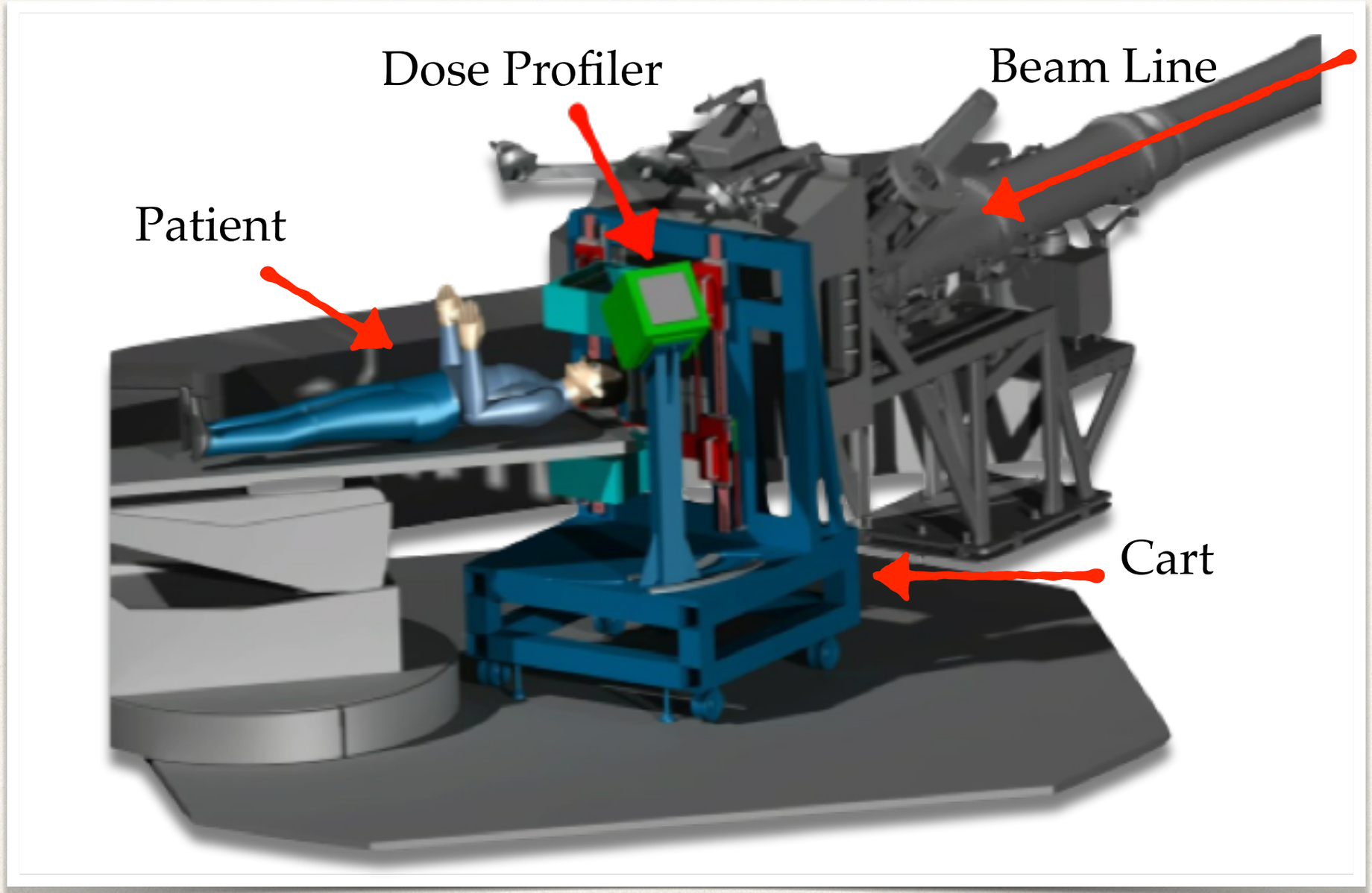
For the inter-fractional beam range monitoring purpose, a new device has been developed: the ***Dose Profiler.***
Clinical trial on patients @ CNAO started in 2019

PRIN MIUR 2010	INFN RDH project	Centro Fermi project

INnovative Solutions for In-beam DosimEtry in Hadrontherapy

The Dose Profiler project

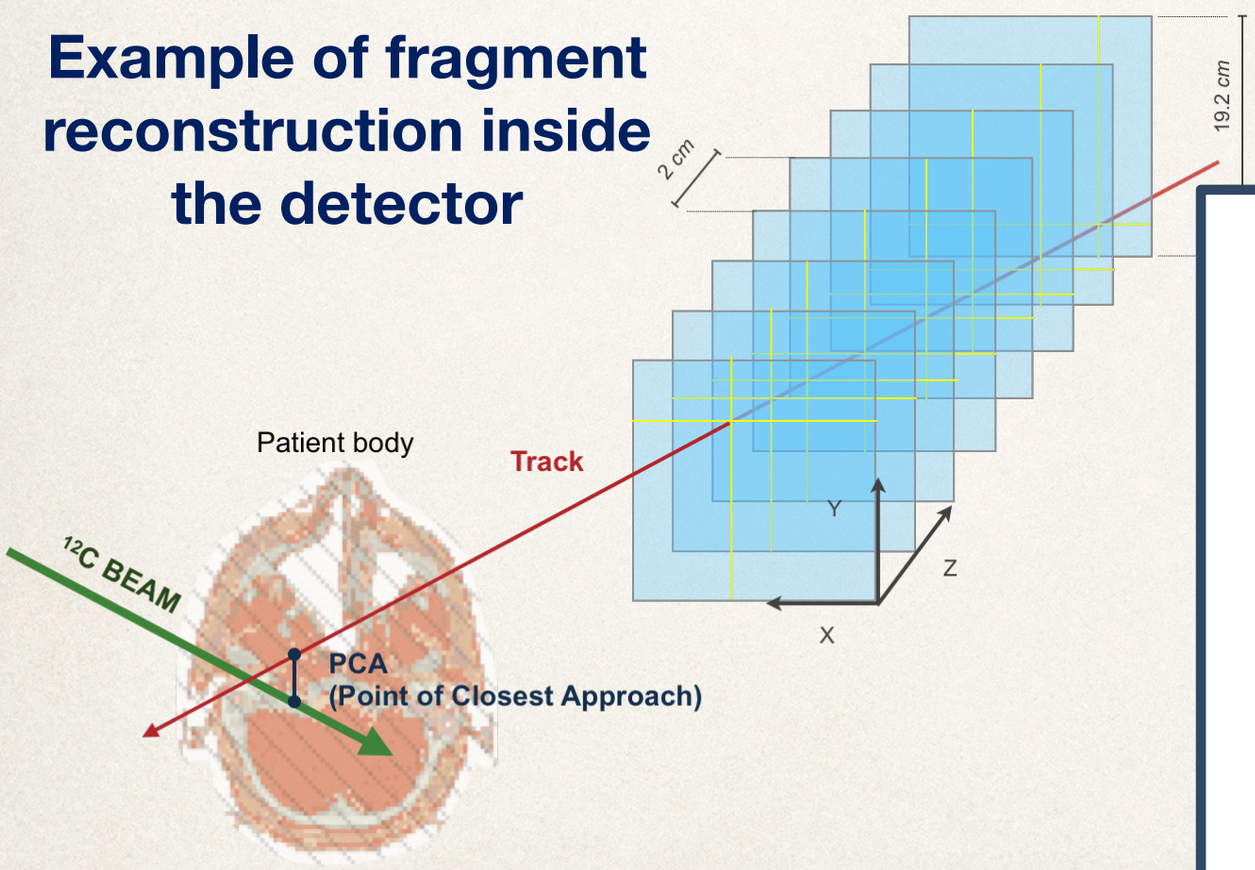
The Dose Profiler is a tracker of <u>secondary charged particles</u>

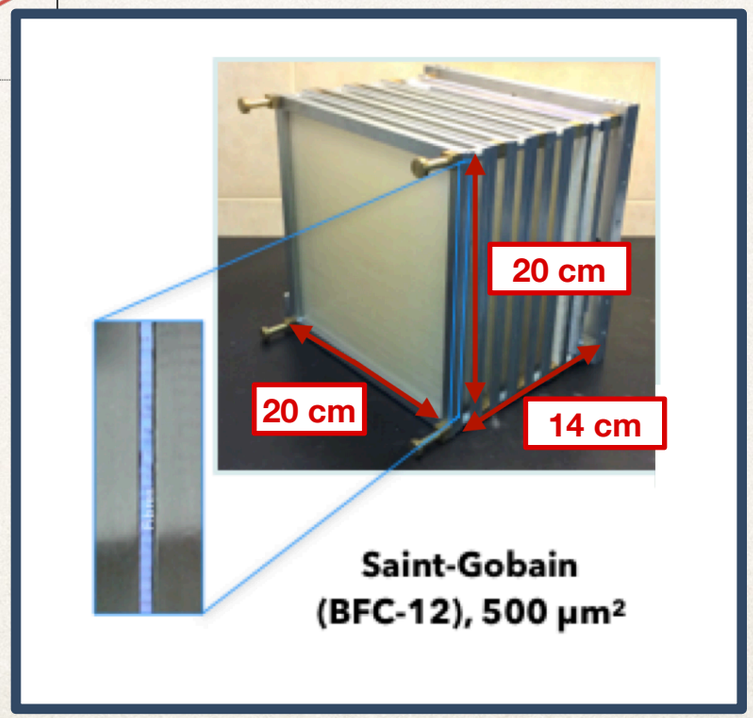


Detector Overview

- 8 planes each one composed of 2 orthogonally oriented layers of **plastic scintillating fibres** (squared **500 μm**, double cladding) are used to track the incoming particles
- 3072 **SiPMs readout** (1 mm^2)
- Interface with the **Dose Delivery system** of CNAO

Example of fragment reconstruction inside the detector



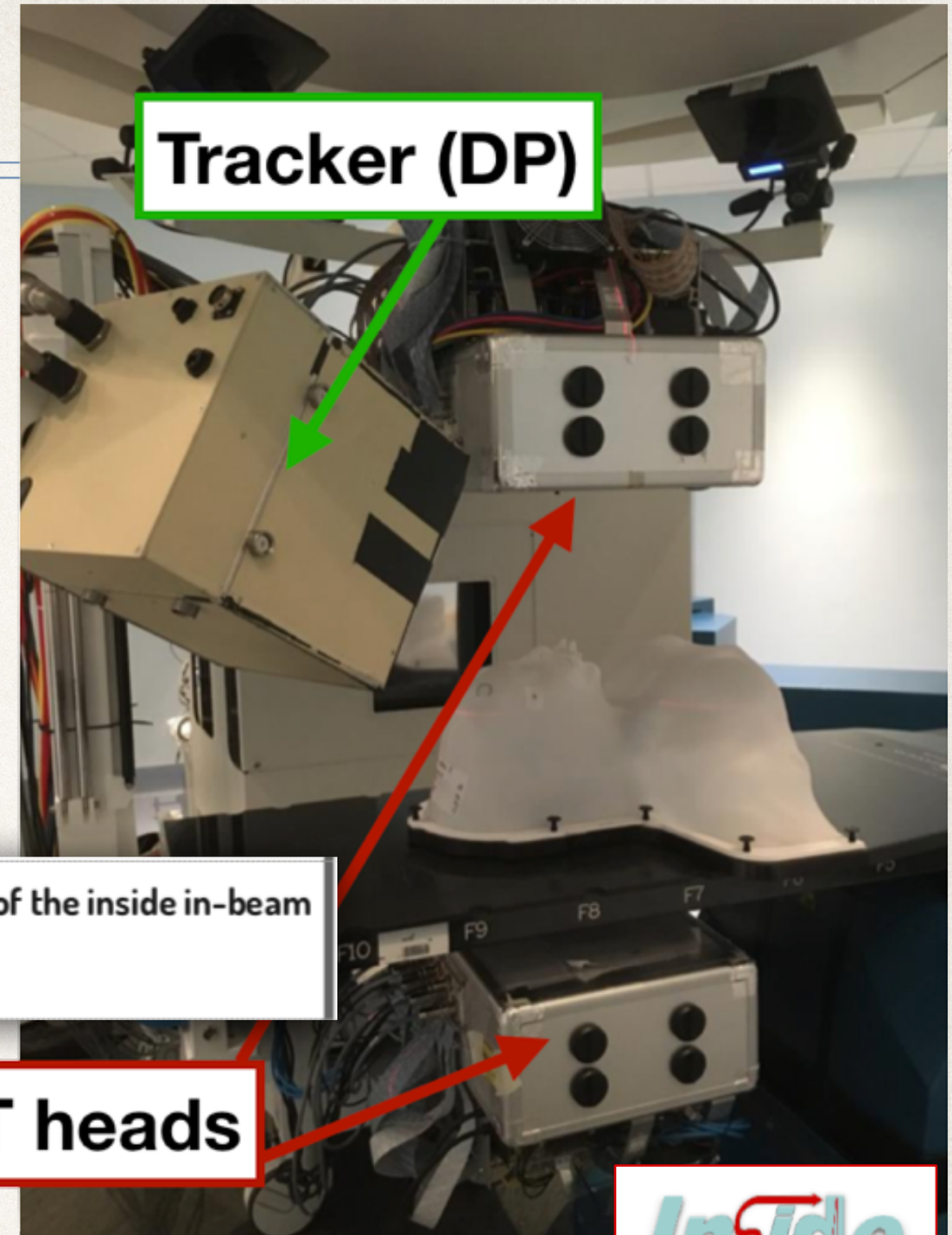


Detector Overview

The DP is integrated within the **INSIDE** system @ CNAO with a PET device using a bi-modal approach: **charged fragments** detection and ß+ activity map measurement for **carbon ion** and **proton** treatments monitoring, respectively.

Clinical results of in-vivo inter-fractional monitoring in particle therapy by means of the inside in-beam PET

Elisa Fiorina – **ON-LINE** doi: 10.3389/fphy.2020.578388

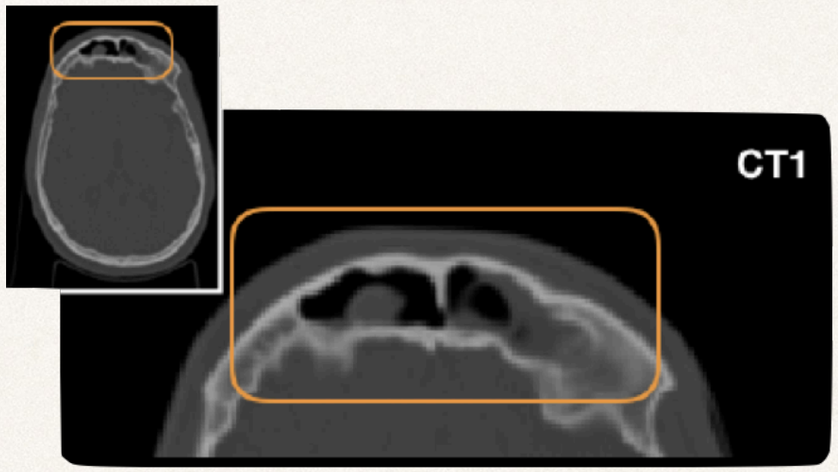


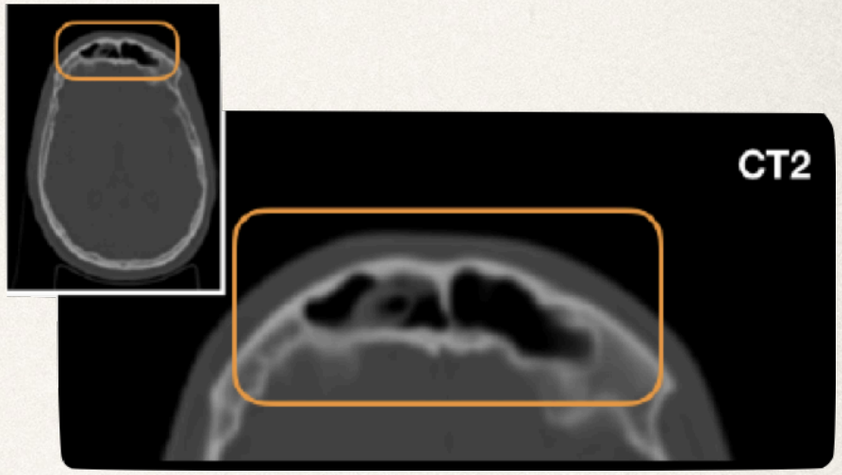
DP is placed at **50 cm** from the treatment room isocenter and at **60° wrt the beam direction.**

Inter-fractional Monitoring

- Carbon ion treatments at CNAO typically lasts ~ **4 weeks**
- A **CT scan** is performed and used as input for the treatment planning
- The ^{12}C beam is delivered in **20-30 fractions**
- The decision to perform a mid-treatment CT and eventually to re-plan the treatment is taken only accordingly to the pathology under treatment and on the basis of the collected statistics of patients with similar pathologies

Example of morphological changing occurred during the treatment

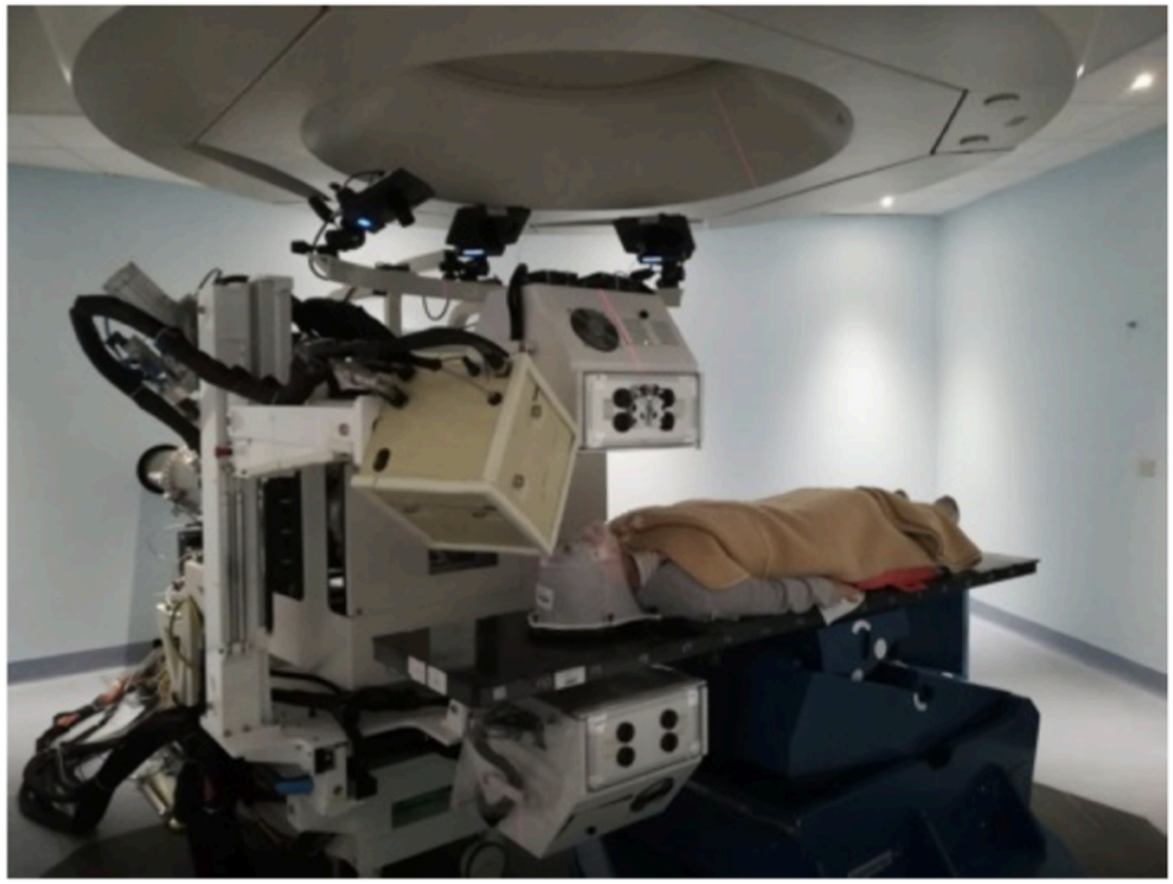




Monitoring strategy: As the fragments production yield along the beam path depends on the **density** and the **atomic mass** of the crossed tissues, the dis-homogeneities onset can be monitored **comparing the reconstructed emission map of the fragments in different fractions of the treatment** to help the decision on when a replanning CT is needed.

Clinical Trial: 8-12/2019@CNAO

- A clinical trial (ClinicalTrials.gov Identifier: NCT03662373) is started at CNAO in August 2019 to evaluate the Dose Profiler capability and sensitivity in detecting morphological changes arising in pathologies of the **neck-head district.** At present, data on 10 patients have been collected.

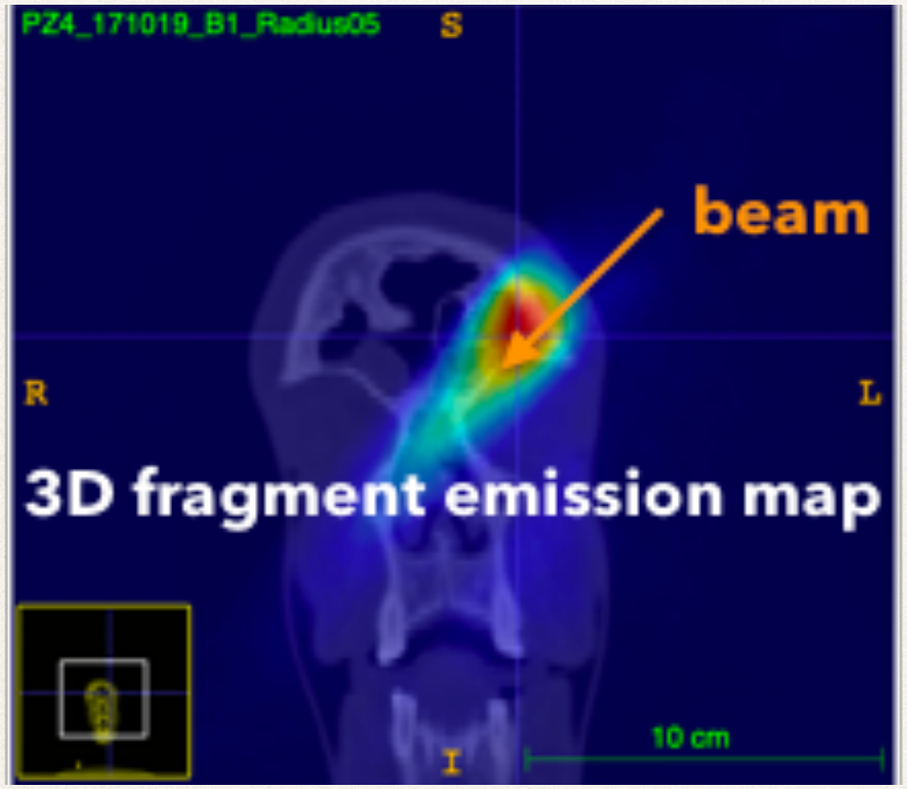


Patient ID	Pathology	Re-evaluation CT	Re-planning
PZ1	ACC	7° fraction	no
PZ2	ACC	5° and 10° fraction	no
PZ3	ACC	no	no
PZ4	ACC	8° fraction	no
PZ5	clival chordoma	no	no
PZ6	ITAC	7° fraction	yes
PZ7	clival chordoma	no	no
PZ8	ACC	7° fraction	no
PZ9	clival chordoma	no	no
PZ10	ITAC	8° fraction	yes

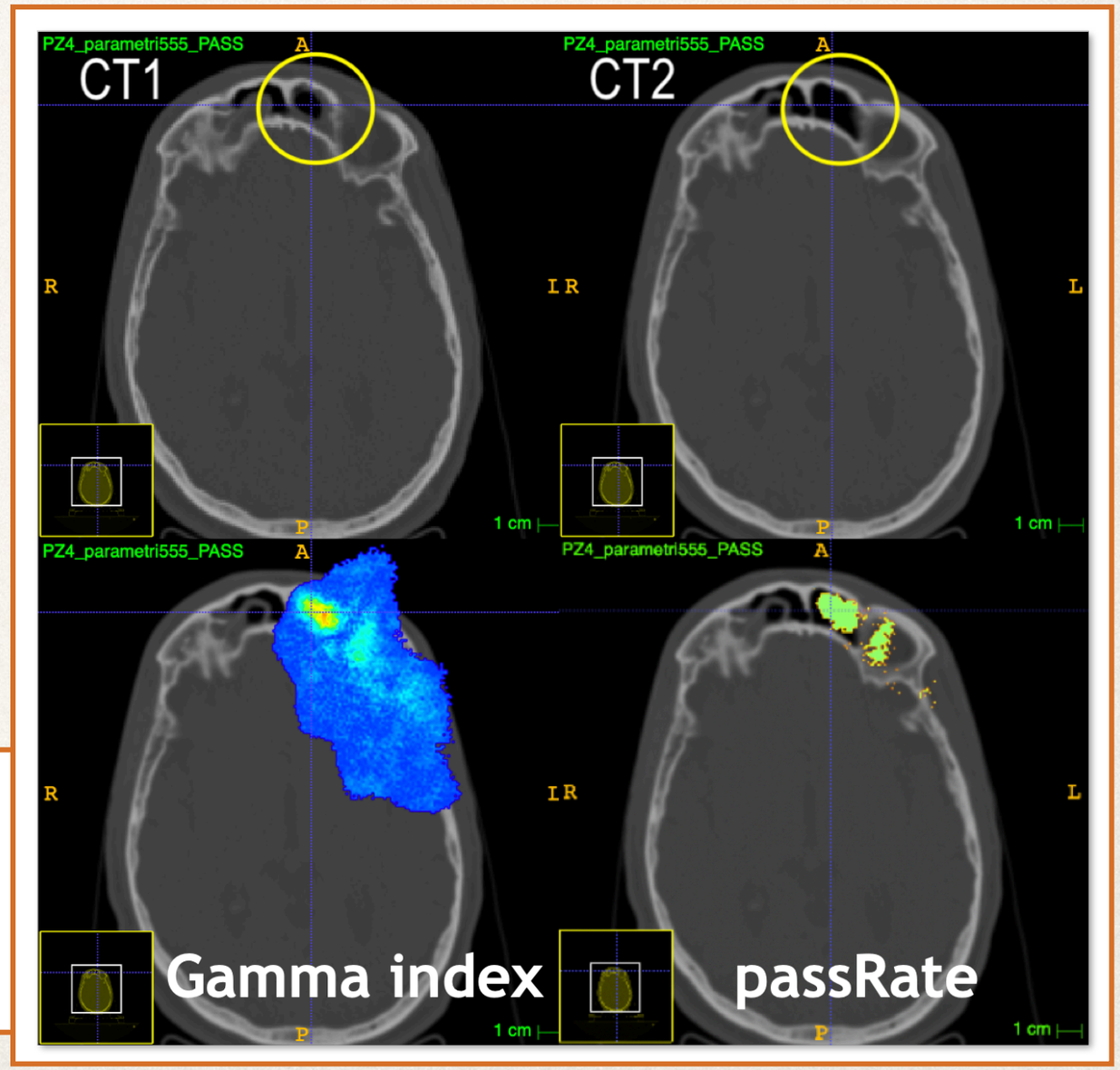
The **1D inter-fractional monitoring results** have been published
Fischetti, M. *et al.*, *Sci Rep* 10, 20735 (2020)
https://doi.org/10.1038/s41598-020-77843-z

3D Inter-fractional Monitoring

- Data on PZ4 are here shown: **CT1 before 16 October; CT2 the 29 October**
- The 3D map of emission points of detected fragments are reconstructed in each fraction
- The difference of maps taken at the first fraction and at the replanning-CT fraction is evaluated in terms of gamma-index (pass rate) map



PZ4 underwent the emptying of the frontal sinuses, as noticed by a mid-term CT (CT2). **Such modification has been clearly identified by the gamma-index map.**



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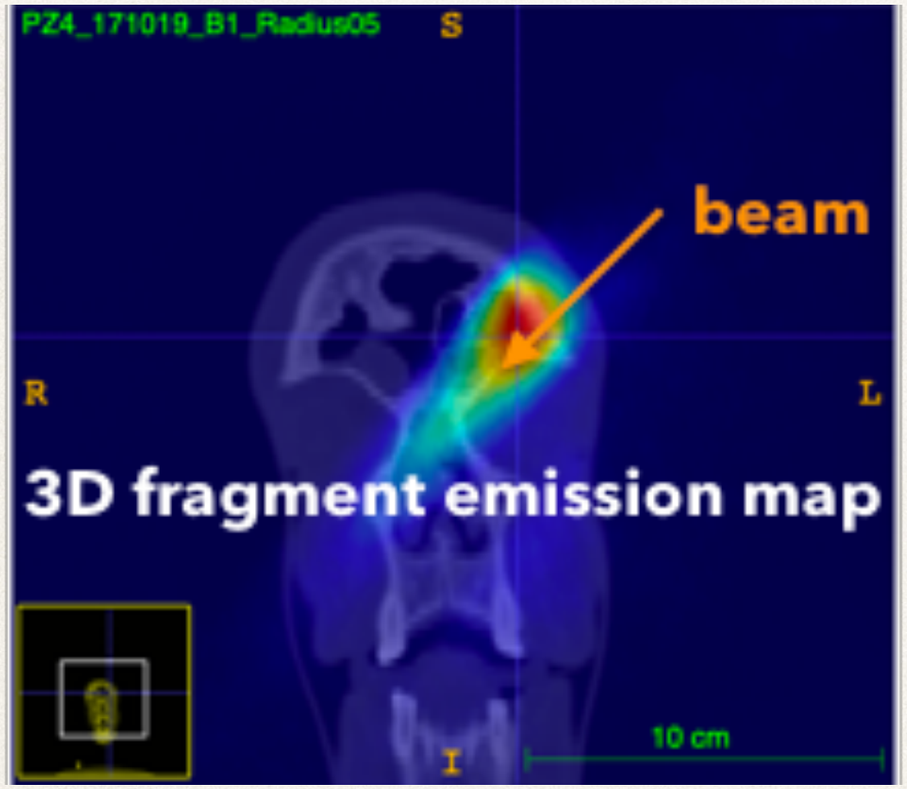
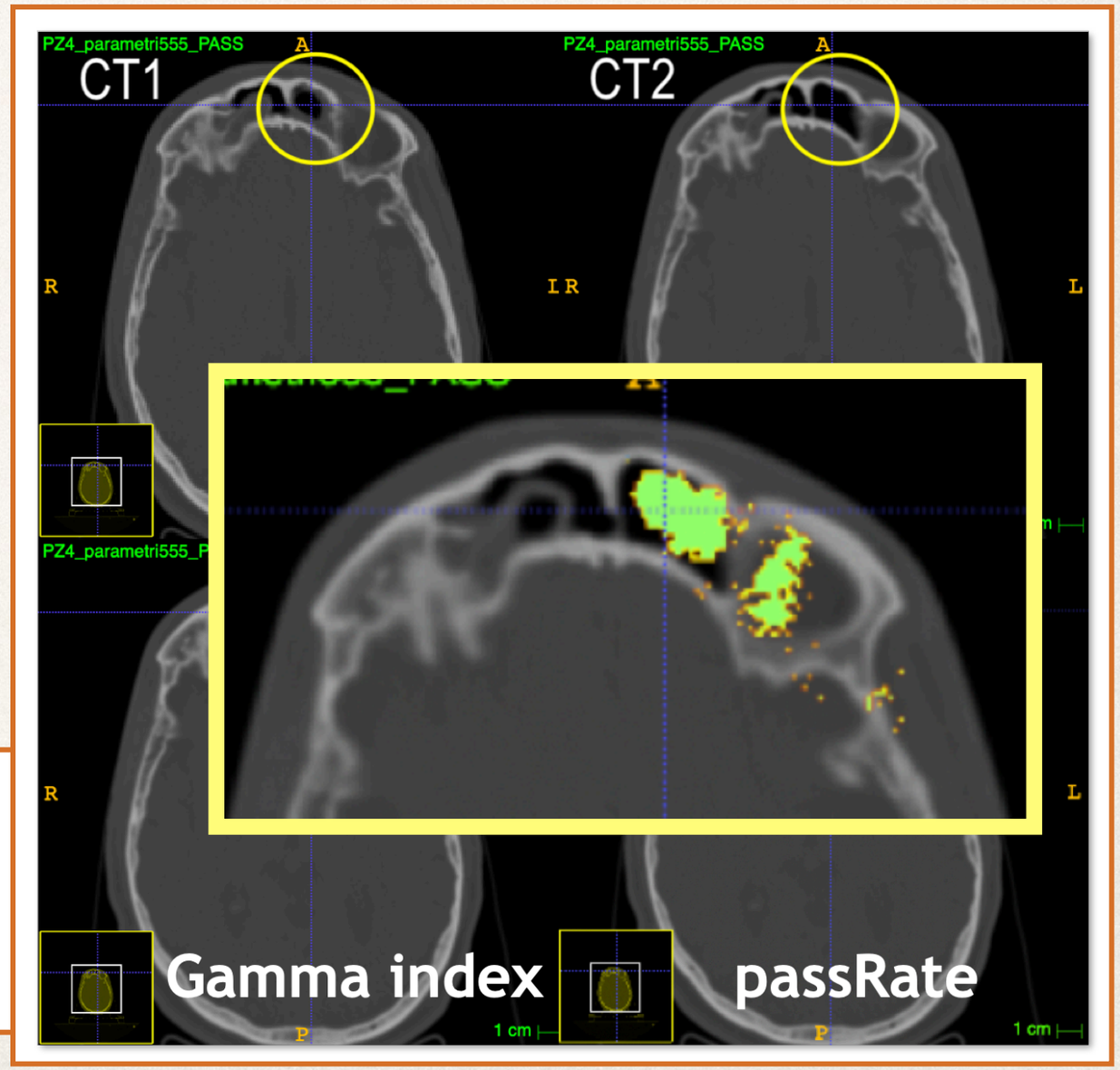
- The difference of maps taken at the first fraction and at the replanning-CT fraction is evaluated in terms of gamma-index (pass rate) map



PZ4 underwent the emptying of the frontal sinuses, as noticed by a mid-term CT (CT2). **Such modification has been clearly identified by the gamma-index map.**



3D Inter-fractional Monitoring

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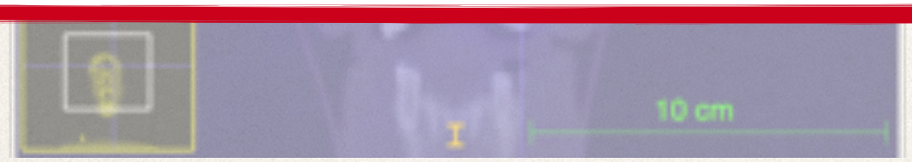
For the first time ever, patients treated with 12C have been monitored and morphological changes occurred during the treatment have been identified.

Another clinical trial campaign is going to start in 2022.



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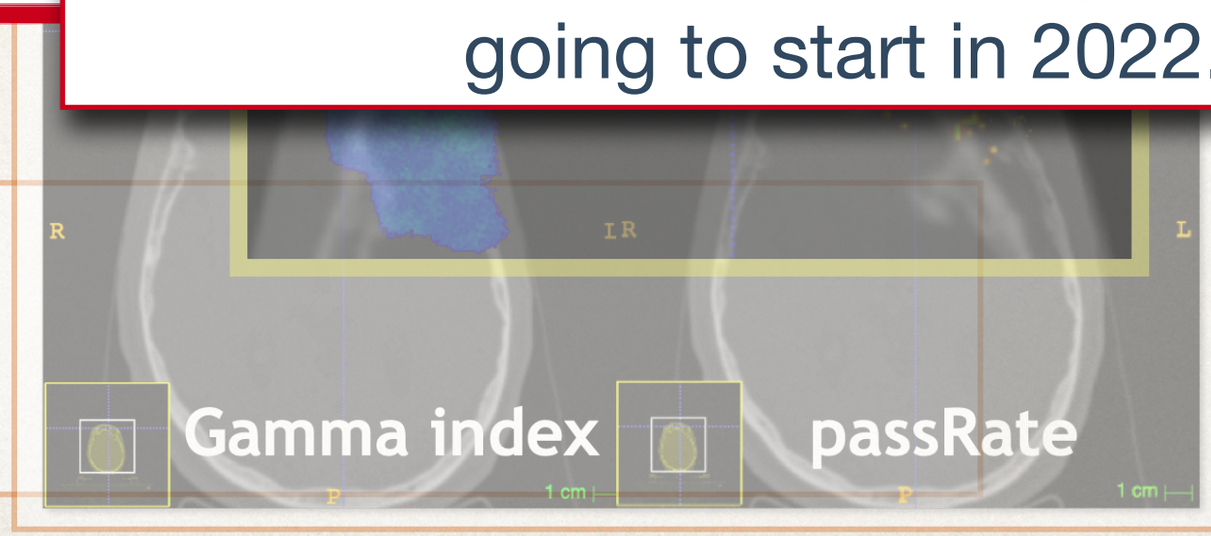
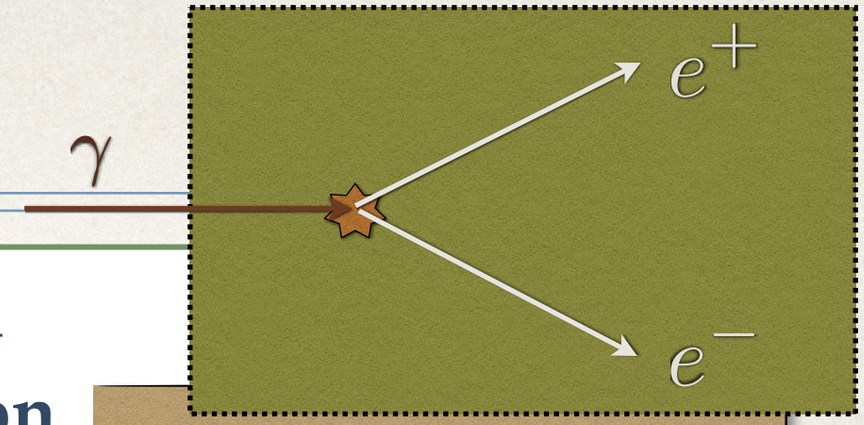


The PAPRICA project

For the beam range monitoring purpose, a new technique has been proposed within a young researcher grant: **the PAPRICA (*PAir PRoduction Imaging ChAmber*) *project.***

The detector is under construction and will be tested in-beam in 2022.

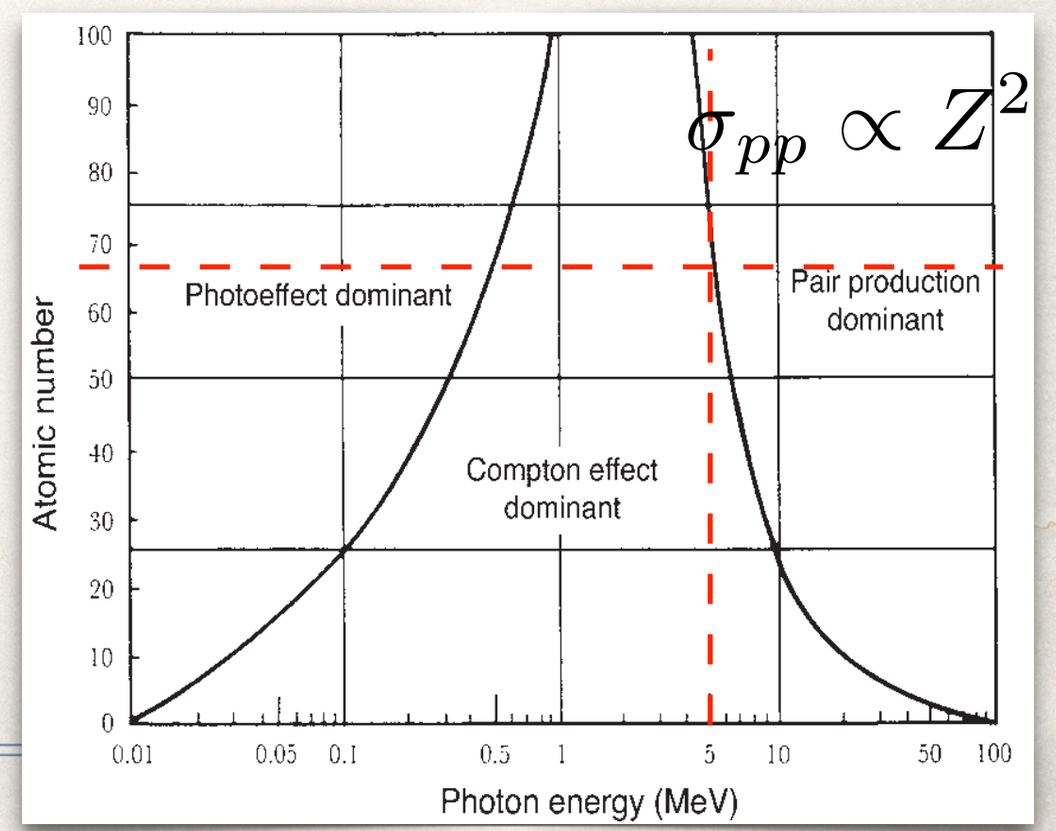
The PAPRICA project



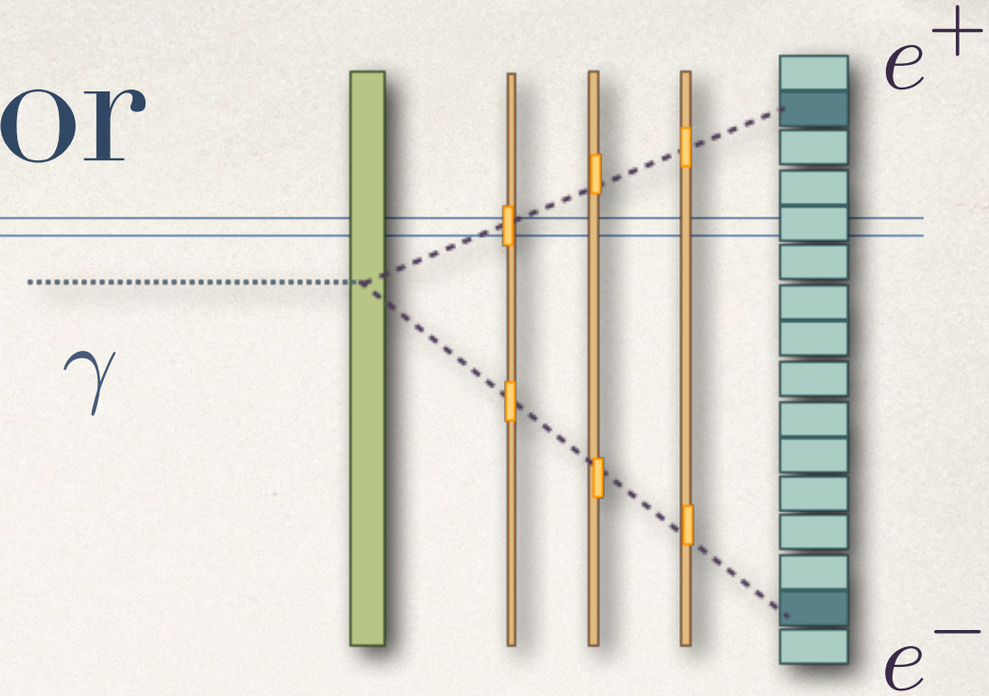
$$E_\gamma \sim E_{e-} + E_{e+}$$
$$\vec{p}_\gamma \sim \vec{p}_{e-} + \vec{p}_{e+}$$

PAPRICA proposes a **novel 3D prompt gamma imaging strategy**, exploiting the **pair production** mechanism of prompt photons for range monitoring purpose.

- Technique used by pair telescopes in astrophysics applications for cosmic photons imaging E > 30 MeV
- Never explored in the lower PG energy range E ~ 2-10 MeV
- Topological event signature: no *n* bkg
- No collimation
- Easy to 3D reconstruct the PG emission point
- Potentially to be used both in proton and 12C PT



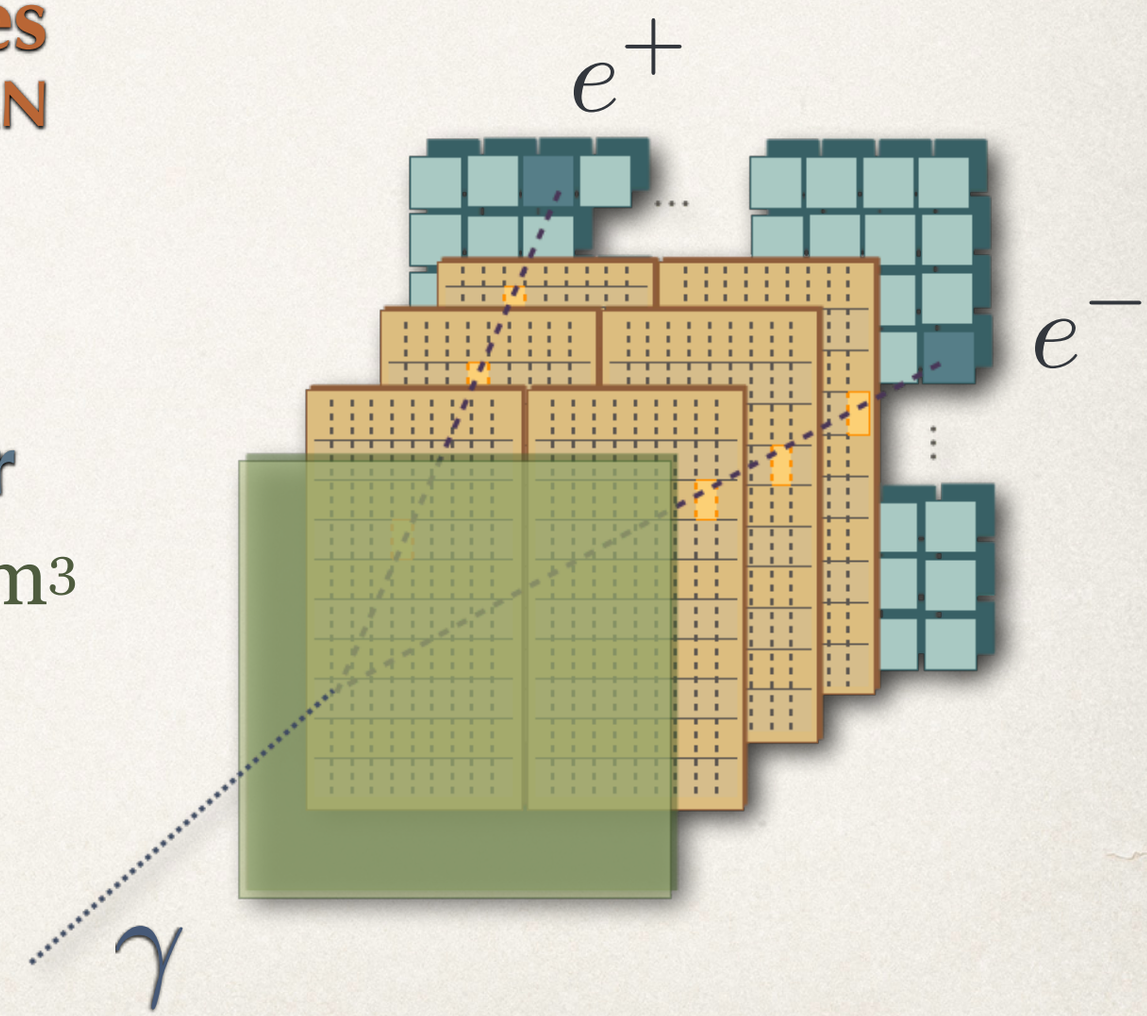
The PAPRICA detector



- **CONVERTER plane: LYSO fibers**
  high Zeff (66), fiber thickness 1.5 mm
  active medium (trigger and reco)

- **TRACKER: MAPS ALPIDE* modules**
  *ALICE@CERN
  low budget material
  intrinsic resolution < 10 μm

- **CALORIMETER: plastic scintillator**
  2 matrices 8 x 8 pixels, 6 x 6 x 50 mm^3
  low leptons backscattering
  same converter readout
  energy resolution < 3%



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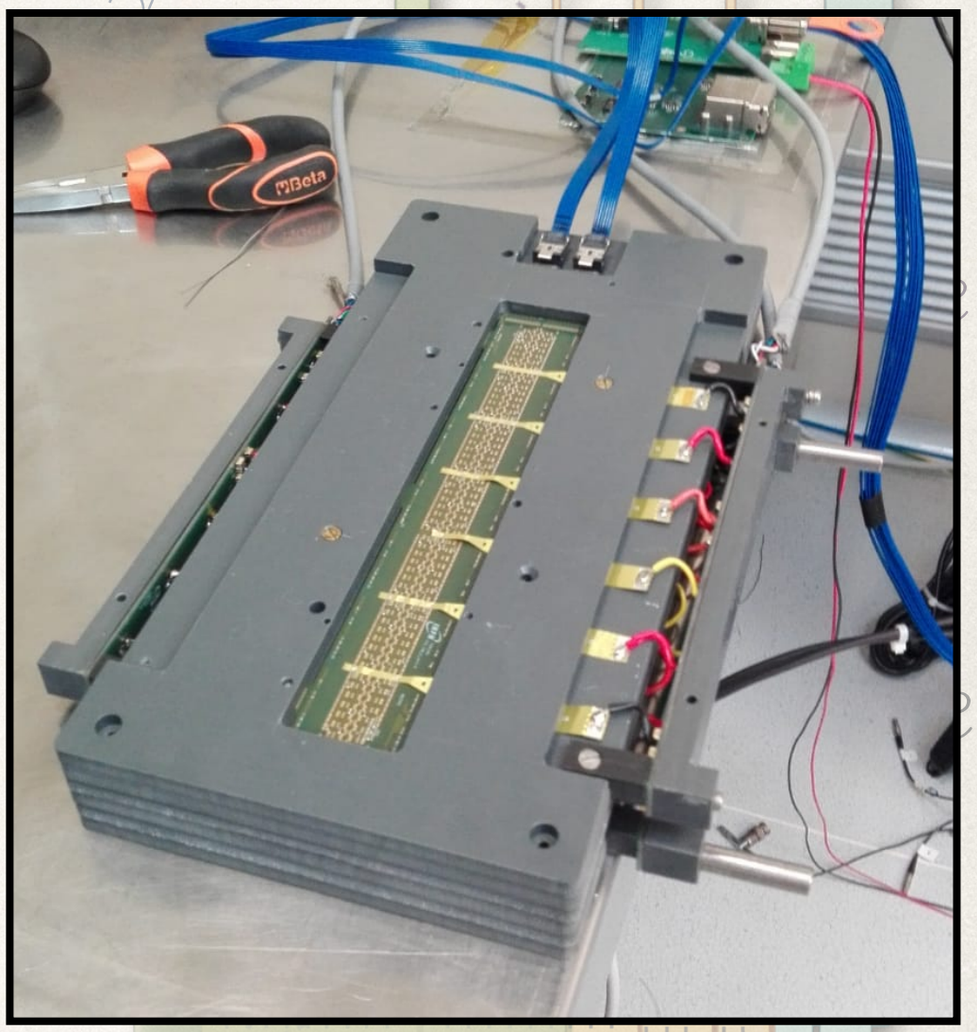

The PAPRICA detector

- **CONVERT**
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- **TRACKER:**
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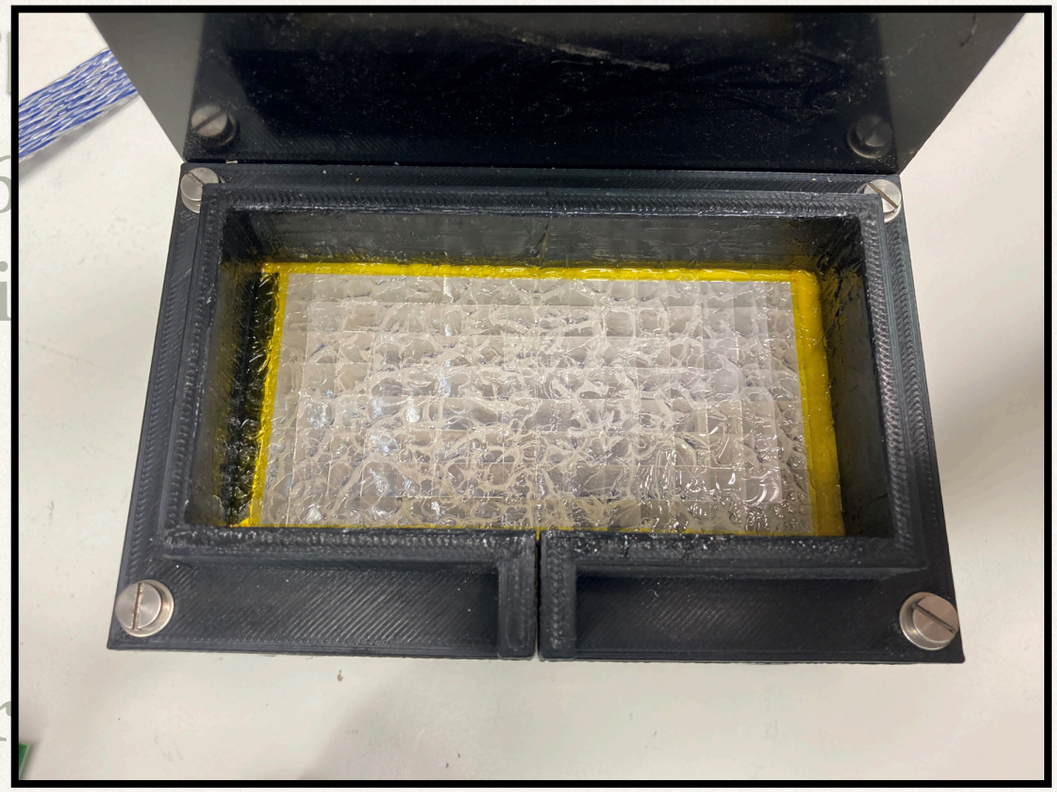
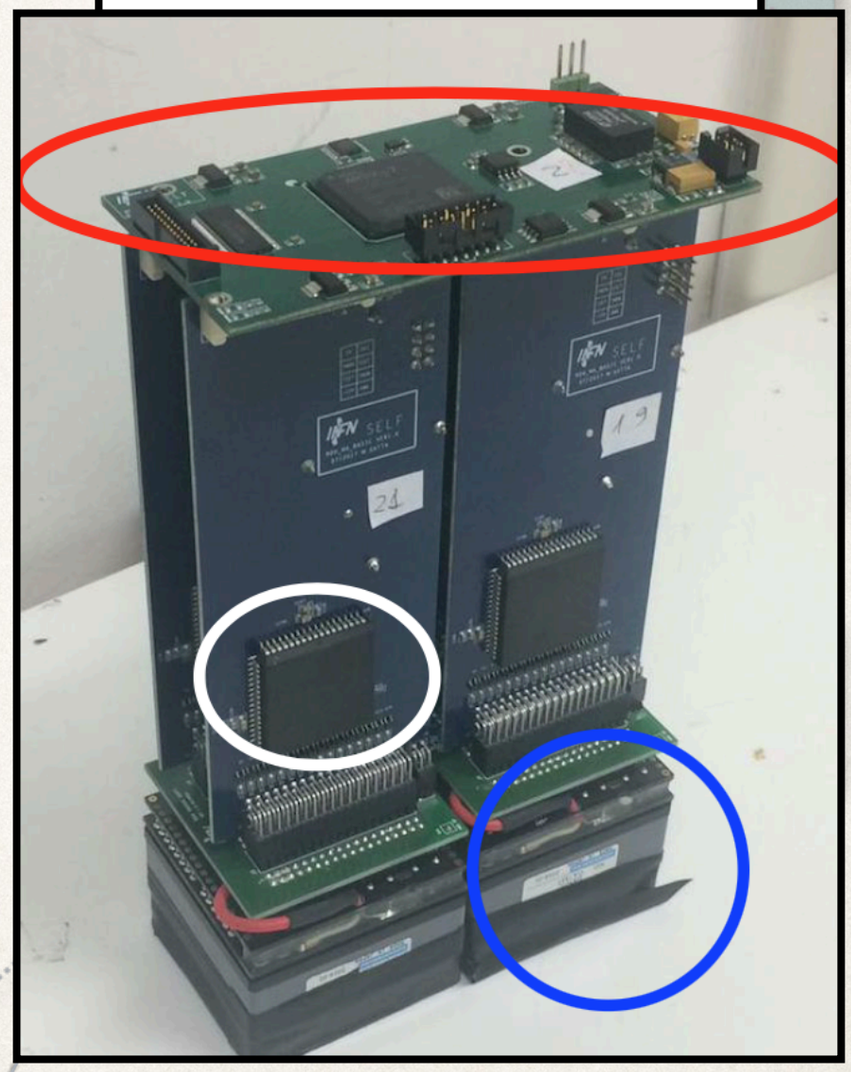


MAPM
ASIC 32 channels
FPGA



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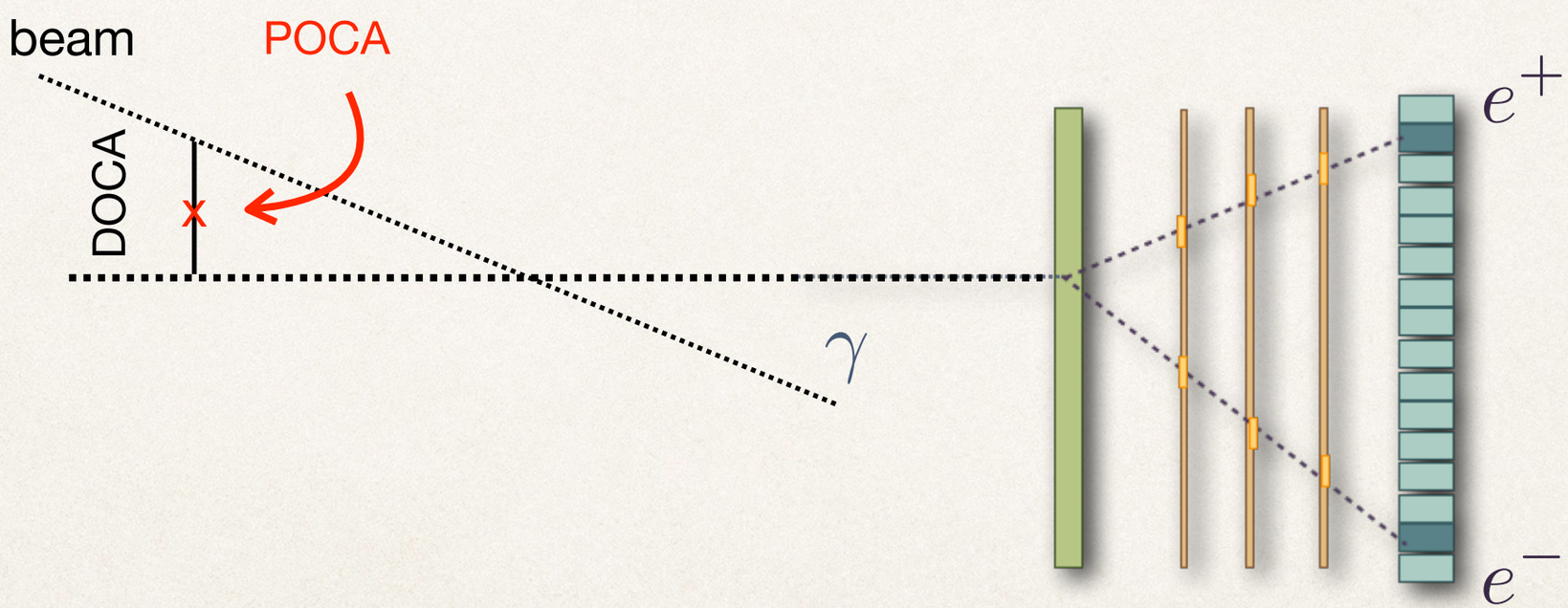
  4 matrices 8 x 8 pixels, 6 x 6 x 50 mm^3
  low leptons backscattering
  same converter readout
  energy resolution < 3%

Resolution Study (MC)

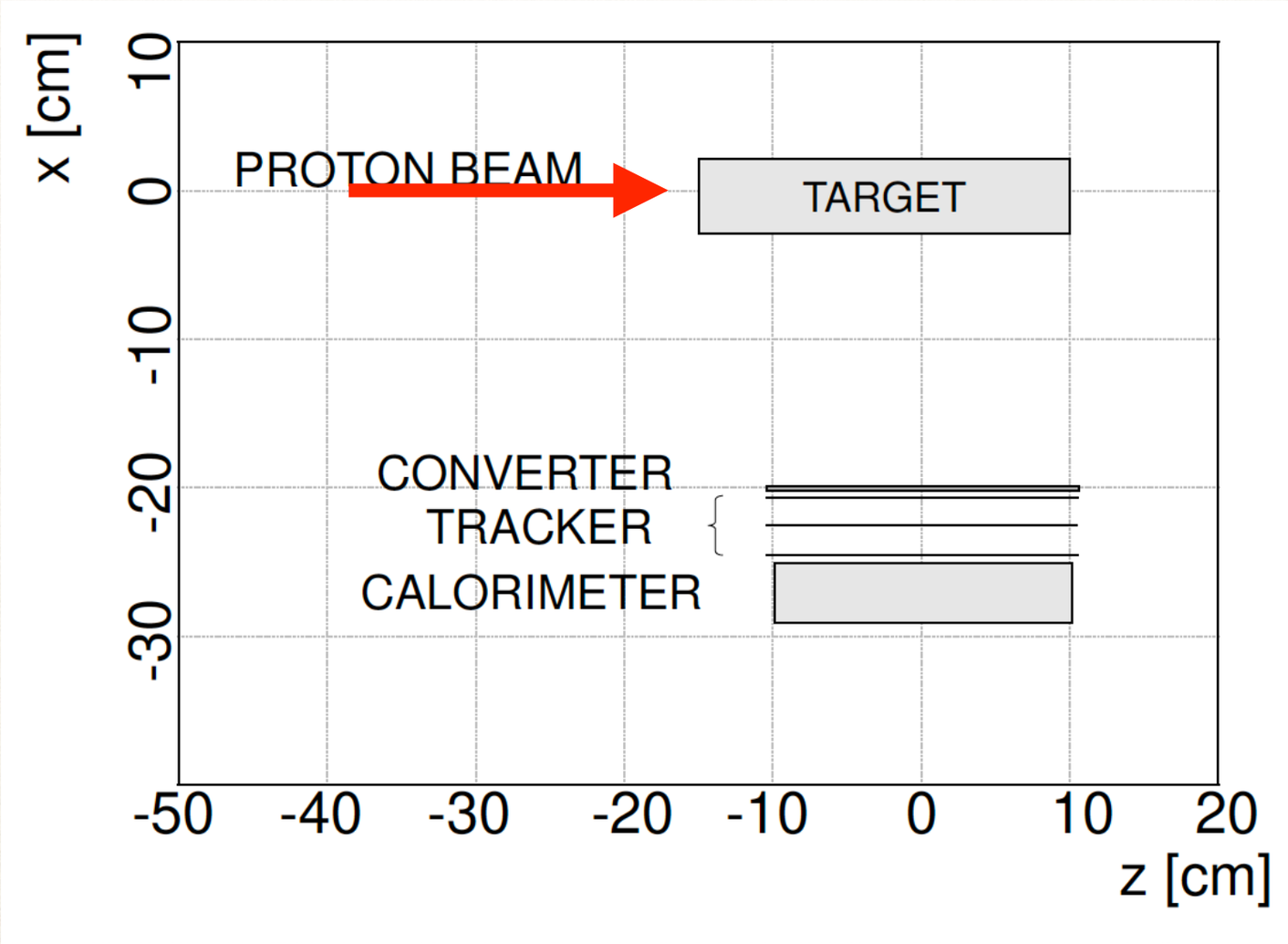
- The **detector geometry has been optimised** by exploiting MC (FLUKA) simulations
- In **MC**, lepton pairs are reconstructed as in a **real signal event** (energy loss, resolutions)
- Prompt photons **directions are reconstructed** exploiting the pair production kinematics and the emission points are obtained as the point of closest approach (POCA) between the photon and beam directions*



*Toppi, M. *et al., Front. Phys. 9:568139* (2021) **https://doi.org/10.3389/fphy.2021.568139**

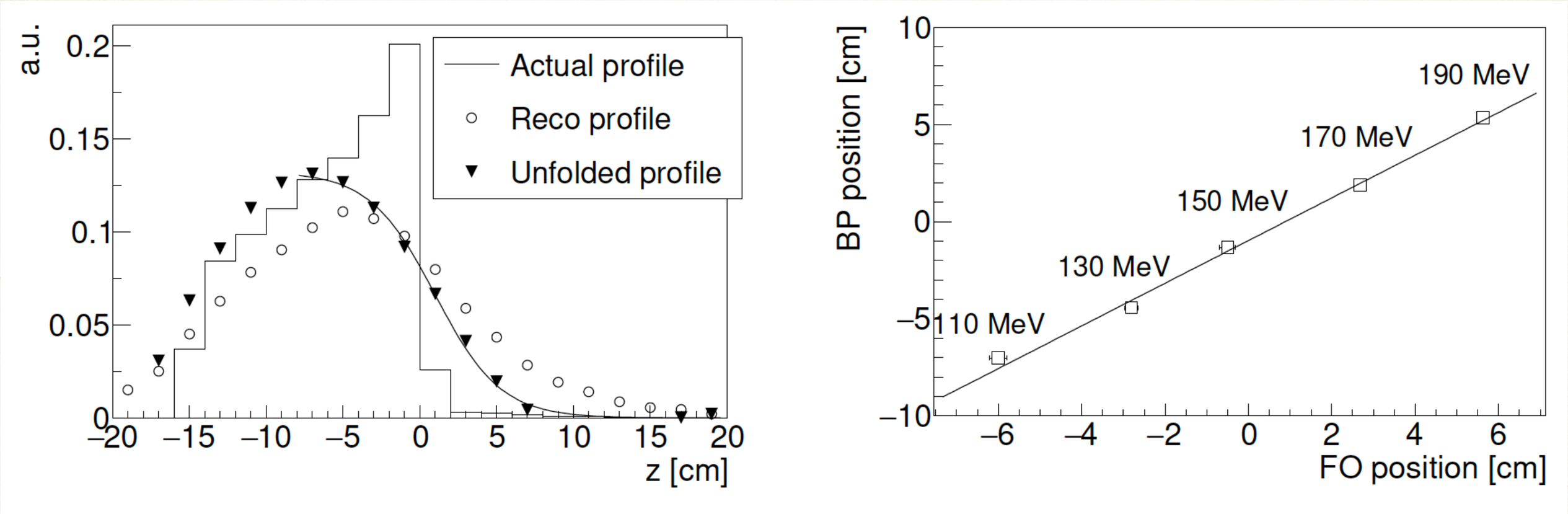
Resolution Study (MC)

- A simulation of a 160 MeV proton beam impinging on a PMMA ($C_5O_2H_8$) target has been performed



Resolution Study (MC)

- A simulation of a 160 MeV proton beam impinging on a PMMA ($C_5O_2H_8$) target has been performed
- An **unfolding procedure** to retrieve the true emission position was needed due to a bias in the 1D reconstruction and a **calibration** to evaluate the Bragg peak position (i.e. the beam range) was applied to reconstructed data*



*Calvi, G. *et al.*, *IL NUOVO CIMENTO 44 C (2021) 147* **https://doi.org/10.1393/ncc/i2021-21147-9**

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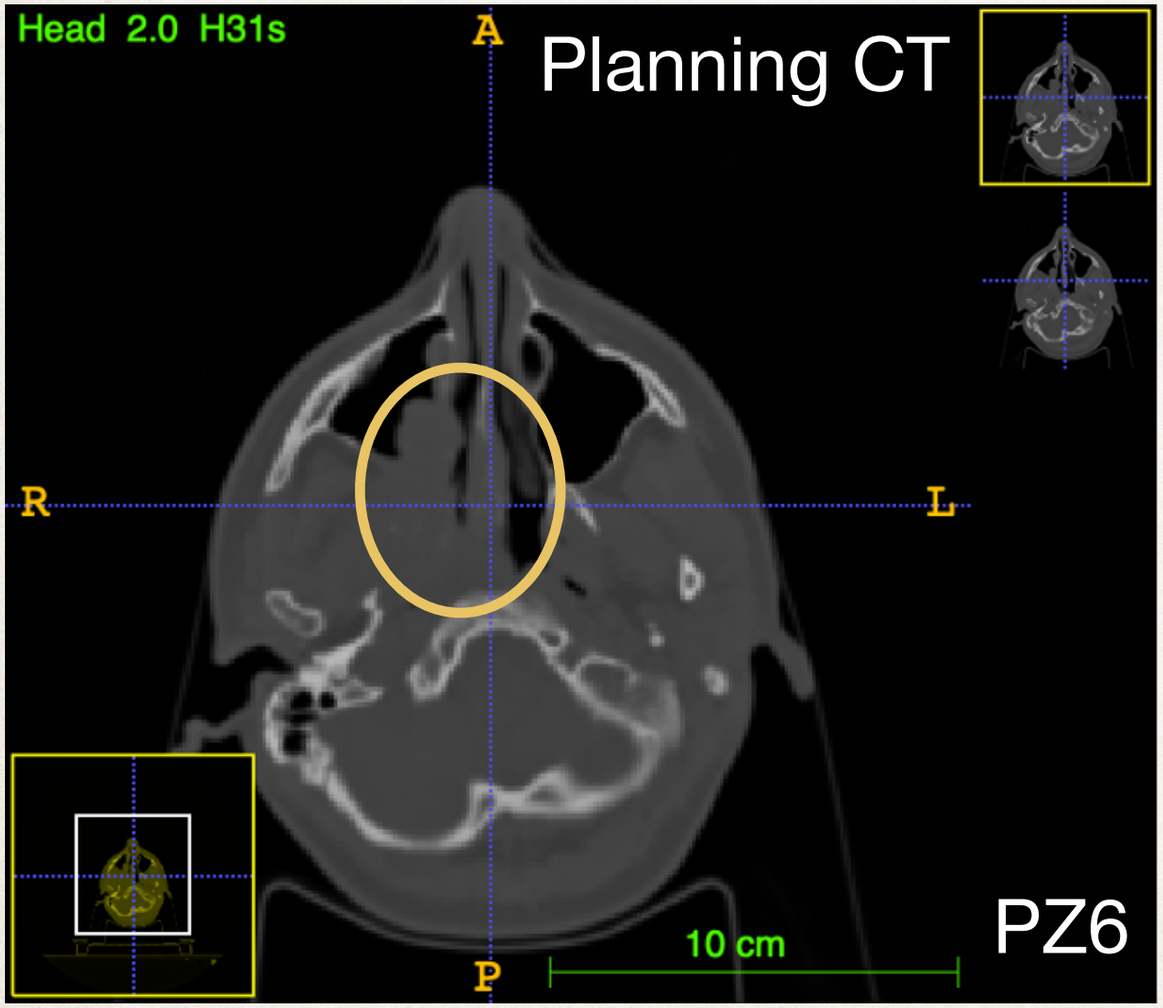
- The **accuracy** achieved in the measurement of the 160 MeV proton Bragg peak position is approximately **4 mm***

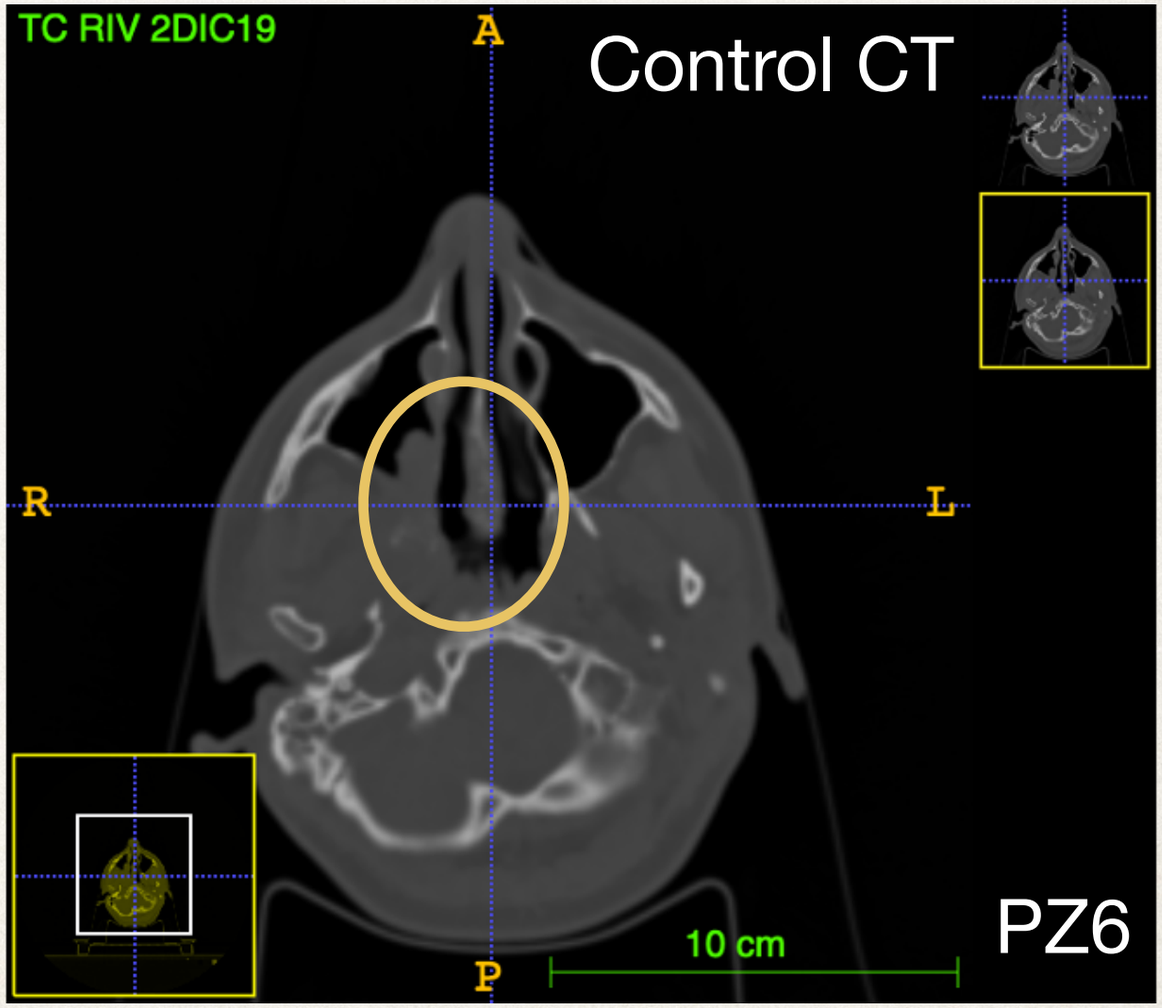
Promising result!

*Calvi, G. *et al., IL NUOVO CIMENTO 44 C (2021) 147* **https://doi.org/10.1393/ncc/i2021-21147-9**

3D Inter-fractional Monitoring (MC)

- A **Monte Carlo study** has been performed on a patient of the **clinical trial at CNAO**, treated with protons and monitored with the **INSIDE-PET system***. The patient had an Adenoid Cystic Carcinoma, where morphological changes occurred, spotted by the PET system and confirmed by the control CT.

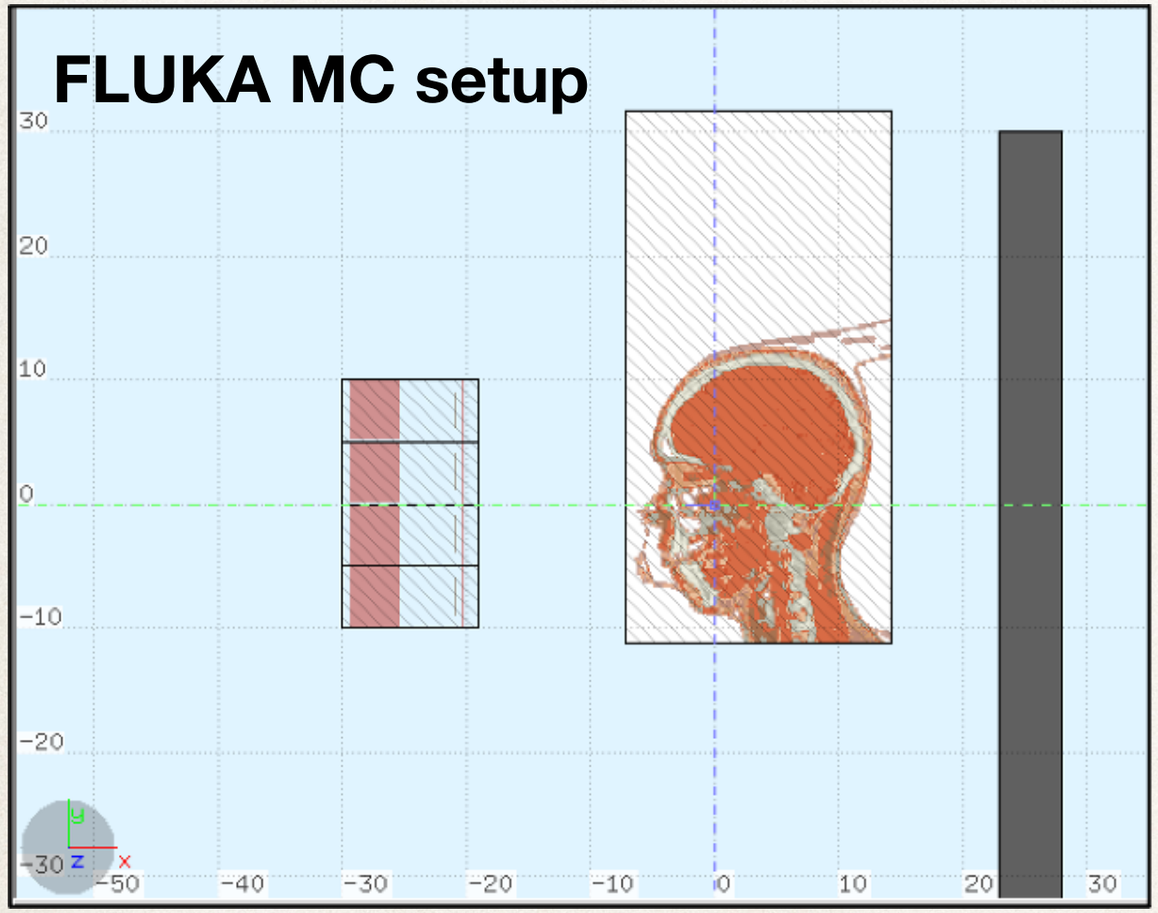


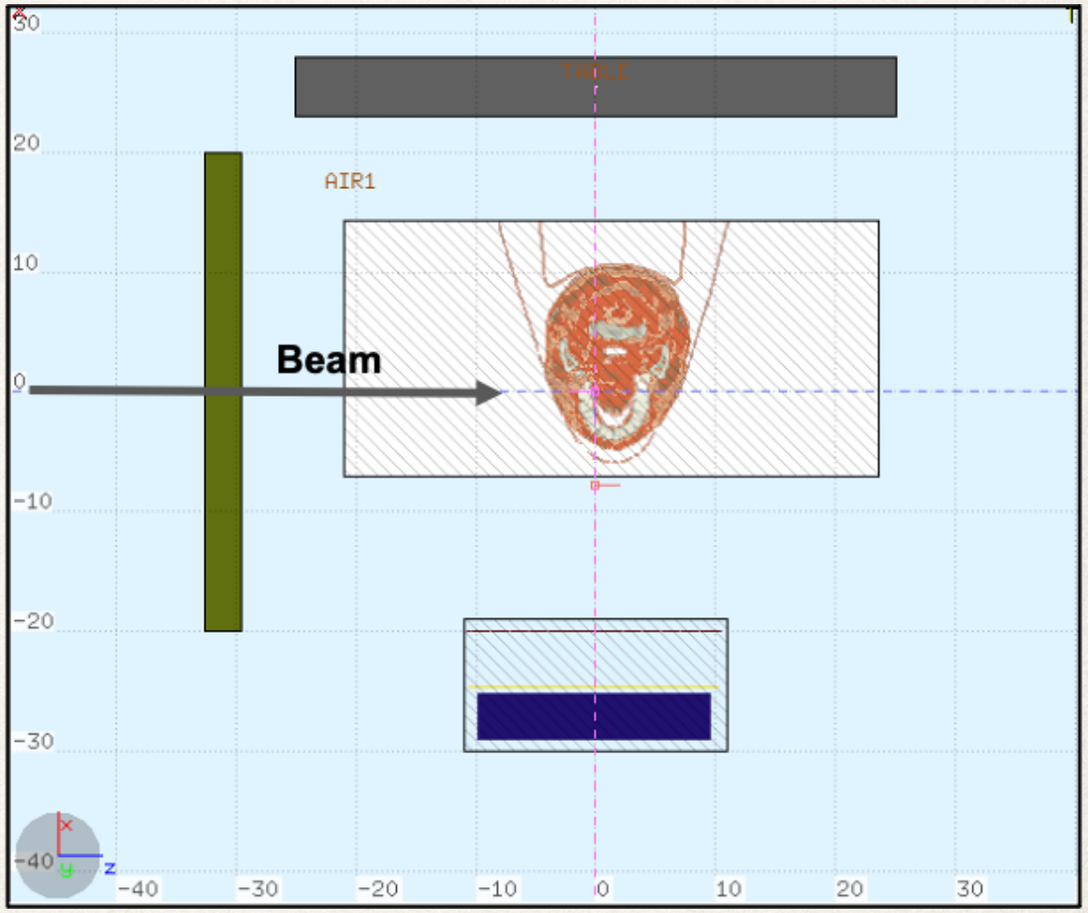


*Fiorina, E. *et al.*, *Frontiers in Physics* 8 (2021) 578388 **https://doi.org/10.3389/fphy.2020.578388**

3D Inter-fractional Monitoring (MC)

- PAPRICA has been simulated as 4 modules, to have a 1 sr detector
- 2 simulations (FLUKA) of the **full treatment delivered on the planning and control CT**





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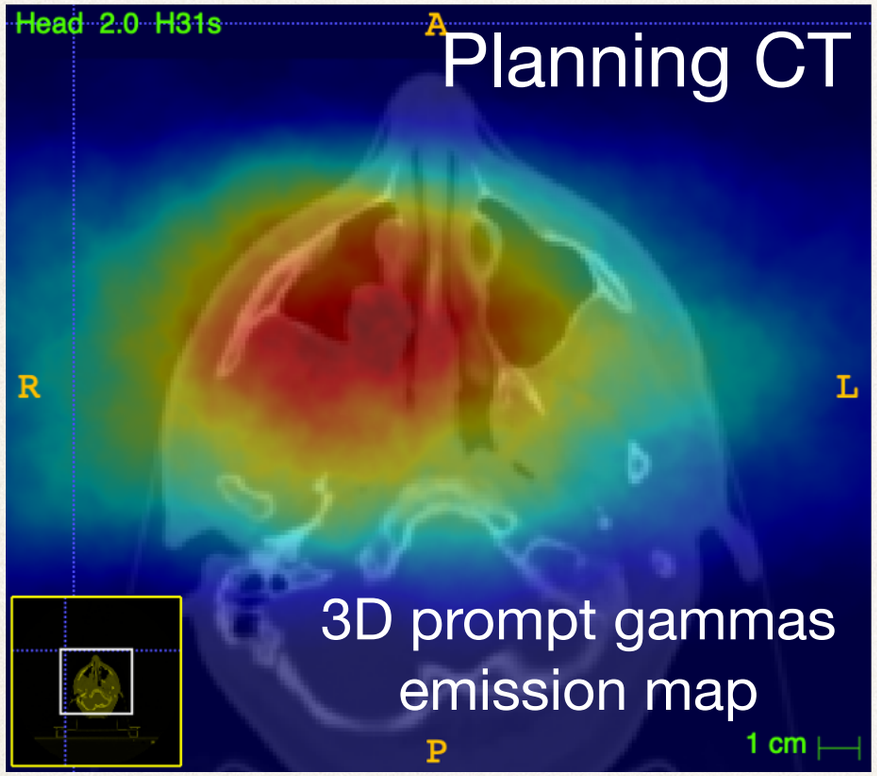
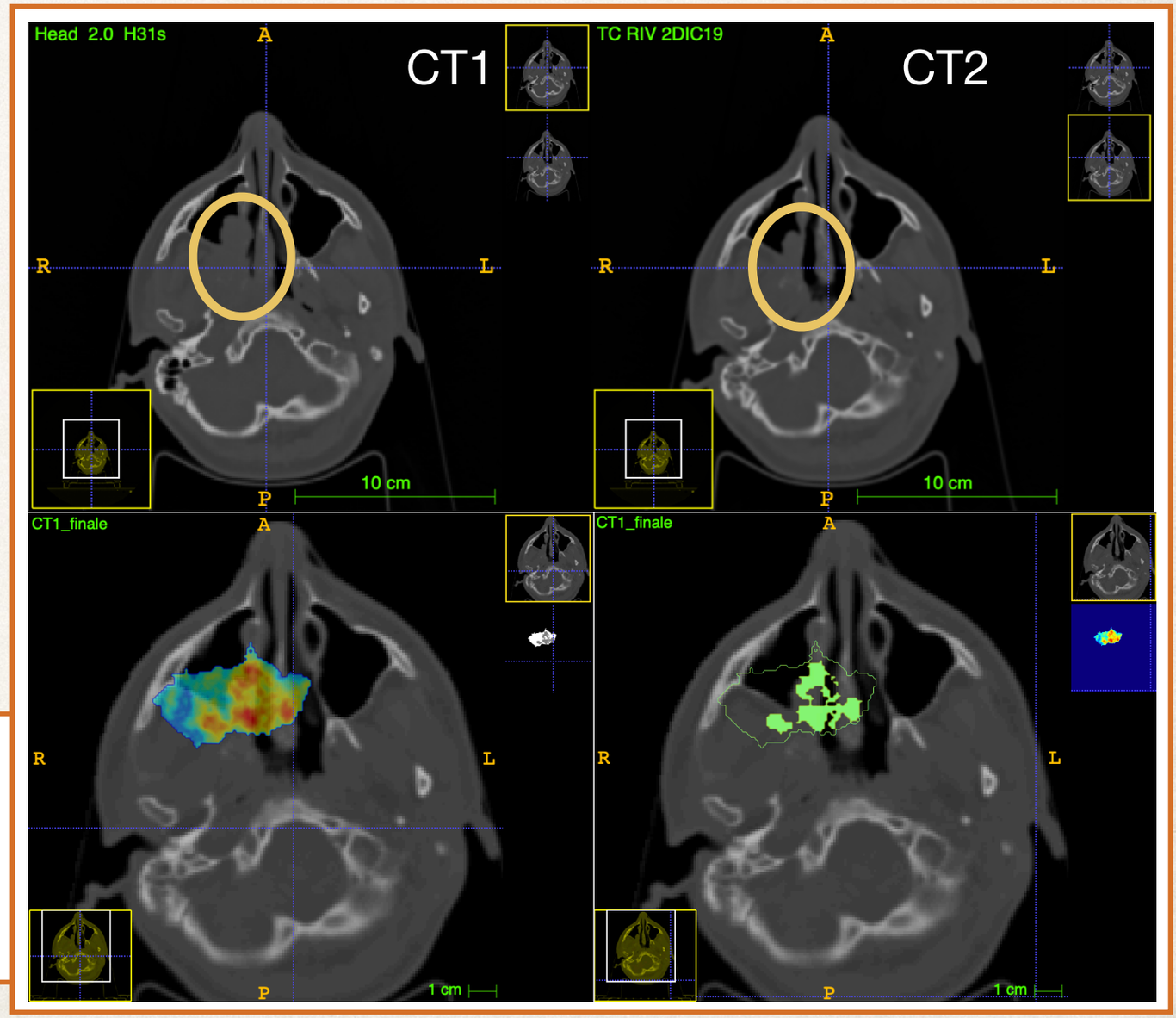


PZ6 underwent the emptying of the nasal cavity, as noticed by a mid-term CT (CT2). **Such modification has been clearly identified by the gamma-index map.**



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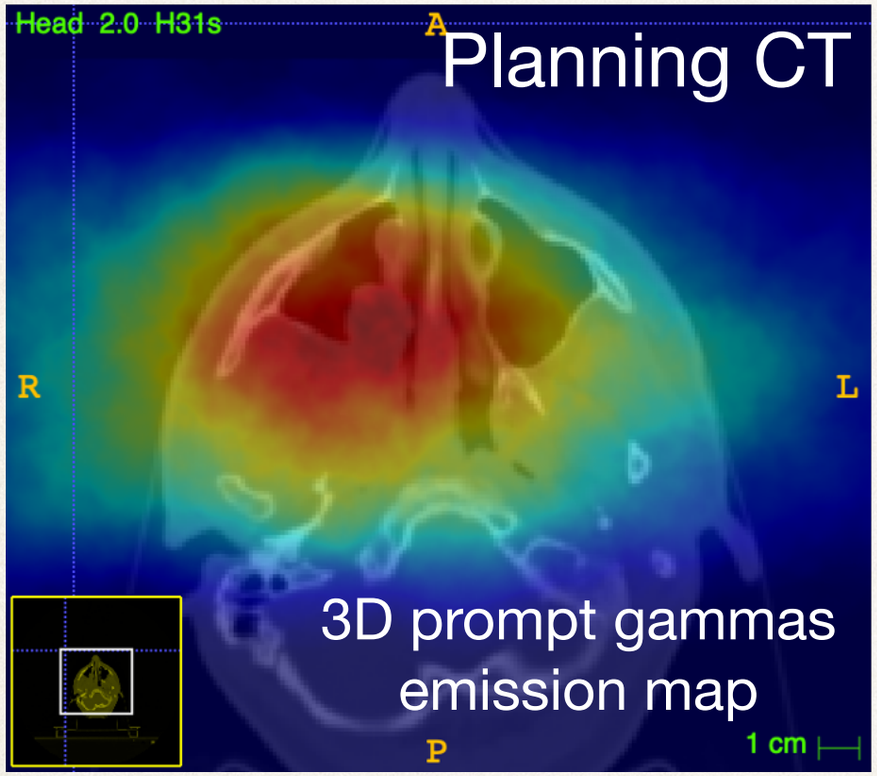

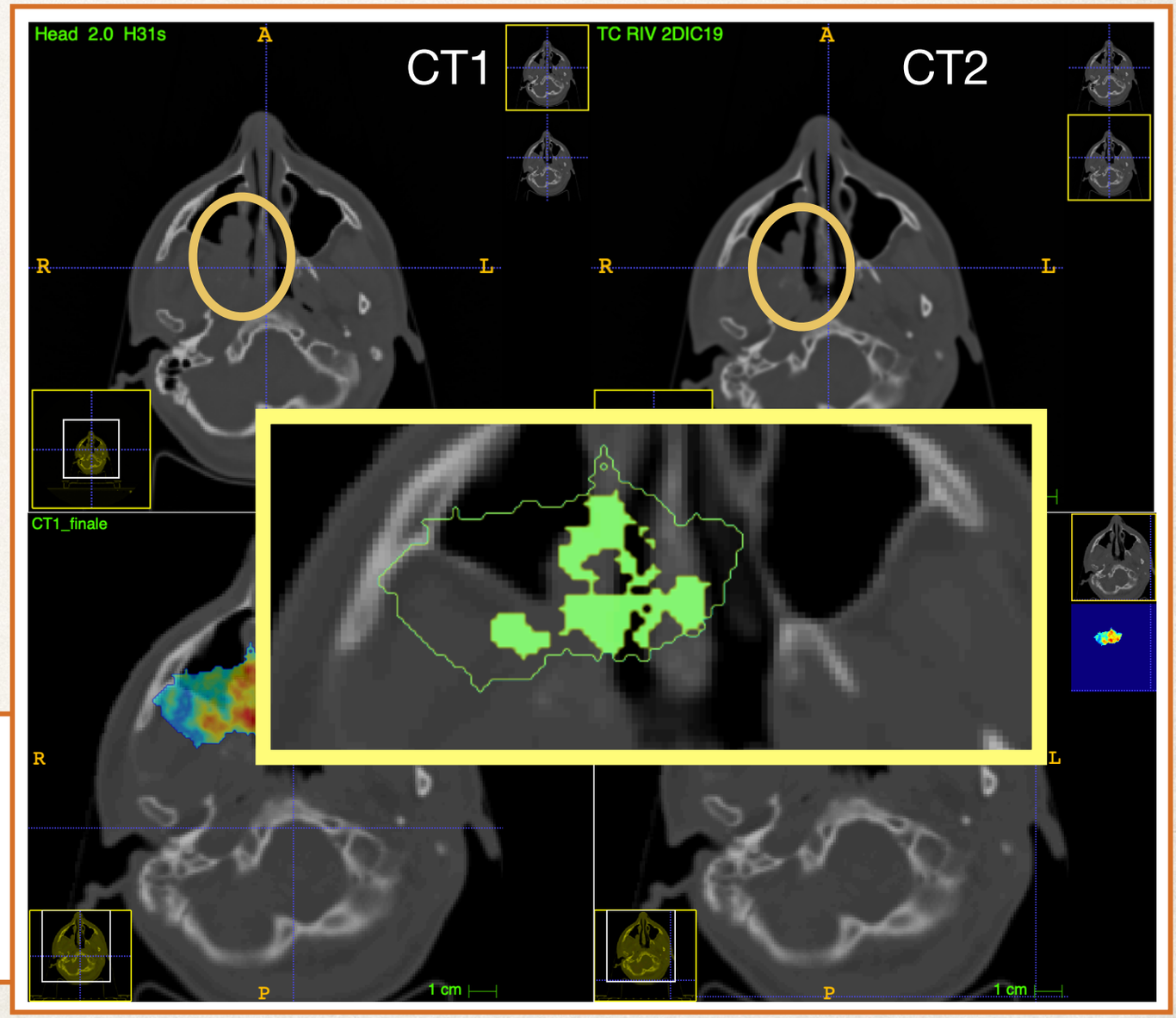

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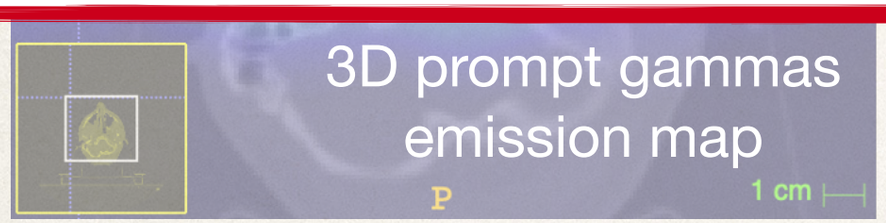
A study on the parameter of the gamma index test is going, to optimise the PAPRICA sensitivity to spot 3D morphological changes.

The detector is under construction and will be tested on beam in 2022.



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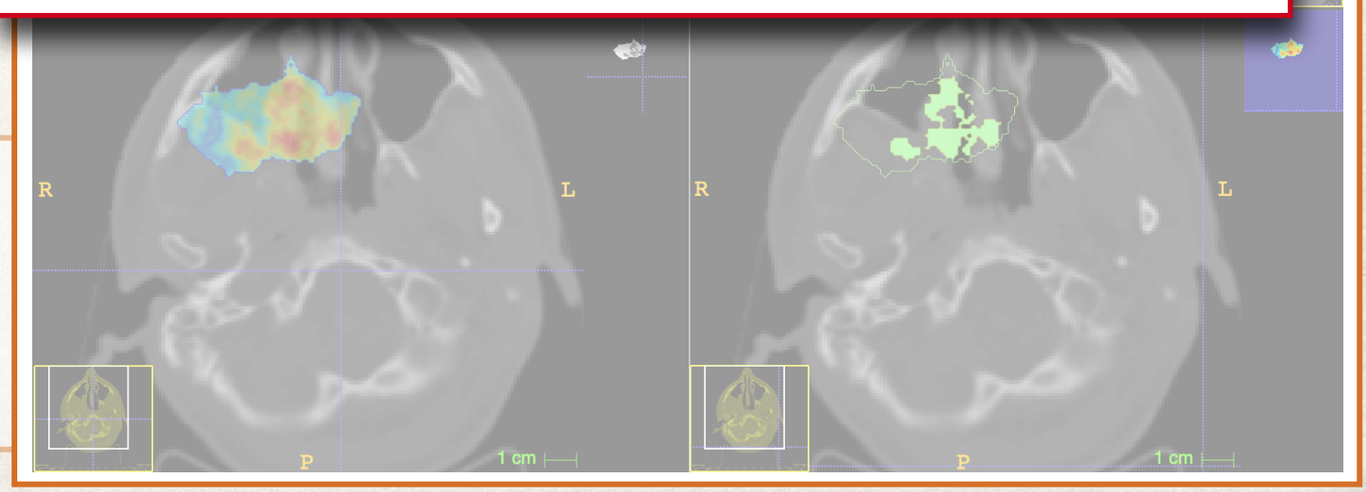


The FOOT experiment

The aim of the FOOT (FragmentatiOn Of Target) experiment* is to measure the nuclear fragmentation cross sections of interest in Particle Therapy and radioprotection in space.

The Collaboration

Aachen: Hetzel Ronja[3], Stahl Achim[3],

Bari: Galati Giuliana[29], Pastore Alessandra[29],

Bologna: Biondi Silvia[4,20], Bruni Graziano[4], Colombi Sofia[4], Franchini Matteo[4,20], Massimi Cristian[4,20], Mengarelli Alberto[4], Ridolfi Riccardo[4,20], Sartorelli Gabriella[4,20], Selvi Marco[4], Spighi Roberto[4], Villa Mauro[4,20], Zarrella Roberto[4,20], Zoccoli Antonio[4,20],

CEADEN: Arteche Diaz Raul[30], Lopez Torres Ernesto[30,17],

CNAO: Meneghetti Alessio[5], Pullia Marco[5], Savazzi Simone[5],

Frascati: Clozza Alberto[7], Iarocci Enzo[7], Laurenza Martina[7], Sanelli Claudio[7], Sciubba Adalberto[7,22], Spiriti Eleuterio[7], Tomassini Sandro[7], Toppi Marco[7,22],

GSI: Durante Marco[6,32], Reidel Claire-Anne[6], Schuy Christoph[6], Weber Ulrich[6],

GSSI: Gentile Valerio[31],

Milano: Battistoni Giuseppe[8], Dong Yunsheng[8,23], Mattei Ilaria[8], Muraro Silvia[8], Valle Serena Marta[8],

Nagoia: Sato Osamu[9],

Napoli: Alexandrov Andrey[10,19,33,34], De Lellis Giovanni[10,19], Di Crescenzo Antonia[10,19], Lauria Adele[10,19], Montesi Maria Cristina[10,19], Valeri Tioukov[10],

Perugia: Alpat Behcet[11], Ambrosi Giovanni[11], Barbanera Mattia[11], Fiandrini Emanuele[11,24], Ionica Maria[11], Kanxheri Keida[11], Placidi Pisana[11,25], Servoli Leonello[11], Silvestre Gianluigi[11,24],

Pisa: Belcari Nicola[2,1], Bisogni Maria Giuseppina[2,1], Carra Pietro[2,1], Ciarrocchi Esther[2,1], Del Guerra Alberto[2,1], Francesconi Marco[2,1], Galli Luca[1], Kraan Aafke Christine[1], Massa Maurizio[1], Moggi Andrea[1], Morrocchi Matteo[1,2], Rosso Valeria[2,1], Sportelli Giancarlo[2,1],

Roma: De Simoni Micol[12,26], Fischetti Marta[12,22], Franciosini Gaia[12,26], Marafini Michela[12,21], Patera Vincenzo[12,22], Sarti Alessio[12,22], Schiavi Angelo[12,22], Traini Giacomo[12,26],

Roma Tor V.: Morone Maria Cristina[13,27],

Strasbourg: Finck Christian[14], Sécher Alexandre[14], Vanstalle Marie[14],

Trento: Bellinzona Elettra[15], Di Ruzza Benedetto[15], La Tessa Chiara[15,16], Scifoni Emanuele[15], Tommasino Francesco[15,16],

Torino: Argirò Stefano[28,17], Bartosik Nazar[17], Cavanna Francesca[17], Cerello Piergiorgio[17], Donetti Marco[17,5], Ferrero Veronica[17], Fiorina Elisa[17], Giraudo Giuseppe[17], Pastrone Nadia[17], Pennazio Francesco[17], Ramello Luciano[18,17], Scavarda Lorenzo[28,17], Sitta Mario[18,17],

*Battistoni, G. *et al., Frontiers in Physics 8 (2021) 568242* **https://doi.org/10.3389/fphy.2020.568242**

FOOT in Particle Therapy

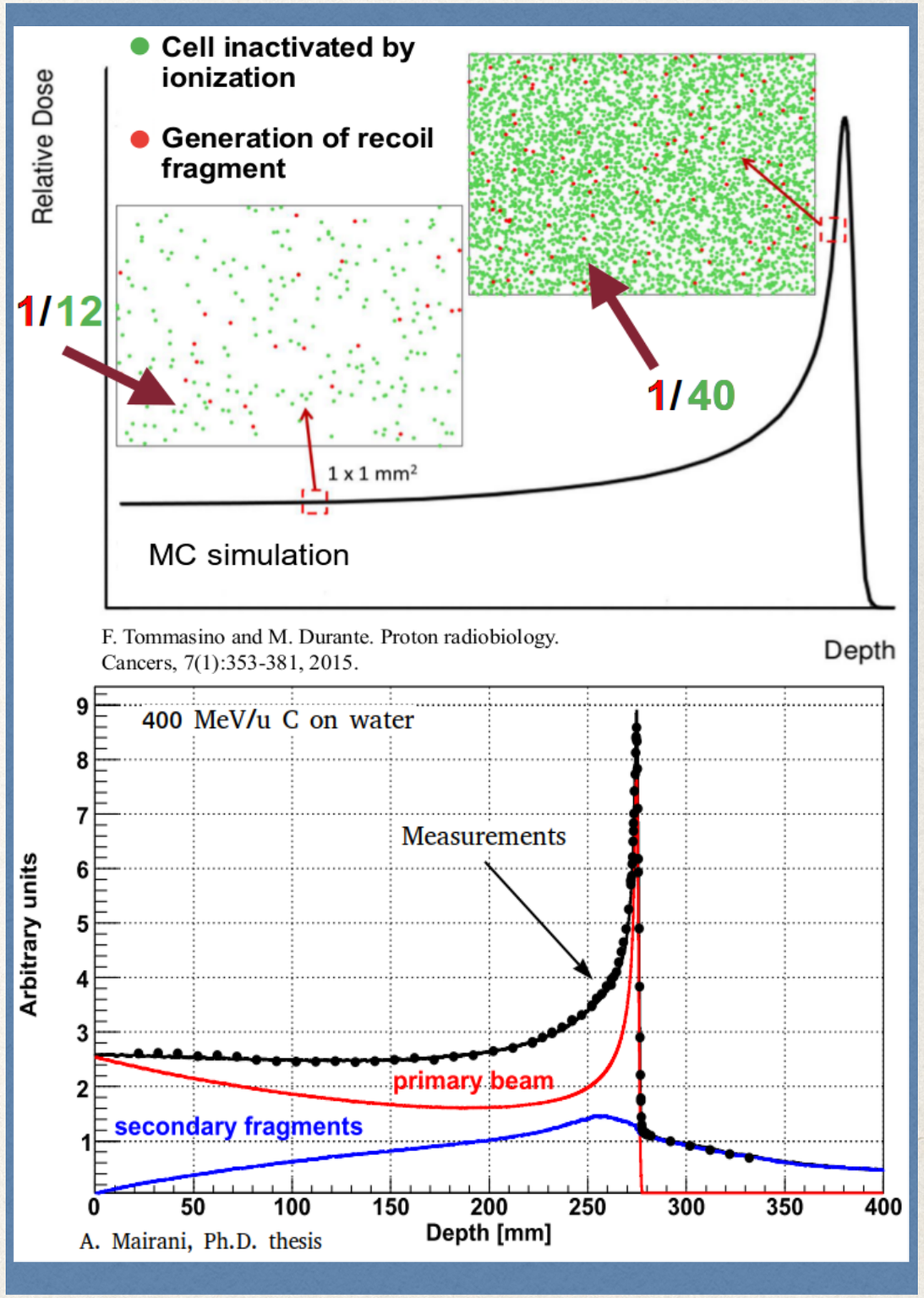
Target Fragmentation in proton therapy:

- Fragments with low ranges (~μm)
- Dose deposition in beam entrance channel

Projectile fragmentation in heavy ion therapy:

- Fragments with similar direction and velocity of primaries, but with lower mass
- Dose deposition beyond the Bragg peak

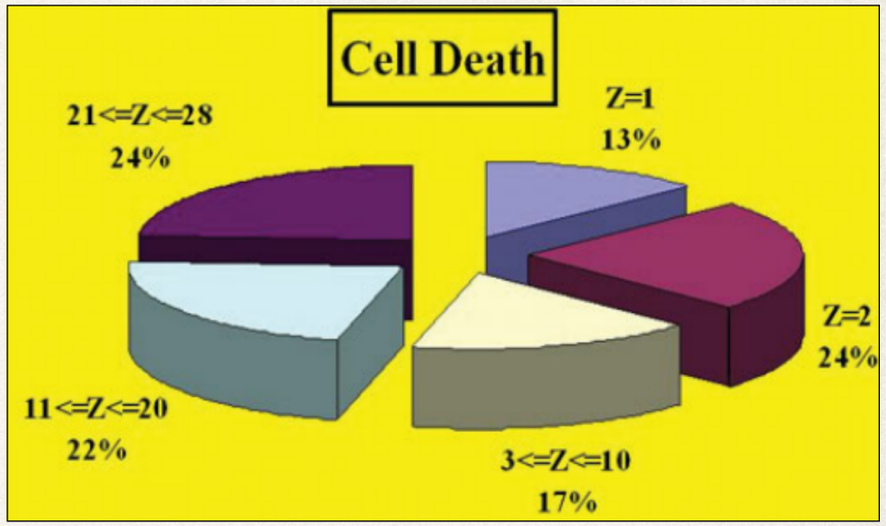
Need of fragmentation cross sections to benchmark MC tools and to improve the nuclear interaction models adopted in the current treatment planning systems (TPS)



FOOT in Radioprotection in Space

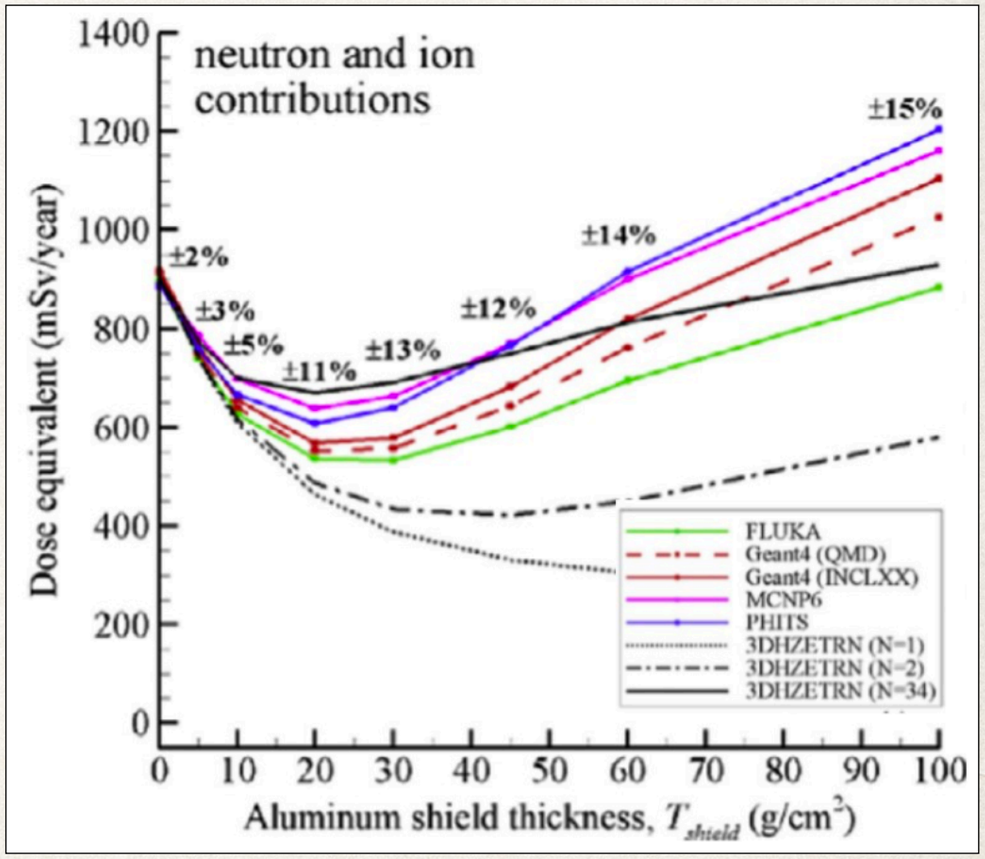
Main radiation hazards in future long term and far from Earth space missions to Moon and Mars:

- Galactic cosmic radiations ($E<10^{20}$ eV) and Solar particles events ($E<10^{5}$ eV)
- Particle species: H~85-90%, He~10-14%, Z>2~1%



High contribution to the equivalent dose from:

- Primary light ions (mainly He) and fragments produced by primary high Z and Energy particles
- Secondary neutrons that can penetrate deeply



Slaba T. C. et al, Life Sciences in Space Research 12 (2017) 1–15
doi:10.1016/j.lssr.2016.12.003

Large discrepancies between transport codes, mainly for light fragments and neutrons

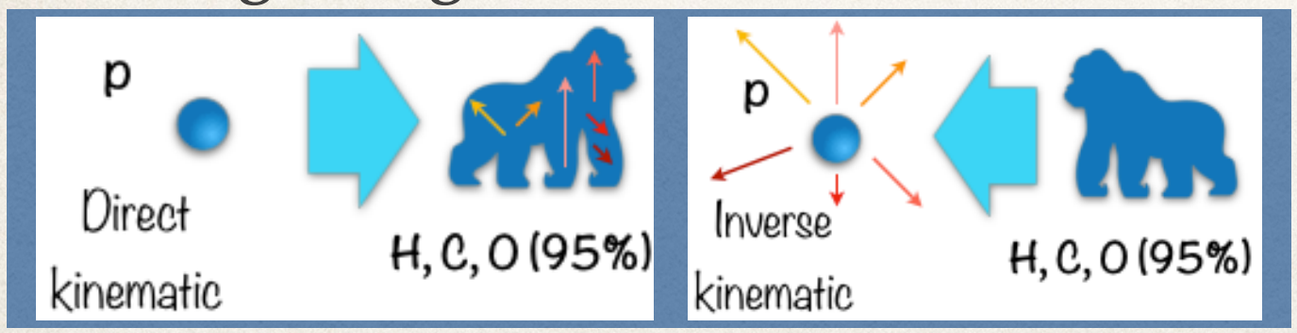
Measurement Strategy

Target material

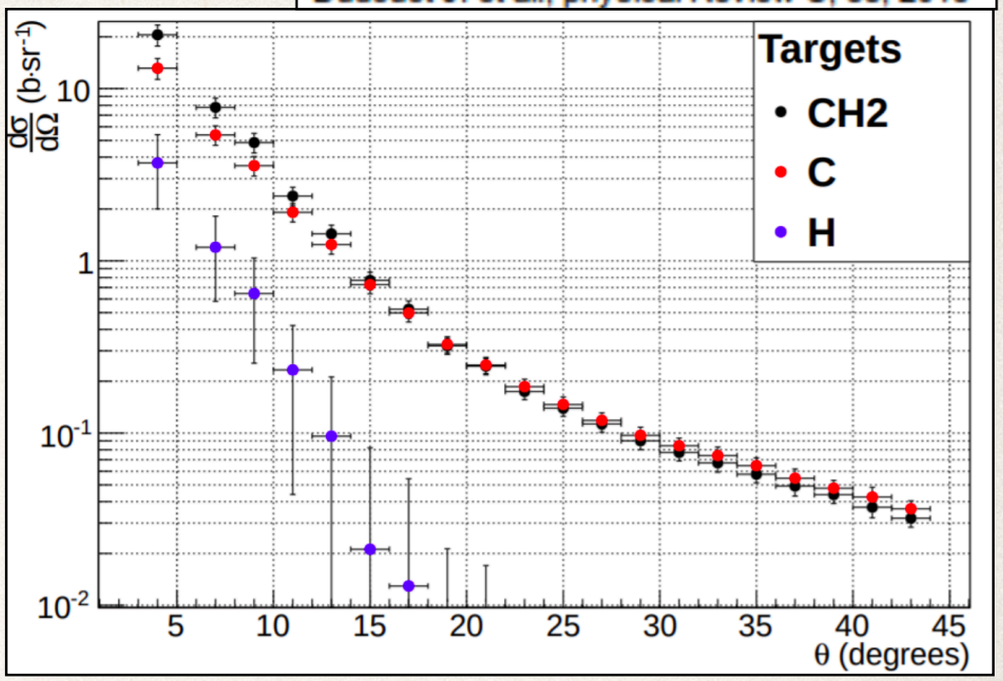
- Body composition: ^{16}O (61%), ^{12}C (23%), H (10%)
- Difficulties with gaseous target of ^{16}O and H
- **Use of C, CH_2 and PMMA targets**

Target fragmentation measurements

- Target fragments produced in proton therapy have ranges of ~ μm
- Technical difficulties for a direct detection
- **Use of an inverse kinematic approach for the target fragmentation measurements**



Dudouet J. et al., physical Review C, 88, 2013



Expected average physical parameters for target fragments produced in water by a 180 MeV proton beam

Fragment	E (MeV)	LET (keV/μm)	Range (μm)
^{15}O	1.0	983	2.3
^{15}N	1.0	925	2.5
^{14}N	2.0	1137	3.6
^{13}C	3.0	951	5.4
^{12}C	3.8	912	6.2
^{11}C	4.6	878	7.0
^{10}B	5.4	643	9.9
^{8}Be	6.4	400	15.7
^{6}Li	6.8	215	26.7
^{4}He	6.0	77	48.5
^{3}He	4.7	89	38.8
^{2}H	2.5	14	68.9

GoodHead D.T., Radiation protection dosimetry, 122, 2006

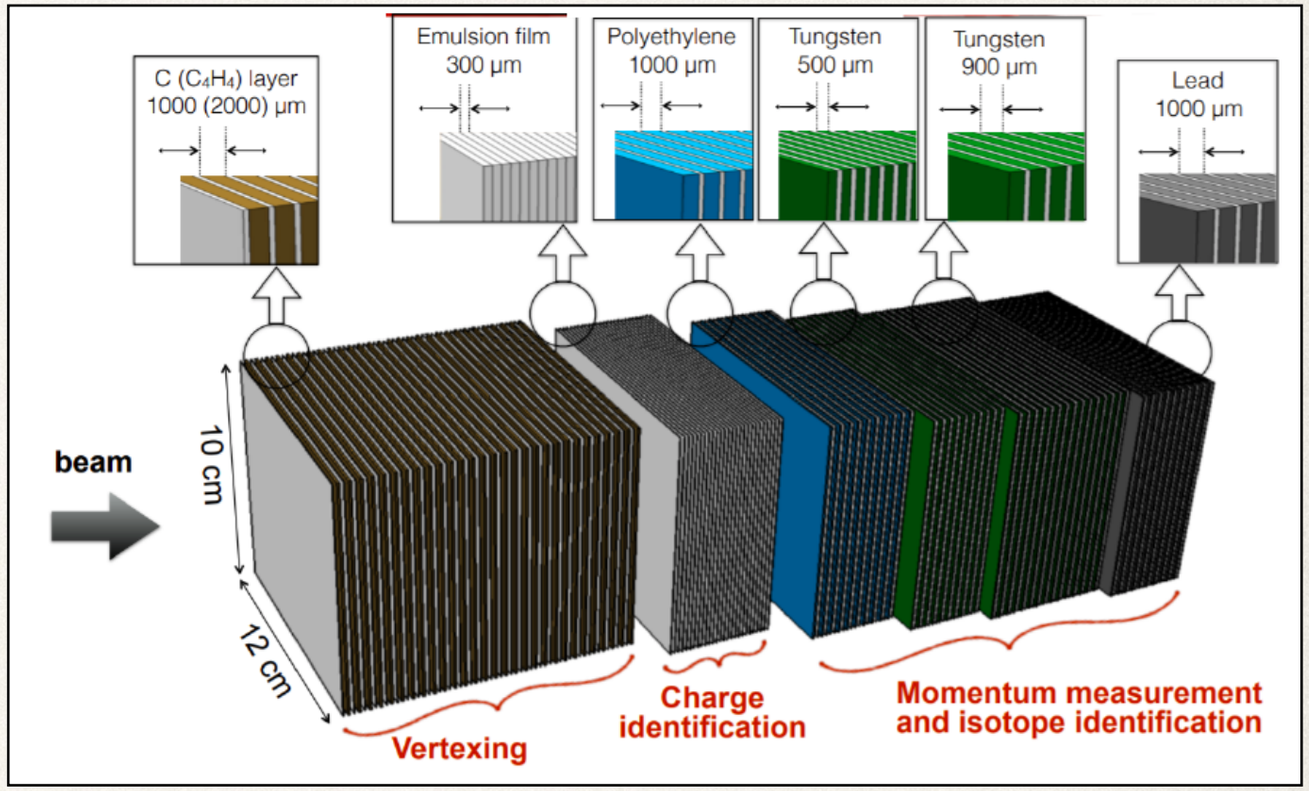
The Emulsion Spectrometer

The emulsion spectrometer is a compact detector realised with the technology adopted in the OPERA experiment.

Emulsion Cloud Chamber adopted to detect the fragments with Θ<70° and Z≤3

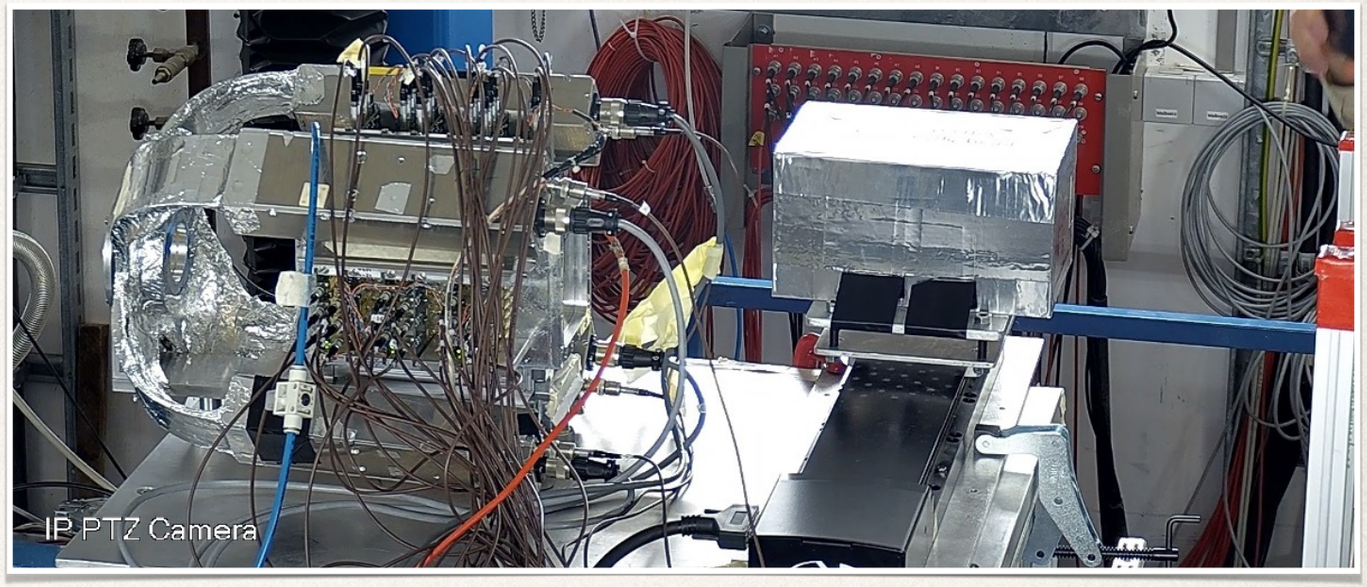
Detector composition:

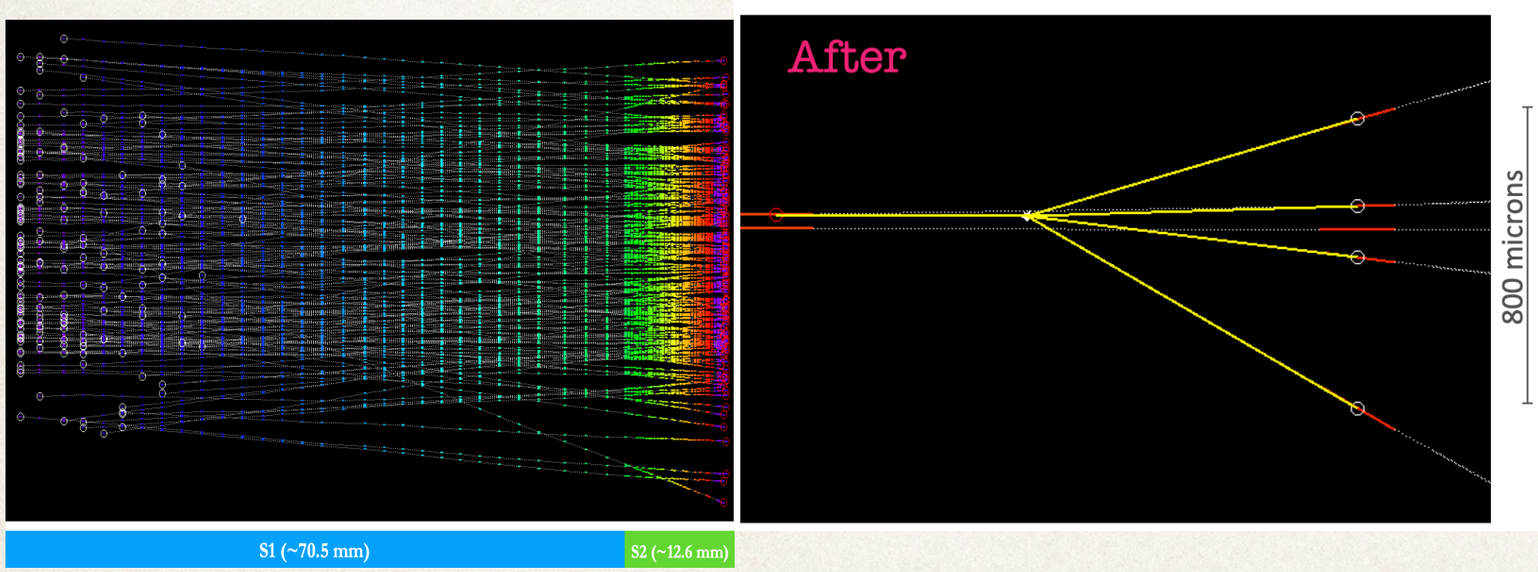
- **Vertexing region**: identify the nuclear interaction vertices
- **Charge id. region**
- **Absorbing region**: momentum and mass id. exploiting the track length and the Multiple Coulomb Scattering effect



The Emulsion Spectrometer

- Assessment of **detector performances***
- **Data taking at GSI** with ^{16}O @ 200-400 MeV/u on C and C_2H_4 (cross section evaluation ongoing)**

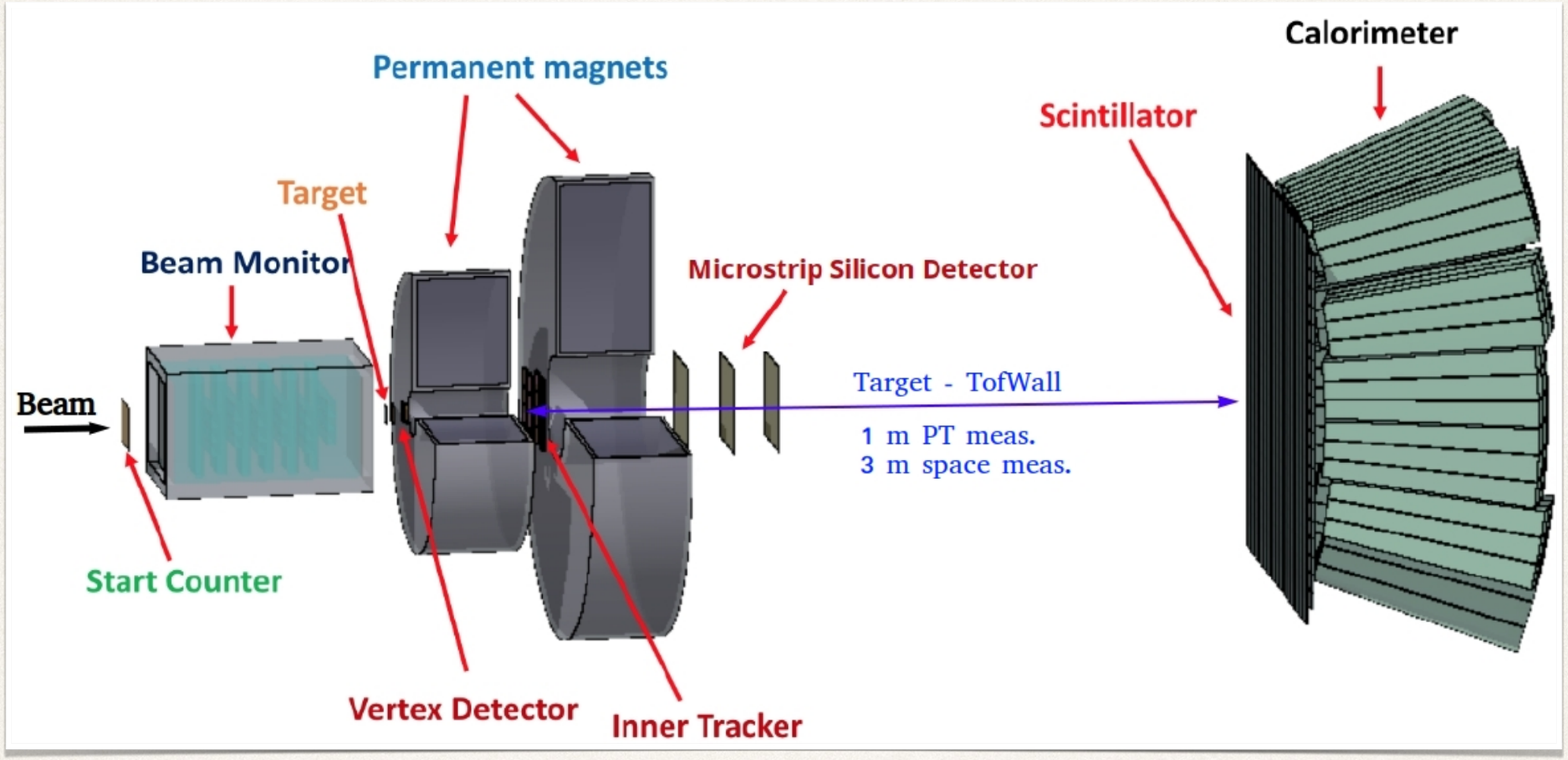




*Montesi, M.C. *et al., Open physics 17 (2019) 1* **https://doi.org/10.1515/phys-2019-0024**

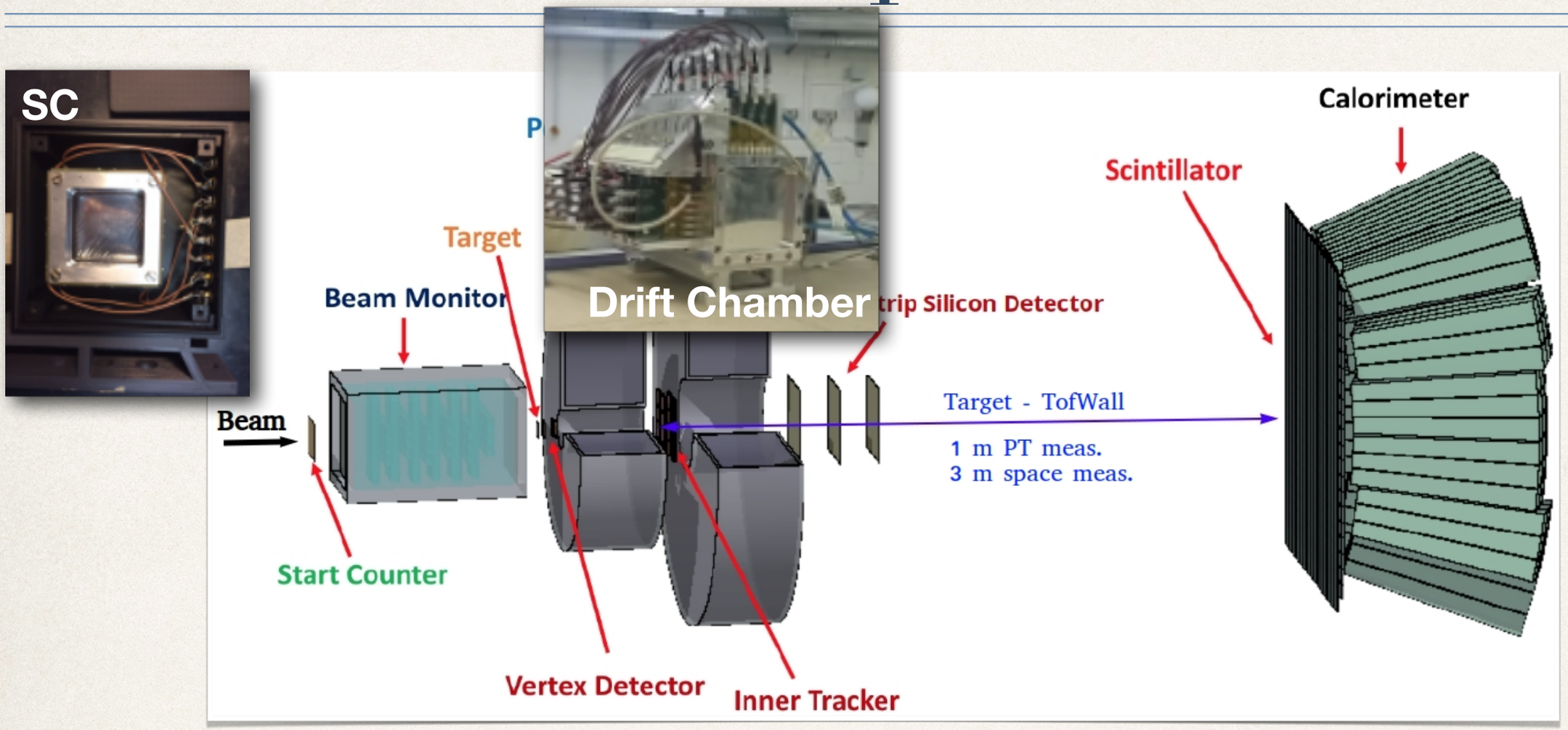
Galati, G. *et al., Open physics 19 (2021) 1* **https://doi.org/10.1515/phys-2021-0032

The Electronic Spectrometer



Different electronic sub detectors adopted to detect the fragments with $\Theta<10^{o}$ and $Z\geq3$

The Electronic Spectrometer

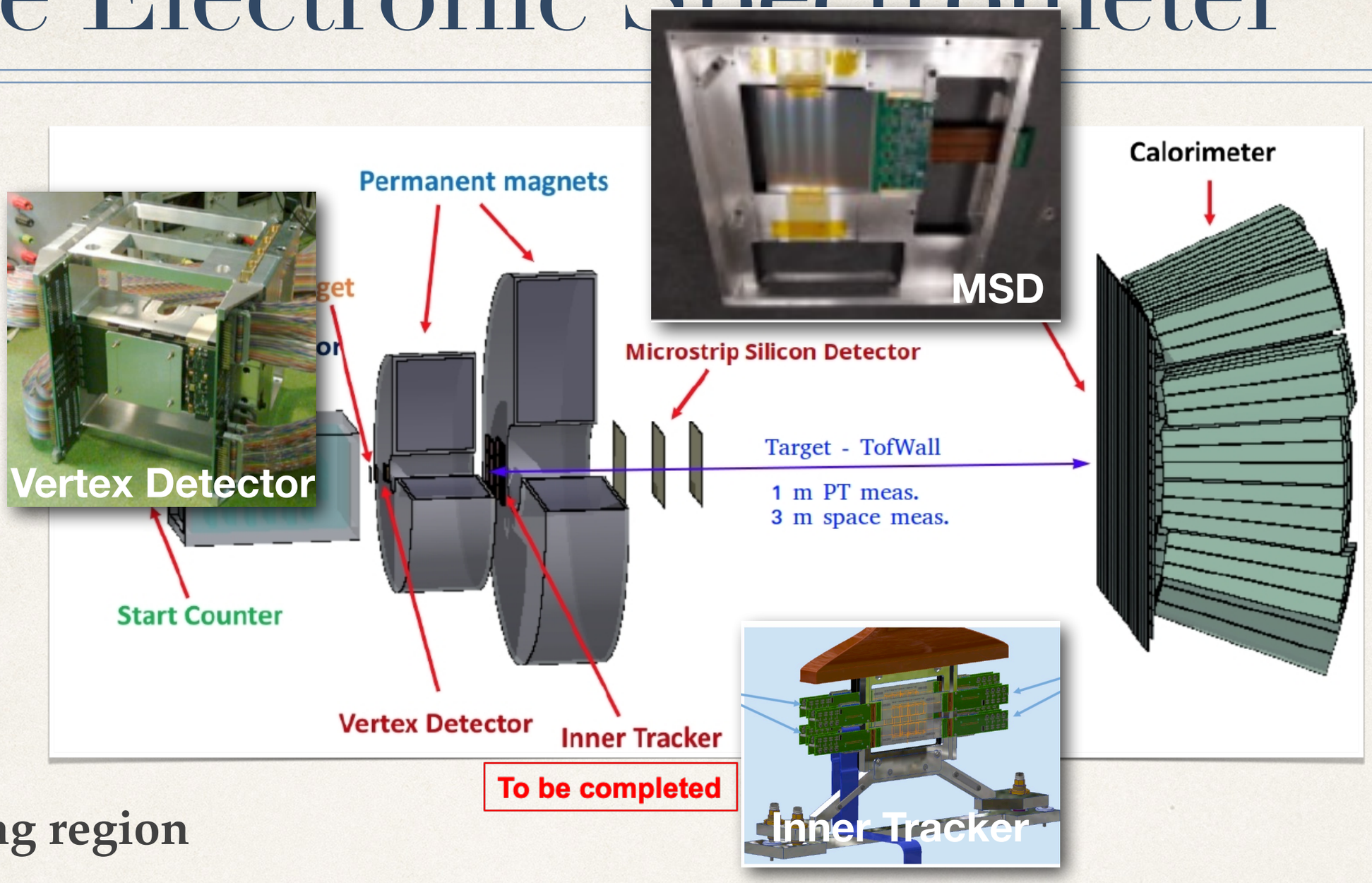


Pre target region

- Plastic scintillator: trigger and Time of Flight (TOF)
- Drift chamber: beam direction and position*

*Dong, Y. *et al.*, NIM A 986 (2021) 164786 https://doi.org/10.1016/j.nima.2020.164756

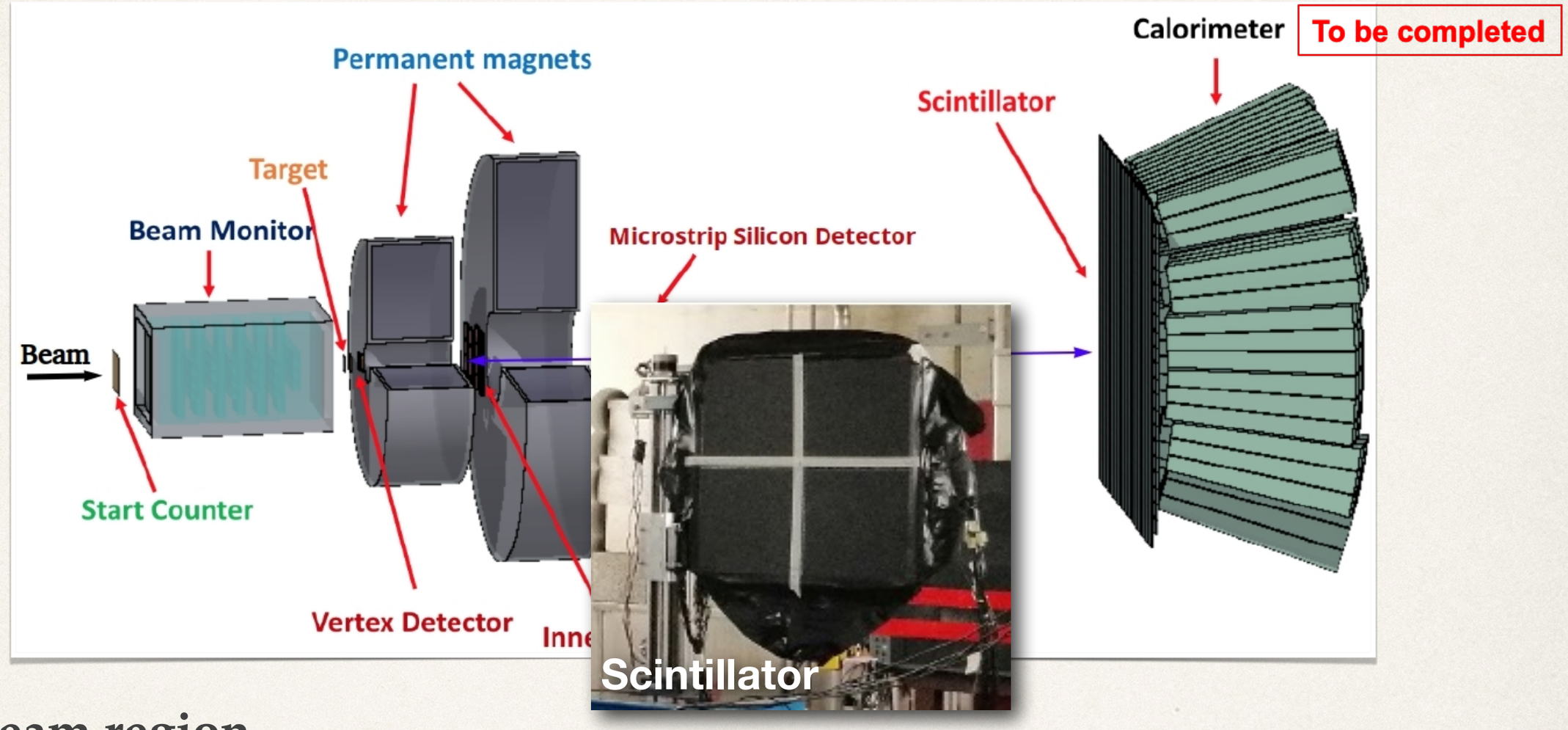
The Electronic Spectrometer



Tracking region

- Silicon pixel and strip detectors: particle momentum and track reconstruction
- Two permanent magnets in Halbach configuration: provide up to 1.4 T perpendicular to the beam axis

The Electronic Spectrometer



Downstream region

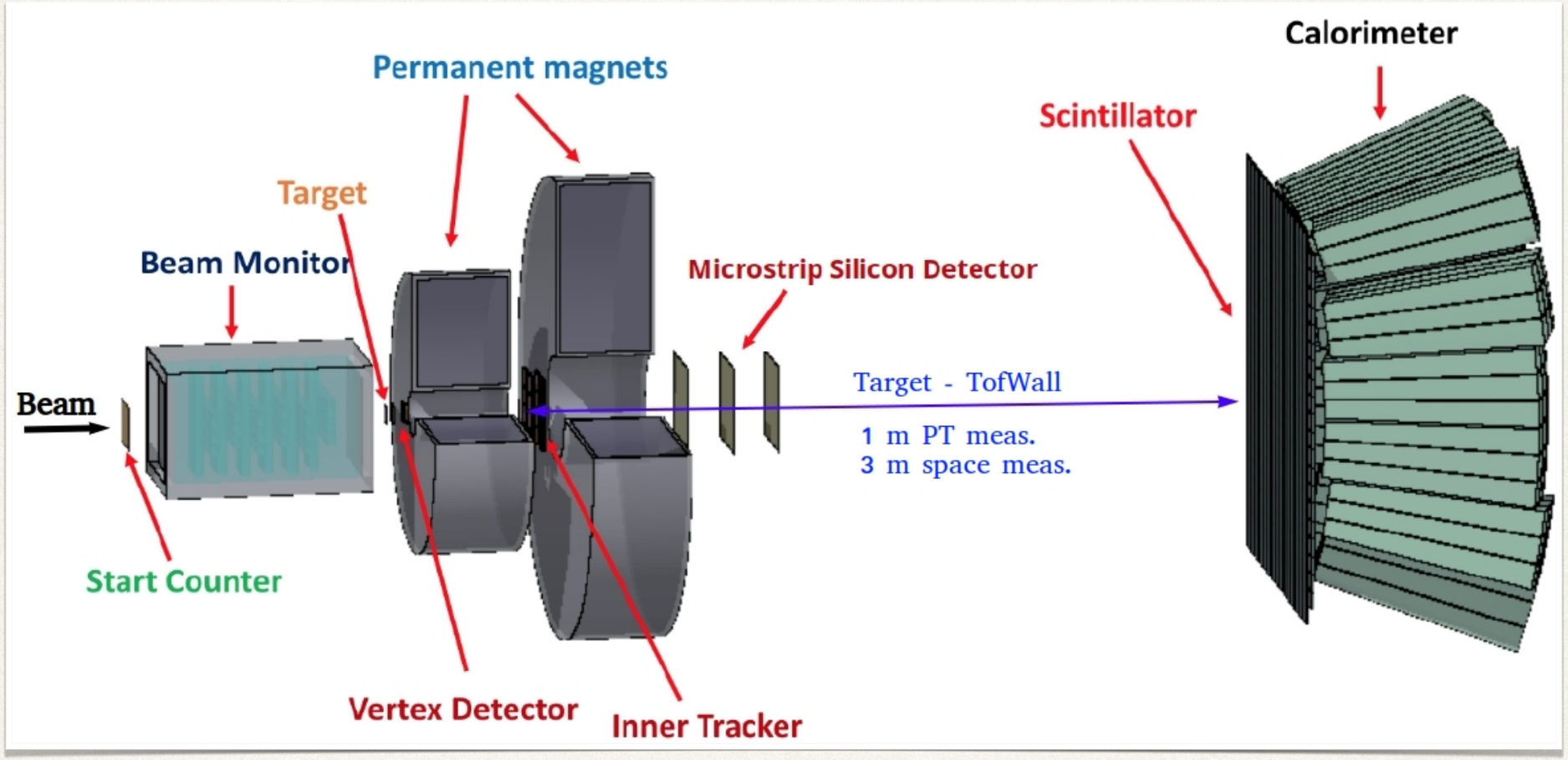
- Plastic scintillator bars: dE/dx and TOF *,**,***
- Calorimeter: kinetic energy

*Galli, L. *et al.,* NIM A 953 (2020) 163146 https://doi.org/ 10.1016/j.nima.2019.163146

**Morrocchi, M. *et al.,* IEEE Trans. Nucl. Sci. 68 (2020) https://doi.org/10.1109/TNS.2020.3041433

***Kraan, A.C. *et al.,* NIM A 1001 (2021) 165206 https://doi.org/10.1016/j.nima.2021.165206

The Electronic Spectrometer



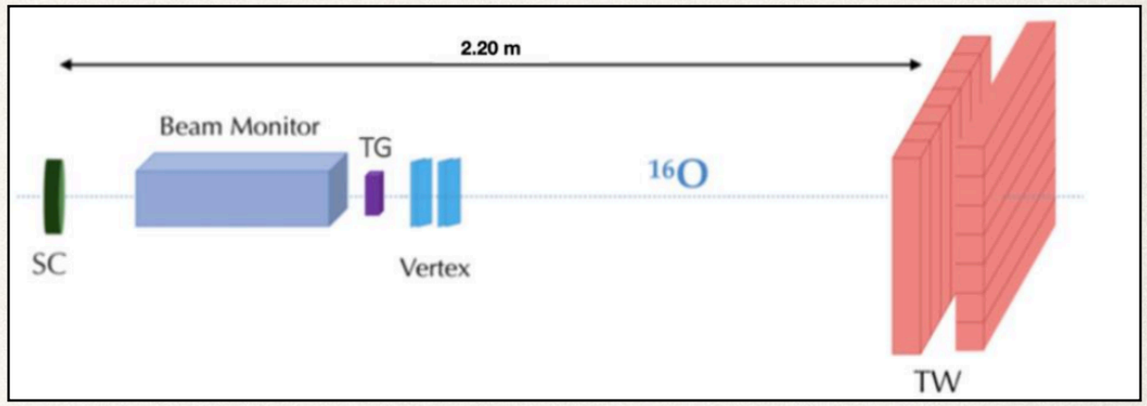
- Charge id: $\beta = L/(c \cdot TOF)$; $dE/dx \sim z^2 \cdot f(\beta)$
- Mass id: $A_1 = \frac{1}{u}\frac{P\sqrt{1-\beta^2}}{\beta}$; $A_2 = \frac{E_{kin}}{u} \cdot \frac{1+\sqrt{1+\gamma^2\beta^2}}{\gamma^2\beta^2}$; $A_3 = \frac{E_{kin}^2 - P^2}{2E_{kin}u}$

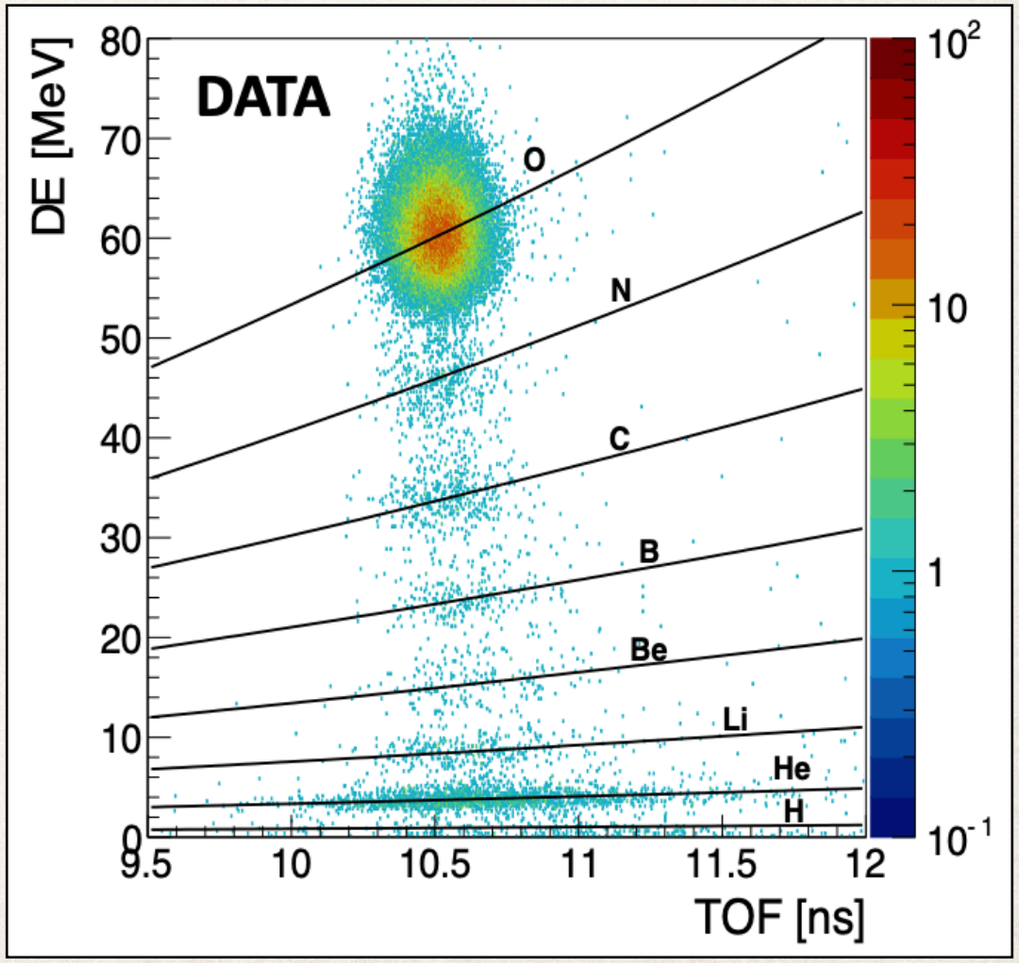
Electronic setup data taking

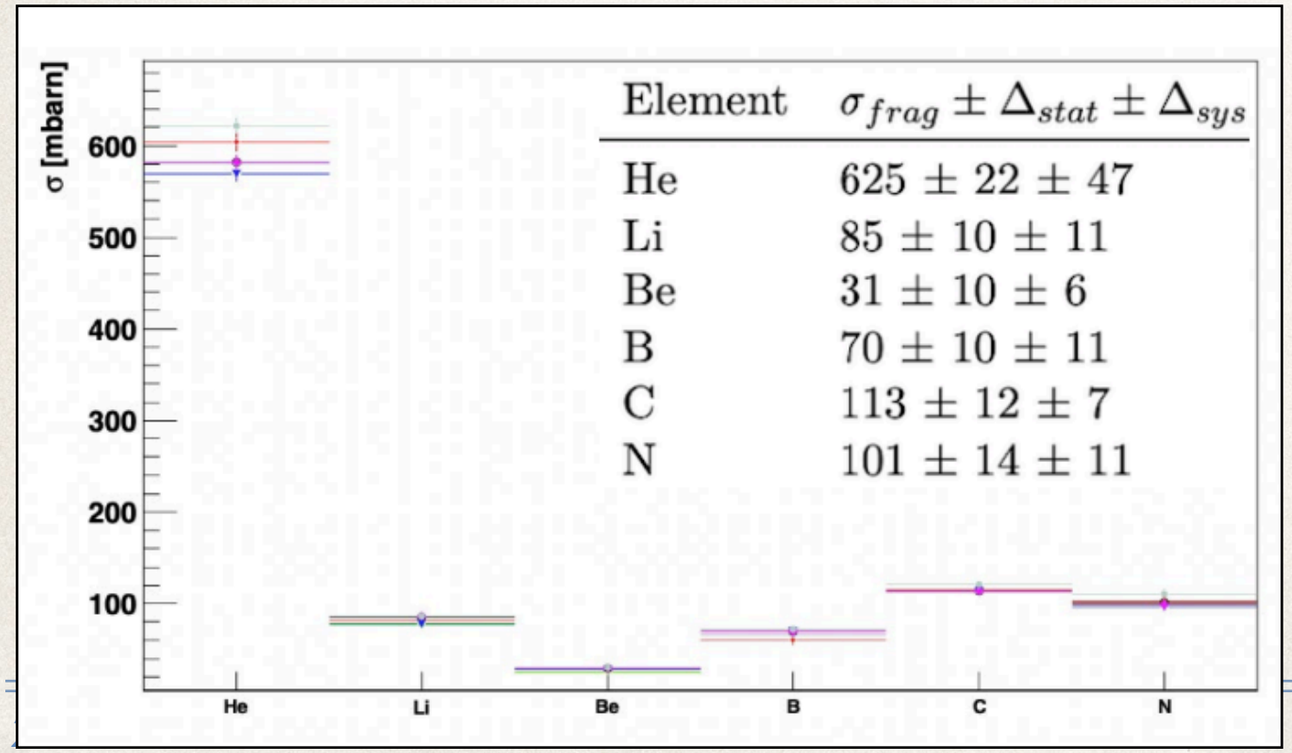
Characterisation completed for almost all the detectors.

First data taking at GSI with ^{16}O @ 400 MeV/u on C

- Scintillators, drift chamber and vertex detector
- TOF and dE/dx —> Total cross section meas.





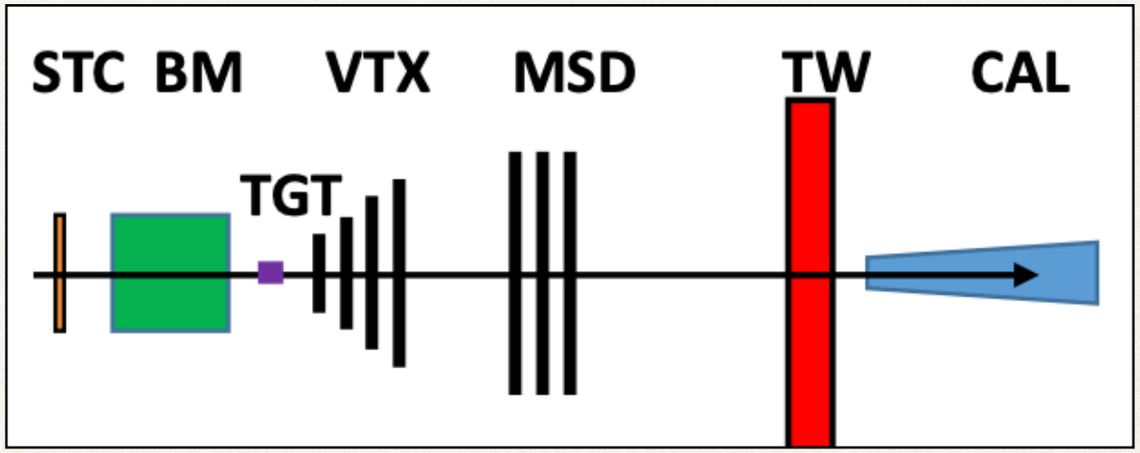


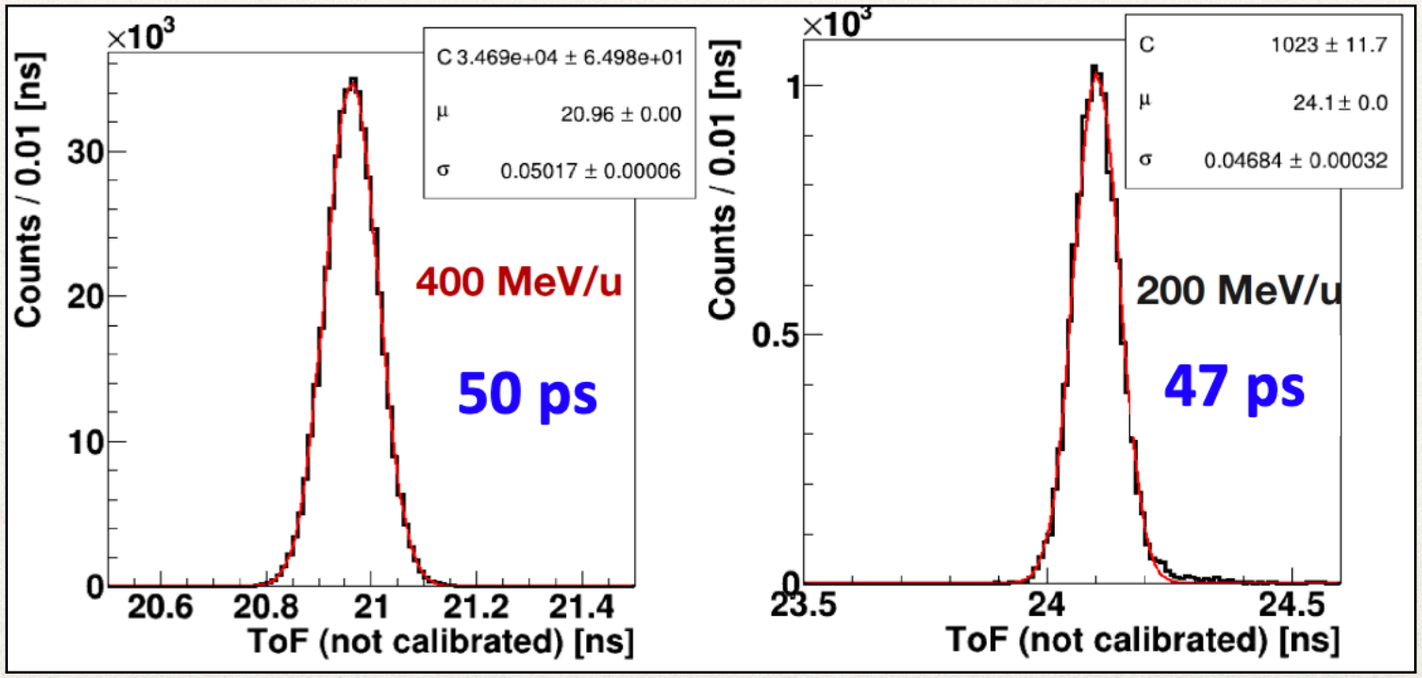
Element	$\sigma_{frag} \pm \Delta_{stat} \pm \Delta_{sys}$
He	$625 \pm 22 \pm 47$
Li	$85 \pm 10 \pm 11$
Be	$31 \pm 10 \pm 6$
B	$70 \pm 10 \pm 11$
C	$113 \pm 12 \pm 7$
N	$101 \pm 14 \pm 11$

Electronic setup data taking

Data taking at GSI with ^{16}O @ 200-400 MeV/u on C and C_2H_4

- Scintillators, drift chamber, tracking detectors and a calorimeter module + neutron detectors
- Data analysis just started





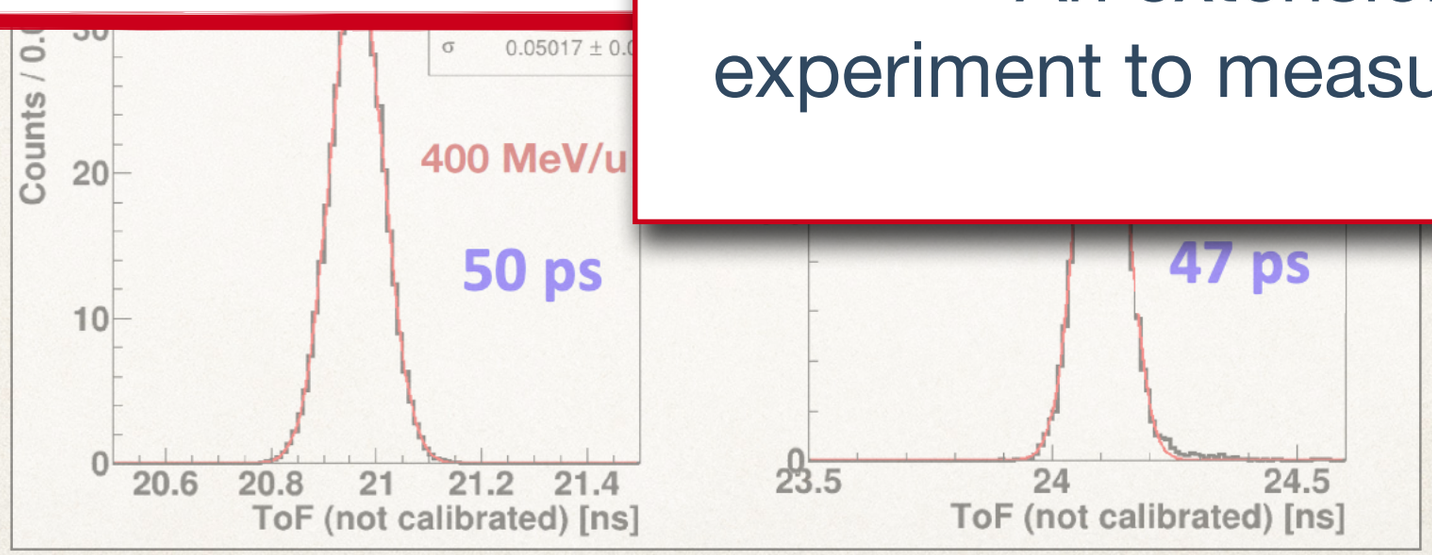
Electronic setup data taking

Data taking at GSI with 16O @ 200-400 MeV/u on C and C_2H_4

- Scintillators, drift chamber, tracking detectors and a calorimeter module + neutron detectors

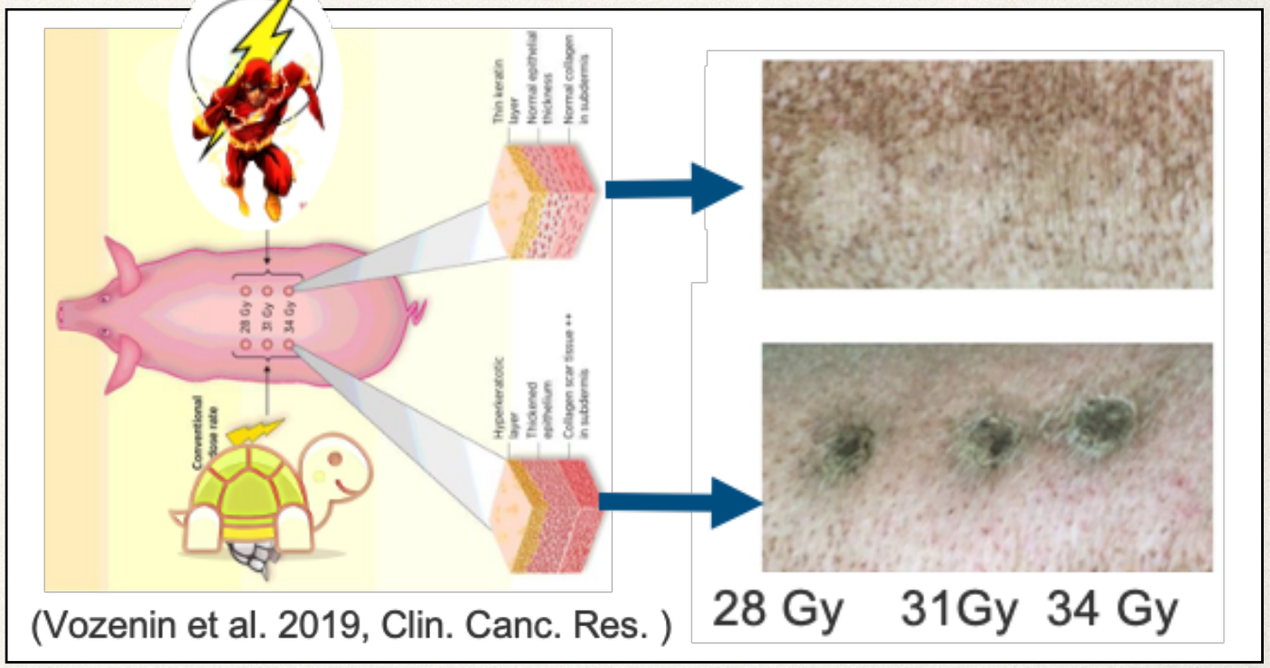
The FOOT full detector will be ready at the beginning of 2022 and new data takings are foreseen at CNAO, GSI, HIT.

An extension of the FOOT experiment to measure neutrons is under study.



Upcoming Activities

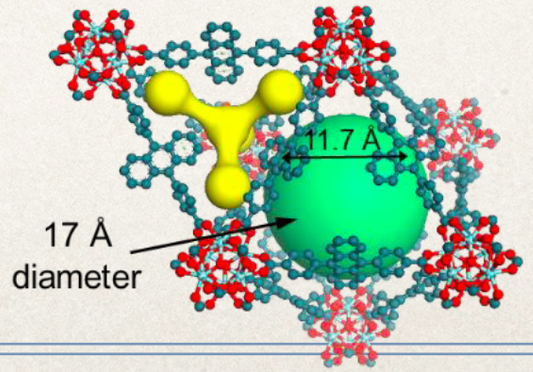
- **FRIDA** (Flash Radiotherapy with hIgh Dose-rate particle beAms): CALL CSN5 (INFN)

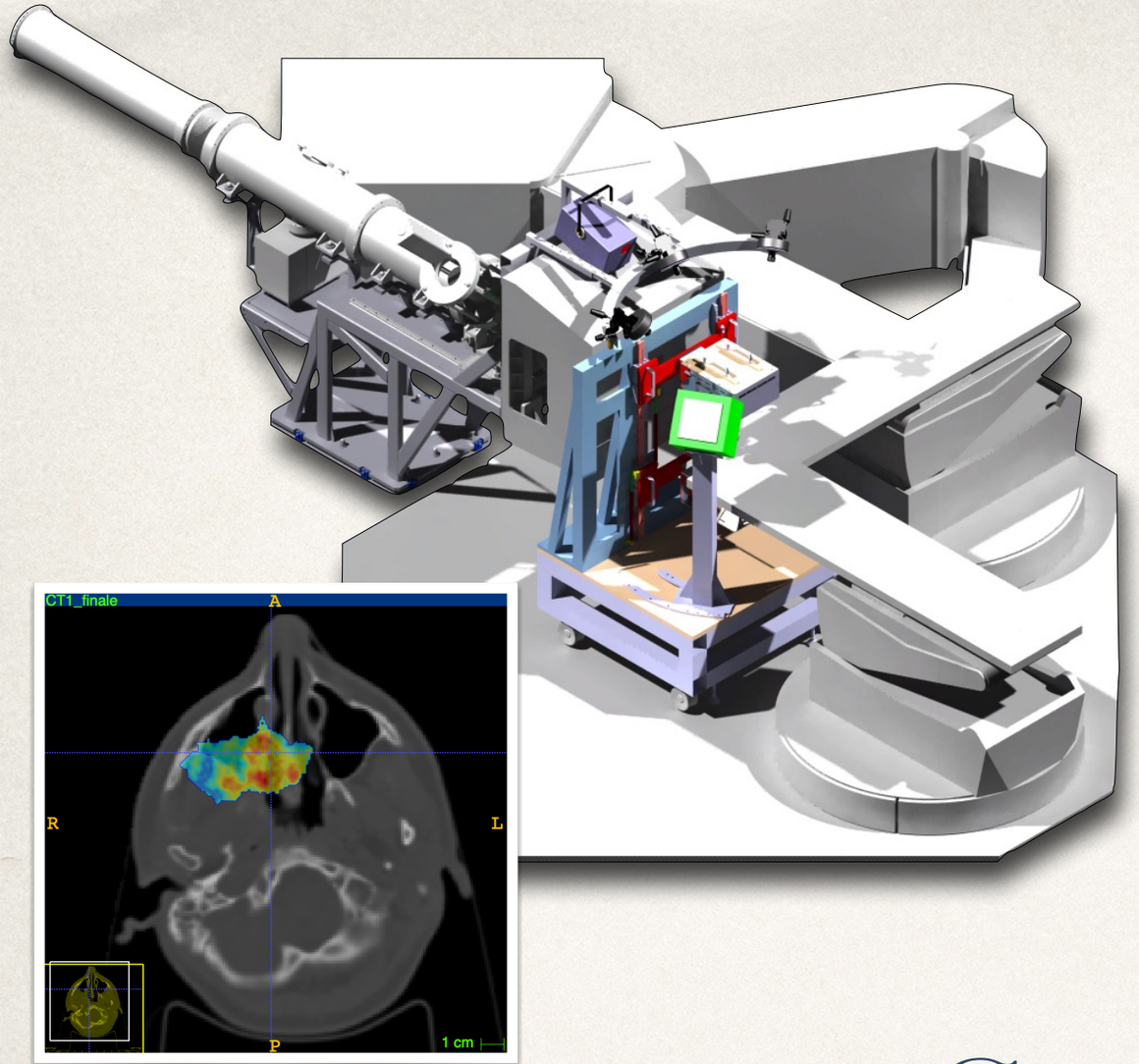


(Vozenin et al. 2019, Clin. Canc. Res.)

- **SHERPA** (Scintillating HEterostructures for high Resolution fast PET imAging): **PRIN2020**, PI Angelo Monguzzi (Università degli Studi Milano Bicocca)

https://www.mur.gov.it/it/atti-e-normativa/decreto-direttoriale-n-2435-del-20-10-2021





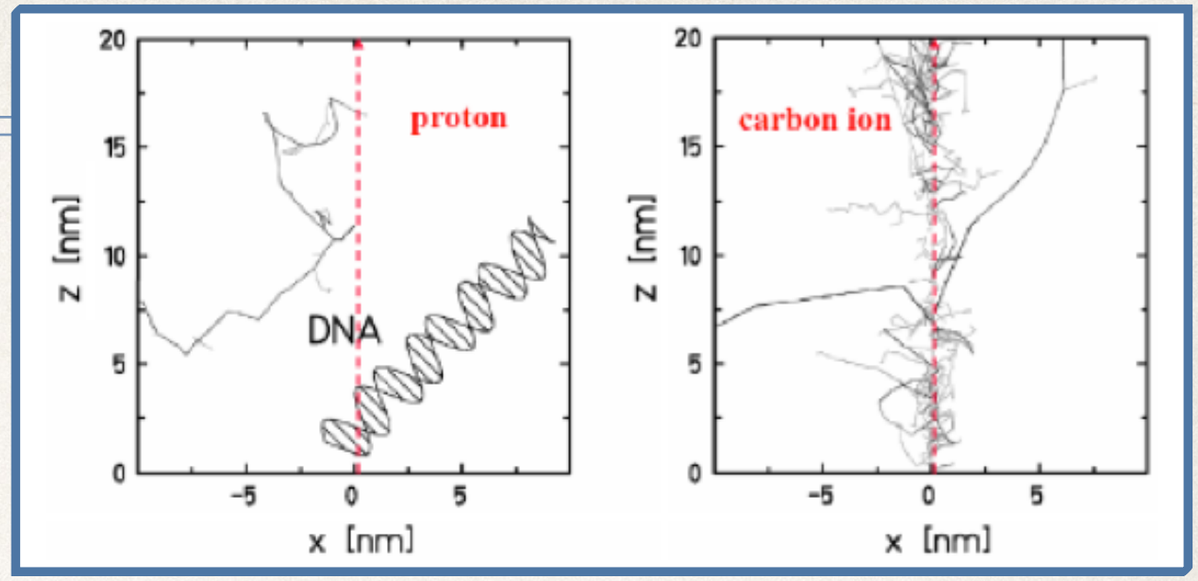
Grazie per l'attenzione

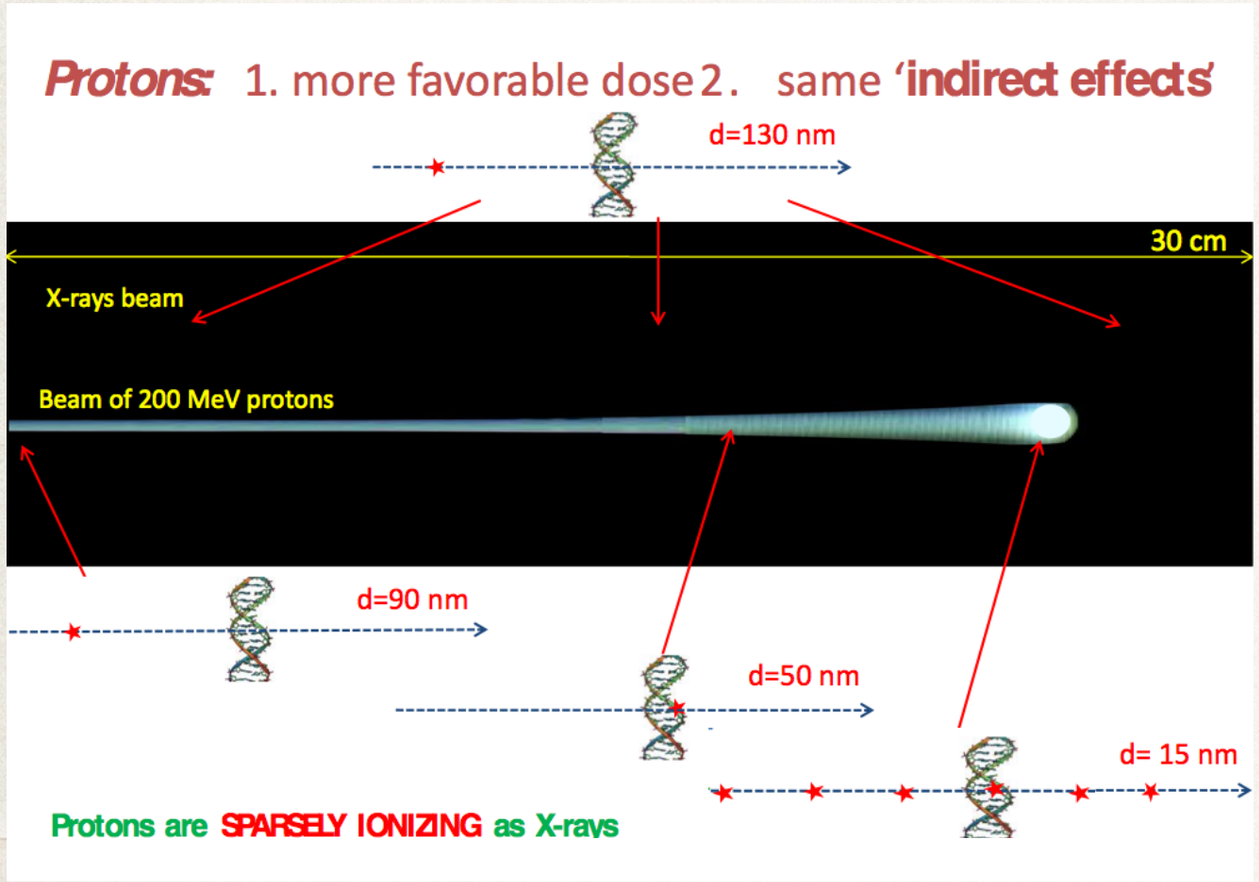
ilaria.mattei@mi.infn.it

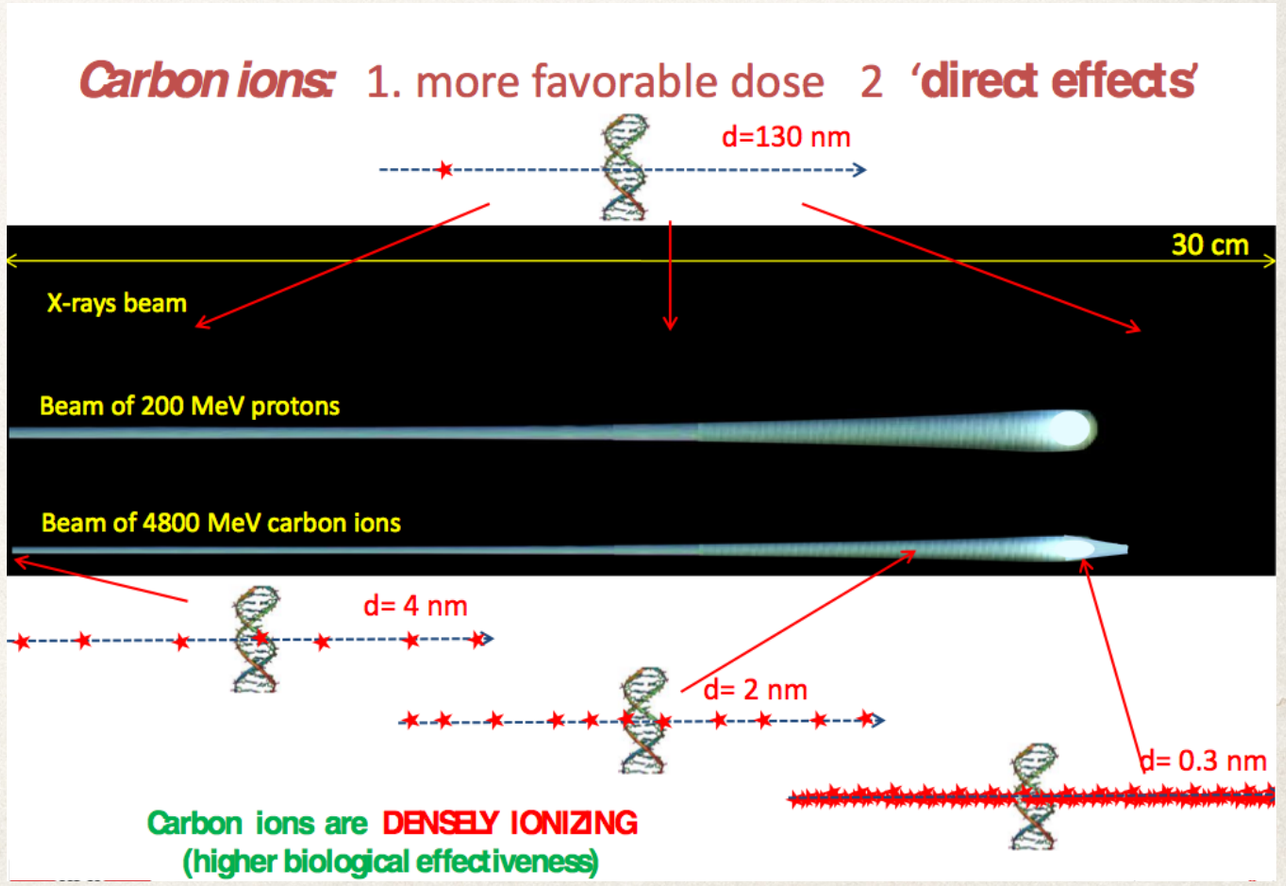
SPARES

Protons vs ^{12}C

- **Ionization density (LET)**

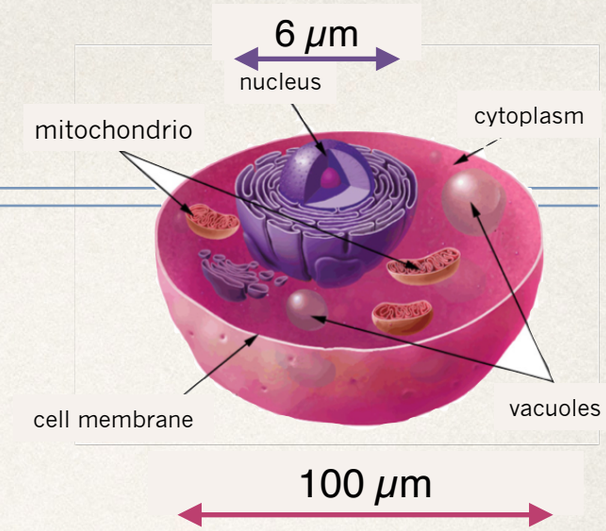






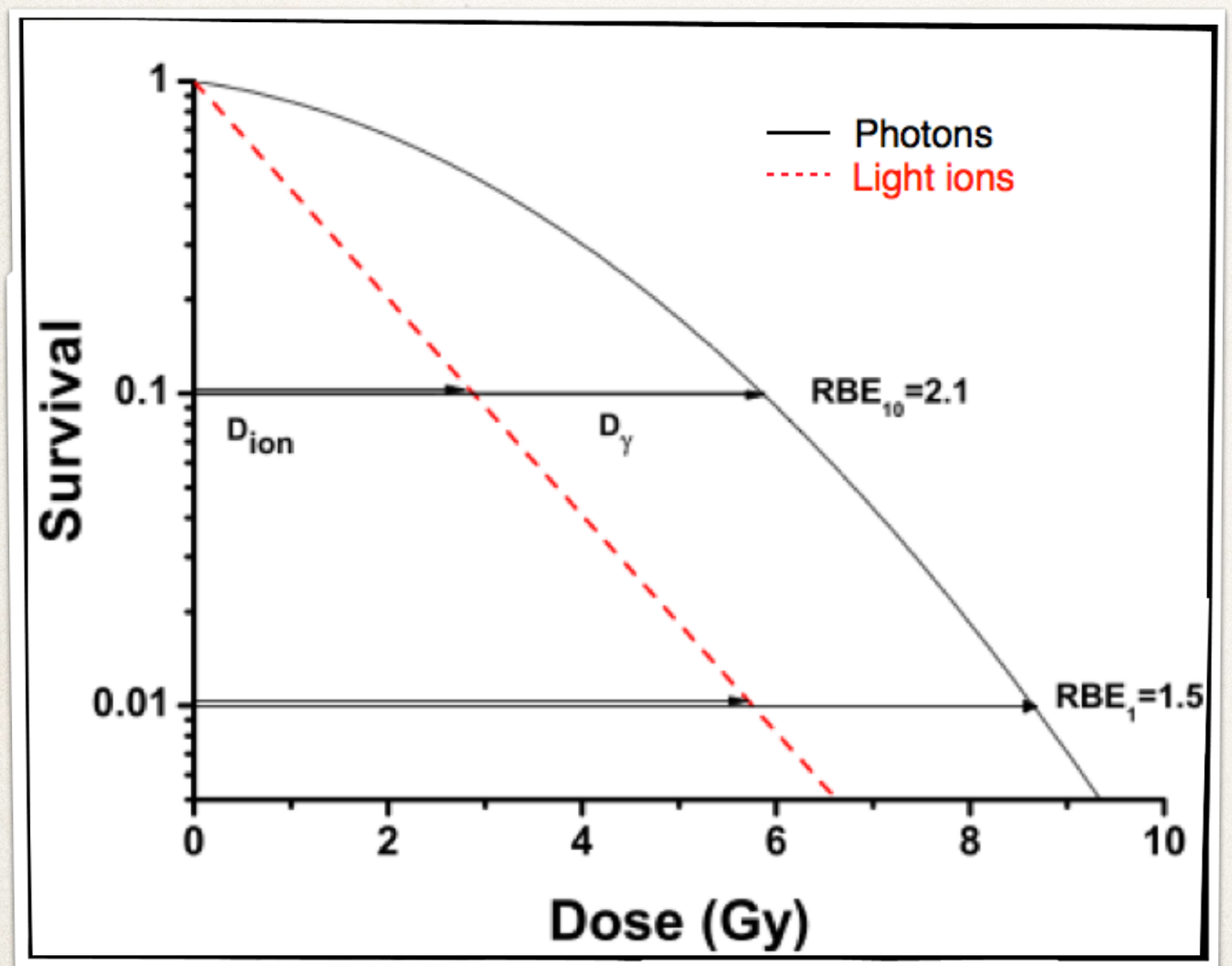
For the <u>beam delivery techniques</u>: MS is exploited for PROTONS (passive) but NOT for heavier ions (fragmentation=>active)

RBE



- **Survival Fraction**

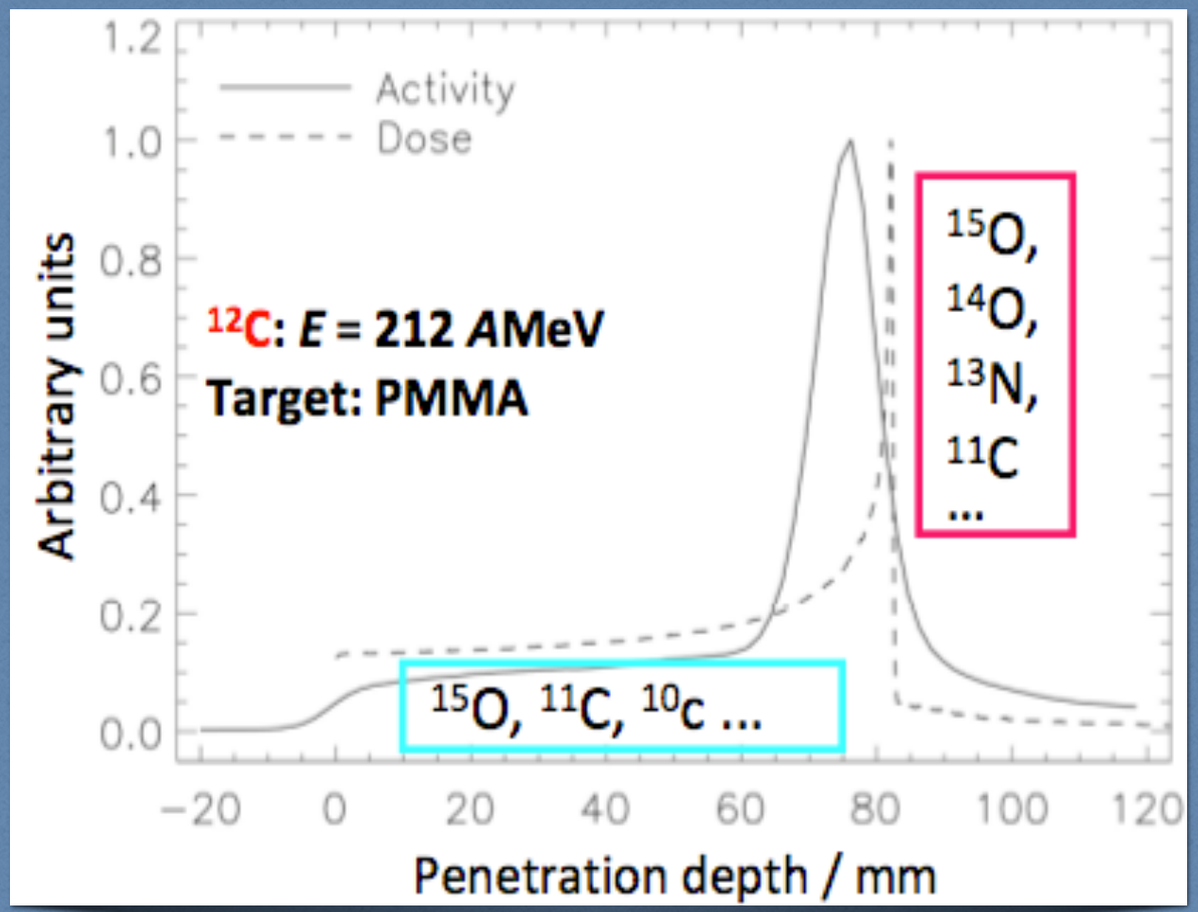
$$S = \frac{N_{surv}}{N_{seed}} = e^{-(\alpha D + \beta D^2)}$$

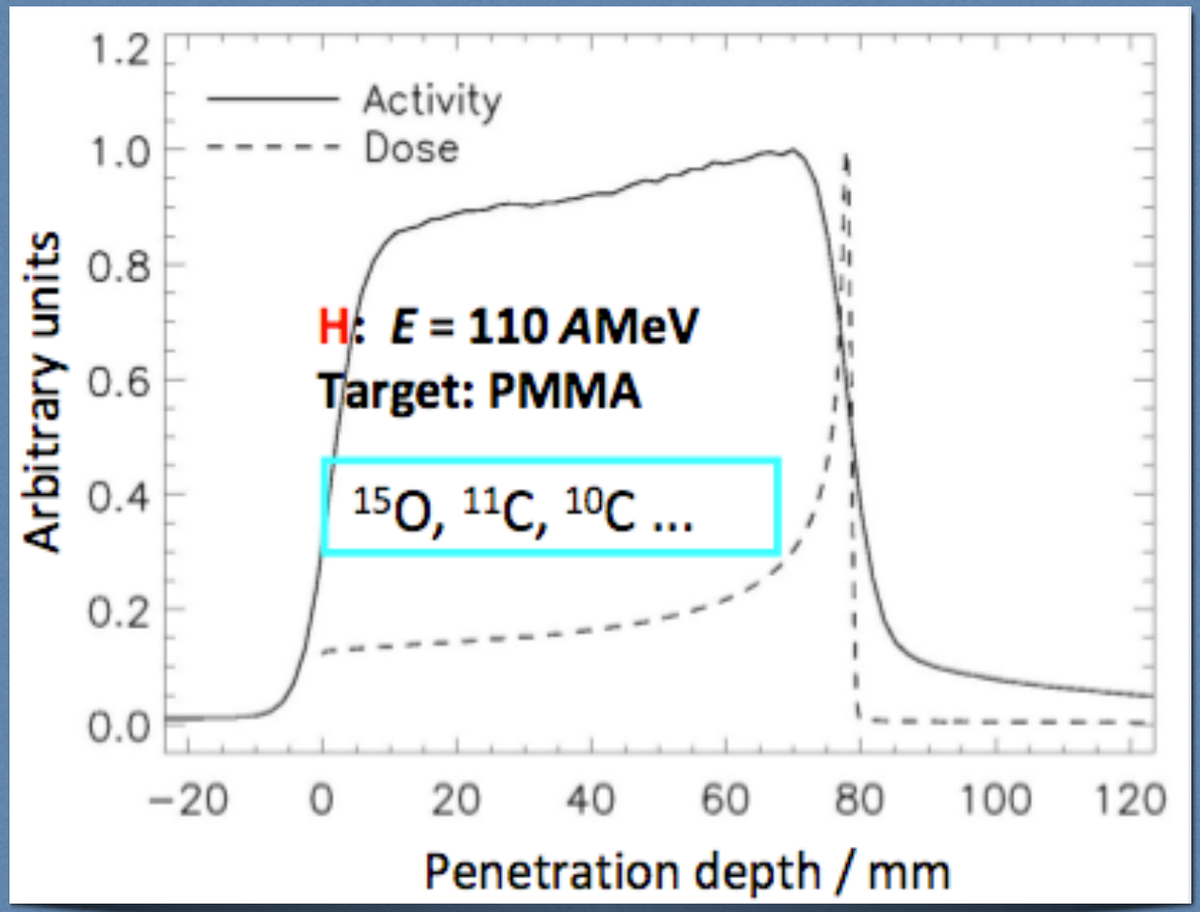


- **Relative Biological Effectiveness**

$$RBE = \frac{D_\gamma}{D_{ch}}\Big|_{iso}$$

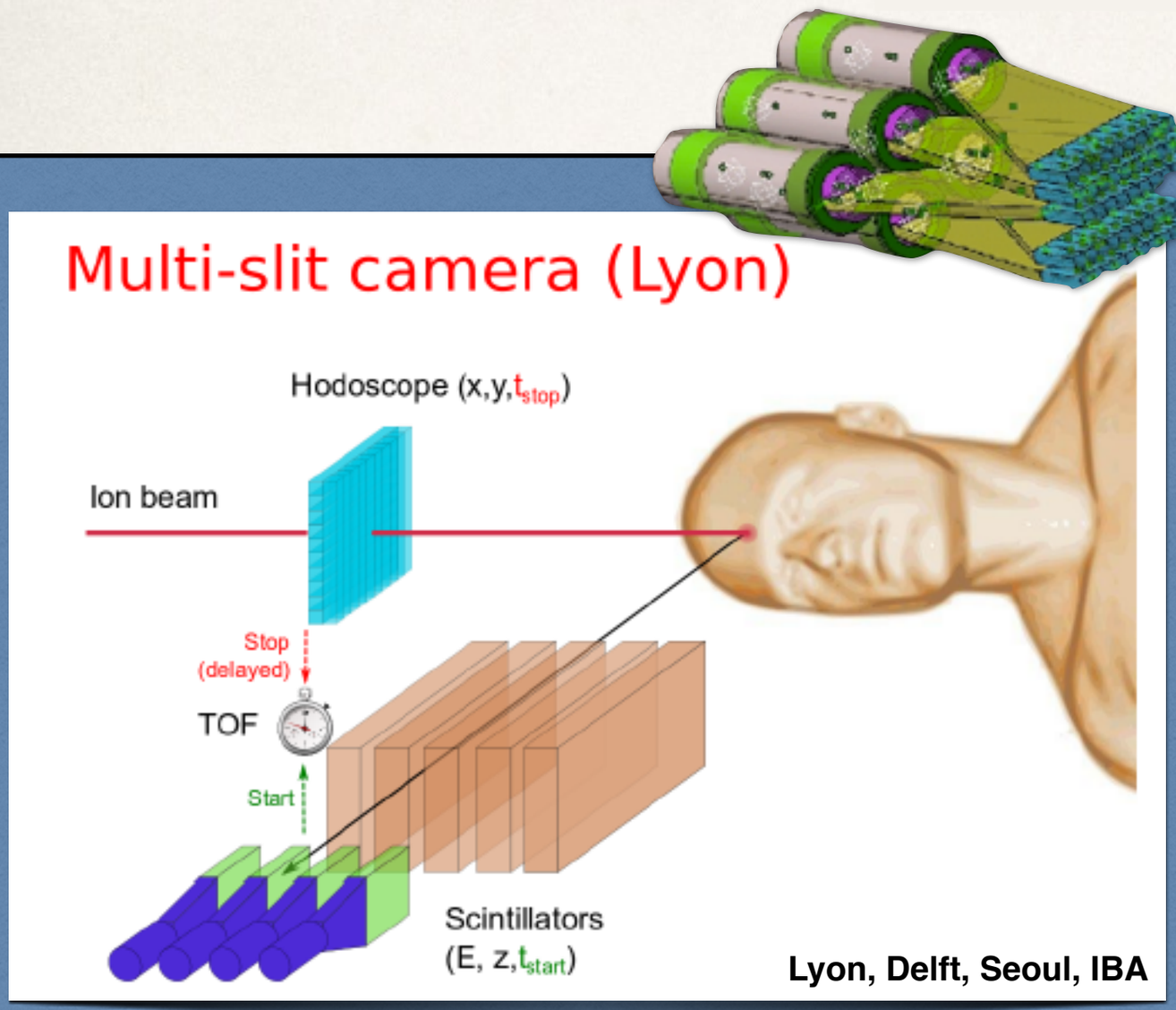
Dose Monitoring: PET-γ





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

Dose Monitoring: Prompt-γ



- Difficult to stop and collimate prompt photons (large energy spectrum: 1-10MeV)
- Huge neutron background
- Abundant Secondaries

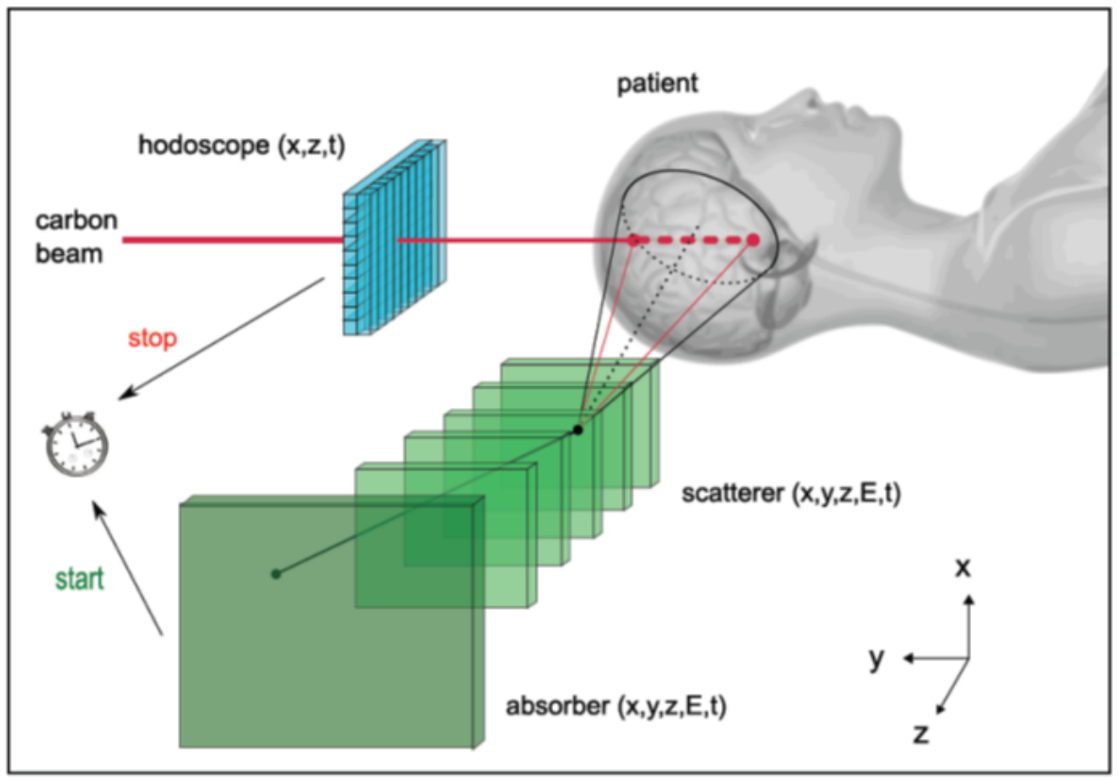
Balance of promptly emitted particles outside the target:

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

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

Dose Monitoring: Prompt-γ

Compton Camera



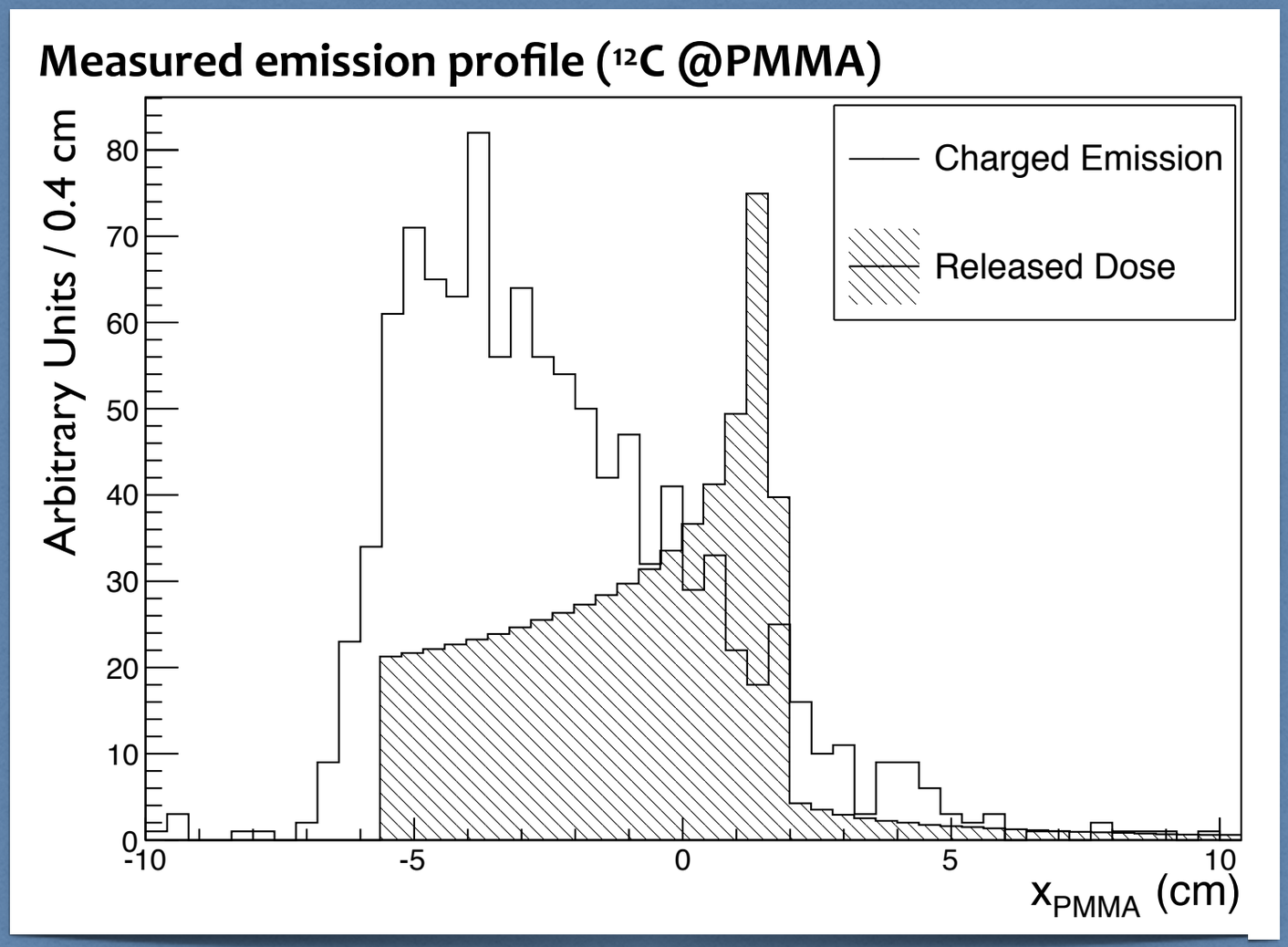
- No collimation: potentially higher efficiency
- Potentially better spatial resolution (< 1cm PSF)
- If beam position known simplified reconstruction
- 3D-potential imaging (several cameras)

Courtesy of D.Dauvergne PET symposium 2014

Main issue: necessity to work at reduced intensity

Dose Monitoring: Charged Fragments

Charged secondary particles: protons, deuterons and tritons..

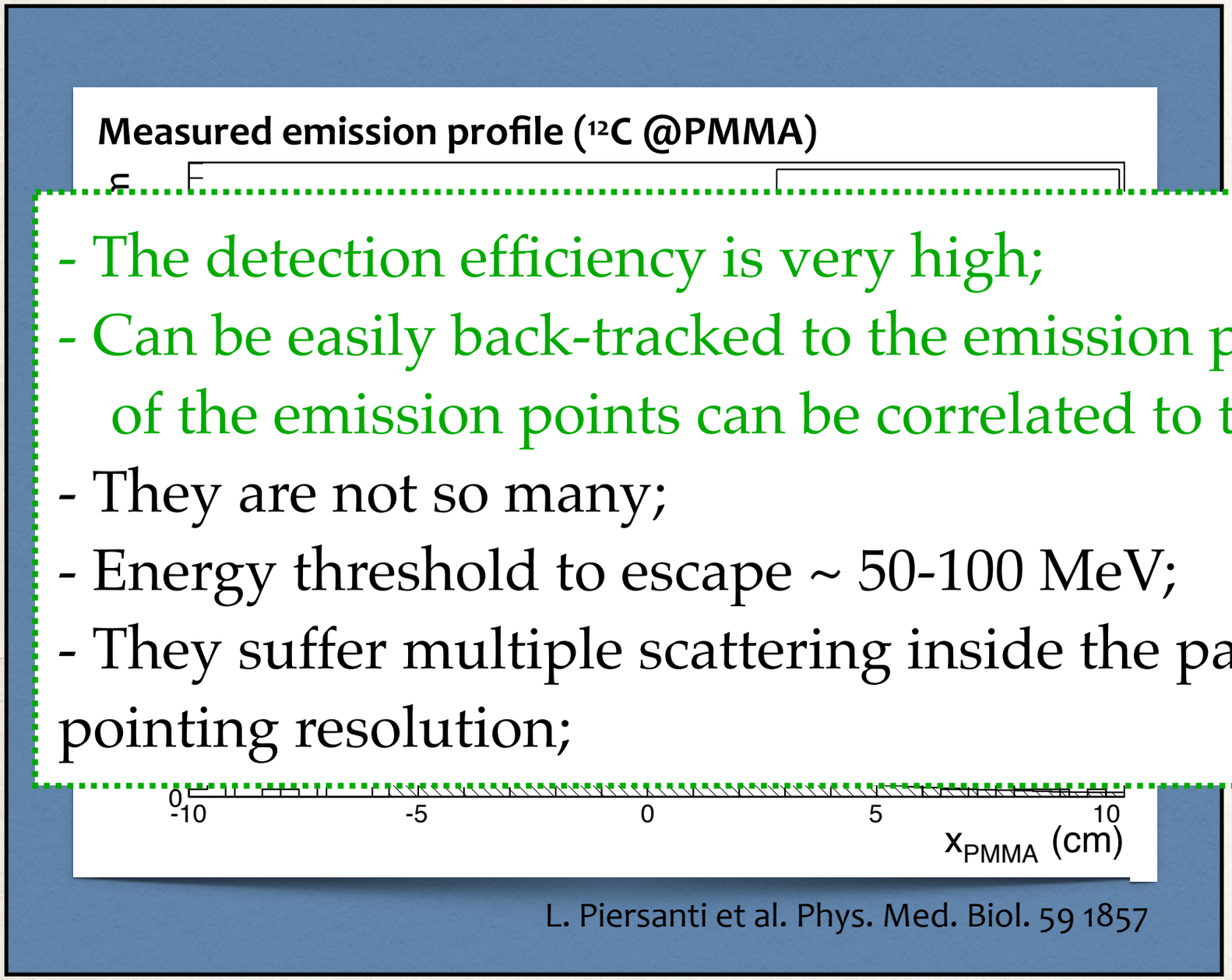


L. Piersanti et al. Phys. Med. Biol. 59 1857

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

Dose Monitoring: Charged Fragments

Charged secondary particles: protons, deuterons and tritons..



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;

Charged Fragments: Detection Angle

The main contributions to the uncertainty of the emission point determination of secondary charged particles are:

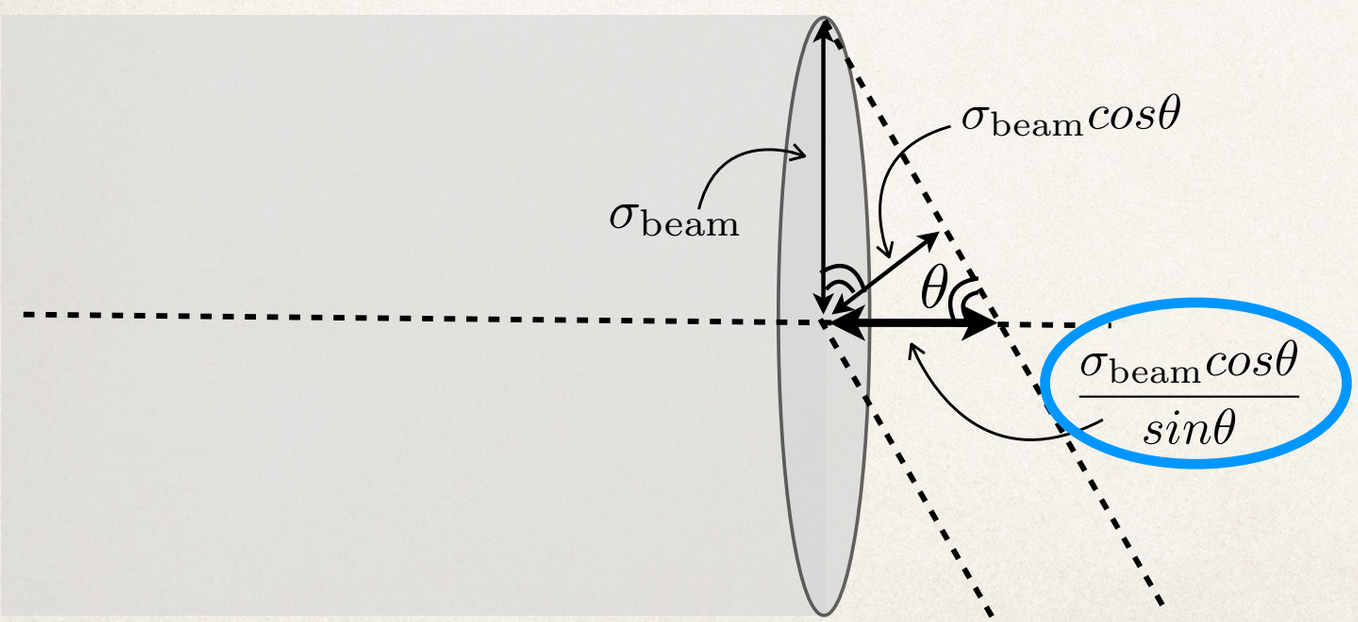
- the Multiple Scattering inside the target ($\propto \sqrt{x}$, E^{-1})
- the statistics ($\propto \vartheta$)
- The DCH resolution (to the beam line)
- the beam spot dimension (~ 2 mm - 1.5 cm)

COMPENSATION:

Low ϑ (high stat)

Large E => Low MS

Large x => Large MS



LOWERED AT LARGE ANGLES

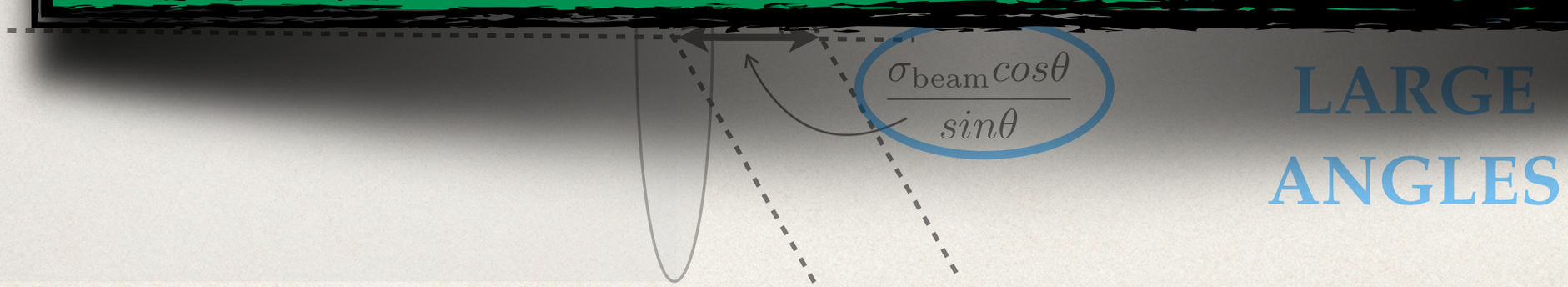
Charged Fragments: Detection Angle

The main contributions to the uncertainty of the emission point determination of secondary charged particles are:

- the Multiple Scattering inside the target ($\propto \sqrt{x}$, E^{-1})

COMPENSATION:

In a treatment room, very often the positions at low ϑ are not available to a monitor device, in particular in the treatment configuration where the patient body is aligned with the beam axis.

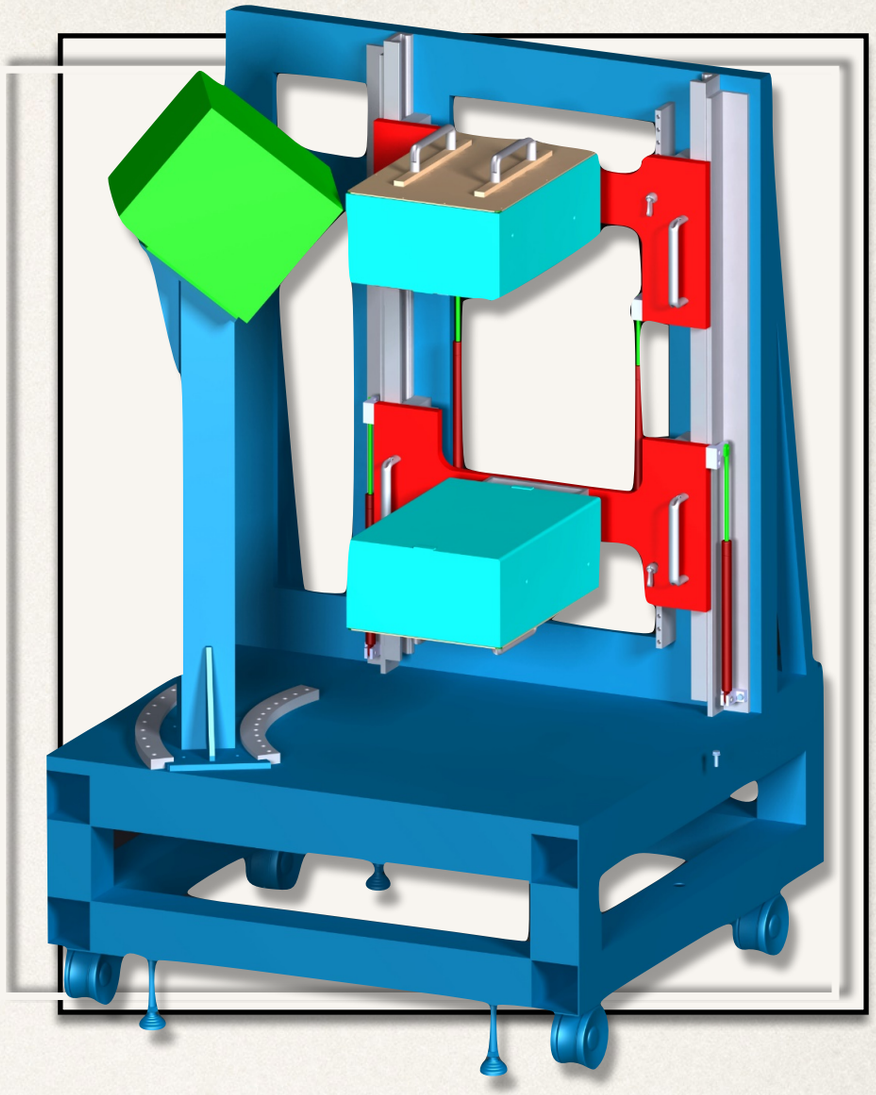


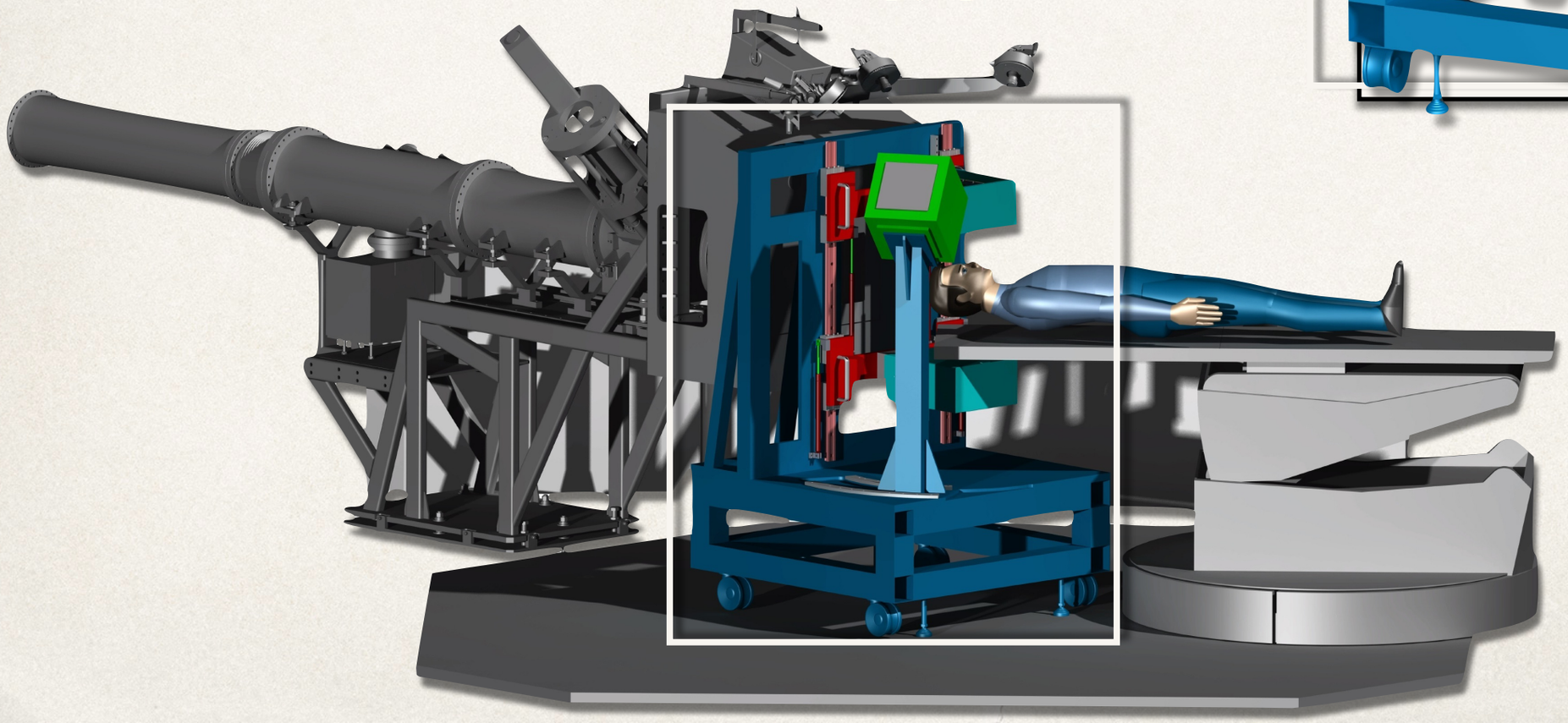
LARGE ANGLES

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.

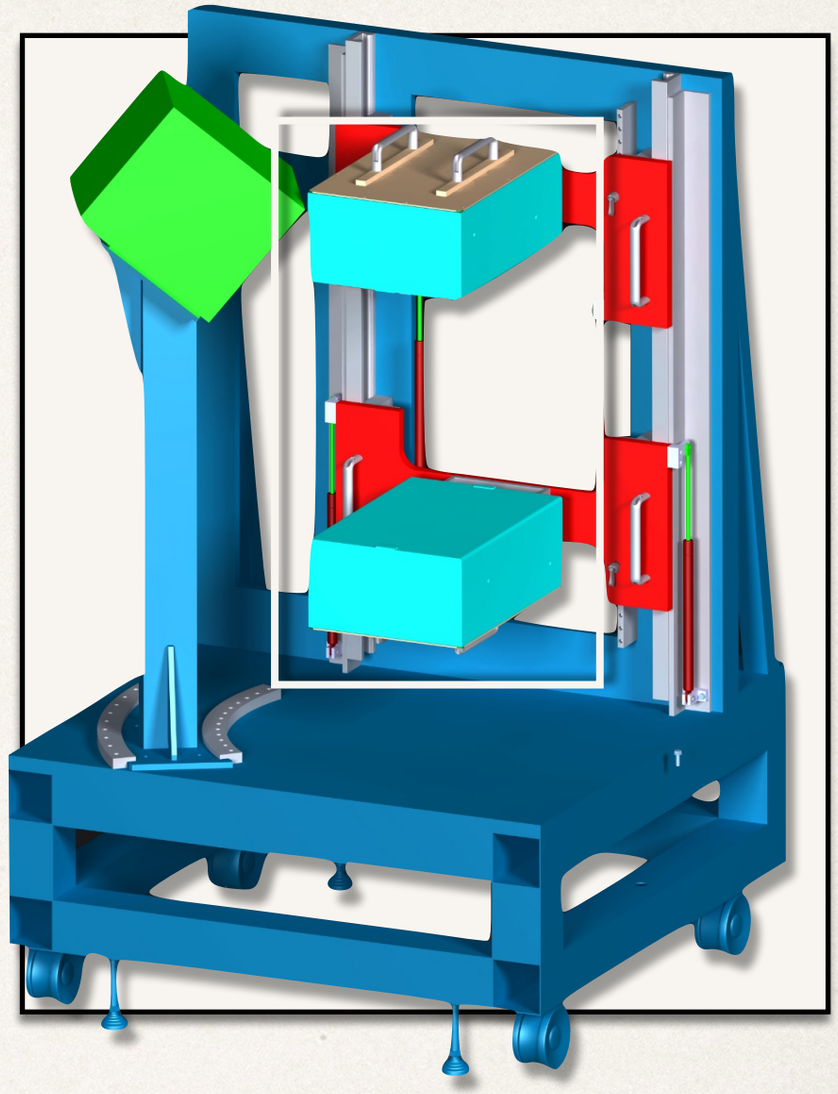
For the **CNAO** measurements we design a cart in order to hold up the detectors minimizing the interferences with therapy procedures





The INSIDE Project

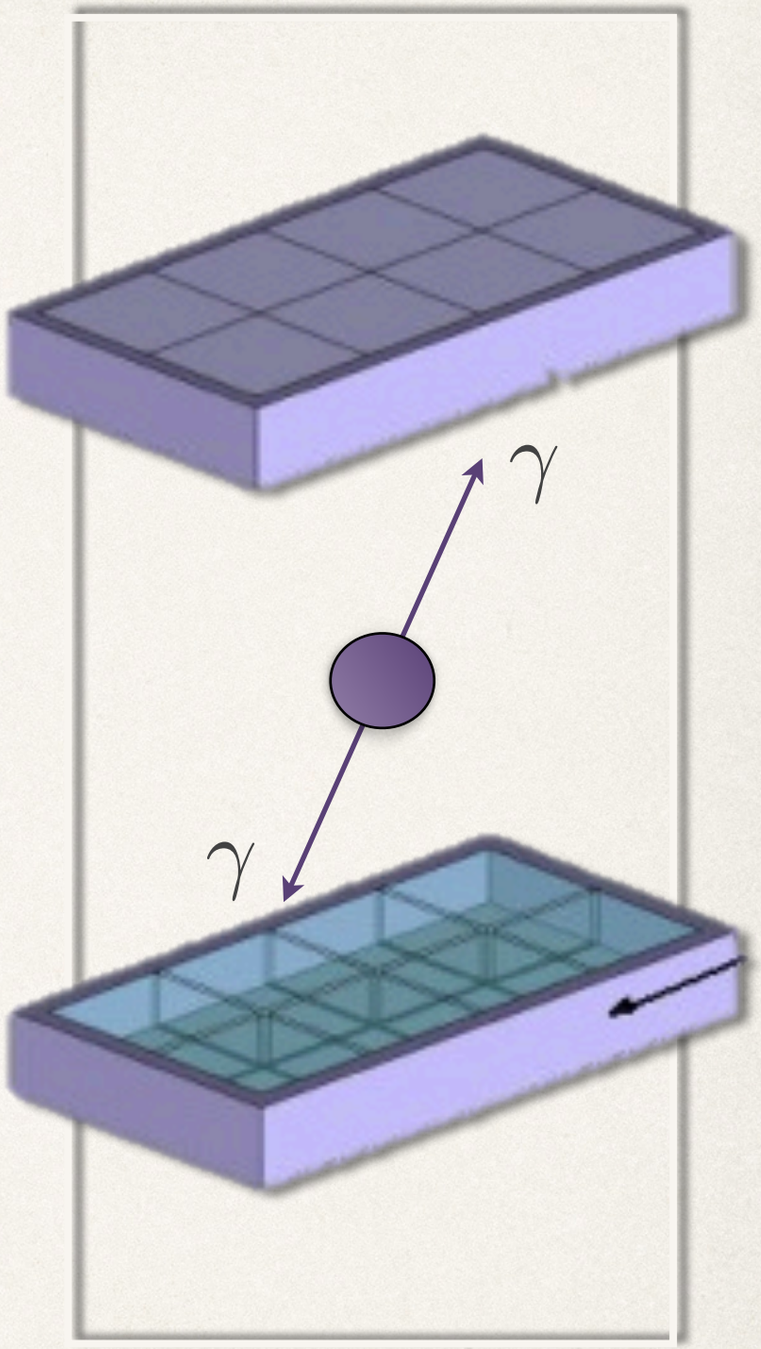
- Detectors to measure the 511 keV photons in order to reconstruct the β^+ activity map;
- Full in-beam PET system able to sustain annihilation, prompt photon and neutron rates during the beam irradiation (in-beam and inter-spill);



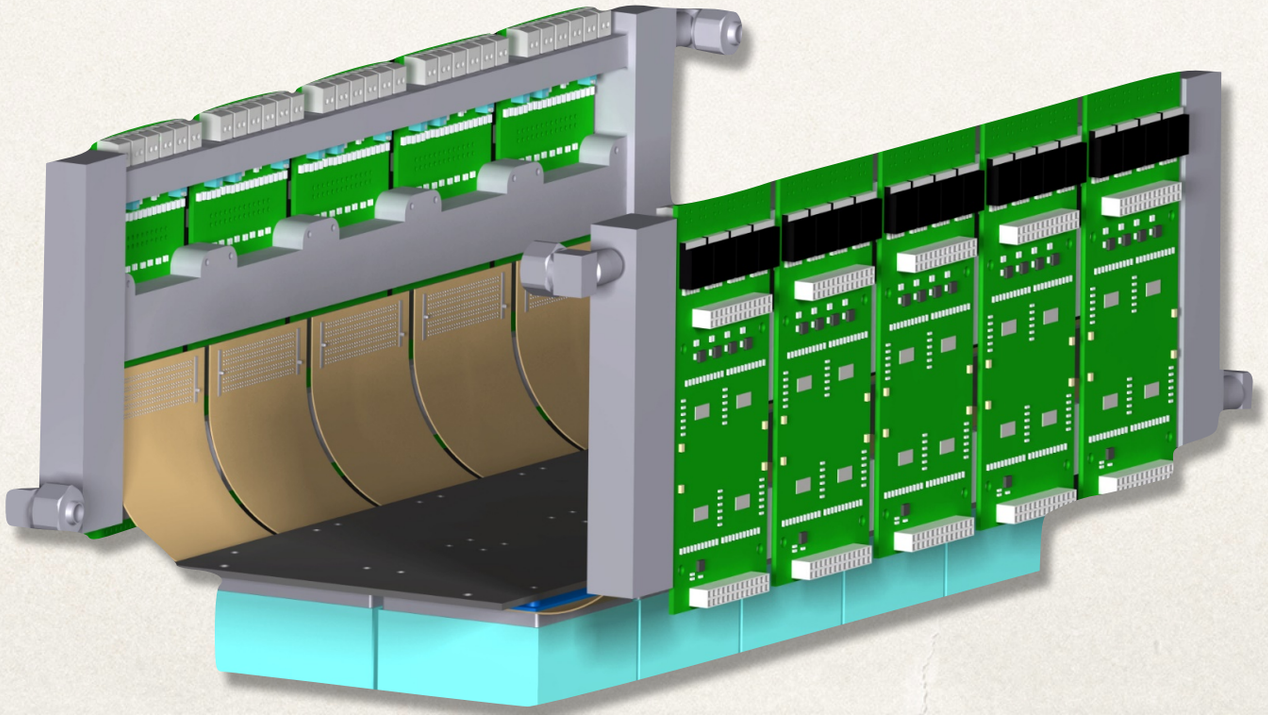
Total sensitive area of a module: 5 cm x 5 cm

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

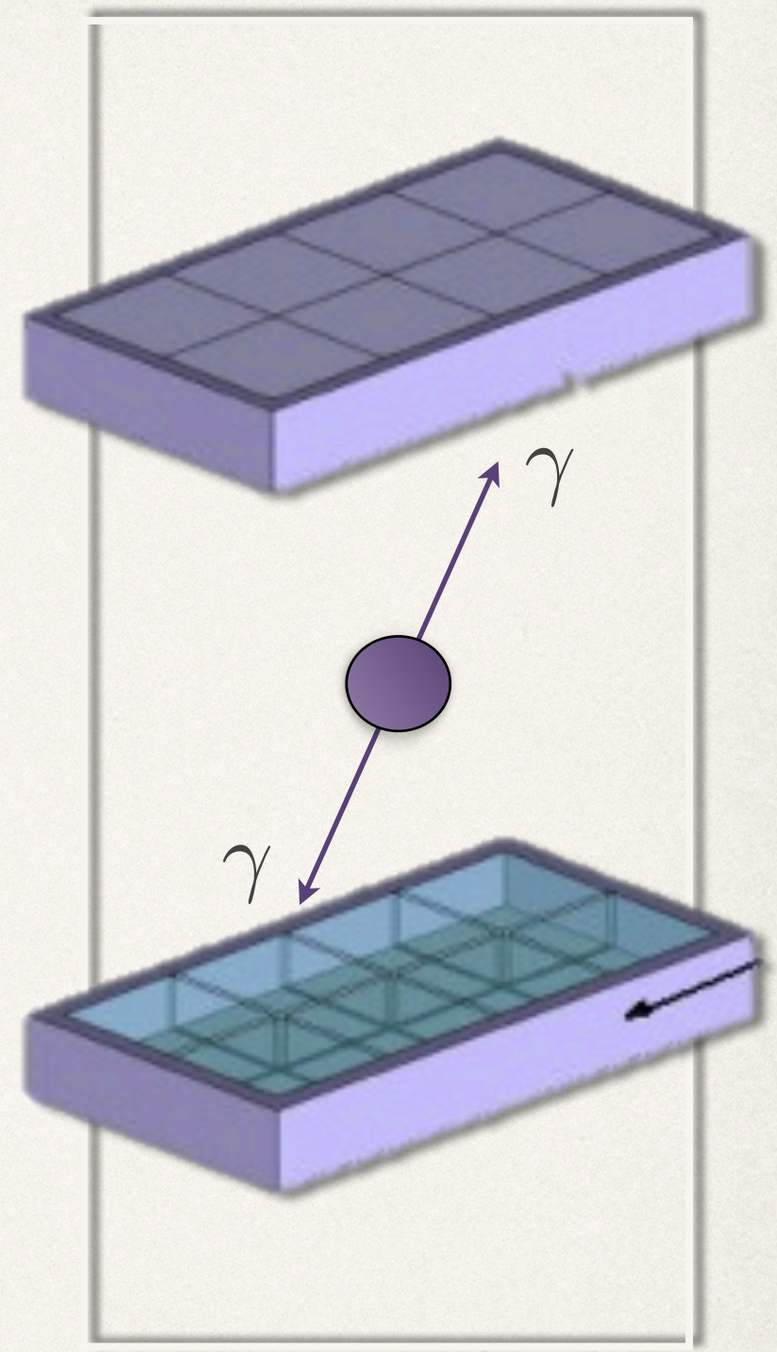
- Detectors to measure the 511 keV photons in order to reconstruct the β^+ activity map;

- 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.

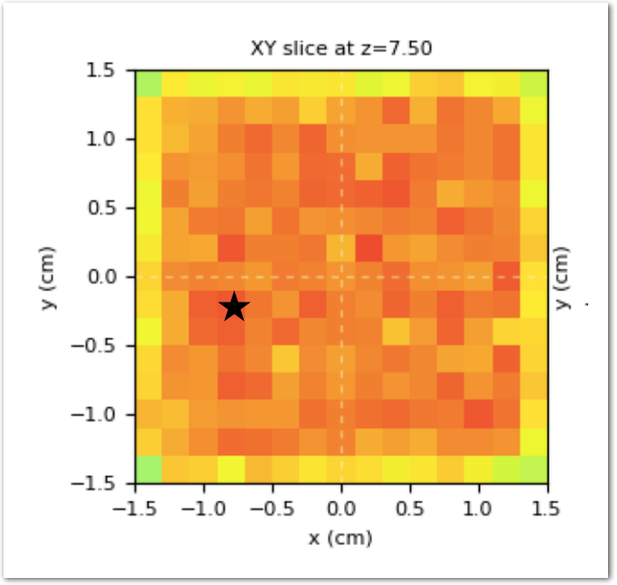
The **resolution** of the two PET heads system in the β^+ activity reconstruction map is expected to be between 1 and **2 mm (FWHM)** in beam direction.



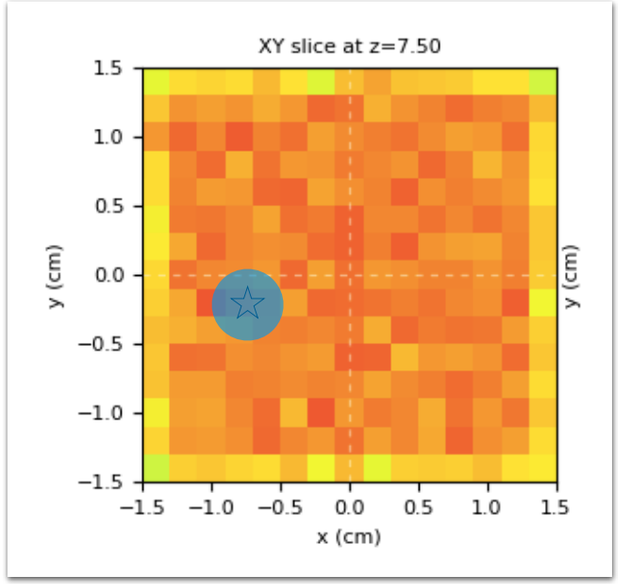
=> 511 keV back-to-back

Gamma index analysis

First Map



Second Map



γ-index 2mm/3%

$$\Gamma(\vec{r_e}, \vec{r_r}) = \sqrt{\frac{|\vec{r_e} - \vec{r_r}|^2}{\Delta d^2} + \frac{[D_e(\vec{r_e}) - D_r(\vec{r_r})]^2}{\Delta D^2}}$$

D= dose (D_r of the reference map, D_e of the evaluation map)

r = position of the evaluated point (r_r of the reference map, r_e of the evaluation map)

$$\gamma(\vec{r_r}) = \min\{\Gamma(\vec{r_e}, \vec{r_r})\}\forall\{\vec{r_e}\}$$

γ≤1 = test passed

γ>1 = test NOT passed

pass rate ≥ 92% clinical acceptance